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Editorial

Athletic Incontinence: Proposal of a New Term for a New Woman

Incontinência de atletas: proposta de novo termo para uma nova mulher

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In 1896, Baron Pierre de Coubertin inaugurated the first modern era Olympic Games. At that time, women could not participate in the competitions, as sports in general were considered dangerous for women's health. At the Paris Olympics (1900), of the 997 enrolled athletes, 22 were women who competed in sailing, tennis and golf.[1] Women's participation increased considerably, and in the 2016 Olympic Games, which were held in the city of Rio de Janeiro, almost half of the athletes were women.[2]

However, the "slogan" proposed by Baron de Coubertin during the creation of the International Olympic Committee, "Citius, Altius, Fortius" (faster, higher, stronger), has caused

Fig. 1 Physiopathology of athletic incontinence.

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numerous problems to the health of female athletes.[3] Irregular or absent menstrual cycles, inadequate eating behaviors, muscular injuries, stress fractures and pelvic floor dysfunctions have been increasing among physically active women.[4]

Women who practice high-impact, high-intensity exercises are eight times more likely to suffer from involuntary urine loss when compared with sedentary women in the same age group.[5] The sports at risk for this condition include acrobatic trampoline (trampoline), long distance running, volleyball and basketball.[6] Unlike stress urinary incontinence, in which urine leakage occurs during coughing, sneezing, or lifting weight, these young women report the symptom only during exercise.[7] Therefore, the term athletic incontinence would be the most appropriate for these patients who complain only during physical exercise and do not lose urine during their other activities.

Athletic incontinence affects young, nulliparous women with an adequate body mass index.[8] These women do not have the classic risk factors for pelvic floor dysfunction, such as age, parity and obesity.[9]

The pathophysiology of athletic incontinence is complex, and includes biomechanical factors (impact on and displacement of the pelvic floor during exercise), increased intra-abdominal pressure, decreased energy availability (a condition that interferes with the hypothalamic control of the menstrual cycle, leading to hypoestrogenism), and joint hypermobility (►**Fig. 1**).[7,10]

The urodynamic exam of these patients is not able to reproduce the situation in which urine leakage occurs, and the conventional pad test is flawed.[11] Pelvic floor muscle training may improve athletic incontinence, but the specificity of each modality should be adjusted.[12] Many of these physically active women use vaginal devices such as tampons or pessaries to minimize urine loss.[13] Restrictive diets and the use of licit and illicit supplements are common, and should be evaluated before the treatment.[7]

We conclude, therefore, that athletic incontinence is a specific condition that occurs in young and nulliparous women only while they are practicing sports. For this reason, it should be evaluated and treated differently from the other categories of urinary incontinence.

Conflicts of Interest
The authors have no conflicts of interest to disclose.

References

1 O'Brien M, Robertson A. Women and sport. Scott Med J 2010; 55(02):25–28
2 Church H, Murdoch-Eaton D, Patel R, Sandars J. What can medical educators learn from the Rio 2016 Olympic Games? Med Teach 2017;39(06):665–666
3 Seiler S. Same Citius, Altius, Fortius…more women, crashes, and McTwists? Int J Sports Physiol Perform 2014;9(01):122–127
4 Joy EA, Van Hala S, Cooper L. Health-related concerns of the female athlete: a lifespan approach. Am Fam Physician 2009;79(06): 489–495
5 Almeida MB, Barra AA, Saltiel F, Silva-Filho AL, Fonseca AM, Figueiredo EM. Urinary incontinence and other pelvic floor dysfunctions in female athletes in Brazil: A cross-sectional study. Scand J Med Sci Sports 2016;26(09):1109–1116
6 Fozzatti C, Riccetto C, Herrmann V, et al. Prevalence study of stress urinary incontinence in women who perform high-impact exercises. Int Urogynecol J Pelvic Floor Dysfunct 2012;23(12):1687–1691
7 Araújo MP, Oliveira Ed, Zucchi EV, Trevisani VF, Girão MJ, Sartori MG. [The relationship between urinary incontinence and eating disorders in female long-distance runners]. Rev Assoc Med Bras (1992) 2008;54(02):146–149
8 Eliasson K, Edner A, Mattsson E. Urinary incontinence in very young and mostly nulliparous women with a history of regular organised high-impact trampoline training: occurrence and risk factors. Int Urogynecol J Pelvic Floor Dysfunct 2008;19(05):687–696
9 Hagovska M, Švihra J, Buková A, et al. Prevalence of urinary incontinence in females performing high-impact exercises. Int J Sports Med 2017;38(03):210–216
10 Dias N, Peng Y, Khavari R, et al. Pelvic floor dynamics during high-impact athletic activities: A computational modeling study. Clin Biomech (Bristol, Avon) 2017;41:20–27
11 Barton A, Serrao C, Thompson J, Briffa K. Transabdominal ultrasound to assess pelvic floor muscle performance during abdominal curl in exercising women. Int Urogynecol J Pelvic Floor Dysfunct 2015;26(12):1789–1795
12 Da Roza T, de Araujo MP, Viana R, et al. Pelvic floor muscle training to improve urinary incontinence in young, nulliparous sport students: a pilot study. Int Urogynecol J Pelvic Floor Dysfunct 2012;23(08):1069–1073
13 Glavind K. Use of a vaginal sponge during aerobic exercises in patients with stress urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 1997;8(06):351–353

Reference Ranges for Ultrasonographic Measurements of the Uterine Cervix in Low-Risk Pregnant Women

Valores de referência das medidas ultrassonográficas do colo uterino em gestantes de baixo risco

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Abstract

Objective To define transvaginal ultrasound reference ranges for uterine cervix measurements according to gestational age (GA) in low-risk pregnancies.

Methods Cohort of low-risk pregnant women undergoing transvaginal ultrasound exams every 4 weeks, comprising measurements of the cervical length and volume, the transverse and anteroposterior diameters of the cervix, and distance from the entrance of the uterine artery into the cervix until the internal os. The inter- and intraobserver variabilities were assessed with the linear correlation coefficient and the Student *t*-test. Within each period of GA, 2.5, 10, 50, 90 and 97.5 percentiles were estimated, and the variation by GA was assessed with analysis of variance for dependent samples. Mean values and Student *t*-test were used to compare the values stratified by control variables.

Results After confirming the high reproducibility of the method, 172 women followed in this cohort presented a reduction in cervical length, with an increase in volume and in the anteroposterior and transverse diameters during pregnancy. Smaller cervical lengths were associated with younger age, lower parity, and absence of previous cesarean section (C-section).

Conclusion In the studied population, we observed cervical length shortening throughout pregnancy, suggesting a physiological reduction mainly in the vaginal portion of the cervix. In order to better predict preterm birth, cervical insufficiency and premature rupture of membranes, reference curves and specific cut-off values need to be validated.

Keywords

- ultrasound
- uterine cervix
- cervical length
- reference ranges
- low-risk pregnancy

Resumo

Objetivo Elaborar curvas de referências de medidas ultrassonográficas de colo uterino por idade gestacional (IG) em gestações de baixo risco.

Métodos Coorte de gestantes de baixo risco, submetidas a ultrassom transvaginal repetido a cada 4 semanas, com medida do comprimento, dos diâmetros antero-

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posterior e transverso, da distância entre a entrada da artéria uterina no colo e o orifício interno, e do volume do colo. Foi avaliada a variabilidade inter e intraobservador entre as medidas com o coeficiente de correlação linear e teste *t* de Student. Para cada faixa de IG, estimaram-se os percentis 2,5, 10, 50, 90 e 97,5 dos valores das medidas, com a variação por IG avaliada por análise de variância para amostras dependentes. As comparações dos valores por variáveis de controle foram feitas por meio dos cálculos de médias e teste t de Student.

Resultados Assegurada a alta reprodutibilidade do método, as 172 mulheres acompanhadas na coorte apresentaram redução das medidas de comprimento de colo com o decorrer da gestação, com aumento de volume e dos diâmetros anteroposterior e transverso. O menor comprimento cervical foi associado à menor idade materna, menor paridade, e ausência de cesárea prévia.

Conclusão Na população estudada foi observada redução no comprimento cervical com o decorrer da gestação, sugerindo encurtamento fisiológico principalmente à custa da porção vaginal do colo. Há a necessidade de validar tais curvas de referência e pontos de corte específicos para uma melhor predição de risco de parto pré-termo, insuficiência cervical, e amniorrexe prematura.

Palavras-chave
- ultrassom
- colo uterino
- comprimento cervical
- valores de referência
- gestação de baixo risco

Introduction

Approximately 15 million preterm births occur per year globally.[1] According to the World Health Organization, premature babies are those delivered before 37 weeks of pregnancy.[1] Currently, preterm births are among the largest direct causes of neonatal deaths in the world, accounting for 35% of 3.2 million deaths occurring each year.[2] It is estimated that the prevalence of preterm births is around 10% worldwide, being higher in countries with large populations, such as the United States, China and India, and in low- and middle-income countries such as Nigeria, Pakistan, and Indonesia, among others. These countries, including Brazil, are responsible for the largest number of preterm births in the world.[2]

Twin pregnancies or pregnancies with a history of preterm births are groups at a higher risk for preterm birth.[3] However, demographic, socioeconomic, and ethnic characteristics may have an impact on these rates.[3,4] Other clinical features can also play an important role in determining the risk of preterm birth, including maternal chronic diseases, alloimmune and autoimmune alterations, chromosomal abnormalities, uterine malformations, cervix surgeries, low body mass index (BMI), smoking, periodontal disease,[3] as well as genital and urinary tract infections.[5] Some authors point out that certain phenotypic groups can be more susceptible to preterm birth,[6] while others suggest that racial differences can also be a determining factor.[4] However, although some risk factors are associated with prematurity, little is still known about the real causes of preterm birth.

A strategy for the early identification of women at higher risk of preterm birth is monitoring the physiological changes preceding labor.[7–9] Among these modifications, the cervical effacement process seems to be an important predictor of preterm birth. Cervix alterations, which start a few weeks before labor, are a consequence of biochemical mechanisms that will culminate with cervical effacement and labor.[10]

The cervical stroma is composed of ~ 80 to 85% of fibrous connective tissue and 10% of smooth muscle, determining a passive biomechanical force not derived from muscular contractility itself.[10] In parturition, the stroma of the uterine cervix undergoes a complex biochemical and biomechanical alteration, progressing from a completely closed and long cervix to a wedge-shaped cervix until reaching the total shortening of the cervix and the thinning of the walls.

Cervical shortening, when diagnosed ultrasonographically between weeks 20 and 24, is an important risk factor for preterm birth.[11] This has been identified in populations with different risk profiles, varying from pregnant women with low-risk, single and asymptomatic gestations to women with high-risk pregnancies due to either a history of preterm birth or twin pregnancy.[12]

Along with the previous history of preterm birth, the measurement of the cervical length by transvaginal ultrasound (US) scan is currently the most appropriate available parameter for the prediction of preterm birth. It is highly recommended in several widely recognized guidelines, since there is evidence on interventions that may reduce the risk of prematurity.[13] Both the daily administration of vaginal progesterone[14] and the use of cervical pessaries[15] are recognized as alternative treatments to reduce the risk of preterm birth in women with a short cervix.

Since at least two decades ago, there is a consensus regarding the concept that the shorter the cervix, the higher the risk of prematurity. However, there are still divergences regarding the parameter to be considered as the best cut-off point for the prediction of preterm birth in different populations, with values ranging from less than 25 mm[16–20] to less than 15 mm.[21]

Some authors suggest that the cervical length varies according to the population, and that may imply different risks that also depend on the specific gestational ages (GAs).[4] Therefore, the definition of reference ranges for cervical measurements from different populations could be helpful to define a more appropriate propedeutic and therapeutic approach. With an US evaluation, it would be possible to establish standards for a reference population, thus enabling the identification of the early changes that lead to labor.

The purpose of this study was to define reference ranges for values of US measurements of the uterine cervix among low-risk pregnant women with GAs between 12 and 36 weeks, and to discuss these findings in the light of the current knowledge.

Methods

This was a prospective cohort study involving a single group of low-risk pregnant women. Those with GA below 16 weeks (estimated by reliable amenorrhea and/or early confirmatory US) were included, and transvaginal and abdominal US exams were repeated at intervals ranging from 2 to 4 weeks, with the first evaluation occurring between 12 and 16 weeks. The study was conducted over a period of 18 months to allow the necessary number of pregnant women to be included and monitored until delivery.

Complete information on the measurements of the cervix of all participating women was collected, as well as information on epidemiology, evolution of pregnancy and childbirth. Women with any obstetric or clinical pathological conditions that could be associated with spontaneous or induced preterm birth, such as diabetes, hypertension, heart and rare diseases, with risk factors for preterm birth, such as a history of prematurity, cerclage, recurrent miscarriage, uterine cervix surgery, uterine malformation, uterine myomatosis, fetal malformation, and premature rupture of membranes were excluded. The development of any of the aforementioned conditions during pregnancy was considered a reason to exclude the pregnant women from the study, but all data collected until that moment were considered in the analysis.

The calculation of the sample size considered the mean cervical length of 44.2 mm and a standard deviation (SD) of 4.1 mm,[22] with a 2% difference from the populational mean, and a type I error of 0.01. The number needed to assess the mean length of the uterine cervix was calculated individually for each GA range, and the largest estimated size was chosen, that is, 144 women for the 33–36-week period. Considering a possible loss of up to 35% during follow-up, a minimum number of 200 pregnant women was estimated to be necessary to compose the sample.

The measurements obtained by US examination for each pregnant woman was the uterine cervix length, using the technique proposed by the Fetal Medicine Foundation, with the addition of a 90-degree rotation of the transducer, focusing the middle third of the cervix to enable the measurement of the transverse and anteroposterior diameters (►**Fig. 1** and ►**Fig. 2**). Finally, the distance between the entrance of the right or left uterine arteries into the uterine cervix until the internal os was also evaluated, using an oblique cross section to determine the supravaginal length of the cervix. The volume of the cervix was calculated using the formula for the volume of a cylinder, $\pi R^2 h$, where R corresponded to the half of the transverse diameter of the cervix, and h, to its length. The total duration of the US abdominal examination was ~ 25 minutes, while the transvaginal examination lasted around 10 minutes. The machine used for the US exam was the Toshiba Xario (Toshiba, Minato, Tokyo, Japan) with a multifrequencial probe of 3.6 to 8.8 MHz endocavity transducer for the endovaginal exam (Toshiba Xario PVT-661 VT Transducer).

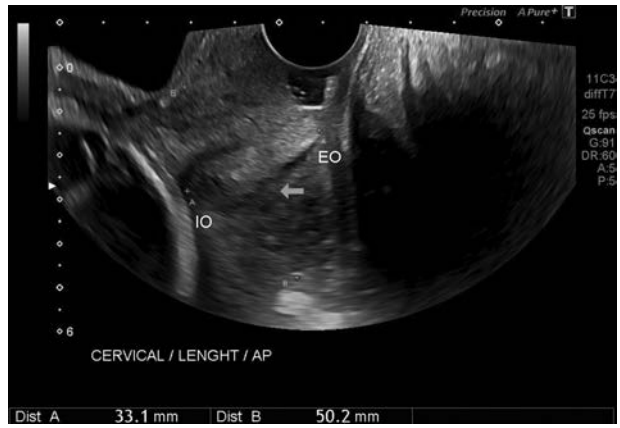

Fig. 1 Ultrasound scan showing the measurement procedure for the uterine cervix. A-A: cervical length from the internal os (IO) to the external os (EO), with the cervical channel (arrow). B-B: Antero-posterior (AP) diameter of the uterine cervix.

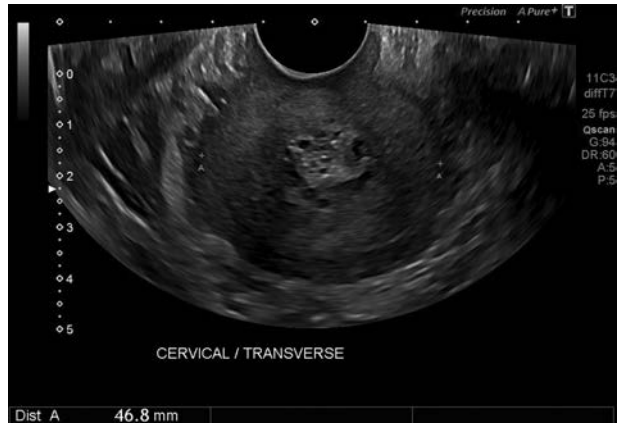

Fig. 2 Ultrasound scan showing the measurement procedure for the uterine cervix. A-A: transverse diameter of the uterine cervix.

The study was evaluated and approved by the Institutional Review Board of our institution (letter of approval number 367–2000). The pregnant women were identified among those attending prenatal care at the outpatient clinic, who were then invited to participate in the study. After agreeing to participate, they signed an informed consent form and underwent the first US exam. After that, the women had US exams scheduled monthly, which coincided with their prenatal care visits. The study followed all principles of the Declaration of Helsinki, which was reviewed in 2008. All the pregnant women had US

exams performed by the same examiner. Only the group of women participating in the pilot study underwent the second exam, on the same day, performed by a different examiner, for the assessment of the interobserver variability; the exam was subsequently performed again by the first examiner for the assessment of the intraobserver variability. In those two situations, the observers were blind to all measurements to avoid the possibility of being biased by the knowledge of the previous measurements.

For the data analysis, a normal distribution was assumed for all collected data. At first, for the evaluation of inter- and intraobserver variabilities, the mean values (±SD) of each US measurement obtained by the first examiner were compared with those obtained by the second examiner, with the differences compared using the Student *t*-test, as well as by the mean proportional variation between the two measurements. The variability was considered the lowest the highest was the linear correlation coefficient r when crossing the two measurements for all of the pregnant women. Reference ranges curves were then defined for the uterine cervix measurements, which were summarized by points at each four-week interval of GA, starting at week 12 until week 36. The curves were constructed from the medians of the measurements (percentile 50) and the confidence interval (CI) that determined the maximum (percentiles 90 and 97.5) and minimum limits (percentiles 10 and 2.5) of the curves. A comparison of the values was performed with the Friedman non-parametric analysis of variance throughout GA (since the residuals did not have a normal distribution) for repeated measurements of the same subject.

Likewise, the comparison analysis of the mean values for uterine cervix length measurements was conducted for each group determined by main control variables, including age, ethnicity/skin color, parity, cesarean section (C-section) history, smoking habits, and sexual activity. Their mean values and SDs were compared using the Student *t*-test. These statistical procedures were performed using the Epi-Info (Centers for Disease Control and Prevention, Atlanta, GA, US) and the Statistical Analysis System (SAS, SAS Institute, Cary, NC, US) softwares.

Results

For the pilot study, 38 women were evaluated. ►**Table 1** shows a small variability, from 0.1% to 9.8%, which means that the reproducibility was high, since the variations did not exceed 10%. Only the interobserver variabilities for the cervix canal width and for the anteroposterior diameter were significant, the only ones with a variation higher than 5%.

A total of 201 pregnant women were included in the study, and 172 concluded their participation with complete data, although not all of them underwent all the 6 planned exams. Of the 29 losses (14.4%), 18 were because they either gave up being cared for at the institution or they were referred elsewhere for delivery, 4 had an abortion, 2 had fetal death, 2 had preterm premature rupture of membranes, 2 had fetal malformations, and 1 had a cervical cerclage performed. They were then excluded from the analysis.

Upon admission to the study, the majority of women were between 20 and 24 years of age, white, married or had a partner, and had finished primary school. About one-third of them were pregnant for the first time, and almost 50% of them had never given birth. One-fourth of them had a history of abortion or C-section. A small minority smoked regularly during pregnancy (►**Table 2**).

The measurements of the uterine cervix length decreased slowly, yet significantly, with GA. However, the values regarding the distance between the entry point of the uterine artery into the cervix until the internal os showed a very slight increase variation with GA (►**Table 3**, ►**Fig. 3**, ►**Fig. 4**). The measurements of the anteroposterior and transverse diameters of the cervix, as well as the estimated cervical volume, showed a small but significant increase with the progression of GA (►**Table 4**, ►**Figs. 5–7**).

The measurements of the uterine cervix length were controlled according to some possibly confounding

Table 1 Inter- and intraobserver variability of the ultrasonographic measurements of the uterine cervix (pilot sample $n = 38$)

Variability	r	Mean ± SD	Mean ± SD	Mean Difference	Variability (%)	t	*p*
Interobserver		1st measurement	2nd measurement				
Cervical length	0.93	36.6 ± 8.1	35.9 ± 7.8	0.75	2.1	1.57	0.126
Chanel width	0.90	5.4 ± 2.2	4.8 ± 2.2	0.53	9.8	3.42	0.0015
Anteroposterior diameter	0.83	34.6 ± 5.0	32.8 ± 5.8	1.78	5.1	3.35	0.0019
Angle of the internal os	0.82	147 ± 21	145 ± 22	1.55	1.1	0.73	0.46
Intraobserver		1st measurement	2nd measurement				
Cervical length	0.93	36.6 ± 8.1	36.7 ± 7.9	−0.03	0.1	−0.06	0.95
Chanel width	0.87	5.4 ± 2.2	5.2 ± 2.1	0.20	3.7	1.20	0.24
Anteroposterior diameter	0.85	34.6 ± 5.0	34.2 ± 5.3	0.34	0.9	0.76	0.45
Angle of the internal os	0.79	147 ± 2	143 ± 19	3.50	2.4	1.65	0.11

Abbreviations: r, linear correlation coefficient; SD, standard deviation; t, Student's t test.

Table 2 Main sociodemographic characteristics of the sample population

Characteristics	n (%)
Maternal age	
≤ 19	36 (20.9)
20–24	61 (35.4)
25–29	40 (23.2)
≥ 30	35 (20.3)
Ethnicity/Skin color	
White	123 (71.5)
Non-white	49 (28.5)
Marital status	
Married	79 (45.9)
Single	27 (15.7)
Stable union	65 (37.8)
Separated	1 (0.6)
Schooling	
Incomplete primary school	77 (44.8)
Complete primary school	28 (16.3)
Incomplete high school	32 (18.6)
Complete high school	29 (16.9)
Incomplete higher education	4 (2.3)
Complete higher education	2 (1.2)
Number of pregnancies	
1	61 (35.5)
≥ 2	111 (64.5)
Parity	
0	82 (47.7)
≥ 1	90 (52.3)
Previous abortion	
0	132 (76.7)
≥ 1	40 (23.3)
Previous cesarean section	
No	132 (76.7)
Yes	40 (233)
Smoking	
Never	122 (70.9)
Not during pregnancy	24 (14.0)
1–10 cigarettes/day	16 (9.3)
11–20 cigarettes/day	4 (2.3)
> 20 cigarettes/day	1 (0.6)
Only initial pregnancy	5 (2.9)
Gestational age at first ultrasound exam (weeks)	
12	24 (14.0)
13	45 (26.3)
14	24 (14.0)
15	47 (27.5)
16	31 (18.1)
Total	**172 (100.0)**

Table 3 Values of percentiles 2.5, 10, 50, 90 and 97.5 for the uterine cervical length and for the distance from the uterine artery to the internal os by ultrasound, according to gestational age, among low-risk pregnant women

Gestational age (n)					
Cervical length (mm) ($p < 0.01$)*					
	p 2.5	**p 10**	**p 50**	**p 90**	**p 97.5**
12–16 (168)	31.5	36.1	44.1	57.1	64.4
17–20 (167)	30.2	33.2	40.8	51.4	59.8
21–24 (167)	29.4	33.9	41.4	51.7	55.5
25–28 (165)	27.6	31.6	40.8	48.5	53.5
29–32 (168)	21.0	29.3	38.1	46.8	50.5
33–36 (168)	19.5	26.4	35.8	44.7	49.0
Distance from the uterine artery to the internal os (mm) ($p = 0.03$)*					
	p 2.5	**p 10**	**p 50**	**p 90**	**p 97.5**
12–16 (168)	13.8	17.5	23.5	31.2	36.9
17–20 (167)	16.0	17.7	23.5	31.2	35.9
21–24 (167)	15.9	18.9	24.7	31.7	36.3
25–28 (165)	14.6	17.7	24.7	33.9	39.6
29–32 (168)	13.3	17.5	24.2	30.2	33.5
33–36 (168)	14.0	17.3	23.2	30.8	35.6

Note: *Friedman non-parametric analysis of variance for repeated measurements.

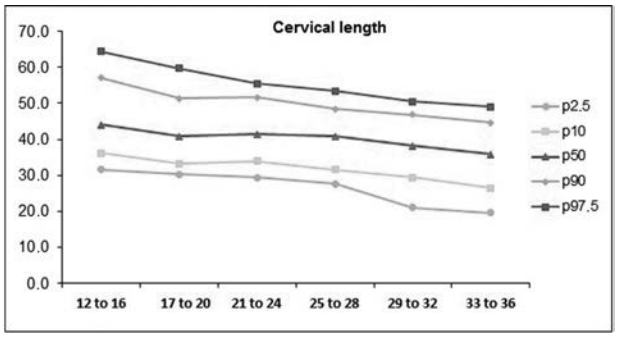

Fig. 3 Curve of values for uterine cervical length by ultrasonography, according to gestational age, among low-risk pregnant women.

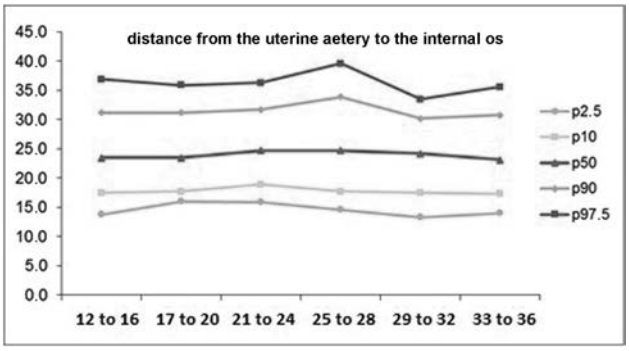

Fig. 4 Curve of percentile values for the distance fromthe uterine artery to the internal os, according to gestational age, among low-risk pregnant women.

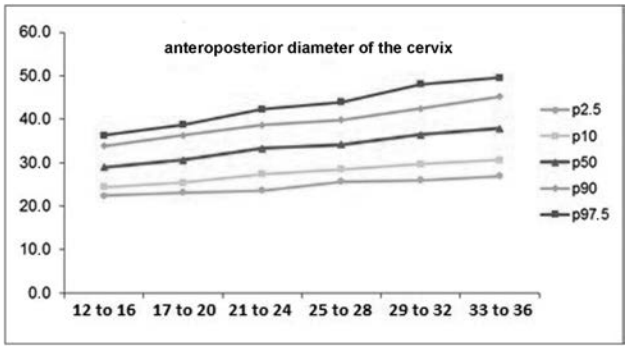

Fig. 5 Curve of percentile values for the anteroposterior diameter of the cervix, according to gestational age, among low-risk pregnant women.

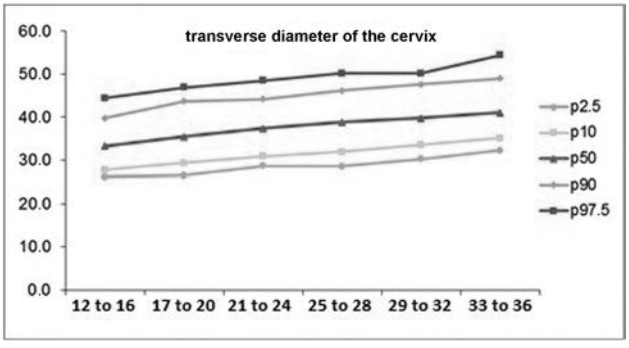

Fig. 6 Curve of percentile values for the transverse diameter of the cervix, according to gestational age, among low-risk pregnant women.

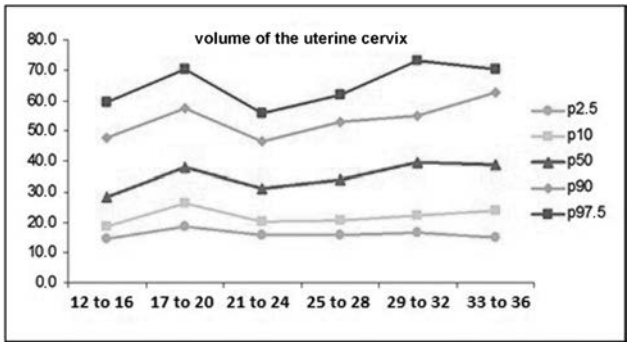

Fig. 7 Curve of percentile values for the volume of the uterine cervix by ultrasonography, according to gestational age, among low-risk pregnant women.

Table 4 Values of percentiles 2.5, 10, 50, 90 and 97.5 for the anteroposterior and transverse diameters, and for the volume of the uterine cervix by ultrasonography, according to gestational age, among low-risk pregnant women

Anteroposterior diameter of the cervix (mm) ($p < 0.01$)*					
Gestational age (n)	p 2.5	p 10	p 50	p 90	p 97.5
12–16 (168)	22.4	24.4	29.0	33.9	36.3
17–20 (167)	23.1	25.4	30.6	36.3	38.8
21–24 (167)	23.6	27.4	33.3	38.7	42.3
25–28 (165)	25.7	28.5	34.2	39.9	44.0
29–32 (168)	26.0	29.7	36.5	42.5	48.1
33–36 (168)	26.9	30.6	37.9	45.2	49.6
Transverse diameter of the cervix (mm) ($p < 0.01$)*					
	p 2.5	p 10	p 50	p 90	p 97.5
12–16 (168)	26.2	27.8	33.3	39.8	44.4
17–20 (167)	26.5	29.4	35.5	43.7	46.9
21–24 (167)	28.7	30.9	37.4	44.2	48.5
25–28 (165)	28.6	32.0	38.8	46.2	50.2
29–32 (168)	30.3	33.6	39.8	47.6	50.2
33–36 (168)	32.3	35.2	41.1	49.0	54.4
Volume of the cervix (cm^3) ($p < 0.01$)*					
	p 2.5	p10	p 50	p 90	p 97.5
12–16 (168)	14.7	18.4	28.3	47.6	59.3
17–20 (167)	18.4	26.4	37.8	57.4	70.4
21–24 (167)	15.7	20.2	31.0	46.4	55.8
25–28 (165)	15.9	20.4	33.9	53.0	61.7
29–32 (168)	16.6	22.1	39.8	54.9	73.3
33–36 (168)	14.9	23.8	38.9	62.5	70.3

Note: *Friedman non-parametric analysis of variance for repeated measurements.

factors. ►**Table 5** shows that the cervical length had significantly higher values for women over 25 years of age, with 1 or more previous deliveries, and with a previous C-section. These values were not associated with the women's ethnicity/skin color, smoking habits, or the frequency of sexual intercourse.

Discussion

This was one of the few studies on cervical length measurements conducted among a Brazilian population involving a prospective evaluation throughout pregnancy until childbirth with a dependent sample strictly defined as low-risk. A detailed evaluation of multiple US parameters was conducted, enabling the definition of reference range curves for those measurements with percentile values, especially for the cervical length, which is more useful and applicable in practice. For decades, there has been great concern about the heterogeneity observed in studies of the uterine cervix for the prediction of preterm birth. Currently, there still is some

Table 5 Variability of uterine cervical length according to some control variables (mean ± standard deviation)

Characteristics	Gestational age (weeks)						n
	12–16	17–20	21–24	25–28	29–32	33–36	
Maternal age							
Up to 24 years	44.3 ± 8.2	41.3 ± 7.3	41.2 ± 6.9	39.1 ± 6.6	36.2 ± 7.8	33.7 ± 7.4	97
≥ 25 years	47.2 ± 8.5	43.2 ± 6.9	42.4 ± 6.9	41.8 ± 7.3	39.4 ± 7.4	37.5 ± 6.7	75
p^*	0.02	0.08	0.25	0.01	0.008	0.0008	
Ethnicity/Skin color							
White	45.5 ± 8.1	42.1 ± 6.5	41.5 ± 6.2	40.6 ± 6.6	37.2 ± 7.1	35.2 ± 7.2	123
Non-white	45.7 ± 9.3	42.3 ± 8.7	42.4 ± 8.3	39.4 ± 8.0	38.5 ± 9.2	35.9 ± 7.8	49
p^*	0.85	0.89	0.43	0.3	0.33	0.53	
Parity							
0	43.7 ± 7.9	41.4 ± 6.9	40.8 ± 5.6	38.8 ± 6.4	36.0 ± 7.2	33.6 ± 7.6	82
1+	47.2 ± 8.6	42.9 ± 7.3	42.6 ± 7.8	41.6 ± 7.3	39.1 ± 7.9	37.0 ± 6.8	90
p^*	0.006	0.17	0.08	0.01	0.01	0.002	
Previous cesarean section							
No	44.9 ± 8.3	41.6 ± 7.2	41.1 ± 6.4	39.4 ± 6.6	36.8 ± 7.9	34.3 ± 7.1	132
Yes	47.7 ± 8.8	44.0 ± 6.7	43.8 ± 8.0	43.1 ± 7.5	40.3 ± 6.3	38.9 ± 7.1	40
p^*	0.07	0.06	0.03	0.003	0.01	0.0005	
Smoking							
Never	45.8 ± 8.6	41.8 ± 7.2	41.5 ± 6.5	39.8 ± 6.9	36.8 ± 7.5	35.1 ± 7.0	122
Sometimes	44.9 ± 8.1	43.0 ± 6.9	42.4 ± 7.7	41.5 ± 7.2	39.5 ± 8.1	36.1 ± 8.1	50
p^*	0.55	0.32	0.42	0.17	0.04	0.41	
Sexual activity during pregnancy							
Up to once a week	46.9 ± 8.9	42.9 ± 7.8	42.5 ± 7.4	40.4 ± 7.4	38.2 ± 8.6	35.9 ± 7.5	87
≥ twice a week	44.1 ± 7.8	41.4 ± 6.4	40.9 ± 6.2	40.2 ± 6.6	37.0 ± 6.8	34.9 ± 7.2	85
p^*	0.02	0.16	0.15	0.86	0.32	0.38	

Note: *Student *t*-test

debate on the differences observed in uterine cervix measurements regarding different populations, the GA at screening, the recommended periodicity for the US exams, and even regarding how their outcomes should be evaluated.[23]

Although this cohort was specifically followed in a single service, the examination technique used in this study was similar to what is currently practiced. Discussions are likely to be raised concerning some issues of this study, such as the characteristics of the women cared for in this healthcare facility, and whether the sample represents the population of low-risk pregnant women in the country, which could be a limitation of the study. We found that the technique used in this study was appropriate for the purposes of the investigation, especially considering that inter- and intraobserver variabilities were low.

Among all cases followed-up until the end of pregnancy, not a single preterm birth occurred. This was somewhat unexpected, since the preterm birth rate for the general pregnant population in Brazil is around 10%.[2] However, it also possibly reveals that the inclusion/exclusion criteria used made it possible to select a very low-risk sample of pregnant women. If the selection of a very specific population may imply, on one hand, limitations for generalizations, on the other hand, the absence of preterm births can be understood as a benchmark, allowing to adequately show the physiology of the natural shortening of the uterine cervix in fully regular gestations.

The length of the uterine cervix showed a statistically significant decrease during pregnancy. The 50th percentile ranged from 44.1 mm at 12–16 weeks to 35.8 mm at 33–36 weeks. In a similar Brazilian study,[24] the authors found 36 mm for the 50th percentile at week 23, and 29 mm at week 34. These values are smaller than the ones from our study, and that could possibly be explained by the fact that the aforementioned study had a preterm birth rate of 8.8% between weeks 34 and 37. However, despite the difference, the same pattern of cervical shortening was observed with GA.

The uterine cervix seems to become slightly longer with maternal age, even though no changes were observed in its anteroposterior and transverse diameters. However, these values increased also with parity. These two findings are consistent with another Brazilian study that demonstrated

that the uterine cervix is significantly shorter in women younger than 20 years and primiparous.[25] In addition in our study, a previous C-section was also associated with longer cervical length. These findings may suggest that pregnancies are most likely to cause an increase in the length of the cervix, and then the age and history of C-section would be just confounding factors for this association, since they are also parity-related.

The values of the anteroposterior and transverse diameters also presented a minor increase with GA, outlining an assumption that the shortening and enlargement of the cervix could occur, simultaneously and physiologically, with the increase in GA. The volume also presented a minor increase during pregnancy, which was statistically significant, from 28 cm^3 at 12–16 weeks to 39cm^3 at 33–36 weeks. This could even explain the reason why several shortened uterine cervices during pregnancy did not result in preterm births. In ►**Fig. 8** we present a schematic model of how this physiological shortening progresses during the course of gestation. In addition, other studies involving much larger populations also concluded that the cervical length decreased significantly with GA.[26]

Another issue refers to the actual clinical relevance of a small difference found in cervical length when comparing two measurements. A difference of 2 mm, for instance, is in fact greater than the inherent variability of the measurement method (0.75 mm), exceeding the margin of error of the US. Our hypothesis is that, although there is a difference, it should be interpreted within a natural physiological development of pregnancy, thus showing a gradual decrease in the length of the cervix over the weeks that may or may not be associated with maternal characteristics. In addition, particular attention should also be paid to the pressure the examiner applies to the probe, which could make a difference in the measurement taken, as well as the existence of a concomitant uterine contraction that could also modify the shape and length of the cervix.

By establishing an anatomical reference that divided the cervix into two parts, it was possible to evaluate the behavior of the measurements of these parts at different GAs. The measurement of the distance between the entrance of the uterine artery into the cervix until the internal os showed a very low variation during gestation, suggesting that the decrease in the length of the uterine cervix during pregnancy is most probably due to the shortening of the distal portion of the cervix, the vaginal portion.

The change in cervical length was the largest observed when compared with other measurements also changing during pregnancy. It seems to be the simplest and easiest to be obtained and reproduced. Some authors suggest that the initial evaluation of the cervix can be obtained also with an abdominal exam.[27] However, the unpredictable effect of the volume of the bladder on the elongation of the cervix and the difficulty of its visualization due to obstruction by fetal parts can lead to unsatisfactory images in up to 25% of the cases.[27] Different from what has already been said about the transvaginal evaluation, this method still presents significant divergences in its standardization,[28,29] and it does not exclude the need for the complementary transvaginal exam, when the cervical shortening is identified.[28]

The main objective of this study was to define reference range values of US measurements of the uterine cervix for low-risk pregnant women according to GA, from 12 to 36 weeks, and to associate these values with some obstetric, sociodemographic and lifestyle variables. It was not the purpose of this study to assess the ability of those measurements to predict preterm birth.

A significant difference in the length of the cervix with maternal age was observed, which is in agreement with a study that evaluated 40,000 women and proposed a model for the prediction of preterm birth, showing a sensitivity of around 55% when considering only the cervical length; the sensitivity increased to 69% when the obstetric history and the maternal age were added to the model.[30]

In a systematic review conducted in 2010, Domin et al[31] suggested that, for preterm delivery prediction, the US assessment of the cervix, when stratified by GA, was more sensitive after 20 weeks than prior to that (58% versus 28.2%), although it was less specific (82% versus 98.5%). That means that when a pregnant woman with a shortened cervix is identified with less than 20 weeks of GA, the risk of this woman progressing to a preterm delivery is close to 100%. However, when evaluating women over 20 weeks of GA, the risk of identifying women

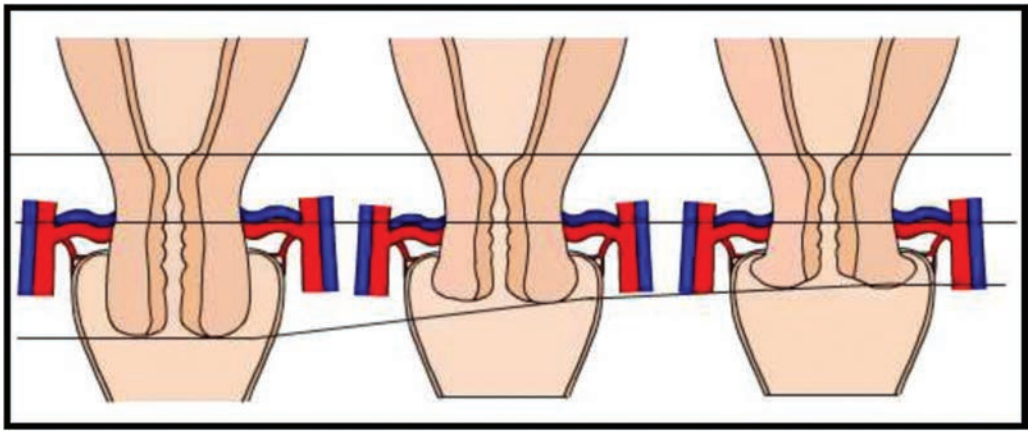

Fig. 8 Graphic representation of the proposed model to shorten the uterine cervix during pregnancy.

who may progress to preterm birth is almost twice higher than when the cervix is evaluated before 20 weeks. The authors also performed a stratification by maternal risk, and concluded that the test showed a better performance for low-risk women, considering that the area under the receiver operating characteristic (ROC) curve was 0.88 for low-risk versus 0.80 for high-risk women.

In a recent meta-analysis, Conde-Agudelo and Romero[8] identified the absence of standard reference values for cervical length as a limitation of the studies, but they concluded that the performance of a single measurement between 18 and 24 weeks was not better than the serial evaluations.

All of these findings may allow us to conclude that the expected cervical changes during pregnancy are the shortening and the enlargement of the cervix with a slight increase in volume, and that the specific values depend on some specific factors regarding the pregnant woman, such as maternal age and obstetric history.

The scientific literature on the topic could be considered biased, since the majority of the studies is only performed on populations from high-income countries. The discrepancy is clearly observed in review articles, with an absolute predominance of studies from the USA and Europe.[8,9,13,15,31,32] One could, therefore, ask how to adequately address the risk factors for populations as racially mixed as the Brazilian population. The interpretation of data on ethnicity is still conflicting. In the Preterm Prediction Study,[33] for instance, ethnicity was a factor that contributed to the risk of preterm birth in nulliparous women, but it could be argued that this effect could be the result of other confounding factors, such as the poor social environment.

In Brazil, a large multi-center study[34] involving more than 5,000 women from the 3 most populous regions of the country was not able to find any evidence of behavioral or sociodemographic factors, including ethnicity/skin color, associated with preterm delivery. Moreover, recent data also suggest that even different physiological changes can occur during the gestational period in Caucasian and in Afro-descendent women.[2] This is based on evidence that shows that newborns with a lower GA, mostly afro-descendants,[35] do not show the same rates of respiratory complications, intensive care needs, or neonatal mortality as the Caucasians.[2]

Conclusion

It seems clear that we are going down a path in which universal screening for cervical length will be recommended; however, in order for this to become a reality, stricter criteria are needed. The best approach for the assessment of the low-risk population should probably be a single evaluation with a transvaginal US exam, possibly during the fetal morphological evaluation, at around 20 weeks of GA. Thus, the definition of reference ranges for cervical measurements during pregnancy, especially those showing lower limits (percentiles 2.5 and 10), for a low-risk population, should enable diagnoses of changes occurring in those measurements. In order for this to happen, it will be necessary to validate such curves and appropriate cut-off points in similar populations for the prediction of the risk of preterm birth, cervical insufficiency, or even premature rupture of membranes.

In a country with relatively scarce resources for healthcare such as Brazil, where medical routine imposes decision-making based on a limited amount of information, the parameters to be used should be precise to avoid inappropriate managements that generate extra expenses caused by unnecessary treatments and repetition of exams.

Conflict of Interests

Cecatti JG is an Associate Editor of Revista Brasileira de Ginecologia e Obstetrícia, and did not participate in the evaluation process of this article.

Contributors

Andrade KC, Bortoletto TG, Almeida CM, Daniel RA, Avo H, Pacagnella RC, and Cecatti JG contributed to the conception of the study, the critical review of the intellectual content, and the final approval of the version to be published.

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References

1 Preterm birth: Fact Sheet. World Health Organization Web site. Published November 2016. http://www.who.int/mediacentre/factsheets/fs363/en/. Accessed March 10, 2017
2 Blencowe H, Cousens S, Chou D, et al; Born Too Soon Preterm Birth Action Group. Born too soon: the global epidemiology of 15 million preterm births. Reprod Health 2013;10(Suppl 1):S2
3 Koullali B, Oudijk MA, Nijman TA, Mol BW, Pajkrt E. Risk assessment and management to prevent preterm birth. Semin Fetal Neonatal Med 2016;21(02):80–88
4 Buck JN, Orzechowski KM, Berghella V. Racial disparities in cervical length for prediction of preterm birth in a low risk population. J Matern Fetal Neonatal Med 2017;30(15):1851–1854
5 Bittar RE, Zugaib M. [Risk predictors for preterm birth]. Rev Bras Ginecol Obstet 2009;31(04):203–209
6 Manuck TA, Esplin MS, Biggio J, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Genomics and Proteomics Network for Preterm Birth Research. The phenotype of spontaneous preterm birth: application of a clinical phenotyping tool. Am J Obstet Gynecol 2015;212(04):487.e1–487.e11
7 Romero R, Nicolaides K, Conde-Agudelo A, et al. Vaginal progesterone in women with an asymptomatic sonographic short cervix in the mid-trimester decreases preterm delivery and neonatal morbidity: a systematic review and metaanalysis of individual patient data. Am J Obstet Gynecol 2012;206:124.e1–124.e19
8 Conde-Agudelo A, Romero R. Predictive accuracy of changes in transvaginal sonographic cervical length over time for preterm birth: a systematic review and metaanalysis. Am J Obstet Gynecol 2015;213(06):789–801
9 Li Q, Reeves M, Owen J, Keith LG. Precocious cervical ripening as a screening target to predict spontaneous preterm delivery among asymptomatic singleton pregnancies: a systematic review. Am J Obstet Gynecol 2015;212(02):145–156
10 House M, Kaplan DL, Socrate S. Relationships between mechanical properties and extracellular matrix constituents of the

cervical stroma during pregnancy. Semin Perinatol 2009; 33(05):300–307
11 Sinno A, Usta IM, Nassar AH. A short cervical length in pregnancy: management options. Am J Perinatol 2009;26(10):761–770
12 Vaisbuch E, Romero R, Erez O, et al. Clinical significance of early (< 20 weeks) vs. late (20-24 weeks) detection of sonographic short cervix in asymptomatic women in the mid-trimester. Ultrasound Obstet Gynecol 2010;36(04):471–481
13 Suhag A, Berghella V. Short cervical length dilemma. Obstet Gynecol Clin North Am 2015;42(02):241–254
14 Romero R, Nicolaides KH, Conde-Agudelo A, et al. Vaginal progesterone decreases preterm birth ≤ 34 weeks of gestation in women with a singleton pregnancy and a short cervix: an updated meta-analysis including data from the OPPTIMUM study. Ultrasound Obstet Gynecol 2016;48(03):308–317
15 Abdel-Aleem H, Shaaban OM, Abdel-Aleem MA. Cervical pessary for preventing preterm birth. Cochrane Database Syst Rev 2013; (05):CD007873
16 Fox NS, Rebarber A, Roman AS, Klauser CK, Saltzman DH. Association between second-trimester cervical length and spontaneous preterm birth in twin pregnancies. J Ultrasound Med 2010; 29(12):1733–1739
17 Ramaeker DM, Simhan HN. Sonographic cervical length, vaginal bleeding, and the risk of preterm birth. Am J Obstet Gynecol 2012; 206(03):224.e1–224.e4
18 Wozniak S, Czuczwar P, Szkodziak P, Milart P, Wozniakowska E, Paszkowski T. Elastography in predicting preterm delivery in asymptomatic, low-risk women: a prospective observational study. BMC Pregnancy Childbirth 2014;14:238
19 Kuusela P, Jacobsson B, Söderlund M, et al. Transvaginal sonographic evaluation of cervical length in the second trimester of asymptomatic singleton pregnancies, and the risk of preterm delivery. Acta Obstet Gynecol Scand 2015;94(06):598–607
20 Miller ES, Tita AT, Grobman WA. Second-trimester cervical length screening among asymptomatic women: an evaluation of risk-based strategies. Obstet Gynecol 2015;126(01):61–66
21 Heath VC, Southall TR, Souka AP, Novakov A, Nicolaides KH. Cervical length at 23 weeks of gestation: relation to demographic characteristics and previous obstetric history. Ultrasound Obstet Gynecol 1998;12(05):304–311
22 Podobnik M, Bulić M, Smiljanić N, Bistricki J. Ultrasonography in the detection of cervical incompetency. J Clin Ultrasound 1988; 16(06):383–391
23 Guzman ER, Ananth CV. Cervical length and spontaneous prematurity: laying the foundation for future interventional randomized trials for the short cervix. Ultrasound Obstet Gynecol 2001; 18(03):195–199
24 Silva SV, Damião R, Fonseca EB, Garcia S, Lippi UG. Reference ranges for cervical length by transvaginal scan in singleton pregnancies. J Matern Fetal Neonatal Med 2010;23(05):379–382
25 Palma-Dias RS, Fonseca MM, Stein NR, Schmidt AP, Magalhães JA. Relation of cervical length at 22-24 weeks of gestation to demographic characteristics and obstetric history. Braz J Med Biol Res 2004;37(05):737–744
26 Hoesli IM, Strutas D, Tercanli S, Holzgreve W. Charts for cervical length in singleton pregnancy. Int J Gynaecol Obstet 2003;82(02):161–165
27 Peng CR, Chen CP, Wang KG, Wang LK, Chen CY, Chen YY. The reliability of transabdominal cervical length measurement in a low-risk obstetric population: Comparison with transvaginal measurement. Taiwan J Obstet Gynecol 2015;54(02):167–171
28 Friedman AM, Schwartz N, Ludmir J, Parry S, Bastek JA, Sehdev HM. Can transabdominal ultrasound identify women at high risk for short cervical length? Acta Obstet Gynecol Scand 2013; 92(06):637–641
29 Hernandez-Andrade E, Romero R, Ahn H, et al. Transabdominal evaluation of uterine cervical length during pregnancy fails to identify a substantial number of women with a short cervix. J Matern Fetal Neonatal Med 2012;25(09):1682–1689
30 To MS, Skentou CA, Royston P, Yu CKH, Nicolaides KH. Prediction of patient-specific risk of early preterm delivery using maternal history and sonographic measurement of cervical length: a population-based prospective study. Ultrasound Obstet Gynecol 2006;27(04):362–367
31 Domin CM, Smith EJ, Terplan M. Transvaginal ultrasonographic measurement of cervical length as a predictor of preterm birth: a systematic review with meta-analysis. Ultrasound Q 2010; 26(04):241–248
32 Conde-Agudelo A, Romero R, Nicolaides K, et al. Vaginal progesterone vs. cervical cerclage for the prevention of preterm birth in women with a sonographic short cervix, previous preterm birth, and singleton gestation: a systematic review and indirect comparison metaanalysis. Am J Obstet Gynecol 2013;208(01):42.e1–42.e18
33 Mercer BM, Goldenberg RL, Das A, et al. The preterm prediction study: a clinical risk assessment system. Am J Obstet Gynecol 1996;174(06):1885–1893, discussion 1893–1895
34 Passini R Jr, Cecatti JG, Lajos GJ, et al; Brazilian Multicentre Study on Preterm Birth study group. Brazilian multicentre study on preterm birth (EMIP): prevalence and factors associated with spontaneous preterm birth. PLoS One 2014;9(10): e109069
35 Szychowski JM, Owen J, Hankins G, et al; Vaginal Ultrasound Cerclage Trial Consortium. Timing of mid-trimester cervical length shortening in high-risk women. Ultrasound Obstet Gynecol 2009;33(01):70–75

Knowledge and Compliance in Practices in Diagnosis and Treatment of Syphilis in Maternity Hospitals in Teresina - PI, Brazil

Conhecimento e conformidade quanto às práticas de diagnóstico e tratamento da sífilis em maternidades de Teresina - PI, Brasil

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Abstract

Objective To assess the knowledge and compliance of health professionals regarding the diagnostic and treatment practices for syphilis in patients admitted for childbirth in public maternity hospitals in the city of Teresina, in the state of Piauí, Northeastern Brazil.

Methods A cross-sectional study was performed in 2015 with obstetricians and nurses working in the public maternity hospitals in Teresina ($n = 159$) using a self-administered questionnaire, with 5% of losses and 10% of refusals. The study used 21 evaluation criteria: 13 of them were related to knowledge (5 on serological tests and 8 on treatment adequacy); 8 were related to practices (3 on diagnosis, 4 on treatment, and 1 on post-test counseling). The knowledge of and compliance to the practices was estimated as the proportion of health professionals' answers that were in agreement with Brazilian Ministry of Health protocols.

Results The obstetricians were in agreement with two criteria concerning the knowledge of serological tests, one for diagnostic practices, and one for treatment practice. Among nurses, no single match between actual procedures and guidelines was observed.

Conclusions Low compliance with the protocols results in missed opportunities for the diagnosis and treatment of pregnant and postpartum women and their partners. Strategies for training and integrating the various professional groups, improved data recording on prenatal cards, and greater accountability of the hospital team in managing the women's partners are needed to overcome the barriers identified in the study and to interrupt the syphilis transmission chain.

Keywords
- syphilis
- congenital syphilis
- health personnel
- health evaluation
- maternity hospitals

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Resumo

Objetivo Avaliar o conhecimento e a conformidade em práticas de diagnóstico e tratamento no manejo da sífilis por ocasião da admissão para o parto entre os profissionais de saúde atuantes nas maternidades públicas de Teresina, Piauí, na Região Nordeste do Brasil.

Métodos Realizou-se, em 2015, um estudo transversal com a população de médicos obstetras e enfermeiros atuantes nas maternidades públicas de Teresina ($n = 159$) por meio de formulários autoaplicáveis, tendo sido registradas 5% de perdas e 10% de recusas. Foram utilizados 21 critérios de avaliação: 13 relacionados ao conhecimento (5 sobre exames sorológicos e 8 sobre adequação do tratamento) e 8 relacionados às práticas (3 sobre diagnóstico, 4 sobre tratamento, e 1 sobre aconselhamento pós-teste). A conformidade dos conhecimentos e práticas foi estimada como a proporção de respostas dos profissionais em concordância com os protocolos do Ministério da Saúde brasileiro.

Resultados Foi observada concordância em dois critérios de conhecimento sobre exames sorológicos, um relacionado às práticas diagnósticas, e um de prática de tratamento, entre os médicos. Entre os enfermeiros, nenhum critério avaliado apresentou concordância com os critérios padrão.

Conclusões O perfil observado de baixa conformidade quanto aos critérios avaliados resulta em oportunidades perdidas de diagnóstico e tratamento das gestantes/puérperas e de seus parceiros. Estratégias de capacitação e integração das diversas categorias profissionais, melhoria nos registros no cartão de pré-natal e maior responsabilização da equipe hospitalar no manejo do parceiro são necessárias para superar as barreiras encontradas e interromper a cadeia de transmissão da doença.

Palavras-chave

- sífilis
- sífilis congênita
- pessoal de saúde
- avaliação em saúde
- maternidades

Introduction

The most recent available global estimates of syphilis in pregnancy, obtained from World Health Organization (WHO) databases, indicate that ~ 1.4 million pregnant women presented active syphilis infection worldwide in 2008, distributed across Asia (44.3%), Africa (39.3%), the Americas (7.8%), the Pacific (4.0%), the Mediterranean (3.0%), and Europe (1.6%). In the absence of adequate diagnosis and treatment, an estimated 710,000 pregnancies evolve to adverse outcomes associated with the infection, including stillbirth, early fetal deaths, neonatal deaths, prematurity, low birth weight, and infected newborns,[1] with an extremely high burden of disease.[2]

The elimination of congenital syphilis (CS) is a top public health priority. The goal is to reduce the incidence of congenital syphilis to below 0.5 cases per 1,000 live births.[3–5] In Brazil, 19,228 new cases of CS were reported to the Information System on Notifiable Diseases (Sinan, in the Portuguese acronym) in 2015, with an incidence rate of 6.5 per 1,000 live births, which 13 times higher than the goal of elimination.[6]

The principal strategy for the control of CS is the identification and treatment of pregnant women with syphilis infection during prenatal care. However, worldwide, some two thirds of the adverse outcomes associated with syphilis in pregnancy occur in women who received prenatal care but were not tested and/or treated for syphilis.[1] Therefore, in order to achieve the goal of eliminating CS, the WHO established three process goals related to the care provided to pregnant women: offer prenatal care, test for diagnosis of syphilis, and treat the disease during pregnancy, with coverage of at least 95%.[5]

The Brazilian Ministry of Health (MoH) also recommends serological testing at the first prenatal visit, with an additional test at the beginning of the third trimester of pregnancy and another test upon hospital admission for childbirth or curettage. This additional testing aims to identify cases or inadequate treatments during pregnancy,[7] and provides new opportunities for the diagnosis and treatment of the mothers, their partners and newborns at the time of childbirth.[8]

In Brazil, of all cases of CS registered in 2015, 78.4% of the pregnant women had received prenatal care, but only 51.4% underwent a syphilis diagnostic test during pregnancy, only 34.6% underwent it during admission for childbirth or curettage, only 8.9% underwent it after that period, and 5.1% with diagnostic period ignored. From those pregnant women who received prenatal care, 56.5% received inadequate treatment, and 27.3% were untreated, whereas the majority of their partners were untreated (62.3%) or with ignored registered information about treatment (23.8%),[6] thus revealing serious flaws in this care.

An even worse situation was observed in some states of the Northeast of Brazil (the least economically developed region of the country). Piauí is one of the Northeastern states, with a CS rate of 7.8 per 1,000 live births in 2015,[6] and its capital, Teresina, is the state's largest city, with 800,000 inhabitants, and a CS rate of 15.3 per 1,000 live births. In this city, of all cases of CS registered in 2015, 43.2% underwent a syphilis diagnostic

test during admission for childbirth or curettage, and 10.3%, after that period; 76.5% of them were inadequately treated, 21.1% had absence of treatment/ignored information (21.1%), and 77.5% of their partners were not treated.[9]

Given the gap between Brazil's epidemiological situation and the goal of eliminating congenital syphilis, plus the need to intervene to avoid missing the opportunity to diagnose and treat women with syphilis and their newborns, this study aims to assess the knowledge of and compliance to the practices in the diagnosis and treatment of syphilis upon the admission of pregnant women for childbirth by the health professionals working in the public maternity hospitals in Teresina, Piauí, in relation to Brazilian MoH protocols.

Methods

A cross-sectional study was conducted from February 1st to March 31st, 2015, with the obstetricians and nurses working in the public maternity hospitals in Teresina, Piauí (three municipal and one state hospital), in operation during the study period. The sample excluded professionals that were working exclusively in management, administrative, outpatient, and materials and sterilization services or in the maternal intensive care unit (ICU).

The health professionals were contacted by the principal investigator during their ward duty at the maternity hospitals. After an invitation to participate in the study, they received a self-applied questionnaire with multiple-choice questions, to be returned in a sealed, unidentified envelope at the end of their shift or on a date and time suggested by the participant.

Refusals were defined as professionals who stated that they declined to participate, returned the questionnaire blank, or failed to return the questionnaire after scheduling three attempts for this purpose, while losses were defined as professionals that were not contacted because they were on maternity or sick leave or vacation during the study period. A field spreadsheet was used to control the return of the questionnaires, in which there was no key field connected to the questionnaires, which enabled the calculation of the response rate while safeguarding the participants' anonymity.

The professionals' profile was characterized through a descriptive analysis of their demographic and training characteristics and careers, with a point estimate of proportions and respective 95% confidence intervals (95%CIs).

In order to assess the health professionals' knowledge and practices in the management of syphilis in patients admitted for childbirth, we used the normative evaluation as the theoretical reference,[10] according to the guidelines in the MoH protocols, as of the study's starting date.[7,11] The guidelines were summarized in 21 evaluation criteria: 13 of them were related to knowledge (5 on serological tests and 8 on treatment adequacy based on hypothetical clinical cases); 8 were related to practices (3 on diagnosis, 4 on treatment, and 1 on post-test counseling). Agreement was assessed by the group of researchers considering the core of contents, which were expressed in multiple choice questions comparing and contrasting the professionals' answers about their knowledge and practices in the diagnosis and treatment of syphilis vis-à-vis the standard procedures as stated in the manuals.

Compliance with the evaluation criteria was estimated as the proportion of the health professionals' answers that agreed with the MoH protocols, with the respective 95%CI. The criteria were considered compliant when the interval estimate included 95% compliance or greater, according to the standard adopted by the WHO for diagnostic and therapeutic goals for syphilis in pregnancy.[5] The questionnaires were keyed into the EpiData (EpiData Association, Odense, Denmark) software, version 3.1, with duplicate keying-in of 15% of the questionnaires and correction of errors as identified. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, IBM Corp., Armonk, NY, US) software, version 20.

The research project was approved by the Institutional Review Boards of our institutions (CAAE case review no. 861.845). In order to ensure the research subjects' anonymity, rather than an informed consent form, a letter of invitation that contained information on the study and relevant information on the investigators, the same procedure adopted in a previous study, was sent.[12] Thus, filling out and returning the questionnaire were considered expressions of consent by the health professional to participate in the study.

Results

A total of 237 obstetricians and nurses working in the public maternity hospitals in Teresina were considered eligible, of whom 13 (5%) were on vacation or maternity or sick leave, and were thus not invited to participate. Of the 224 health professionals invited to participate in the study, 22 (10%) refused. Of the questionnaires received, 59 were filled out by obstetricians, 100 by nurses who worked with women admitted for childbirth, and 43 by nurses who worked only with the newborns. The latter group was not included in the present study, as our aim was to evaluate the knowledge and practices related to women's care.

Of the 159 professionals that participated in the study, the majority were women (67%), under 40 years of age (65%), who had graduated from higher education less than 10 years before the present study (53%), with less than 10 years of experience working in maternity hospitals (71%), and with job stability in the public service (74%). Among the nurses, there was a statistically higher percentage of women, younger individuals (under 30 years of age), and of respondents with less time since graduation and fewer years of experience working in maternity hospitals when compared with the obstetricians (►**Table 1**).

An analysis of the participants' complementary training showed that 88% of them had attended some kind of graduate course, and 54% of these had a specialization or residency in maternal and child health; the percentages were statistically lower for nurses in both cases.

Total 39% of the professionals stated that they had participated in some training on syphilis management, of whom more than 2/3 (69%) had received their most recent training 1 to 5 years before the study. Nearly 2/3 (64%) of the subjects

Table 1 Demographic, training, and work characteristics of health professionals in public maternity hospitals. Teresina, state of Piauí, Brazil, 2015 ($n = 159$)

	Obstetricians ($n = 59$)		Nurses ($n = 100$)		Total ($n = 159$)	
Variables	**n**	**% (95%CI)***	**n**	**% (95%CI)***	**n**	**% (95%CI)***
Sex						
Female	20	34 (22.4 - 47. 5)	86	86 (77.2–91.8)	106	67 (58.7–73.8)
Male	39	66 (52.5–77.6)	14	14 (8.1–22.7)	53	33 (26.2–41.3)
Age group (years)						
< 30	4	7 (2.2–17.3)	39	39 (29.5–49.3)	43	27 (20.4–34.8)
30–39	25	42 (29.8–55.9)	35	35 (25.9–45.2)	60	38 (30.3–45.8)
40–49	13	22 (12.7–35.0)	14	14 (8.1–22.7)	27	17 (11.7–23.9)
≥ 50	16	27 (16.7–40.5)	9	9 (4.4–16.3)	25	16 (10.6–22.5)
Time since graduation						
< 10 years	15	25 (15.4–38.7)	70	70 (59.9–78.5)	85	53 (45.4–61.3)
≥ 10 years	43	73 (59.5–83.2)	29	29 (20.6–39.1)	72	45 (37.4–53.3)
Time working in the maternity hospital						
< 10 years	26	44 (31.4–57.5)	87	87 (78.4–92.6)	113	71 (63.3–77.8)
≥ 10 years	32	54 (40.8–67.1)	9	9 (4.4–16.8)	41	26 (19.3–33.4)
Employment relationship in maternity hospital						
Stable/public servant	49	83 (70.6–91.1)	69	69 (58.8–77.7)	118	74 (66.6–80.7)
Temporary	10	17 (8.8–29.4)	30	30 (21.4–40.1)	40	25 (18.8–32.8)
Graduate training						
Yes	59	100 (92.4–100.0)	81	81 (71.7–87.9)	140	88 (81.7–92.5)
No	0	0 (0.0–7.6)	17	17 (10.5–26.1)	17	11 (6.5–16.8)
Most recent types of graduate training						
Specialization/residency	53	90 (78.5–95.8)	68	68 (57.8–76.8)	121	76 (68.6–82.3)
Master's	2	3 (0.6–12.7)	13	13 (7.4–21.6)	15	9 (5.5–15.3)
PhD	3	5 (1.3–15.0)	0	0 (0.0–4.6)	3	2 (0.5–5.9)
Other	1	2 (0.1–10.3)	0	0 (0.0–4.6)	1	1 (0.0–4.0)
Most recent type of specialization/residency(***)**						
Maternal and child health	47	89 (76.3–95.3)	18	26 (16.8 - 38.8)	65	54 (44.4–62.7)
ICU/urgency and emergency	1	2 (0.1–11.4)	18	26 (16.8 - 38.8)	19	16 (10.0–23.7)
Family health /public health	0	0 (0.0–8.4)	10	15 (7.6–25.8)	10	8 (4.2–15.0)
Other	6	11 (4.7–23.7)	19	28 (18.1–40.3)	25	21 (14.0–29.2)
Participation in training on syphilis						
Yes	22	37 (25.3–50.9)	40	40 (30.5–50.3)	62	39 (31.5–47.1)
No	36	61 (47.4–73.2)	57	57 (46.7–66.7)	93	58 (50.4–66.2)
Most recent training***						
< 1 year	0	0(0.0–18.5)	3	8 (1.9–21.5)	3	5 (1.2–14.4)
1 to 5 years	13	59 (36.7–78.5)	30	75 (58.5–86.7)	43	69 (56.2–80.1)
> 5 years	9	41 (21.5–63.3)	6	15 (6.2–30.5)	15	24 (14.6–37.0)
Knows MoH manual						
Yes	31	52 (39.2–65.5)	71	71 (60.9–79.4)	102	64 (56.1–71.5)
No	26	44 (31.4–57.5)	25	25 (17.1–34.8)	51	32 (25.0–40.0)

Table 1 (*Continued*)

	Obstetricians ($n = 59$)		Nurses ($n = 100$)		Total ($n = 159$)	
Variables	**n**	**% (95%CI)***	**n**	**% (95%CI)***	**n**	**% (95%CI)***
Last time consulting the MoH manual***						
< 1 year	4	13 (4.2–30.8)	12	17 (9.4–28.0)	16	16 (9.5–24.5)
1 to 5 years	23	74 (55.1–87.4)	48	68 (55.3–77.9)	71	70 (59.6–78.1)
> 5 years	2	6 (1.1–22.8)	9	13 (6.3–23.2)	11	11 (5.8–18.9)
Read MoH manual ***						
Yes, entirely	13	42 (25.1–60.7)	11	16 (8.3–26.4)	24	23 (15.9–33.1)
Yes, partially	16	52 (33.4–69.4)	57	80 (68.8–88.4)	73	72 (61.6–79.8)
No	2	6 (1.1–22.8)	3	4 (1.1–12.7)	5	5 (1.8–11.6)

Abbreviations: 95%CI, 95% confidence interval; ICU, intensive care unit; MoH, Ministry of Health.
Notes: *Proportions of the total obstetricians (59) and nurses (100): the totals for each variable differ due to the small number of "missing" cases; **multiple-choice question; ***question answered by participants that answered yes to the previous question.

reported knowing the MoH manual on prevention of congenital syphilis, and 70% of them had last consulted it between 1 and 5 years before the study. The manual had been read in its entirety by 23% of the professionals.

In relation to the knowledge of serological tests (►**Table 2**), 79% of the obstetricians and nurses identified the Venereal Disease Research Laboratory (VDRL) test as a non-treponemal test, 77% identified the fluorescent treponemal antibody-absorption (FTA-Abs) test and the *Treponema pallidum* hemagglutination assay (TPHA) as treponemal tests, and 50% identified the rapid syphilis test as a treponemal test. The obstetricians showed higher agreement rates for the VDRL and FTA-Abs tests and the TPHA compared with the nurses.

Six percent of the professionals correctly identified the VDRL test's relevant characteristics for the clinical management in pregnancy, while the lowest percentage of correct answers was associated with the fact that this test is also considered qualitative (32%). About 1/3 of the professionals (29%) have correctly indicated the characteristics of the treponemal tests, while 31% have erroneously stated that treponemal tests become "non-reactive" after adequate treatment, and 28% stated that they can be used to control the cure.

Agreement rates about the knowledge of the treatment of syphilis during pregnancy varied from 21% (95%CI: 14.9–28.0%) to 76% (95%CI: 68.6–82.3%) (►**Table 3**), and the lowest proportion of correct answers was for the minimum time between the conclusion of the treatment and childbirth for the mother's treatment to be considered adequate. The results also showed a low proportion of adequate management of the pregnant woman in relation to penicillin allergy (32%), in the evaluation of maternal serological titers following treatment (41%), and in the interval between doses of penicillin benzathine (48%) during the pregnant woman's treatment. The obstetricians showed a statistically higher agreement rate than the nurses in three clinical cases: management of a pregnant woman with a low serological titer during pregnancy and report of adequate prior treatment; prescription of treatment with the correct interval between doses of penicillin benzathine; and treatment of the partner.

Of all the professionals, 74% stated that they recorded on the patient chart and/or on the hospital admission form the results of the serological tests for syphilis contained on the prenatal card and 82% of the treatments received by the woman. Ordering "syphilis serology" for all women admitted for childbirth or curettage was reported by 40% of the professionals, and was statistically more common among obstetricians (96%; 95%CI: 87.2–99.4%). Among nurses, 47% reported not ordering the tests (95%CI: 37.0–57.2%) and 36% reported not being allowed to order them (95%CI: 26.8–46.3%) (►**Table 4**).

Obstetricians and nurses differed significantly in relation to the correct procedure in the treatment of syphilis according to the stage of the disease. Among the obstetricians, 66% (95%CI: 52.5–77.6%) reported the correct treatment of primary syphilis, 52% (95%CI: 39.2–65.5%) reported the correct treatment of secondary syphilis, and 95% (95%CI: 84.9–98.7%) reported the correct treatment of syphilis of unknown duration. The majority of nurses reported not being allowed to prescribe any medicine for the pregnant women in the maternity hospital, regardless of the stage of the disease (58%; 95%CI: 47.7–67.7%).

The offer of 3 recommended instructions during the post-test counseling was reported by 73% of the professionals. More than 1/3 of the professionals (37%) reported calling in the partners of the pregnant women with syphilis to the maternity hospital to order the VDRL test and prescribe treatment.

The main barriers to the adequate management of syphilis in the maternity hospitals were lack of records of the diagnosis on the prenatal card (50%) and of the treatments received during prenatal care (65%); the pregnant women's lack of information on the treatments performed during prenatal care (64%); and difficulties in conversing with the women's partners (50%) (►**Table 5**). The nurses reported statistically greater difficulty in explaining the test result to the pregnant women (41%; 95%CI: 31.4–51.3) when compared with the

Table 2 Agreement of the health professionals' knowledge on laboratory tests in relation to the management of syphilis in pregnancy. Teresina, state of Piauí, Brazil, 2015

Criteria	Obstetricians ($n = 59$)		Nurses ($n = 100$)		Total ($n = 159$)	
	n	% (95%CI)*	N	% (95%CI)*	n	% (95%CI)*
The VDRL test is non-treponemal						
In agreement	54	92 (80.6–96.8)	72	72 (62.0–80.3)	126	79 (71.9–85.1)
Not in agreement/not informed	5	8 (3.1–19.4)	28	28 (19.7–38.0)	33	21 (14.9–28.1)
The rapid syphilis test is treponemal						
In agreement	28	48 (34.5–60.8)	51	51 (40.9–61.0)	79	50 (41.7–57.7)
Not in agreement/not informed	31	52 (39.2–65.5)	49	49 (38.9–59.1)	80	50 (43.3–58.3)
The TPHA and FTA-Abs test are treponemal						
In agreement	54	92 (80.6–96.8)	69	69 (58.8–77.7)	123	77 (69.9–83.4)
Not in agreement/not informed	5	8 (3.1–19.4)	31	31 (22.3–41.1)	36	23 (16.5–30.1)
Characteristics of the VDRL test**						
1. Qualitative test	18	31 (19.5–44.0)	33	33 (24.1–43.2)	51	32 (25.0–40.0)
2. Can become non-reactive after adequate treatment	41	70 (56.0–80.4)	47	47 (37.0–57.2)	88	55 (47.3–63.1)
3. Can be used to control the cure	46	78 (64.9–87.3)	43	43 (33.2–53.3)	89	56 (47.9–63.8)
4. Cross-reactive with other infections	51	86 (74.5–93.5)	28	28 (19.7–38.0)	79	50 (41.7–57.7)
5. Does not know how to interpret the test	0	0 (0.0–7.6)	8	8 (3.8 - 15.6)	8	5 (2.3–10.0)
In agreement (with items 1,2,3, and 4)	9	15 (7.6–27.4)	1	1 (0.1–6.2)	10	6 (3.2–11.6)
Not in agreement / Not informed	50	85 (72.5–92.4)	99	99 (93.8–99.9)	149	94 (88.4–96.8)
Characteristics of the treponemal tests**						
1. Qualitative tests	39	66 (52.5–77.6)	49	49 (38.9–59.1)	88	55 (47.3–63.1)
2. Can become non-reactive after adequate treatment	21	36 (23.9–49.2)	29	29 (20.6–39.1)	50	31 (24.4–39.3)
3. Can be used to control the cure	26	44 (31.4–57.5)	19	19 (12.1–28.3)	45	28 (21.6–36.1)
4. Cross-reactive with other infections	7	12 (5.3–23.5)	11	11 (5.9–19.2)	18	11 (7.0–17.5)
5. Does not know how to interpret the tests	0	0 (0.0–7.6)	19	19 (12.1–28.3)	19	12 (7.5–18.3)
In agreement (only with item 1)	20	34 (22.4–47.5)	26	26 (18.0–35.9)	46	29 (22.2–36.7)
Not in agreement/Not informed	39	66 (52.5–77.6)	74	74 (64.1–82.0)	113	71 (63.3–77.8)

Abbreviations: 95%CI, 95% confidence interval; FTA-Abs, fluorescent treponemal antibody-absorption; TPHA, *Treponema pallidum* hemagglutination assay; VDRL Venereal Disease Research Laboratory.
Notes: *Proportions of the total obstetricians (59) and nurses (100): the totals for each variable differ due to the small number of "missing" cases. **Multiple choice question.

obstetricians (17%; 95%CI: 8.8–29.4%). For the other difficulties, there was no statistically significant evidence of differences between obstetricians and nurses (►**Table 5**).

Discussion

The results of the present study reveal a series of gaps in the knowledge and practices among health professionals involved in obstetric care, whose answers express approaches that fail to agree consistently with the Brazilian MoH[7,11] and international protocols.[4]

The obstetricians agreed with two criteria pertaining to the knowledge of serological tests (the VDRL test as a non-treponemal test, and the TPHA and FTA-Abs test as treponemal tests), one criteria about diagnostic practices ("ordering syphilis serology for all pregnant women admitted for childbirth and curettage"), and one criteria regarding treatment practices ("treatment of syphilis of unknown duration"). Among the nurses, no criterion agreed with the protocols. These findings are worrisome, since this performance could be defined as incompatible with any concerted attempt to curb CS.

Low agreement rates were observed for laboratory tests used to diagnose syphilis, which is essential to properly manage each case. The lowest agreement rate was with the rapid syphilis test. Brazil's health care system only implemented this test in 2011,[13] which might explain the health professionals' lower familiarity with its use. It appears that the implementation strategies used so far have been insufficient to increase the knowledge and uptake of this test. Once applied properly, it may produce relevant benefits in terms of greater

Table 3 Agreement of the health professionals' knowledge concerning the treatment guidelines for the management of syphilis in pregnancy. Teresina, state of Piauí, Brazil, 2015

Criteria	Obstetricians ($n = 59$)		Nurses ($n = 100$)		Total ($n = 159$)	
	n	% (95%CI)*	n	% (95%CI)*	n	% (95%CI)*
(I) Pregnant woman allergic to penicillin						
In agreement	24	41 (28.3–54.2)	27	27 (18.8–37.0)	51	32 (25.0–40.0)
Not in agreement/not informed	35	59 (45.8–71.7)	73	73 (63.0–81.2)	108	68 (60.0–75.0)
(II) Low titer (1:2) at childbirth, no diagnosis, or prior treatment						
In agreement	44	75 (61.3–84.6)	56	56 (45.7–65.8)	100	63 (54.8–70.3)
Not in agreement/not informed	15	25 (15.4–38.7)	44	44 (34.2–54.3)	59	37 (29.7–45.2)
(III) Treatment dose						
In agreement	51	86 (74.5–93.5)	70	70 (59.9–78.5)	121	76 (68.6–82.3)
Not in agreement/not informed	8	14 (6.4–25.5)	30	30 (21.4–40.1)	38	24 (17.6–31.4)
(IV)Time elapsed between the conclusion of the treatment and delivery						
In agreement	11	19 (10.1–31.3)	22	22 (14.6–31.6)	33	21(14.9–28.0)
Not in agreement/not informed	48	81 (68.7–89.9)	78	78 (68.4–85.4)	126	79 (71.9–85.1)
(V) Serological scar						
In agreement	50	85 (72.5–92.4)	60	60 (49.7–69.5)	110	69 (61.3–76.1)
Not in agreement/not informed	9	15 (7.6–27.5)	40	40 (30.5–50.3)	49	31 (23.9–38.7)
(VI) Persistent titer after treatment						
In agreement	24	41 (28.3–54.2)	42	42 (32.3–52.3)	66	41 (33.8–49.6)
Not in agreement/not informed	35	59 (45.8–71.7)	58	58 (47.7–67.7)	93	59 (50.4–66.2)
(VII) Partner not treated						
In agreement	52	88 (76.4–94.7)	67	67 (56.8–75.9)	119	75 (67.2–81.2)
Not in agreement/not informed	7	12 (5.3–23.5)	33	33 (24.1–43.2)	40	25 (18.8–32.8)
(VIII) Interval between treatment doses						
In agreement	38	64 (50.8–76.1)	39	39 (29.5–49.3)	77	48 (40.4–56.4)
Not in agreement/not informed	21	36 (23.9–49.2)	61	61 (50.7–70.4)	82	52 (43.6–59.5)

Abbreviation: 95%CI, 95% confidence interval.
Note: *Proportions of the total obstetricians (59) and nurses (100); due to the small number of "missing" cases, the values were combined as "not in agreement".

case-resolution, user-friendly execution, and gains in biosafety and patient comfort, since it does not require venous puncture. The nurses showed the greatest level of difficulty in interpreting the test result and in explaining the result to the women. Although rapid tests are probably more useful and relevant in primary care settings, health care professionals should be able to interpret test results and evaluate the adequacy of syphilis treatment during pregnancy.

All eight criteria for assessing the physicians' and nurses' knowledge about the treatment failed to agree with the MoH protocols. The lack of knowledge about the treatment of syphilis on the part of physicians and nurses has been reported in previous Brazilian studies focused on health professionals working in primary care. In a study conducted in the city of Recife in 2012,[14] more than 2/3 (69%) of the physicians and nurses knew how to treat a pregnant woman who was allergic to penicillin. In a study conducted in the city of Fortaleza in 2009, approximately half of the nurses did not know how to treat a pregnant woman with a VDRL test titer of 1:1.[15] In another study conducted in the same city and year, 51% of the nurses prescribed the correct dose for secondary syphilis, and 41% knew the correct 7-day interval between doses.[16]

The treatment practices for syphilis reported by the obstetricians showed variable agreement according to the stage of the disease. The most frequent errors observed were overtreatment of the pregnant women, which by itself is not a problem for the prevention of CS. However, it does mean a waste of medicines, which is aggravated by the lack of raw material to formulate the medicine, which happened during the study, besides the fact that it is a painful and unnecessary intervention for the pregnant women.

In April 2015, the recommendation to treat secondary and recent latent syphilis was modified in Brazil, reducing the total dose of penicillin G benzathine from 4,800,000 IU to 2,400,000 IU,[17,18] which is similar to the protocol adopted in

Table 4 Agreement of the health professionals' practices concerning the management of syphilis in pregnancy. Teresina, state of Piauí, Brazil

Criteria	Obstetricians		Nurses		Total	
	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)
Diagnostic practices						
(A) Recording the test results**		Obstetricians ($n = 55$)		Nurses ($n = 68$)		Total (123)
In agreement (test results recorded)	40	73 (58.8–83.4)	51	75 (62.8–84.4)	91	74 (65.2–81.3)
Not in agreement /not informed	15	27 (16.5–41.2)	17	25 (15.6–37.2)	32	26 (18.7–34.8)
(B) "Syphilis serology" ordered		Obstetricians ($n = 59$)		Nurses ($n = 100$)		Total (159)
(1) For all women admitted for childbirth, but not for curettage	1	2 (0.1–10.3)	4	4 (1.3–10.5)	5	3 (1.2–7.6)
(2) Only other criteria*	0	0(0.0–7.6)	4	4 (1.3–10.5)	4	2 (0.8–6.7)
(3) Does not order	1	2 (0.1–10.3)	47	47 (37.0–57.2)	48	30 (23.3–38.0)
(4) Not allowed to order tests	0	0 (0.0–7.6)	36	36 (26.8–46.3)	36	23 (16.5–30.1)
In agreement (for all women admitted for childbirth or curettage)	57	96 (87.2–99.4)	7	7 (3.1–14.4)	64	40 (32.6–48.3)
Not in agreement /not informed	2	4 (0.6–12.7)	93	93 (85.6–96.9)	95	60 (51.7–67.3)
(C)Management of partner						
In agreement (treatment of partner at the maternity hospital)	25	42 (29.8–55.9)	34	34 (25.0–44.2)	59	37 (29.7–45.1)
Other approaches	31	53 (39.2–65.5)	47	47 (37.1–57.2)	78	49 (41.1–57.1)
No management of partner or not informed	3	5 (1.3–15.1)	19	19 (12.1–28.3)	22	14 (9.1–20.4)
Treatment practices						
(A)Recording the treatments performed**		Obstetricians ($n = 55$)		Nurses ($n = 68$)		Total (123)
In agreement	46	84 (70.7–91.8)	55	81 (69.2–89.0)	101	82 (73.9–88.2)
Not in agreement	9	16 (8.2–29.3)	13	19 (10.9–30.8)	22	18 (11.8–26.0)
(B)Treatment of primary syphilis		Obstetricians ($n = 59$)		Nurses ($n = 100$)		Total (159)
Not allowed to prescribe	0	0 (0.0–7.6)	58	58 (47.7–67.7)	58	36 (29.1–44.5)
In agreement (Penicillin G Benzathine 2,400,000 IU)	39	66 (52.5–77.6)	29	29 (20.6–39.1)	68	43 (35.0–50.8)
Does not know how to treat/not informed	20	34 (22.4- 47.5)	13	13 (7.4–21.6)	33	21 (14.9–28.0)
(C)Treatment of secondary syphilis						
Not allowed to prescribe	0	0 (0.0–7.6)	58	58 (47.7–67.7)	58	36 (29.1–34.5)
In agreement (Penicillin G Benzathine 4,800,000 IU)	31	52 (39.2–65.5)	26	26 (18.0–35.9)	57	36 (28.5–43.9)
Does not know how to treat/not informed	28	48 (34.5–60.8)	16	16 (9.7–25.0)	44	28 (21.0–35.4)
(D)Treatment of syphilis of unknown duration						
Not allowed to prescribe	0	0 (0.0–7.6)	58	58 (47.7–67.7)	58	37 (29.1–34.5)
In agreement (Penicillin G Benzathine 7,200,000 IU)	56	95 (84.9–98.7)	32	32 (23.2–42.2)	88	55 (47.3–63.2)
Does not know how to treat/not informed	3	5 (1.3–15.0)	10	10 (5.2–18.0)	13	8 (4.6–13.9)
Post-test counseling						
(1) Always provides orientation on the risks of the disease for the pregnant woman with diagnosis of syphilis and her child	55	93 (82.7–97.8)	81	81 (71.7–87.9)	136	86 (78.9–90.4)
(2) Always provides orientation on the importance of the partner's treatment to avoid reinfection	57	97 (87.2–99.4)	90	91 (82.0–94.8)	147	92 (86.9–95.9)
(3) Always provides orientation on the importance of condom use to avoid reinfection	48	81 (68.7–89.9)	81	81 (71.7–87.9)	129	81 (74.0–86.7)
In agreement (with items 1, 2, and 3)	46	78 (64.9–87.3)	70	70 (59.9 - 78.5)	116	73 (65.2–80.0)
Not in agreement /not informed	13	22 (12.7 - 35.1)	30	30 (21.4 - 40.1)	43	27 (20.4–34.8)

Abbreviation: 95%CI, 95% confidence interval.
Notes: *Only for pregnant women without tests recorded on the prenatal card or who did not receive prenatal care; for all pregnant women with history of syphilis during pregnancy or for all pregnant women with lifetime history of syphilis; ** question only answered by health professionals in charge of women's hospitalization before delivery.

Table 5 Barriers reported by health professionals to the management of syphilis in the maternity hospital. Teresina, state of Piauí, Brazil, 2015 ($n = 243$)

Barriers	Obstetricians ($n = 59$)		Nurses ($n = 100$)		Total ($n = 159$)	
	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)
(1) No record of the diagnosis on the prenatal card	33	56 (42.5–68.6)	47	47 (37.0–57.2)	80	50 (42.3–58.3)
(2) No record of the treatments on the prenatal card	44	75 (61.3–84.6)	60	60 (49.7–69.5)	104	65 (57.4–72.6)
(3) Women's lack of information on treatments received during prenatal care	42	71 (57.7–81.9)	59	59 (48.7–68.6)	101	64 (55.5–70.9)
(4) Other health professionals in the maternity hospital do not record relevant information on syphilis on the patient's chart	17	29 (18.1–42.2)	20	20 (12.9–29.4)	37	23 (17.1–30.7)
(5) Other health professionals in the maternity hospital do not order necessary tests for diagnosis and treatment	5	9 (3.2–19.4)	5	5 (1.8–11.8)	10	6 (3.2–11.6)
(8) Delay in the turnaround time of the results of the tests ordered in the maternity hospital	16	27 (16.7–40.5)	16	16 (9.7–25.0)	32	20 (14.4–27.4)
(9) Difficulty in interpreting the test results	2	3 (0.6–12.7)	11	11 (5.9–19.2)	13	8 (4.6–13.9)
(10) Women's resistance to the waiting time in the postpartum period to receive the test result	12	20 (11.4–33.2)	18	18 (11.3–17.2)	30	19 (13.3–26.0)
(11) Lack of medicines for treatment	2	3 (0.6–12.7)	1	1 (0.0–6.2)	3	2 (0.5–5.8)
(12)Difficulty in conversing with the women's partners	37	63 (49.1–74.6)	42	42 (32.3–52.3)	79	50 (41.7–57.7)
(13)Difficulty in conversing with the women about the possible forms of syphilis infection	12	20 (11.4–33.2)	29	29 (20.6–39.1)	41	26 (19.3–33.4)
(14)Difficulty in informing the women about the consequences of syphilis for her and the infant	7	12 (5.3–23.5)	24	24 (16.3–33.8)	31	20 (13.8–26.7)
(15)Difficulty in explaining the test result to the women	10	17 (8.8–29.4)	41	41 (31.4–51.3)	51	32 (25.0–40.0)
(16)Difficulty in orienting the women on treatment	5	9 (3.2–19.4)	26	26 (18.0–35.9)	31	19 (13.8–26.7)
(17)Difficulty in orienting the women on condom use	7	12 (5.3–23.5)	19	19 (12.1–28.3)	26	16 (11.1–23.2)
No difficulties	2	3 (0.5–12.7)	7	7 (3.1–14.4)	9	6 (2.8–10.8)
Not informed	2	3 (0.5–12.7)	4	4 (1.3–10.5)	6	4 (1.5–8.4)

Abbreviation: 95%CI, 95% confidence interval.
Note: The health professionals could choose more than one answer.

other countries. Strategies aimed at reinforcing the items that remained unaltered, highlighting the changes, and avoiding overtreatment are needed to disseminate and implement this new protocol.

The current study showed limited ordering of tests and treatment prescription by the nurses, revealing their low autonomy in this context. Under Brazilian legislation (Federal Law 7.498/1986 and Resolution 195/1997 of the Federal Council of Nursing – COFEN, in the Portuguese acronym),[19,20] registered nurses who are actual members of the health care team can order routine and complementary tests and prescribe medicines included in public health care protocols and in routines approved by the health care institution. Our study did not assess the causes of this low performance, but some possible explanations include fear of being held accountable for the diagnosis and prescription; the nurses' incomplete knowledge of their professional responsibilities; the feeling that this is the obstetricians' exclusive responsibility; resistance by health care service administrators and attending physicians; less time since graduation and on the job in maternity hospitals among nurses (as shown by the study's empirical data); and the high proportion of nurses without stable employment contracts in the maternity hospital, who are thus subject to greater turnover and are probably less familiar with the protocols.

Evidence from previous studies showed that the outsourcing of job positions in Brazil has been accompanied by lower wages, greater instability and job turnover, accumulation of tasks, and longer work weeks,[21] which can hinder the establishment of routines and effective professional training, generating inadequate practices and increasing the risk of work accidents.[22] In a 2015 publication by the Brazilian MoH, in the city of Vitória da Conquista, in the Northeastern state of Bahia, high workforce turnover was one of the problems mentioned as a barrier to the elimination of congenital syphilis.[23]

Regardless of the reason, the low performance of the nurses is a limiting factor in the efforts to curb syphilis, especially in such a strikingly heterogeneous country as Brazil, where regions and social strata display profoundly diverse realities in the availability of human resources and infrastructure.[24]

In the current study, fewer than half of the health professionals reported calling the partners of pregnant women with syphilis to appear at the maternity hospital to be tested and treated, making evident important missed opportunities for timely diagnosis and treatment. In addition, nearly 50%

reported difficulty in conversing with the women's partners as a barrier to the effective management of syphilis. Other studies in Brazil have revealed the health professionals' difficulty in addressing the women's partners. In four maternity hospitals in the countryside of the Northeastern state of Pernambuco in 2005, a quite modest proportion of partners of pregnant women with syphilis were successfully brought in for concurrent treatment.[25] In public maternity hospitals in the Federal District (Midwestern Brazil), in 2009 and 2010, the principal underlying reason for the inadequate management of the pregnant women was the lack of approach or the inadequate management of the partner.[26] In a large public mother and child hospital in the Southeastern state of São Paulo, no information about the treatment of the sexual partner was available for 73.9% of the cases of maternal syphilis identified from 2007 to 2014.[27] In the city of Rio de Janeiro, Southeastern Brazil, a study in 2007 with prenatal care staff working in public health care units also showed the inadequate management of the partners by physicians and nurses, such as sending the test orders or treatment prescriptions via the pregnant woman rather than addressing the partner directly.[12]

Difficulties in treating the sexual partner are associated with the characteristics of the health care services and policies, which historically do not focus on men's health, and with an underestimation of the relevance of social and cultural issues.[28] The Brazilian MoH drafted guidelines aimed at the communication with the sexual partners of pregnant women with syphilis, preferably via a letter requesting the partner to appear at the health service.[17] However, this strategy seems more appropriate for primary care services. In maternities, the greatest challenge in addressing the partner relates to the fact that he is not hospitalized. On the other hand, the male partner is normally present at the maternity hospital while the woman is hospitalized, which represents a good opportunity to address him. Thus, the professional team at the maternity hospital should devise strategies to approach the partner when he visits the woman in the postpartum period. Although such access is sometimes difficult, it is essential to interrupt the transmission chain, provide counseling, and prevent the infection in future pregnancies.

In the current study, the obstetricians failed to counsel the patients on the importance of condom use. Among the nurses, no counseling practice achieved satisfactory rates. The difficulty of the physicians and nurses in counseling on issues related to sexually transmitted diseases (STDs), like transmission routes, health consequences, treatment, and prevention, was also reported by prenatal care staff working in health units in the city of Rio de Janeiro.[12]

Other barriers frequently mentioned by staff for the adequate management of syphilis in the maternities included lack of records of the diagnostic and treatment data on the women's prenatal card, and the women's lack of information about the treatments performed during prenatal care. These difficulties were also reported in a study in the Federal District of Brazil, with a low proportion of postpartum women with syphilis that had prior knowledge of their diagnosis, in addition to incomplete information on the partner's treatment in the prenatal card and on the patient's chart in the maternity hospitals.[26] In a Brazilian national study conducted between 2011 and 2012 that analyzed almost 17,000 prenatal cards, 89.1% had the result of the first "syphilis serology" recorded, and only 41.1% had the result of the second serology, with regional heterogeneities.[29]

Conclusions

The present study, which was conducted among obstetricians and nurses working in the public maternity hospitals in the city of Teresina, in the state of Piauí (in the Northeast of Brazil, a region with particularly high CS rates), showed that their knowledge and practices in the management of syphilis in women admitted for childbirth had low levels of agreement with the Brazilian MoH protocols, resulting in missed opportunities for diagnosis, treatment, and counseling of pregnant and postpartum women with syphilis and their partners.

The lack of knowledge about the specific characteristics of the serological tests for the diagnosis of syphilis and about the adequate treatment of the pregnant women and her partners are barriers to the adequate management of the cases of syphilis. Training is considered a strategy with weak results for the implementation of guidelines, but it can increase the familiarity with the guideline contents. In this study, the health professionals had low access to training and manuals about the management of syphilis in pregnancy and the prevention of congenital syphilis. Specific training programs combined with other local strategies for the implementation of guidelines, such as the use of implementation tools, audits and feedback, should emphasize the uptake and adoption of the recommended protocols.

Training the nurses and other strategies to encourage and support their work in the maternity hospital are urgent. These should emphasize the responsibilities and attributions of each group of professionals in the management of syphilis during pregnancy and increase the nurses' involvement in actions related to syphilis control aimed at reducing missed opportunities for diagnosis and providing adequate treatment to the pregnant women and their partners.

There is also a clear need to improve the link between primary care services and maternities, by properly recording on the pregnant women's prenatal card the test results and treatments performed during prenatal care; the integration of the hospital team to approach the male partner at the time of his visit to the postpartum woman also needs to improve. Offering diagnosis, treatment, and adequate counseling for the women and their partners are essential actions to interrupt the syphilis transmission chain. Women's counseling would also reduce the lack of information on tests and treatments during antenatal care, which was reported by the health professionals as a barrier to syphilis control.

Conflict of Interests

The authors have no potential conflict of interests to declare.

References

1 Newman L, Kamb M, Hawkes S, et al. Global estimates of syphilis in pregnancy and associated adverse outcomes: analysis of multinational antenatal surveillance data. PLoS Med 2013;10(02): e1001396

2 Kuznik A, Habib AG, Manabe YC, Lamorde M. Estimating the public health burden associated with adverse pregnancy outcomes resulting from syphilis infection across 43 countries in Sub-Saharan Africa. Sex Transm Dis 2015;42(07):369–375

3 Boletim Epidemiológico - Sífilis [Internet]. Brasília (DF): Ministério da Saúde; 2015 [cited in Sep 10, 2016].4(1). Available at: http://www.aids.gov.br/sites/default/files/anexos/publicacao/2015/57978/_p_boletim_sifilis_2015_fechado_pdf_p__18327.pdf

4 Pan American Health Organization. Regional initiative for the elimination of mother-to-child transmission of HIV and congenital syphilis in Latin America and the Caribbean: regional monitoring strategy. 2nd ed. Washington (DC): PAHO; 2012

5 Word Health Organization. Global guidance on criteria and processes for validation: elimination of mother-to-child transmission (EMTCT) of HIV and syphilis. Geneva: WHO; 2014

6 Boletim Epidemiológico - Sífilis [Internet]. Brasília (DF): Ministério da Saúde; 2016 [cited in Sep 10, 2016].5(35). Available at: http://www.aids.gov.br/sites/default/files/anexos/publicacao/2016/59209/2016_030_sifilis_publicao2_pdf_51905.pdf

7 Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Programa Nacional de DST e AIDS [Internet]. Protocolo para a prevenção de transmissão vertical de HIV e sífilis: manual de bolso. Brasília (DF): Ministério da Saúde; 2007 [cited in Dec 12, 2016]. Available at: http://bvsms.saude.gov.br/bvs/publicacoes/protocolo_prevencao_transmissao_verticalhivsifilis_manualbolso.pdf

8 Workowski KA, Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64(RR-03):1–137

9 Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de DST, AIDS e Hepatites Virais [Internet]. Indicadores e dados básicos da sífilis nos municípios brasileiros. 2016 [cited in May 8, 2017]. Available at: http://indicadoressifilis.aids.gov.br/

10 Brousselle A, Champagne F, Contandriopoulos AP, Hartz Z. Avaliação: conceitos e métodos. Rio de Janeiro: Editora Fiocruz; 2011

11 Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica [Internet]. Atenção ao pré-natal de baixo risco. Brasília (DF): Ministério da Saúde; 2012 [cited in Sep 10, 2016]. Available at: http://bvsms.saude.gov.br/bvs/publicacoes/cadernos_atencao_basica_32_prenatal.pdf

12 Domingues RMSM, Lauria LdeM, Saraceni V, Leal MdoC. [Treatment of syphilis during pregnancy: knowledge, practices and attitudes of health care professionals involved in antenatal care of the Unified Health System (SUS) in Rio de Janeiro City]. Cien Saude Colet 2013;18(05):1341–1351

13 Brasil. Ministério da Saúde [Internet]. Portaria n. 1.459, de 24 de junho de 2011. Institui, no âmbito do Sistema Único de Saúde - SUS - a Rede Cegonha. 2011 [cited in Dec 10, 2016]. Available at: http://www.saude.mt.gov.br/atencao-a-saude/arquivo/3036/rede-cegonha

14 Gomes SF. Conhecimentos, atitudes e práticas dos médicos e enfermeiros das unidades de saúde da família sobre sífilis em gestantes na cidade do Recife-Pe [dissertation]. Recife: Universidade Federal de Pernambuco; 2013

15 Silva DM, Araújo MA, Silva RM, et al. Knowledge of healthcare professionals regarding the vertical transmission of syphilis in Fortaleza -CE, Brazil. Texto Contexto Enferm 2014;23(02): 278–285

16 Andrade RFV, Lima NBG, Araújo MAL, Silva DMA, Melo SP. Conhecimento dos enfermeiros acerca do manejo da gestante com exame de VDRL reagente. DST J Bras Doenças Sex Transm 2011;23 (04):188–193

17 Comissão Nacional de Incorporação de Tecnologias no SUS [Internet]. Protocolo clínico e diretrizes terapêuticas: infecções sexualmente transmissíveis. Brasília (DF): Ministério da Saúde; 2015 [cited in Sep 10, 2016]. Available at: http://conitec.gov.br/images/Consultas/Relatorios/2015/Relatorio_PCDT_IST_CP.pdf

18 Comissão Nacional de Incorporação de Tecnologias no SUS [Internet]. Protocolo clínico e diretrizes terapêuticas para a prevenção da transmissão vertical de HIV, sífilis e hepatites virais. Brasília (DF): Ministério da Saúde; 2015 [cited in Sep 10, 2016]. Available at: http://conitec.gov.br/images/Consultas/Relatorios/2015/Relatorio_PCDT_TransmissaoVertical_CP.pdf

19 Brasil [Internet]. Lei n. 7.498, de 25 de junho de 1986. Dispõe sobre a regulamentação do exercício da enfermagem, e dá outras providências. 1986 [cited in Sep 10, 2016]. Available at: http://www.planalto.gov.br/ccivil_03/leis/L7498.htm

20 Conselho Federal de Enfermagem [Internet]. Resolução COFEN 195/1997. Dispõe sobre a solicitação de exames de rotina e complementares por enfermeiro. 1997 [cited in Sep 10, 2016]. Available at: http://www.cofen.gov.br/resoluo-cofen-1951997_4252.html

21 Brasil. Ministério da Saúde. Organização Pan-Americana da Saúde [Internet]. Doenças relacionadas ao trabalho: manual de procedimentos para os serviços de saúde. Brasília (DF): Ministério da Saúde; 2001 [cited in Sep 10, 2016]. Available at: http://bvsms.saude.gov.br/bvs/publicacoes/doencas_relacionadas_trabalho1.pdf

22 Aiken LH, Sloane DM, Klocinski JL. Hospital nurses' occupational exposure to blood: prospective, retrospective, and institutional reports. Am J Public Health 1997;87(01):103–107

23 Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de DST, Aids e Hepatites Virais [Internet]. Caderno de boas práticas: o uso da penicilina na Atenção Básica para a prevenção da sífilis congênita no Brasil. Brasília (DF): Ministério da Saúde; 2015 [cited in Sep 10, 2016]. Available at: http://www.aids.gov.br/sites/default/files/anexos/publicacao/2015/58373/_p_boas_praticas_2015_final_web_pdf_p__32394.pdf

24 Silveira RP, Pinheiro R. Understanding the need for doctors in innerstate Amazon – Brazil. Rev Bras Educ Med 2014;38(04): 451–459

25 Macêdo VC, Bezerra AFB, Frias PG, Andrade CLT. [Evaluation of measures to prevent vertical transmission of HIV and syphilis in public maternity hospitals in four municipalities in Northeast Brazil]. Cad Saude Publica 2009;25(08):1679–1692

26 Magalhães DMS, Kawaguchi IAL, Dias A, Calderon IdeM. [Maternal and congenital syphilis: a persistent challenge]. Cad Saude Publica 2013;29(06):1109–1120

27 Dallé J, Baumgarten VZ, Ramos MC, et al. Maternal syphilis and accomplishing sexual partner treatment: still a huge gap. Int J STD AIDS 2017;28(09):876–880

28 Oliffe JL, Chabot C, Knight R, Davis W, Bungay V, Shoveller JA. Women on men's sexual health and sexually transmitted infection testing: a gender relations analysis. Sociol Health Illn 2013; 35(01):1–16

29 Domingues RM, Szwarcwald CL, Souza Junior PR, Leal MdoC. Prevalence of syphilis in pregnancy and prenatal syphilis testing in Brazil: birth in Brazil study. Rev Saude Publica 2014;48(05): 766–774

Uterine Artery Doppler Velocimetry of Uterine Leiomyomas in Nigerian Women

Dopplervelocimetria da artéria uterina de leiomiomas uterinos em mulheres nigerianas

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Abstract

Objective To describe the blood flow velocities and impedance indices changes in the uterine arteries of leiomyomatous uteri using Doppler sonography.

Methods This was a prospective, case-control study conducted on 140 premenopausal women with sonographic diagnosis of uterine leiomyoma and 140 premenopausal controls without leiomyomas. Pelvic sonography was performed to diagnose and characterize the leiomyomas. The hemodynamics of the ascending branches of both main uterine arteries was assessed by Doppler interrogation. Statistical analysis was performed mainly using non-parametric tests.

Results The median uterine volume of the subjects was 556 cm^3, while that of the controls was 90.5 cm^3 ($p < 0.001$). The mean peak systolic velocity (PSV), end-diastolic velocity (EDV), time-averaged maximum velocity (TAMX), time-averaged mean velocity (Tmean), acceleration time (AT), acceleration index (AI), diastolic/systolic ratio (DSR), diastolic average ratio (DAR), and inverse pulsatility index (PI) were significantly higher in the subjects (94.2 cm/s, 29.7 cm/s, 49.1 cm/s, 25.5 cm/s, 118 ms, 0.8, 0.3, 0.6, and 0.8 respectively) compared with the controls (54.2 cm/s, 7.7 cm/s, 20.0 cm/s, 10.0 cm/s, 92.0 ms, 0.6, 0.1, 0.4, and 0.4 respectively); $p < 0.001$ for all values. Conversely, the mean PI, resistivity index (RI), systolic/diastolic ratio (SDR) and impedance index (ImI) of the subjects (1.52, 0.70, 3.81, and 3.81 respectively) were significantly lower than those of the controls (2.38, 0.86, 7.23, and 7.24 respectively); $p < 0.001$ for all values.

Conclusion There is a significantly increased perfusion of leiomyomatous uteri that is most likely due to uterine enlargement.

Keywords
- leiomyoma
- uterine artery embolization
- Doppler ultrasonography

Resumo

Objetivo Descrever as velocidades do fluxo sanguíneo e as alterações dos índices de impedância nas artérias uterinas leiomiomatoso utilizando a ultrassonografia Doppler.

Métodos Estudo prospectivo, caso-controle, realizado em 140 mulheres pré-menopáusicas com diagnóstico ultrassonográfico de leiomioma uterino e em 140 controles na pré-menopausa sem leiomiomas. A ultrassonografia pélvica foi realizada para

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diagnosticar e caracterizar os leiomiomas. A hemodinâmica dos ramos ascendentes de ambas as artérias uterinas principais foi avaliada por meio de interrogatório Doppler. A análise estatística foi feita principalmente por meio de testes não paramétricos.

Resultados A média do volume uterino dos das pacientes foi de 556 cm^3, enquanto a dos controles foi de 90,5 cm^3 ($p < 0,001$). A média de velocidade de pico sistólico (VPS), a velocidade diastólica final (VDF), a velocidade máxima do tempo médio (VMTM), a velocidade média do tempo médio (VMdTM), o tempo de aceleração (TA), o índice de aceleração (IA), a relação diástole/sístole (RDS), a proporção diastólica média (PDM) e o índice de pulsatilidade (IP) inversa foram significativamente maiores em pacientes (94,2 cm/s, 29,7 cm/s, 49,1 cm/s, 25,5 cm/s, 118 ms, 0,8, 0,3, 0,6 e 0,8, respectivamente) do que nos controles (54,2 cm/s, 7,7 cm/s, 20,0 cm/s, 10,0 cm/s, 92,0 ms, 0,6, 0,1, 0,4 e 0,4, respectivamente); $p < 0,001$ para todos os valores. Por outro lado, o IP médio, o índice de resistividade (IR), a relação sístole/diástole (RSD) e o índice de impedância (II) nas pacientes (1,52, 0,70, 3,81 e 3,81, respectivamente) foram significativamente mais baixos do que os dos controles (2,38, 0,86, 7,23 e 7,24, respectivamente); $p < 0,001$ para todos os valores.

Conclusão Existe um aumento significativo da perfusão dos úteros leiomiomatosos, que provavelmente se deve ao alargamento uterino.

Palavras-chave
- leiomioma
- embolização da artéria uterina
- ultrassonografia com Doppler

Introduction

Leiomyomas/fibroids are benign uterine tumors **that are more common in black people**. Gray-scale ultrasonography is a reliable method of diagnosing these tumors, and it can be supplemented with Doppler mode to provide additional hemodynamic information.

Though the pulsatility index (PI) is currently the preferred Doppler index in Obstetrics and Gynecology because it is sensitive to alterations in waveform shape and it analyzes the entire cardiac cycle,[1] several other useful Doppler indices have been documented in the literature. Previous studies reported increased peak systolic velocity (PSV) and time-averaged maximum velocity (TAMX), as well as diminished pulsatility index (PI), resistivity index (RI), and systolic-diastolic ratio (SDR) in myomatous uteri compared with controls.[2–6]

The purposes of this study are: to compare the changes within the main uterine artery of myomatous uteri and normal uteri using several Doppler indices (in addition to the traditional ones); to explore the relationship between these changes in uterine volume and the clinical symptoms; and to compare the main uterine artery Doppler changes in women with recurrent leiomyoma (after a previous myomectomy) and those with primary tumors (without previous surgical or medical intervention).

Methods

This prospective, non-randomized, case-control study was performed over a one-year period in the Department of Radiology of our institution as approved by the Ethics in Research Committee of the hospital. The study participants were consecutively recruited, and consisted of 140 premenopausal women with sonographic features of uterine leiomyomas, as previously described by other authors,[4,7,8] and 140 premenopausal controls with normal leiomyoma-free uteri **and normal endometrial stripe thickness**. Recurrent leiomyoma was defined as the presence of a dominant leiomyoma larger than 4 cm in size following previous myomectomy.[9] The exclusion criteria were: pregnancy, post-menopausal status (cessation of menses for more than 12 months), recent childbirth (less than 1 year prior to presentation), **adenomyosis/endometriosis**, and coexisting pelvic pathologies, like ovarian tumors and pelvic inflammatory disease. Informed consent was obtained from all participants.

The participants' demographic and gynecologic histories were obtained, including age, parity, and history of previous myomectomy. Their body mass index was also determined.

All the participants underwent sonography via the transabdominal route using MINDRAY real-time ultrasound machine model DC-7 (Shenzhen Mindray Bio-medical Electronics, Nanshan, Shenzhen, China) with a convex transducer (with a frequency of 3.8-5.0 MHz) and Doppler functionality.

Transabdominal sonography was performed by applying the transducer to the abdominopelvic region to scan the uterus in at least two planes (transverse and longitudinal planes). The following sonographic parameters were recorded: the uterine length, the anteroposterior diameter, and the transverse diameter, which were used to estimate the uterine volume using the ellipsoid formula. The length of the uterus was measured in the longitudinal plane from the fundus to the external cervical os; its anteroposterior diameter was measured perpendicular to the plane of the length, while the transverse diameter was measured from cornu to cornu on a transverse image. The volume of the largest leiomyoma nodule was similarly determined using the prolate ellipse formula. The uterine volume and dominant leiomyoma volume were divided into large and

small if they were larger or smaller than 200 cm^3 respectively.[5] The other sonographic parameters recorded included: leiomyoma type (intramural, subserous, submucous, panmural, pedunculated, or in more than one site) and presence of degenerative changes (cystic, calcific, or mixed).

The Doppler interrogation was performed as previously described by other authors.[10,11] The transducer was placed longitudinally in the midline above the symphysis pubis. A longitudinal section of the uterus and the cervical canal was obtained to identify the internal cervical os. The transducer was then moved from side to side to the lateral border of the uterus until the para-cervical vascular plexus was seen. The color Doppler function was activated, and the uterine artery was identified at the level of the junction between the uterine body and the cervix, as it starts to make its ascent to the uterine body. Measurements were taken at this point, before the uterine arteries branch into the arcuate arteries. The pulsed Doppler gate (sample volume = 1 mm) was placed in the center of the vessel, and a Doppler insonation angle of less than 60 degrees was used to obtain a measurement line parallel to the arterial wall. The Doppler signal was updated until there was a clear and consistent waveform. Doppler velocimetry was repeated three times each in both the right and left uterine arteries, with an interval of at least 2 minutes between the measurements. The average value of the two arteries was used for analysis. The measurements were obtained after the visualization of at least three to five consecutive arterial waveforms of similar amplitude. Blood velocity waveforms with the lowest RI or highest velocities were recorded.[12–14] A spectral analysis was performed electronically (auto-trace) from a smooth curve fitted to the average waveform over three to five cardiac cycles to obtain the following parameters: peak systolic velocity (PSV), end-diastolic velocity (EDV), systolic/diastolic ratio (SDR or S/D ratio = PSV/EDV),[6] resistivity index (RI= [PSV – EDV]/PSV),[15] pulsatility index (PI = [PSV – EDV] ÷ [{PSV + EDV}]/2}),[16] time-averaged maximum velocity (TAMX), time-averaged mean velocity (Tmean), and acceleration time (AT). The diastolic/systolic ratio or end-diastolic ratio (DSR or D/S ratio = EDV/PSV),[17] impedance index (ImI = [S x D]/D^2),[18] inverse PI [= 1/PI],[19] diastolic average ratio (DAR = EDV/TAMX),[20] and the acceleration index (AI = PSV/AT)[21] were also calculated from the electronically generated indices.

The color and pulsed Doppler parameters, including the high pass filter, the sample volume and the velocity scale were optimized for the detection of slow flow.[21,22] Low filtration (color wall filter of 50–100 Hz) was used to detect the diastolic flow in the arteries.[23] The color box was kept small, covering only the area of interest, and the Doppler gain was set just below noise level. All of the participants were scanned by the first author.

The study data was analyzed with the Statistical Package for the Social Sciences (SPSS), version 20, for Windows (IBM Corp., Armonk, NY, US). The Mann-Whitney U test was used to compare the means because the uterine volumes and the accompanying Doppler indices were skewed and not normally distributed. Due to similar reasons, the Spearman correlation analysis was used to determine the correlation between the variables. The chi-squared test was used to compare two categorical variables, while the Kruskal-Wallis test was used when more than two variables were compared. The level of statistical significance was set at $p \leq 0.05$.

Results

A total of 280 premenopausal women were recruited consecutively for this prospective, case -control study comprising 140 subjects with uterine leiomyoma and 140 leiomyoma-free controls. **The subjects' general characteristics are displayed in ►Table 1.**

Nineteen subjects (13.6%) were asymptomatic, while 121 (86.4%) had various leiomyoma-related symptoms. Menorrhagia with abdominal swelling and/or pain was the most common presenting symptom, which was observed in 24 (17.1%) subjects. However, menorrhagia alone, and in various combinations with other symptoms, like infertility and dysmenorrhea, was a feature in 70 (50%) subjects. Fourteen subjects (10%) had recurrent leiomyoma after previous myomectomy, with a median time interval of 5 years (range = 2–15 years) after surgery. Eight (57.1%) of these presented ≤ 5 years post-myomectomy, while 6 (42.9%) of them were > 5 years post-myomectomy.

The subjects had a median uterine volume of 556 cm^3 (range = 37–9,384 cm^3) which was significantly larger ($p < 0.001$) than that of the controls, who had a median uterine volume of 90.5 cm^3 (range = 21–304 cm^3). When a

Table 1 Subjects' characteristics

Variable	Patients	Controls	Statistic	df	*p*
	n = 140	n = 140			
Age in years					
*Mean ± SD**	37.9 ± 7.4	30.5 ± 8.3	7.9	278	< 0.001
*n (%)***					
< 20	0 (0.0)	13 (9.3)	46.0	4	< 0.001
20–29	18 (12.9)	51 (36.4)			
30–39	68 (48.6)	56 (40.0)			
40–49	45 (32.1)	18 (12.9)			
≥ 50	9 (6.4)	2 (1.4)			
Parity, *n (%)*					
Nulliparous	79 (56.4)	70 (50.0)	2.3	3	0.5
Primiparous	21 (15.0)	19 (13.6)			
Multiparous (2–4)	32 (22.9)	43 (30.7)			
Grand multip. (> 4)	8 (5.7)	8 (5.7)			
Weight (Kg)	66.8 ± 15.2	63.7 ± 16.0	1.7	278	0.1
Height (m)	1.61 ± 0.06	1.6 ± 0.1	-0.1	278	0.9
BMI (kg/m^2)	25.7 ± 5.3	24.6 ± 6.1	1.7	278	1.0

Abbreviations: BMI, body mass index; df, degree of freedom.
Notes: *Independent samples *t*-test used to compare the means.
** Chi-squared test applied for the proportions.

cut-off value of 200 cm^3 was used to divide the participants' uteri into large and small, 126 (90%) and 14 (10%) subjects had large and small uteri respectively, compared with 5 (3.6%) and 135 (96.4%) controls with large and small uteri respectively. This difference was statistically significant ($p < 0.001$).

Degenerative changes were observed in 69 (49.3%) subjects: 35 (25%) had cystic degeneration, 22 (15.7%) had calcific degeneration, and 12 (8.6%) had both cystic and calcific degenerations.

All the evaluated Doppler indices of the main uterine artery showed statistically significant differences between the subjects and controls (►**Table 2**). The main uterine arteries of the subjects had significantly higher PSV, EDV, TAMX, Tmean, AT, AI, DSR, DAR and inverse PI, but significantly lower PI, RI, SDR and ImI than the main uterine arteries of the controls.

All the main uterine artery Doppler indices, except the AI, showed statistically significant differences between the subjects with uterine volume $\leq$ 200 cm^3 and those with uterine volume 200 cm^3. The latter group had higher flow velocities and lower resistance to flow than the former (►**Table 3**).

Symptomatic subjects (all symptoms inclusive) had significantly higher main uterine artery PSV, EDV, TAMX, and AI than the asymptomatic subjects. Furthermore, there were statistically significant differences in all the main uterine artery Doppler indices, except the AT and DAR, between the subjects with menorrhagia and those without. Those with menorrhagia had higher flow velocities and lower resistance to flow (►**Table 4**).

Table 2 Comparison of main uterine artery Doppler indices of the subjects and controls

Doppler indices	Subjects	Controls	$p^{\dagger}$
	n = 140	n = 140	
PSV (cm/s)	94.2 ± 39.3	54.2 ± 16.4	< 0.001
EDV (cm/s)	29.7 ± 19.1	7.7 ± 2.6	< 0.001
TAMX (cm/s)	49.1 ± 26.4	20.0 ± 7.2	< 0.001
Tmean (cm/s)	25.5 ± 16.4	10.0 ± 4.2	< 0.001
PI	1.5 ± 0.7	2.4 ± 0.4	< 0.001
RI	0.7 ± 0.1	0.9 ± 0.03	< 0.001
SDR	3.8 ± 1.6	7.2 ± 1.5	< 0.001
AT (ms)	117.9 ± 28.0	92.0 ± 22.8	< 0.001
AI	0.8 ± 0.3	0.6 ± 0.2	< 0.001
DSR	0.3 ± 0.1	0.1 ± 0.03	< 0.001
ImI	3.8 ± 1.6	7.2 ± 1.5	< 0.001
DAR	0.6 ± 0.2	0.4 ± 0.1	< 0.001
1/PI	0.8 ± 0.3	0.4 ± 0.1	< 0.001

Abbreviations: 1/PI, inverse pulsatility index; AI, acceleration index; AT, acceleration time; DAR, diastolic average ratio; DSR, diastolic/systolic ratio; EDV, end-diastolic velocity; ImI, impedance index; PI, pulsatility index; PSV, peak systolic velocity; RI, resistivity index; SDR, systolic/diastolic ratio; TAMX, time-averaged maximum velocity; Tmean, time-averaged mean velocity.
Note: † Mann-Whitney U test applied.

Table 3 Comparison of main uterine artery Doppler indices by uterine volume in the subjects

Doppler indices	Uterine volume		$p^{\dagger}$
	$\leq$ 200.0 cm^3	> 200.0 cm^3	
	n = 14	n = 126	
PSV (cm/s)	65.1 ± 14.6	97.4 ± 39.9	< 0.001
EDV (cm/s)	12.8 ± 5.7	31.6 ± 19.1	< 0.001
TAMX (cm/s)	23.8 ± 7.9	51.9 ± 26.2	< 0.001
Tmean (cm/s)	12.7 ± 4.7	26.9 ± 6.7	< 0.001
PI	2.4 ± 1.1	1.4 ± 0.6	< 0.001
RI	0.8 ± 0.1	0.7 ± 0.1	< 0.001
SDR	5.7 ± 1.7	3.6 ± 1.5	< 0.001
AT (ms)	98.5 ± 30.0	120.1 ± 27.1	0.01
AI	0.7 ± 0.3	0.8 ± 0.3	0.20
DSR	0.2 ± 0.1	0.3 ± 0.1	< 0.001
ImI	5.7 ± 1.7	3.6 ± 1.5	< 0.001
DAR	0.6 ± 0.3	0.6 ± 0.2	0.01
1/PI	0.5 ± 0.1	0.8 ± 0.3	< 0.001

Abbreviations: 1/PI, inverse pulsatility index; AI, acceleration index; AT, acceleration time; DAR, diastolic average ratio; DSR, diastolic/systolic ratio; EDV, end-diastolic velocity; ImI, impedance index; PI, pulsatility index; PSV, peak systolic velocity; RI, resistivity index; SDR, systolic/diastolic ratio; TAMX, time-averaged maximum velocity; Tmean, time-averaged mean velocity.
† Mann-Whitney U test applied.

Table 4 Effect of menorrhagia on main uterine artery Doppler indices in the subjects

Doppler indices	Menorrhagia		$p^{\dagger}$
	Present (n = 70)	Absent (n = 70)	
PSV (cm/s)	103.6 ± 39.5	84.8 ± 37.0	0.001
EDV (cm/s)	34.1 ± 19.0	25.3 ± 18.3	0.001
TAMX (cm/s)	55.4 ± 26.7	42.8 ± 24.7	0.001
Tmean (cm/s)	28.8 ± 14.5	22.2 ± 17.6	0.001
PI	1.4 ± 0.7	1.6 ± 0.7	0.03
RI	0.7 ± 0.1	0.7 ± 0.1	0.02
SDR	3.5 ± 1.3	4.1 ± 1.8	0.03
AT (ms)	116.2 ± 28.4	119.6 ± 27.7	0.37
AI	0.9 ± 0.3	0.7 ± 0.3	0.001
DSR	0.3 ± 0.1	0.3 ± 0.1	0.03
ImI	3.5 ± 1.3	4.1 ± 1.8	0.03
DAR	0.6 ± 0.3	0.6 ± 0.2	0.14
1/PI	0.8 ± 0.3	0.7 ± 0.3	0.03

Abbreviations: 1/PI, inverse pulsatility index; AI, acceleration index; AT, acceleration time; DAR, diastolic average ratio; DSR, diastolic/systolic ratio; EDV, end-diastolic velocity; ImI, impedance index; PI, pulsatility index; PSV, peak systolic velocity; RI, resistivity index; SDR, systolic/diastolic ratio; TAMX, time-averaged maximum velocity; Tmean, time-averaged mean velocity.
Note: † Mann-Whitney U test applied.

Table 5 Effect of previous myomectomy on main uterine artery Doppler indices in the subjects

Doppler indices	History of previous myomectomy		$p^{\dagger}$
	Present ($n = 14$)	Absent ($n = 126$)	
PSV (cm/s)	122.1 ± 62.7	91.1 ± 34.8	0.05
EDV (cm/s)	42.0 ± 32.4	28.3 ± 16.6	0.1
TAMX (cm/s)	63.9 ± 42.4	47.4 ± 23.7	0.2
Tmean	36.7 ± 30.6	24.3 ± 13.7	0.1
PI	1.4 ± 0.4	1.5 ± 0.8	0.9
RI	0.7 ± 0.1	0.7 ± 0.1	0.5
SDR	3.4 ± 0.9	3.9 ± 1.7	0.5
AT (mms)	126.7 ± 37.1	116.9 ± 26.8	0.5
AI	0.9 ± 0.3	0.8 ± 0.3	0.1
DSR	0.3 ± 0.1	0.3 ± 0.1	0.5
ImI	3.4 ± 0.9	3.9 ± 1.7	0.5
DAR	0.6 ± 0.1	0.6 ± 0.2	0.1
1/PI	0.8 ± 0.2	0.8 ± 0.3	0.9

Abbreviations: 1/PI, inverse pulsatility index; AI, acceleration index; AT, acceleration time; DAR, diastolic average ratio; DSR, diastolic/systolic ratio; EDV, end-diastolic velocity; ImI, impedance index; PI, pulsatility index; PSV, peak systolic velocity; RI, resistivity index; SDR, systolic/diastolic ratio; TAMX, time-averaged maximum velocity; Tmean, time-averaged mean velocity.
Note: † Mann-Whitney U test applied.

Table 6 Correlation* between uterine volume and Doppler indices of the main uterine artery (UtA)

Doppler indices	Subjects ($n = 140$)		Controls ($n = 140$)	
	Correlation coefficient, r	p	Correlation coefficient, r	p
PSV (cm/s)	0.6	< 0.001	0.4	< 0.001
EDV (cm/s)	0.7	< 0.001	0.3	< 0.001
TAMX (cm/s)	0.7	< 0.001	0.4	< 0.001
Tmean (cm/s)	0.6	< 0.001	0.3	< 0.001
PI	−0.6	< 0.001	−0.3	< 0.001
RI	−0.5	< 0.001	−0.1	0.54
SDR	−0.5	< 0.001	−0.02	0.76
AT (ms)	0.3	< 0.001	0.4	< 0.001
AI	0.4	< 0.001	0.03	0.72
DSR	0.5	< 0.001	0.03	0.75
ImI	−0.5	< 0.001	−0.03	0.75
DAR	0.4	< 0.001	−0.2	0.01

Abbreviations: 1/PI, Inverse pulsatility index; AI, acceleration index; AT, acceleration time; DAR, diastolic average ratio; DSR, diastolic/systolic ratio; EDV, end-diastolic velocity; ImI, impedance index; PI, pulsatility index; PSV, peak systolic velocity; RI, resistivity index; SDR, systolic-diastolic ratio; TAMX, time-averaged maximum velocity; Tmean, time-averaged mean velocity.
Note: * Spearman correlation applied.

There were no statistically significant differences between all the main uterine artery Doppler indices of the subjects with previous myomectomy and of those without (►**Table 5**).

All the main uterine artery Doppler indices of the subjects showed a significant correlation with the subjects' uterine volume. The PSV, EDV, TAMX, and Tmean showed strong positive correlations with the uterine volume (correlation coefficient [r] 0.6), while the PI, RI, SDR, and the ImI showed moderate negative correlations with the uterine volume (r = - 0.4 to - 0.6). The main uterine artery PSV, EDV, TAMX, Tmean, PI, AT, DAR and inverse PI of the controls correlated weakly with the uterine volume (►**Table 6**).

Significantly higher main uterine artery flow velocity indices (except AI and DAR) and significantly lower resistance to flow were noted in subjects who had fibroids with degenerative changes compared with those without degenerative changes.

Discussion

Doppler sonography in Gynecology is an important adjunct to gray-scale sonography, with established roles in the assessment of infertility, uterine leiomyomas, pelvic arteriovenous malformations, hormone replacement therapy, etc.[13,14] In this study, the women with uterine leiomyomas showed a significant increase in uterine perfusion/blood flow compared with the controls, as evidenced by the elevation of uterine artery Doppler indices reflecting blood flow velocity (PSV, EDV, TAMX, Tmean, DAR, AT and AI) with increase in uterine volume, while the indices reflective of the degree of resistance to blood flow or vascular impedance (PI, RI, SDR, ImI, inverse PI) diminished with increase in uterine volume. This decrease in resistance to blood flow could be due to the uncoiling of the uterine artery with uterine enlargement in the leiomyomatous uterus.[6] Similar uterine artery uncoiling and diminution of resistance has been observed in enlarged gravid uteri.[6] The myometrial vasculature also enlarges[24,25] to supply the hypervascular networks present in uterine leiomyomas, which further decreases the resistance to blood flow.

Increase in blood flow velocity indices with increasing uterine volume was also noted in the controls, with weak statistical significance. This suggests that uterine enlargement rather than the mere presence of the leiomyomatous tumor is mainly responsible for the observed alteration in the uterine artery blood flow to the leiomyomatous uteri. Furthermore, women with a uterine volume $> 200\ cm^3$ had significantly higher flow velocities and lower vascular ImIs than those with uterine volume $\leq 200\ cm^3$. This is similar to the results obtained by Farmakides et al[6] and Alatas et al.[5]

Leiomyomas with degenerative changes showed higher flow velocities and lower resistance to blood flow in the main uterine artery. This is in agreement with previous studies,[2,26]

and could be due to the fact that degenerating leiomyomas are often large and rapidly growing, eventually outgrowing their blood supply. Such rapid growth probably requires greater blood supply to support the metabolic activities.

The study also found that the blood flow velocity indices of the main uterine artery were significantly higher in symptomatic subjects compared with asymptomatic subjects. When menorrhagia was considered as a specific symptom, those with menorrhagia had higher main uterine artery blood flow velocity indices and lower vascular resistance indices, which is suggestive of a "compensatory" increase in perfusion when menorrhagia occurs. These two observations suggest that the presence of menorrhagia leads to significant alterations in the main uterine artery Doppler indices. A similar pattern was documented by Hurskainen et al,[27] who reported a significant inverse correlation between the uterine artery PI and the amount of blood loss in menstruating women (those with lower uterine flow impedance bled more), and concluded that there likely is a significant relationship between uterine vascular tone and menorrhagia.[27]

Apart from being a black population study,[22–30] the markedly larger uterine volumes in this study could also be due to the fact that the majority of the patients in this environment present late, often after failure of alternative therapies, or due to the prohibitive cost of orthodox medical treatments. These markedly larger sizes may also explain the much lower Doppler indices in this study compared with those of some previous studies.[2,4,5] Moreover, the median uterine volume of the subjects in this study was 556 cm^3, which is much higher than the reported mean uterine volumes of 128.5 cm^3, 187.4 cm^3, 276.2 cm^3, 305 cm^3, 312 cm^3, and 381.16 cm^3 by Tsuda et al,[31] Alcazar et al,[4] Alatas et al,[5] Tranquart et al,[32] Danisman et al,[14] and Samani et al[12] respectively.

There were no significant differences between the main uterine artery Doppler indices of uteri with recurrent leiomyomas and those with primary tumors. This is most likely due to the fact that there was no statistically significant difference between the uterine volumes of the two groups; increase in uterine volume is the main contributor to the alterations in main uterine artery Doppler indices. Leiomyoma recurrence could be due to de novo growth of new tumors from previously normal myometrial cells post-myomectomy, or due to persistent undetected tumors (remnants) left unintentionally from an incomplete fibroid surgery.[33] Obed et al,[33] who defined recurrence as the presence of a leiomyoma of at least 2 cm in diameter upon ultrasound scan, reported an overall recurrence rate of 20.7% at 10 years post-myomectomy.

The limitations of our study include the fact that the sonographic diagnosis of leiomyoma was not confirmed with histology. However, several studies have shown the increased sensitivity and specificity of the sonographic diagnosis of leiomyomas with more modern ultrasound scanners. There was also difficulty in obtaining accurate measurements of very bulky, leiomyomatous uteri and huge pedunculated leiomyomas extending to the upper abdomen. Split-screen measurements were employed in such cases.

Conclusion

In conclusion, there is increased perfusion of the myomatous uterus, as evidenced by increased blood flow velocity indices and reduced vascular impedance indices in their main uterine artery compared with the controls. These changes are more likely due to increased uterine volume rather than the mere presence of myomas. No significant differences were detected between the main uterine artery Doppler indices of uteri with recurrent leiomyoma and those with primary tumors.

Contributions
Idowu BM, Ibitoye BO and Adetiloye VA contributed with the conception and design, data collection and analysis, interpretation of data, writing of the article, critical review of the intellectual content, and final approval of the version to be published.

Conflicts of Interest
None to declare.

References

1 Gómez O, Figueras F, Fernández S, et al. Reference ranges for uterine artery mean pulsatility index at 11-41 weeks of gestation. Ultrasound Obstet Gynecol 2008;32(02):128–132
2 Kurjak A, Kupesic-Urek S, Miric D. The assessment of benign uterine tumor vascularization by transvaginal color Doppler. Ultrasound Med Biol 1992;18(6-7):645–649
3 Sladkevicius P, Valentin L, Marsál K. Transvaginal Doppler examination of uteri with myomas. J Clin Ultrasound 1996;24(03): 135–140
4 Alcázar JL, Griffioen M, Jurado M. Uterine artery blood flow in women with uterine myomas. Eur J Ultrasound 1997;5(03): 165–169
5 Alataş G, Aksoy E, Akarsu C, Yakin K, Bahçeci M. The effect of uterine volume on uterine artery Doppler velocimetry in the myomatous state. Gynecol Obstet Invest 1997;43(01):55–59
6 Farmakides G, Stefanidis K, Paschopoulos M, Mamopoulos M, Lolis D. Uterine artery Doppler velocimetry with leiomyomas. Arch Gynecol Obstet 1998;262(1-2):53–57
7 Muram D, Gillieson M, Walters JH. Myomas of the uterus in pregnancy: ultrasonographic follow-up. Am J Obstet Gynecol 1980;138(01):16–19
8 Laughlin SK, Baird DD, Savitz DA, Herring AH, Hartmann KE. Prevalence of uterine leiomyomas in the first trimester of pregnancy: an ultrasound-screening study. Obstet Gynecol 2009; 113(03):630–635
9 Myers SL, Baird DD, Olshan AF, et al. Self-report versus ultrasound measurement of uterine fibroid status. J Womens Health (Larchmt) 2012;21(03):285–293
10 Lefebvre J, Demers S, Bujold E, et al. Comparison of two different sites of measurement for transabdominal uterine artery Doppler velocimetry at 11-13 weeks. Ultrasound Obstet Gynecol 2012; 40(03):288–292
11 Hollis B, Mavrides E, Campbell S, Tekay A, Thilaganathan B. Reproducibility and repeatability of transabdominal uterine artery Doppler velocimetry between 10 and 14 weeks of gestation. Ultrasound Obstet Gynecol 2001;18(06):593–597
12 Samani FG, Jabbary R, Taghizadeh S. Study on uterine artery blood flow in myomatous uterus. Life Sci J 2012;9(04):583–586

13 Sosić A, Skupski DW, Streltzoff J, Yun H, Chervenak FA. Vascularity of uterine myomas: assessment by color and pulsed Doppler ultrasound. Int J Gynaecol Obstet 1996;54(03):245–250
14 Danisman N, Ekici E, Isik AZ, Zorlu CG, Gokmen O. Transvaginal color Doppler analysis of benign uterine leiomyomas. Turk J Med Sci 1998;28:179–181
15 Pourcelot L. Applications cliniques de l'examen Doppler transcutane. In: Peronneau P, eds. *Velocimetrie Ultrasonore Doppler*. Paris: INSERM; 1974:780–785
16 Gosling RG, King DH. Ultrasonic angiology. In: Marcus AW, Adamson J, eds. *Arteries and Veins*.. Edinburgh: Churchill Livingstone; 1975:61–98
17 Allen KS, Jorkasky DK, Arger PH, et al. Renal allografts: prospective analysis of Doppler sonography. Radiology 1988;169(02): 371–376
18 Vetter K, Gonser M, Voigt HJ. Indices for the evaluation of Doppler sonograms. In: Sohn C, Voigt HJ, Vetter K, eds. *Doppler Ultrasound in Gynecology and Obstetrics*.. Stuttgart: Thieme; 2004:25–39
19 Kawai M, Kano T, Kikkawa F, Maeda O, Oguchi H, Tomoda Y. Transvaginal Doppler ultrasound with color flow imaging in the diagnosis of ovarian cancer. Obstet Gynecol 1992;79(02): 163–167
20 Maulik D, Yarlagadda P, Youngblood JP, Ciston P. Comparative efficacy of umbilical arterial Doppler indices for predicting adverse perinatal outcome. Am J Obstet Gynecol 1991;164(6 Pt 1): 1434–1439, discussion 1439–1440
21 Secil M, Dogra VS. Color flow Doppler evaluation of uterus and ovaries and its optimization techniques. Ultrasound Clin 2008; 3:461–482
22 Bhatt S, Dogra VS. Doppler imaging of the uterus and adnexae. Ultrasound Clin 2006;1:201–221
23 Dubbins PA. Doppler ultrasound of the female pelvis. In: Allan PL, Dubbins PA, Pozniak MA, McDicken WN, eds. *Clinical Doppler Ultrasound*. 2nd ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2006:287–313
24 Farrer-Brown G, Beilby JOW, Rowles PM. Microvasculature of the uterus. An injection method of study. Obstet Gynecol 1970; 35(01):21–30
25 Farrer-Brown G, Beilby JOW, Tarbit MH. The vascular patterns in myomatous uteri. J Obstet Gynaecol Br Commonw 1970;77(11): 967–975
26 Szabó I, Szánthó A, Csabay L, Csapó Z, Szirmai K, Papp Z. Color Doppler ultrasonography in the differentiation of uterine sarcomas from uterine leiomyomas. Eur J Gynaecol Oncol 2002;23(01): 29–34
27 Hurskainen R, Teperi J, Paavonen J, Cacciatore B. Menorrhagia and uterine artery blood flow. Hum Reprod 1999;14(01):186–189
28 Kjerulff KH, Langenberg P, Seidman JD, Stolley PD, Guzinski GM. Uterine leiomyomas. Racial differences in severity, symptoms and age at diagnosis. J Reprod Med 1996;41(07):483–490
29 Marshall LM, Spiegelman D, Barbieri RL, et al. Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. Obstet Gynecol 1997;90(06):967–973
30 Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol 2003;188(01): 100–107 Doi: 10.1067/mob.2003.99
31 Tsuda H, Kawabata M, Nakamoto O, Yamamoto K. Clinical predictors in the natural history of uterine leiomyoma: preliminary study. J Ultrasound Med 1998;17(01):17–20
32 Tranquart F, Brunereau L, Cottier JP, et al. Prospective sonographic assessment of uterine artery embolization for the treatment of fibroids. Ultrasound Obstet Gynecol 2002;19(01):81–87
33 Obed JY, Bako B, Usman JD, Moruppa JY, Kadas S. Uterine fibroids: risk of recurrence after myomectomy in a Nigerian population. Arch Gynecol Obstet 2011;283(02):311–315

Pelvic Floor 3D Ultrasound of Women with a TVT, TVT-O, or TVT-S for Stress Urinary Incontinence at the Three-year Follow-up

Ultrassonografia tridimensional do assoalho pélvico após 3 anos de correção cirúrgica de incontinência urinária de esforço por sling retropúbico, transobturador, ou de incisão única

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Abstract

Objective Using three-dimensional ultrasound (3D-US), we aimed to compare the tape position and the angle formed by the sling arms in different techniques of mid-urethral sling insertion for the surgical treatment of stress urinary incontinence, three years after surgery. In addition, we examined the correlations between the US findings and the clinical late postoperative results.

Methods A prospective cross-sectional cohort study of 170 patients who underwent a sling procedure between May 2009 and December 2011 was performed. The final sample, with US images of sufficient quality, included 26 retropubic slings (tension-free vaginal tape, TVT), 42 transobturator slings (tension-free vaginal tape-obturator, TVT-O), and 37 single-incision slings (tension-free vaginal tape-Secur, TVT-S). The images (at rest, during the Valsalva maneuver, and during pelvic floor contraction) were analyzed offline by 2 different observers blinded against the surgical and urinary continence status. Group comparisons were performed using the Student *t*-test, the chi-squared and the Kruskal-Wallis tests, and analyses of variance with Tukey multiple comparisons.

Results Differences among the groups were found in the mean angle of the tape arms (TVT = 119.94°, TVT-O = 141.93°, TVT-S = 121.06°; $p < 0.001$) and in the distance between the bladder neck and the tape at rest (TVT = 1.65 cm, TVT-O = 1.93 cm, TVT-S = 1.95 cm; $p = 0.010$). The global objective cure rate was of 87.8% (TVT = 88.5%, TVT-O = 90.5%, TVT-S = 83.8%; $p = 0.701$). The overall subjective cure rate was of

Keywords
- urinary incontinence
- ultrasonography
- pelvic floor

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83.8% (TVT = 88.5%, TVT-O = 88.5% and TVT-S = 78.4%; $p = 0.514$). The slings were located in the mid-urethra in 85.7% of the patients (TVT = 100%, TVT-O = 73.8%, TVT-S = 89.2%; $p = 0.001$), with a more distal location associated with obesity (distal: 66.7% obese; mid-urethra: 34% obese; $p = 0.003$). Urgency-related symptoms were observed in 23.8% of the patients (TVT = 30.8%, TVT-O = 21.4%, TVT-S = 21.6%; $p = 0.630$).

Conclusions The angle formed by the arms of the sling tape was more obtuse for the transobturator slings compared with the angles for the retropubic or single-incision slings. Retropubic slings were more frequently located in the mid-urethra compared with the other slings, regardless of obesity. However, the analyzed sonographic measures did not correlate with the urinary symptoms three years after the surgery.

Resumo

Objetivo Comparar por meio de ultrassom tridimensional (US-3D) a posição e o ângulo entre os braços da faixa, em diferentes técnicas de inserção de *sling* de uretra média, para tratamento de incontinência urinária de esforço, 3 anos após a cirurgia, correlacionando os achados ultrassonográficos aos resultados clínicos pós-operatórios.

Métodos Este é um estudo de coorte transversal prospectivo de 170 pacientes que se submeteram a um procedimento de *sling* entre maio de 2009 e dezembro de 2011. Foi possível avaliar as imagens de US em 105 pacientes: 26 com *tension-free vaginal tape* (TVT), 42 com *tension-free vaginal tape-obturator* (TVT-O) e 37 com *tension-free vaginal tape-Secur* (TVT-S). As imagens (em repouso, em manobra de Valsalva e em contração perineal) foram analisadas por dois observadores diferentes, que desconheciam o tipo de *sling* utilizado na cirurgia, assim como as queixas da paciente. A análise estatística foi realizada por meio dos testes *t* de Student, qui-quadrado, Kruskal-Wallis, e análise de variância com comparações múltiplas de Tukey.

Resultados As médias dos ângulos entre os braços da faixa foram: TVT = 119,94°, TVT-O = 141,93°, TVT-S = 121,06° ($p < 0,001$). As médias das distâncias entre o colo vesical e a faixa, em repouso, foram: TVT = 1,65 cm, TVT-O = 1,93 cm, TVT-S = 1,95 cm ($p = 0,010$). A taxa de cura objetiva dos *slings* foi de 87,8% (TVT = 88,5%, TVT-O = 90,5% e TVT-S = 83,8%; $p = 0,701$). A taxa de cura subjetiva foi de 83,8% (TVT = 88,5%, TVT-O = 88,5% e TVT-S = 78,4%; $p = 0,514$). Os *slings* estavam na uretra média em 85,7% (TVT = 100%, TVT-O = 73,8% e TVT-S = 89,2%; $p = 0,001$) dos pacientes, e a localização mais distal foi associada a obesidade (distal: 66,7% obesas; uretra média: 34% obesas; $p = 0.003$). Os sintomas de urgência foram observados em 23,8% das pacientes (TVT = 30,8%, TVT-O = 21,4%, TVT-S = 21,6%; $p = 0,630$). Não houve diferenças significativas quando se comparam os achados ultrassonográficos e os grupos de pacientes com sintomas de urgência, cura subjetiva e objetiva.

Conclusão O ângulo formado pelos braços da faixa foi mais obtuso no TVT-O quando comparado com o TVT ou o TVT-S. Os TVTs foram localizados mais frequentemente na uretra média quando comparados com os outros dois grupos, mesmo em pacientes obesas. Entretanto, as medidas ultrassonográficas não tiveram correlação com os sintomas urinários três anos após a cirurgia.

Palavras-Chave
- incontinência urinária
- ultrassonografia
- assoalho pélvico

Introduction

The current standard surgical treatment for stress urinary incontinence (SUI) involves tension-free mid-urethral sling (MUS) placement, either using the retropubic or transobturator approach, which has a reported success rate of up to 80% at the long-term follow-up.[1] More recently, single-incision slings were developed to minimize some of the risks related to MUSs, such as infection and chronic pain. However, this technique has not been well-accepted by the medical community due to the variability in insertion techniques and the diversity of materials used to ensure the fixation of the

device, which has interfered with continence success. Thus, traditional MUSs are considered significantly superior to mini-slings in terms of cure outcomes.[2–4]

Although MUS operations are considered safe, complications such as urinary obstruction and postoperative urgency may occur. Imaging techniques can provide assistance in the diagnosis of these complications.[5] Ultrasonography (US) is a widespread tool used to assess the anatomy and function of the pelvic floor structures. It is a non-invasive, reproducible, and technically simple method to visualize the lower urinary tract, particularly the urethra and the bladder, and an endovaginal or translabial convex probe can be used.[6] Moreover, translabial three-dimensional ultrasound (3D-US) allows good visualization of the suburethral polypropylene sling tape in orthogonal planes (axial, coronal, mid-sagittal), and can be used to explain the pathogenesis of voiding dysfunction following synthetic sling procedures.[7] Thus, US during the postoperative period has shown an increasing role in the monitoring of surgically treated patients, especially for complications such as urinary retention and urinary disorders. However, there are few studies that correlate the information obtained by 3D-US and the prognostic and predictive markers of SUI treatment with synthetic slings.[7]

Therefore, the present study utilized translabial 3D-US 3 years after surgeries for the cure of SUI to evaluate and compare the spatial position of the polypropylene sling tape for 3 different SUI correction techniques: MUS using the retropubic approach (tension-free vaginal tape, TVT), the transobturator approach (tension-free vaginal tape-obturator, TVT-O), and the single-incision sling (tension-free vaginal tape-Secur, TVT-S). In addition, the relationship between the 3D-US findings and the objective/subjective cure rates and urgency-related symptoms was examined. Our hypothesis was that the angle formed by the arms of the tape following TVT insertion is the most acute, causing more post-operative urgencies, whereas the angle following TVT-O insertion is more obtuse and, consequently, results in more failures of SUI correction. In addition, we expected the TVT-S, which is not currently on the market, to act similarly to the TVT. Moreover, we hypothesized that if the tape is located in the mid-urethra, the better the long-term clinical postoperative results.

Methods

Subjects

A prospective cross-sectional cohort study of patients who underwent a sling procedure at the Urogynecology and Vaginal Surgery Sector of our institution between May 2009 and December 2011 was performed. All patients who underwent the surgery during the study period were invited (via phone) to participate. The inclusion criteria were: women over 18 years-old who had undergone SUI treatment with MUS (using the retropubic or transobturator routes) or a single-incision sling without any concomitant pelvic floor surgical procedures. In addition, the patient should have had a preoperative diagnosis of SUI without detrusor overactivity. The exclusion criteria were as follows: incomplete medical records relating to surgical hospitalization, urinary incontinence previously treated by surgery with a polypropylene implant, or undergoing new treatments for urinary incontinence during the follow-up period. Total of 170 patients were eligible to participate in the study (48 with TVTs, 56 with TVT-Os, and 66 with TVT-Ss). Among these, 115 accepted the invitation, being thus selected and placed in each group according to the surgery performed (TVT: 26; TVT-O: 46; TVT-S: 43). However, 10 evaluated patients were excluded from the analysis (2 women presented with 2 synthetic slings at US, and 3D-US images did not have perfect technical quality in 8 cases), resulting in a final sample of 105 patients (TVT: 26; TVT-O: 42; TVT-S: 37). The patient selection process is depicted in ►**Fig. 1**.

An urodynamic study was performed before the surgery, and the results of the Valsalva leak point pressure (VLPP, mean and standard deviation) were 67.64 $\pm$ 19.20 cmH2O, 87.57 $\pm$ 32.14 cmH2O and 85.14 $\pm$ 27.05cmH2O, for the TVT, TVT-O and TVT-S groups respectively.

A sample power calculation was performed using the results of a previous publication,[7] which involved the evaluation of the angles formed by the arms of the polypropylene tape in sonographic images at rest and during the Valsalva maneuver. At rest, the mean values considered in the sample calculation were 116° and 137°, respectively for the TVT and TVT-O groups, and the overall standard deviation considered was 7. During the Valsalva maneuver, the mean values were 130° (TVT) and 140° (TVT-O), with a standard deviation of 10. Considering the power of the sample of 80%, 4 patients per group at rest and 17 patients per group during the Valsalva maneuver would be necessary. A p-value < 0.05 was considered statistically significant.

The study was approved by the National Ethics in Research Committee, and the trial was appropriately registered on www.clinicaltrials.gov (NCT 02406638). All participants provided written informed consent, and the research was performed according to the Declaration of Helsinki, as revised in 2008.

Procedures

The TVT surgery was performed according to the classical technique,[8] using Gynecare TVT (Ethicon Inc., Somerville, New Jersey, US). The TVT-O procedure was performed according to the inside-out technique proposed by de Leval,[9] using the Gynecare TVT Obturator System (Ethicon Inc., Somerville, New Jersey, US). The single-incision sling (TVT-Secur, Gynecare TVT Secur System, Ethicon Inc., Somerville, New Jersey, US) was inserted using the "U" insertion technique.[10] The manufacturer discontinued the commercialization of the TVT-S in 2012.[11]

Three-dimensional US imaging and a clinical evaluation were performed between April 2013 and June 2014. The physical examination involved stress tests, including the 250-ml bladder volume and the 20-minute pad tests.[12] In addition, the quality of life was assessed using the King Health Questionnaire (KHQ), which had been previously validated for the Portuguese language.[13] Objective cure was defined as the absence of urinary leakage during the stress tests. Subjective

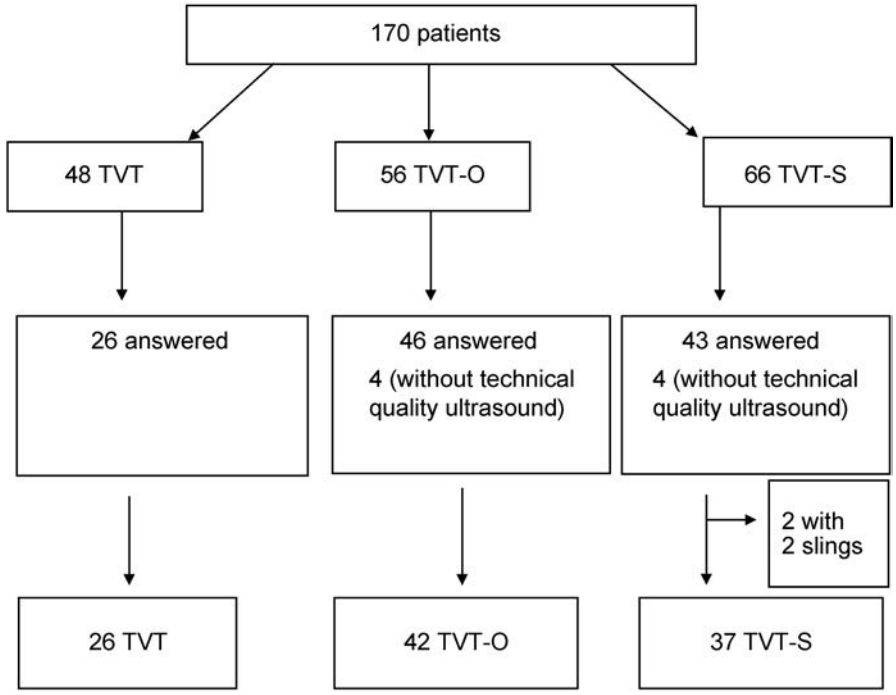

Fig. 1 Patient selection flowchart: the patient selection process is depicted. Abbreviations: TVT, tension-free vaginal tape (retropubic sling); TVT-O, tension-free vaginal tape-obturator (transobturator sling); TVT-S, tension-free vaginal tape-Secur (single-incision sling).

cure was defined as the absence of self-reported urinary leakage as indicated by a KHQ symptoms scale score of 0. The presence of urgency-related symptoms was also evaluated using the KHQ symptoms scale.

Three-dimensional US was performed after voiding, with the patient in the lithotomy position, with the hips flexed and abducted; it was performed at rest, during the Valsalva maneuver, and during perineal contraction. The 3D-US equipment (Voluson 730 Expert, General Electric [GE] Healthcare, Zipf, Austria) included a convex volumetric transducer covered by a plastic transducer (4–8 Mhz) with an acquisition angle of 85°.

The obtained images of the pelvic floor were later evaluated using the 4D View (version 14, ext 0; GE Kretz Ultrasound, GE Healthcare, Zipf, Austria) software on a computer with the Windows system. For the analysis of the images, the sagittal plane (two-dimensional [2D] image) was selected with the sight line through the pubis, the urethra, and the polypropylene sling tape.[14] The assessors of the ultrasound data were blinded against all clinical data. The measurements of the urethral length (UL) and the distance between the bladder neck and the central point of the tape (BT) were performed using a 2D-US image in the mid-sagittal plane (►**Fig. 2**). The tape displacement in relation to the UL was measured as the difference between the ratio of the BT and UL at rest and during the Valsalva maneuver or pelvic floor contraction. For an evaluation of the relative position of the tape, we divided the BT by the UL, and the resulting number was used to classify the position of the tape within the urethra. The tape was considered to be: in the proximal-third (closest to the bladder neck) if the result was between 0 and 0.33; in the middle-third if the result was between 0.34 and 0.66; and in the distal-third (closest to the external urethral ostium) if the result was between 0.67 and 1.0.

The OmniView volume contrast imaging (VCI) mode (GE Healthcare, Zipf, Austria) was used during the image analysis, sliding digitally with a straight line passing through the lower edge of the pubic symphysis, the urethra, and the lower tape. In order to improve visibility, VCI was selected, with a thickness of 3.0 mm, which allowed the visualization of the pubis, the urethra, the vagina, the tape, and the rectum (►**Fig. 2**).[15] The OmniView-VCI mode was used to evaluate the angle formed by the tape arms (A°), as well as the distance between the posterior inferior symphysis margin and the echogenic center of the urethra (PU), and the distance between the echogenic center of the urethra and the tape (UT) (►**Fig. 2**). The mobility of the urethra during movement was calculated as the difference between the PU at rest and the PU during the Valsalva maneuver or pelvic floor contraction.

Statistical analyses were performed using the Minitab software (Minitab, Inc., State College, PA, US), version 16. The Mann-Whitney test was used for the continuous non-parametric variables, and the Student *t*-test was used for the continuous parametric variables. The Chi-squared, Fisher, Kruskal-Wallis, and Pearson correlation tests were used for the nominal variables. Analyses of variance (ANOVAs) for continuous variables were performed using the Tukey multiple comparison procedure. A p-value < 0.05 was considered statistically significant.[16,17]

Results

The three surgical groups (26 TVT, 42 TVT-O, and 37 Minisling TVT-S) were similar in terms of age, body mass index (BMI), the number of vaginal or caesarean deliveries, and hormonal status, as shown in ►**Table 1**. At the time of the

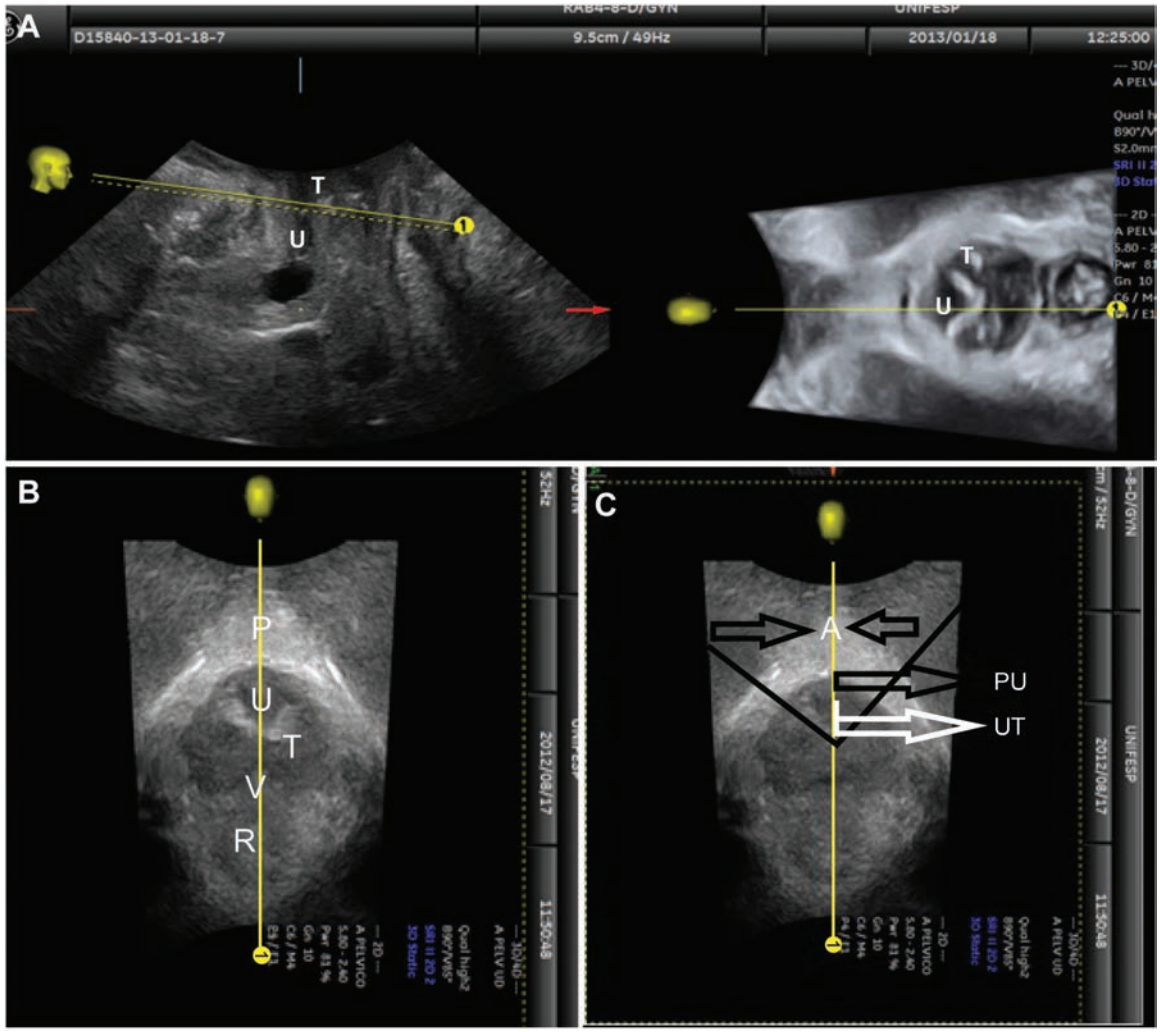

Fig. 2 Example images: (**A**) a 2D-US mid-sagittal plane (left) and 3D OmniView axial image (right) image of the pelvic floor are shown. Note the sling position (white hyperechoic structure – T) and urethra (hypoechoic structure – U). Two images below - OmniView mode: The axial plane on the OmniView mode with pelvic floor organs, at the left (**B**), and measurements, at the right (**C**), is shown. Abbreviations: A°, angle between the two arms of the sling; P, symphysis pubis; PU, distance between the symphysis pubis and the urethra; R, rectum; T, polypropylene tape (sling); U, urethra; UT, distance between the tape and the urethra; V, vagina.

evaluation, the postoperative time ranged between 36 and 40 months.

The 2D-US measurements obtained in the mid-sagittal plane are presented in ►**Table 2**. The UL at rest, during the Valsalva maneuver, and during pelvic floor contraction did not significantly differ among the three groups. In contrast, there were differences among the groups regarding the BT. Specifically for the TVT group, the tape was significantly

Table 1 Patient characteristics

	TVT ($n = 26$) Mean (SD)	TVT-O ($n = 42$) Mean (SD)	TVT-S ($n = 37$) Mean (SD)	p
Age (Years)	58.35 (9.79)	55.00 (10.77)	54.51 (13.2)	0.384[a]
BMI (Kg/m^2)	27.87 (3.66)	30.41 (5.16)	29.50 (5.35)	0.121[a]
Caesarean delivery	0.42 (0.86)	0.52 (0.89)	0.62 (0.83)	0.372[b]
Vaginal delivery	1.89 (1.11)	2.71 (2.11)	3.05 (2.73)	0.130[b]
Menopause (%)	22 (84.60%)	26 (61.90%)	24 (64.86%)	0.122[c]

Abbreviations: BMI, body mass index; SD, standard deviation; TVT, tension-free vaginal tape (retropubic sling); TVT-O, tension-free vaginal tape-obturator (transobturator sling); TVT-S, tension-free vaginal tape-Secur (single-incision sling).
Notes: [a]ANOVA; [b]Kruskal-Wallis test; [c]Chi–squared test. The values are represented as mean and SD (range) and n (%), and are attributed to patients who underwent surgical treatment for stress urinary incontinence using a retropubic sling (TVT), a transobturator sling (TVT-O), or a single-incision sling (TVT-S).

Table 2 Midsagittal sonographic and OmniView-VCI mode measurements

	TVT ($n = 26$) Mean (SD)	TVT-O ($n = 42$) Mean (SD)	TVT-S ($n = 37$) Mean (SD)	p
Urethral length: rest (cm)	3.34 (0.37)	3.24 (0.40)	3.36 (0.45)	0.38*
Urethral length: Valsalva (cm)	3.26 (0.30)	3.18 (0.40)	3.25 (0.42)	0.63*
Urethral length: contraction (cm)	3.56 (0.42)	3.34 (0.39)	3.53 (0.49)	0.07*
BT: rest (cm)	1.65(0.26)	1.93 (0.38)	1.95 (0.51)	0.01*
BT: Valsalva (cm)	1.67 (0.24)	1.85 (0.37)	1.89 (0.50)	0.08*
BT: contraction (cm)	1.81 (0.38)	2.03 (0.39)	2.03 (0.57)	0.11*
Mid-urethra tape n (%): rest	26 (100%)	31 (73.8%)	33 (89.2%)	0.008*
Mid-urethra tape n (%):Valsalva	26 (100%)	33 (78.6%)	29 (78.4%)	0.036*
Mid-urethra tape n (%): contraction	26 (100%)	31 (73.8%)	32 (86.5%)	0.013*
A°: rest	119.94 (19.66)	141.93 (14. 25)	121.06 (14. 24)	< 0.001*
A°: Valsalva	130.79 (21.78)	14.,48 (13. 23)	124.40 (24. 79)	< 0.001*
A°: contraction	120.94 (16.63)	144.77 (16. 51)	126.53 (18. 20)	< 0.001*
PU: rest (cm)	1.68 (0.28)	1.53 (.,25)	1.64 (0.29)	0.08*
PU: Valsalva (cm)	1.72 (0.29)	1.59 (0.28)	1.64 (0.14)	0.19*
PU: contraction (cm)	1.65 (0.27)	1.49 (0.29)	1.66 (0.31)	0.02*
UT: rest (cm)	0.67 (0.14)	0.73 (0.15)	0.71 (0.11)	0.21*
UT: Valsalva (cm)	0.65 (0.13)	0.68 (0.14)	0.75 (0.14)	0.01*
UT: contraction (cm)	0.60 (0.01)	0.65 (0.15)	0.66 (0.10)	0.16*

Abbreviations: A°, angle of the two arms of the sling; BT, distance between the bladder neck and the tape; PU, distance between the symphysis pubis and the urethra; SD, standard deviation; TVT, tension-free vaginal tape (retropubic sling); TVT-O, tension-free vaginal tape-obturator (transobturator sling); TVT-S, tension-free vaginal tape-secure (single-incision sling); UT, distance between the tape and the urethra.
Notes: ANOVA, Tukey multiple comparisons. The midsagittal sonographic measurements and OmniView-VCI mode measurements of patients who underwent surgical treatment for stress urinary incontinence using a retropubic sling (TVT), a transobturator sling (TVT-O), or a single-incision sling (TVT-S) are provided.

closer to the bladder neck compared with the other groups during rest ($p = 0.001$), but not during the Valsalva maneuver ($p = 0.08$) or pelvic floor contraction ($p = 0.11$). There was no significant difference in the displacement of the tape among the three groups.

The location of the sling relative to the urethra was different among the groups at rest and during movement (rest: $p < 0.001$; Valsalva: $p = 0.008$; pelvic floor contraction: $p < 0.001$). Specifically in the TVT group, all tapes (100%) were located in the mid-urethra during rest and during movement (Valsalva maneuver and pelvic floor contraction). However, for the TVT-O group, only 31 out of 42 tapes (73.8%) were located in the mid-urethra at rest, and for the TVT-S group, 33 out of 37 tapes (89.2%) were located in the mid-urethra at rest. Furthermore, during the Valsalva maneuver, 78.6% of tapes in the TVT-O group and 78.4% in the TVT-S group were located in the mid-urethra. During pelvic floor contraction, only 73.8% of the tapes in the TVT-0 group and 86.5% in the TVT-S group were located in the mid-urethra.

Of the 15 patients with the tape located in the distal urethra, 66.7% had a BMI > 30 kg/m^2 (obese status). In contrast, of the 90 patients with the tape located in the mid-urethra, only 34% were obese as assessed by BMI (mid-urethra versus distal urethra: $p = 0.003$). The total sample had 40/105 (38%) obese patients.

The measurements taken using the OmniView-VCI mode are shown in ►**Table 2**. The angle formed by the arms of the sling was not significantly different between the TVT and TVT-S groups, but was more obtuse in the TVT-O group compared with the other groups during rest ($p < 0.001$), during the Valsalva maneuver ($p < 0.001$), and during pelvic floor contraction ($p < 0.001$). There were no significant group differences regarding the PU, at rest or during movement. While the UT at rest and during pelvic floor contraction did not show differences among the groups, during the Valsalva maneuver, the UT significantly differed among the groups ($p = 0.01$), with a smaller UT in the TVT group compared with the TVT-S group. No significant differences among the groups regarding urethral mobility during the Valsalva maneuver and during pelvic floor contraction were found ($p = 0.78$ and $p = 0.51$ respectively).

Information on subjective and objective cure is presented in ►**Table 3**. A subjective cure was achieved by 88 of the 105 patients (83.8%), with no difference among the groups ($p = 0.701$). An objective cure was verified in 92/105 (87.8%) patients, with no difference among the groups ($p = 0.514$). The presence of urgency-related symptoms

Table 3 Urinary symptoms

	TVT	TVT-O	TVT-S	TOTAL	*p*
Subjective cure	23 (88.5%)	36 (85.7%)	29 (78.4%)	88 (83.8%)	0.514[a]
Objective cure	23 (88.5%)	38 (90.5%)	31 (83.8%)	92 (87.8%)	0.701[b]
Urgency symptoms	8 (30.8%)	9 (21.4%)	8 (21.6%)	25 (23.8%)	0.630[a]
TOTAL	26 (100%)	42 (100%)	37 (100%)	105 (100%)	

Abbreviations: TVT, tension-free vaginal tape (retropubic sling); TVT-O, tension-free vaginal tape-obturator (transobturator sling); TVT-S, tension-free vaginal tape-secure (single-incision sling).
Notes: [a]Chi-squared test; [b]Fisher exact test. The subjective and objective cure rates and the rate of urgency-related symptoms for patients who underwent surgical treatment for stress urinary incontinence using a retropubic sling (TVT), a transobturator sling (TVT-O), or a single-incision sling (TVT-S) are provided.

Table 4 Associations between ultrasound measurements and urinary symptoms

	Subjective cure			Objective cure			Urgency symptoms		
	YES ($n = 88$) M (SD)	NO ($n = 17$) M (SD)	*p*	YES ($n = 92$) M (SD)	NO ($n = 13$) M (SD)	*p*	YES ($n = 25$) M (SD)	NO ($n = 25$) M (SD)	*p*
BT: rest (cm)	1.87 (0.38)	1.86 (0.62)	0.96*	1.85 (0.38)	1.98 (0.66)	0.50*	1.76 (0.52)	1.76 (0.52)	0.25*
BT: Valsalva (cm)	1.8 (0.35)	1.95 (0.59)	0.29*	1.79 (0.35)	2.02 (0.66)	0.24*	1.85 (0.48)	1.85 (0.48)	0.74*
BT: contraction (cm)	1.96 (0.44)	2.01 (0.60)	0.80*	1.95 (0.43)	2.12 (0.64)	0.37*	1.93 (0.50)	1.93 (0.50)	0.60*
Ratio BT/UL: rest	0.57 (0.09)	0.55 (0.12)	0.62*	0.56 (0.09)	0.57 (0.12)	0.71*	0.53 (0.11)	0.53 (0.11)	0.09*
Ratio BT/UL: Valsalva	0.56 (0.09)	0.57 (0.13)	0.68*	0.56 (0.09)	0.58 (0.14)	0.61*	0.56 (0.02)	0.56 (0.02)	0.64*
Ratio BT/LU: contraction	0.57 (0.09)	0.57 (0.09)	0.10*	0.57 (0.10)	0.58 (0.10)	0.62*	0.56 (0.10)	0.56 (0.10)	0.56*
A(°): rest	129.2° (18.5)	127.9° (21.3)	0.81*	128.3° (18.8)	133.9° (19.6)	0.35*	128.5° (21.5)	128.5° (21.5)	0.89*
A (°): Valsalva	136.6° (23.0)	133.2° (22.6)	0.58*	135.6° (23.0)	139.3° (22.2)	0.94*	136.3° (21.4)	136.3° (21.4)	0.99*
A (°): contraction	132.4° (18.9)	132.5° (25.2)	0.99*	131.4° (19.0)	139.9° (24.8)	0.26*	133.3° (23.2)	133.3° (23.2)	0.82*
Urethral mobility: rest-Valsalva (cm)	-0.03 (0.24)	-0.06 (0.31)	0.73*	-0.04 (0.25)	-0.05 (0.31)	0.87*	-0.08 (0.23)	-0.08 (0.23)	0.31*
Urethral mobility: rest-contraction (cm)	0.03 (0.21)	0.04 (0.31)	0.36*	0.03 0.21	0.03 (0.32)	0.52*	0.011 (0.27)	0.011 (0.27)	0.86*

Abbreviations: A, Angle of the two arms of the sling; BT, distance between the bladder neck and tape; M, mean; SD, standard deviation; UL, urethral length.
Notes: Student *t*-test. The results of the analyses examining the potential associations between sonographic measurements and urinary symptoms are provided for patients who underwent surgical treatment for stress urinary incontinence using a retropubic sling (TVT), a transobturator sling (TVT-O) or a single-incision sling (TVT-S).

Table 5 Quality of life assessments (King Health Questionnaire)

	TVT-R Mean	TVT-O Mean	TVT-S Mean	*p*
General health	29.81	24.40	25.68	0.28*
Incontinence impact	12.82	13.49	13.51	0.92*
Limitations to daily activities	10.26	8.33	13.06	0.67*
Limitations to physical activities	11.54	7.14	11.56	0.56*
Social limitations	10.26	3.70	6.01	0.62*
Impact on personal relationships	3.92	3.09	5.36	0.86*
Impact on emotions	6.41	9.52	9.31	0.73*
Impact on sleep arrangement	8.97	6.75	5.41	0.58*
Severity measure	13.14	10.52	9.01	0.69*

Abbreviations: TVT, tension-free vaginal tape (retropubic sling); TVT-O, tension-free vaginal tape-obturator (transobturator sling); TVT-S, tension-free vaginal tape-secur (single-incision sling).
Notes: Kruskal Wallis test. Quality of life data as assessed using the King Health Questionnaire are provided for patients who underwent surgical treatment for stress urinary incontinence using a retropubic sling (TVT), a transobturator sling (TVT-O) or a single-incision sling (TVT-S).

was observed in 25/105 (23.8%) patients, with no difference among the groups ($p = 0.630$).

Correlations between the tape's spatial position and the clinical results are shown in ►**Table 4**. No significant relationships were found, except for the displacement of the tape in relation to the UL between rest and contraction, which was slightly greater in the direction of the bladder neck in patients with urgency-related symptoms compared with those without symptoms ($p = 0.03$). No significant differences among the groups were found for the domains of the KHQ (►**Table 5**).

Discussion

Three-dimensional US imaging of the pelvic floor is a non-invasive and reproducible technique for the evaluation of postoperative MUS, and it enables a dynamic assessment of the polypropylene sling tape, with good visibility during rest, pelvic floor contraction, and the Valsalva maneuver.[7]

The BT found in the present study is consistent with previously published data.[18,19] In addition, for the majority of the patients (85.7%), the sling was located in the mid-urethra, and all other patients had slings located in the distal urethra (14.3%). These results are also similar to those obtained by others researchers.[19–21] We observed that 66.7% of the patients with the tape located in the distal urethra had a BMI > 30 kg/m^2 (obese status), while among those with the tape located in the mid-urethra, only 34% were obese. Thus, obesity appears to be a factor favoring a more distal position of the sling. However, the tape remained located in the mid-urethra in all individuals in the TVT group, thus showing a better location in obese patients as well, three years after the surgery.

The angle formed by the tape arms was less obtuse in the TVT and TVT-S groups compared with the TVT-O group (at rest, during the Valsalva maneuver, and during pelvic floor contraction), with no differences between the TVT and TVT-S groups. This finding was as we expected, and it may be explained by features of the sling insertion technique.[7,22] For the TVT-O, the insertion was in a "hammock" position, while for the TVT and TVT-S, the insertion was in a "U" position. The "U" position was considered the best way to insert the TVT-S before its commercialization was discontinued.

It is interesting to note that no differences among the surgical techniques were identified with regard to tape displacement or urethra mobility, in rest or during movement, which is as expected, given that the three surgical procedures are meant to stabilize urethral mobility.

The distance between the urethra and the tape was smaller in the TVT group compared with the TVT-S group during the Valsalva maneuver only. This finding could suggest a higher frequency of postoperative urgency-related symptoms with the TVT. However, similarly to previous studies, we did not observe any differences between TVT and TVT-O groups in terms of this sonographic measure.[22]

Even though no associations between the position of the MUS tape and the clinical results were found, it was noted that, in patients with urgency-related symptoms, the tape tended to move more toward the bladder neck during the Valsalva maneuver. On the other hand, during pelvic floor contraction, there was a greater displacement of the tape toward the bladder neck in patients who reported urgency-related symptoms compared with patients without these symptoms. This may be a mechanism that explains the onset of de novo urgency in the postoperative period.

A lack of correlation between the tape position and the clinical outcomes has been previously reported[6,20,23] and was confirmed in the present study, suggesting that factors other than tape position could influence the results of the insertion of the MUS.[23,24] Although some sonographic measurements reached statistical significance in the group comparisons, the differences are on the order of millimeters, and are not clinically significant.

The limitations of the present study include the cross-sectional design, with only a midterm postoperative follow-up. Therefore, we were not able to compare the preoperative and postoperative results or evaluate the earlier failures requiring surgical re-intervention, which could be related to tape position, as suggested by other studies.[24,25] However, our study sample does reproduce the results from the literature regarding the objective and subjective cure rates and the frequency of urinary urgency symptoms, according to the different surgical techniques.[1,2]

Conclusion

In conclusion, we observed differences in the synthetic sling position three years after surgery when comparing different routes of insertion. In the retropubic approach, the tape was

more frequently located in the mid-urethra compared with the transobturator route and the single-incision sling. Regarding the angle of the sling arms, it was more obtuse with the transobturator route, and it was, in a similar manner, more acute with the retropubic route and the single-incision sling. Although a relationship between the position of the MUS tape and the subjective/objective cure three years after surgery was not demonstrated, there was a correlation between the movement of the tape during pelvic floor contraction and the presence of symptoms of urgency.

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Conflicts of Interest
Authors have no conflicts of interest to disclose.

Registration
Clinical Trials.gov Protocol Registration System, http://www.clinicaltrials.gov, NCT 02406638, Pelvic Floor 3D USG Three Years After Mid-urethral Slings (TVT-R, TVT-O, TVT-S).

References

1 Ogah J, Cody DJ, Rogerson L. Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women: a short version Cochrane review. Neurourol Urodyn 2011;30(03):284–291
2 Mostafa A, Lim CP, Hopper L, Madhuvrata P, Abdel-Fattah M. Single-incision mini-slings versus standard midurethral slings in surgical management of female stress urinary incontinence: an updated systematic review and meta-analysis of effectiveness and complications. Eur Urol 2014;65(02):402–427
3 Bianchi-Ferraro AM, Jarmy-DiBella ZI, de Aquino Castro R, Bortolini MA, Sartori MG, Girão MJ. Randomized controlled trial comparing TVT-O and TVT-S for the treatment of stress urinary incontinence: 2-year results. Int Urogynecol J Pelvic Floor Dysfunct 2014;25(10):1343–1348
4 Schimpf MO, Rahn DD, Wheeler TL, et al; Society of Gynecologic Surgeons Systematic Review Group. Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;211(01):71.e1–71.e27
5 Chantarasorn V, Shek KL, Dietz HP. Sonographic appearance of transobturator slings: implications for function and dysfunction. Int Urogynecol J Pelvic Floor Dysfunct 2011;22(04):493–498
6 Dietz HP. Ultrasound imaging of the pelvic floor. Part II: three-dimensional or volume imaging. Ultrasound Obstet Gynecol 2004;23(06):615–625
7 Chene G, Cotte B, Tardieu AS, Savary D, Mansoor A. Clinical and ultrasonographic correlations following three surgical anti-incontinence procedures (TOT, TVT and TVT-O). Int Urogynecol J Pelvic Floor Dysfunct 2008;19(08):1125–1131
8 Ulmsten U, Henriksson L, Johnson P, Varhos G. An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 1996;7(02):81–85, discussion 85–86
9 de Leval J. Novel surgical technique for the treatment of female stress urinary incontinence: transobturator vaginal tape inside-out. Eur Urol 2003;44(06):724–730
10 Bianchi-Ferraro AM, Jarmy-Di Bella ZI, Castro RdeA, Bortolini MA, Sartori MG, Girão MJ. Single-incision sling compared with transobturator sling for treating stress urinary incontinence: a randomized controlled trial. Int Urogynecol J Pelvic Floor Dysfunct 2013;24(09):1459–1465
11 Ethicon, a Johnson & Johnson Company, makes allegedly dangerous transvaginal mesh and hernia mesh products [Internet]. 2012 [cited 2016 Jan 12]. Available from: http://www.yourlawyer.com/topics/overview/johnson-johnson-ethicon-gynecare-transvaginal-mesh-complications-side-effects-lawsuits
12 Hahn I, Fall M. Objective quantification of stress urinary incontinence: a short, reproducible, provocative pad-test. Neurourol Urodyn 1991;10(05):475–481
13 Fonseca ESM, Camargo ALM, Castro RA, et al. Validation of a quality of life questionnaire (King's Health Questionnaire) in Brazilian women with urinary incontinence. Rev Bras Ginecol Obstet 2005;27(05):235–242
14 Dietz HP. Pelvic floor ultrasound in incontinence: what's in it for the surgeon? Int Urogynecol J Pelvic Floor Dysfunct 2011;22(09):1085–1097
15 Tonni G, Lituania M. OmniView algorithm: a novel 3-dimensional sonographic technique in the study of the fetal hard and soft palates. J Ultrasound Med 2012;31(02):313–318
16 Agrest A. Categorical data analysis. New York: Wiley Interscience; 1990
17 Neter J, Kutner MH, Nachtsheim CJ, Wasserman W. Applied linear statistical models. 4th ed. Boston: Irwin; 1996
18 deTayrac R, Deffieux X, Droupy S, Chauveaud-Lambling A, Calvanèse-Benamour L, Fernandez H. A prospective randomized trial comparing tension-free vaginal tape and transobturator suburethral tape for surgical treatment of stress urinary incontinence. Am J Obstet Gynecol 2004;190(03):602–608
19 Foulot H, Uzan I, Chopin N, Borghese B, Chapron C. Monarc transobturator sling system for the treatment of female urinary stress incontinence: results of a post-operative transvaginal ultrasonography. Int Urogynecol J Pelvic Floor Dysfunct 2007;18(08):857–861
20 Duckett J, Aggarwal I, Patil A, Vella M. Effect of tension-free vaginal tape position on the resolution of irritative bladder symptoms in women with mixed incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2008;19(02):237–239
21 Dietz HP, Mouritsen L, Ellis G, Wilson PD. Does the tension-free vaginal tape stay where you put it? Am J Obstet Gynecol 2003;188(04):950–953
22 Lin KL, Juan YS, Lo TS, Liu CM, Tsai EM, Long CY. Three-dimensional ultrasonographic assessment of compression effect on urethra following tension-free vaginal tape and transobturator tape procedures. Ultrasound Obstet Gynecol 2012;39(04):452–457
23 Dietz HP, Mouritsen L, Ellis G, Wilson PD. How important is TVT location? Acta Obstet Gynecol Scand 2004;83(10):904–908
24 Kociszewski J, Rautenberg O, Kolben S, Eberhard J, Hilgers R, Viereck V. Tape functionality: position, change in shape, and outcome after TVT procedure–mid-term results. Int Urogynecol J Pelvic Floor Dysfunct 2010;21(07):795–800
25 Spelzini F, Cesana MC, Verri D, Polizzi S, Frigerio M, Milani R. Three-dimensional ultrasound assessment and middle term efficacy of a single-incision sling. Int Urogynecol J Pelvic Floor Dysfunct 2013;24(08):1391–1397

Regional and Socioeconomic Differences in the Coverage of the Papanicolau Test in Brazil: Data from the Brazilian Health Survey 2013

Diferenças regionais e socioeconômicas na cobertura do exame Papanicolau no Brasil: Dados da Pesquisa Nacional de Saúde 2013

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Abstract

Purpose To evaluate the coverage of the Papanicolaou test in Brazil and the associated factors.

Methods Cross-sectional study based on data from the Brazilian Health Survey 2013 comprising the proportion of 25- to 64-year-old women who had undergone a Papanicolaou test within the previous 3 years, categorized by sociodemographic variables and access to healthcare services.

Results The screening coverage in Brazil was of 79.4% (95% confidence interval [95%CI]: 78.4–80.3), showing significant differences between the different states of the country, with the highest rate in the state of Roraima (86.5; 95%CI: 83.5–89.4), and the lowest one in the state of Maranhão (67.7; 95%CI: 61.3–74.0). Undergoing the test was significantly more frequent among married women (83.6%; 95%CI: 82.4–84.8), those with higher educational levels (88.7%; 95%CI: 87.0–90.5), of white ethnicity (82.6%; 95%CI: 81.3–83.9) and who reside in urban areas (80.1%; 95%CI: 79.1–81.2). Those who had undergone the test more than three years prior to the survey and the ones who had never undergone it were associated with a lower level of education, being of black or brown ethnicity, single or divorced, and rural dwellers.

Conclusions The coverage of cervical cancer screening in Brazil is below the recommended rate and presents regional and sociodemographic disparities.

Keywords
- papanicolaou test
- cervical neoplasms
- women's health
- early detection of cancer
- inequalities in health
- epidemiology

Resumo

Objetivo Avaliar a cobertura do exame Papanicolau no Brasil e os fatores associados.

Métodos Estudo transversal a partir dos dados da Pesquisa Nacional de Saúde 2013 relativos à proporção de mulheres de 25 a 64 anos que realizaram pelo menos um exame Papanicolau nos últimos 3 anos, categorizados por variáveis sociodemográficas e de acesso aos serviços de saúde.

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Palavras-chave
- teste de Papanicolau
- neoplasias do colo do útero
- saúde da mulher
- detecção precoce de câncer
- desigualdades em saúde
- epidemiologia

Resultados A cobertura do rastreio foi de 79,4% no Brasil (intervalo de confiança de 95% [$IC_{95\%}$]: 78,4–80,3), com diferença significativa entre as unidades federativas, sendo maior no estado de Roraima (86,5%; $IC_{95\%}$: 83,5–89,4) e menor no Maranhão (67,7%; $IC_{95\%}$: 61,3–74,0). A realização do exame foi significativamente maior entre as mulheres casadas (83,6%; IC $_{95\%}$: 82,4–84,8), com nível de instrução mais elevado (88,7%; $IC_{95\%}$: 87,0–90,5), de etnia branca (82,6%; $IC_{95\%}$: 81,3–83,9), e que residem em área urbana (80,1%; $IC_{95\%}$: 79,1–81,2). As que realizaram o exame havia mais de 3 anos e as que nunca realizaram estiveram associadas a menor nível de instrução, a mulheres negras e pardas, a ser solteira ou separada, e a moradoras de área rural.

Conclusões A cobertura do rastreio para o câncer e colo de útero no Brasil tem proporção abaixo da recomendada, e apresenta disparidades regionais e sociodemográficas.

Introduction

Cervical cancer is the third most common type of cancer in women, and one of the leading causes of cancer death among women worldwide.[1] With an estimated 529,000 cases and 275,000 deaths per year, the burden of cervical cancer varies considerably among countries, with more than 85% of the global burden of the disease distributed in low- and middle-income countries.[2] The disparity in the incidence and mortality of cervical cancer between low- and high-income countries and the inequalities within each country are mainly related to the prevalence of human papillomavirus (HPV) infection, and to differences in the access to screening and in the treatment of malignant lesions.[3]

Performing a periodic cervical cytopathology examination is the primary screening strategy for cervical cancer and its precursor lesions, because of the acceptable sensitivity and specificity, low cost, safety in the execution and acceptance by women.[4] The evolution of an incipient cervical lesion to an invasive form is slow, and can extend for up to 20 years. This feature enables the effective control of the malignant neoplasm through proper screening.[5]

The introduction of the high-quality screening test using cytology (Papanicolaou test, also called Pap test) has led to a marked reduction in the mortality from cervical squamous cell cancer, which accounts for 80 to 90% of cervical cancers. Since its introduction in the United States in the mid-1950's, cervical cancer, then the most common cause of cancer death in women, now ranks 14th among deaths due to cancer in the country.[6]

In 2011, the American Cancer Society (ACS), in collaboration with other associations, reiterated by consensus the recommendation to perform the screening test for the prevention and early detection of precancerous lesions and cancer itself. The ACS consensus recommends that the exam be performed for women aged between 21 and 65 years, with a 3-year interval for those with negative cytology.[7] Following the recommendations of the World Health Organization (WHO), the Brazilian Cancer Institute established, as a guideline for cervical cancer screening, the performance of the Pap test in women aged between 25 and 64 years, with a 3-year interval between examinations after 2 negative annual tests, to be discontinued after the age of 64, for those women who have had at least 2 consecutive negative tests in the previous 5 years.[8,9]

According to the recommended protocols, the minimum coverage for the test should reach 80% of the target population. However, Brazil still does not have a population-based information system, a crucial item for organized tracking. As a direct consequence of this, there is no control of the women who undergo the examinations, or of the periodicity with which they do it, which characterizes the country in an opportunistic tracking scenario.[9–11]

The high incidence and mortality due to this type of cancer among women in Brazil indicates that the measures adopted to track this disease may not be leading to the expected results.[2] In recent years, a reduction in cervical cancer mortality has been observed in Brazil, but the magnitude of this reduction has been unequally distributed among the Brazilian regions.[12] Aspects related to the inequalities in the supply of and access to the screening examination have been widely studied, and they represent a restrictive step for the control of cervical cancer in several regions of the country.[13]

In Brazil, the National Program for Cervical Cancer Control aims to ensure the access to the preventive examination for women in the priority age group, qualification of diagnosis, and to provide treatment for precursor lesions. Despite the improvement achieved in mortality indicators, this reduction is below the expectations.[14]

Recognizing the scope of a preventive program and the factors related to the low adherence to the proposed model can contribute to the development of more effective public policies, in line with the territorial reality. Identifying inequalities is a key aspect in the monitoring and evaluation of women's healthcare policies.

The objective of this study was to analyze the inequalities in the coverage of cervical cancer screening in Brazil and the social and economic factors related to the non-adherence to the current preventive program.

Methods

This is a cross-sectional descriptive study with data from the Brazilian Health Survey 2013 (*Pesquisa Nacional de Saúde* [PNS, in the Portuguese acronym] 2013),[15] conducted by the Brazilian Institute of Geography and Statistics (IBGE, in the Portuguese

acronym) in partnership with the Brazilian Ministry of Health (BMH) and Oswaldo Cruz Foundation (Fiocruz, in the Portuguese acronym). The research population was composed of adults (aged $\geq$ 18 years) living in private households throughout the country, and those living in tents, military bases, lodges, boats, penitentiaries, penal colonies, prisons, jails, asylums, orphanages, convents and hospitals were excluded.

The sample size was defined considering the desired precision level for the estimates of some indicators of concern. The minimum size defined for the sample was 1,800 households per state. The PNS chose a total of 81,187 households randomly, with 1 individual selected per household. After completing the collection of data, interviews were conducted in 64,348 households, which resulted in a non-response rate of 8.1%.

The sampling plan employed was the three-stage cluster sampling, with stratification of the primary sampling units. The census tracts make up the primary sampling units (PSUs), the households represent second-stage units, and the adult dwellers are the third-stage units.

Sampling weights were defined for the PSUs, the households and all their dwellers, as well as the weight for the selected resident. The latter was calculated considering the weight of the corresponding household, the probability of the resident's selection, adjustments related to non-response by sex, and calibration by total population according to sex and age groups, estimated by the weight of all residents.

All considerations regarding the sampling plan, weighting and effects of the PNS delineation are contained in the publications by Souza-Júnior et al and Damacena et al.[16,17]

The PNS questionnaire was divided into modules that address characteristics of the household, of all residents (schooling, income, work, people with disabilities, coverage of healthcare insurance, use of healthcare services, health of children under 2 years of age, health of the elderly), and of the selected adult population (lifestyles, perception of health status, accidents and violence, chronic diseases, women's health, prenatal care, oral health and medical care).

By means of Module R, the PNS addressed the topic 'women's health,' including questions on preventive testing, reproductive history and family planning. The issues of interest in the present study are related to the proportion (%) of 25- to 64-year-old women who underwent a screening examination for cervical cancer. For the purpose of the present study, the analyzed variable was: 'When was the last time you underwent a screening test for cervical cancer?' It was categorized into 'Proportion of 25- to 64-year-old women who had undergone the examination within the 3 years prior to the survey,' 'Proportion of 25- to 64-year-old women who had undergone the examination more than 3 years prior to the survey,' and 'Proportion of 25- to 64-year-old women who had never undergone the test.' For the calculation of these indicators, the number of women between 25 and 64 years of age who reported never having had sex was used as the denominator.

The proportions of the sample that underwent the cytopathology examination, presented in percentages (%) with their respective 95% confidence intervals (95%CIs), were estimated for the population of women between the ages of 25 and 64 who had already had sex, according to the sociodemographic variables and the variables on the access to the health service. The following variables were used in the description: states (26 states and the Federal District), level of education (no schooling/incomplete elementary school; complete elementary school/incomplete high school; complete high school/ incomplete higher education; complete higher education); ethnicity/ skin color (white, black and brown); civil status (single, married, separated, divorced, widowed); place of residence (urban and rural), coverage of the examination (public and private healthcare networks); the time it took to get the result; and the reason mentioned for the failure to perform the examination. The data were tabulated using the Tabnet tool (IT Depart in SUS, Health Ministery. Available at: http://tabnet.datasus.gov.br) on the website of the Computer Science Department of the Brazilian Unified Healthcare System (Datasus, in the Portuguese acronym), and were expressed in percentages with their 95%CIs. In order to make the tables and figures, the data were organized into Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA, US) spreadsheets.

The PNS project was approved by the Brazilian Commission for Research Ethics (Conep, in the Portuguese acronym) on July 8, 2013, under number 10853812.7.0000.0008. This current study is a research that used secondary data available on official websites of the BMH, and was exempted from evaluation by a research ethics committee, in accordance with Resolution 466/2012 of the Brazilian Health Council.

Results

Among the Brazilian women aged 25–64 years, 79.4% (95%CI: 78.4–80.3) reported having undergone at least 1 cervical cancer screening test within the 3 years prior to the survey. There was a significant difference in the coverage percentage among the states: it was higher in the states of Roraima (95%CI: 83.5–89.4), Santa Catarina (95%CI: 80.5–88.5), and Espírito Santo (95%CI: 79.9–88.5), while the states with the lowest percentages were Maranhão (95%CI: 61.3–74.0), Amapá (95%CI: 64.0–73.6), and Ceará (95%CI: 65.2 -72.8), as shown in ►**Fig. 1**.

The percentages of women aged 25–64 years in Brazil who reported never having undergone the screening test, or who had undergone the test more than 3 years prior to the survey were 9.03% (95%CI: 8.31–9.74) and 11.6% (95%CI: 10.90–12.29) respectively. The states that presented the highest percentages of examinations performed more than 3 years before the survey were Amapá (95%CI: 13.93–22.20), Sergipe (95%CI: 13.56–20.67), Maranhão (95% CI: 12.88–21.25), and Ceará (95%CI: 12.91–19.57), with a significant difference in relation to the other states. It should be noted that the nine states of the Northeast region presented this marker with percentages above the observed national mean (►**Fig. 2**).

The proportion of women aged 25–64 years who had never undergone the cervical cancer screening test was significantly higher in the states of Pará (95%CI: 12.09–20.08), Alagoas (95% CI: 11.60–19.07), Maranhão (95%CI: 9.92–20.60), and Paraíba (95%CI: 11.18–18.38). Of the eleven states that presented these proportions above the national mean, seven belong to the Northeast region of Brazil (►**Fig. 3**).

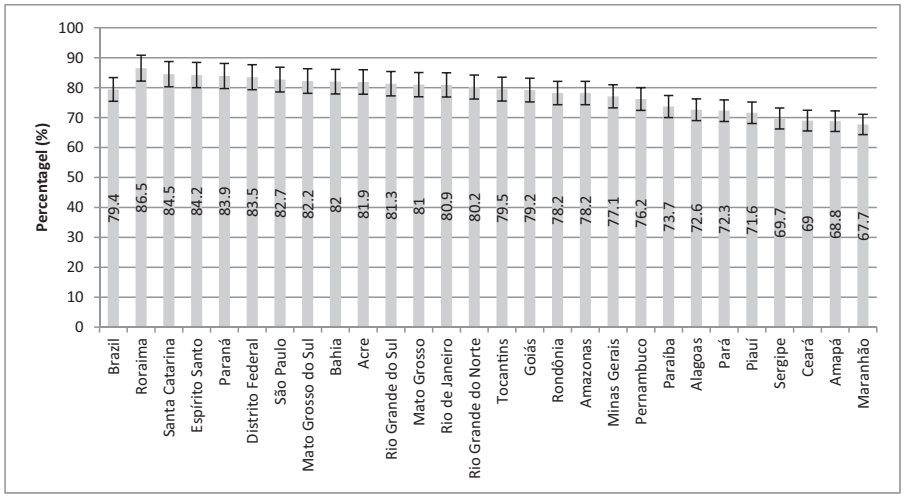

Fig. 1 Percentage of 25- to 64-year-old women who underwent the cytopathology examination within the past 3 years in Brazil as a whole, in the different states, and in the Federal District. Source: Brazilian Health Survey, 2013.[15] Note: The bars represent the 95% confidence intervals of the percentages presented.

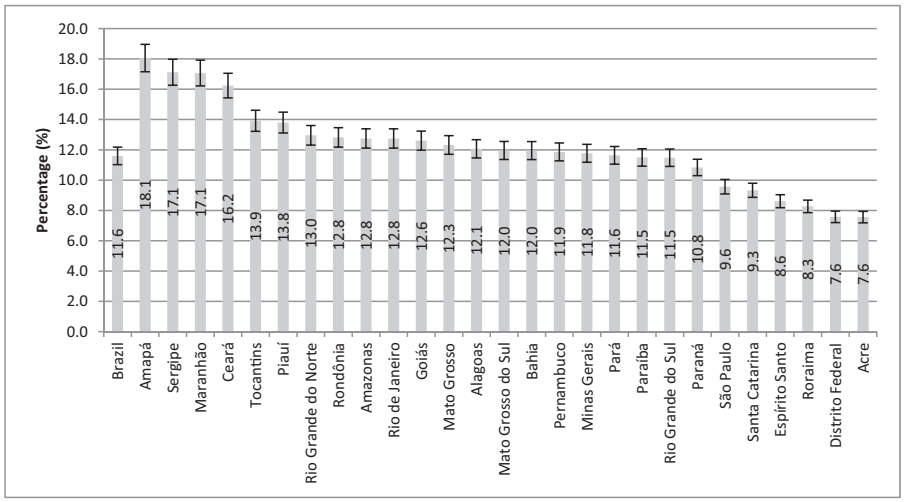

Fig. 2 Percentage of women aged 25 to 64 years who underwent cytopathology examination more than 3 years ago in Brazil as a whole, in the different states, and in the Federal District. Source: Brazilian Health Survey, 2013.[15] Note: The stems represent the 95% confidence intervals of the percentages presented.

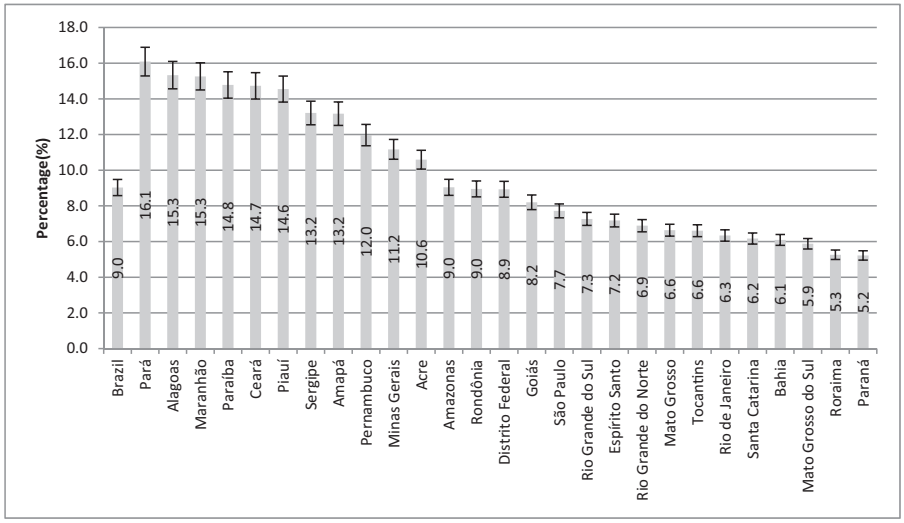

Fig. 3 Percentage of women aged 25 to 64 years who have never undergone the cytopathology examination in Brazil as a whole, in the different states, and in the Federal District. Source: Brazilian Health Survey, 2013.[15] Note: The stems represent the 95% confidence intervals of the percentages presented.

►**Table 1** shows the proportion of women who underwent screening for cervical cancer according to sociodemographic factors and access to health services. The screening within the 3-year period before the study was significantly higher among married women (83.6%; 95%CI: 82.4–84.8), those who presented the two highest levels of education (88.7%; 95%CI: 87.0–90.5, with complete higher education; and 83.3%; 95%CI: 81.8–84.8 ,with complete high school and incomplete higher education), those with white skin color/ethnicity (82.6%; 95%CI: 81.3–83.9), and among those living in urban areas (80.1%; 95%CI: 79.1–81.2). Having healthcare insurance as a means of accessing the test was related to a higher proportion of women who underwent at least 1 examination within the last 3 years (93.4%; 95%CI: 92.5–94.4). The results of the test arrived within ~ 3 months for most women who underwent the screening test up to 3 years prior to the survey.

As for the women who underwent the Pap test more than 3 years before the survey, the percentages were higher among widows (18.12%; 95%CI: 14.87–21.37) and separated women (17.62%; 95%CI: 12.11–23.12), those with no schooling or incomplete elementary school (15.82%; 95%CI: 14.56–17.08), and those with brown skin color/ethnicity (13.24%, 95%CI: 12.15–14.32) compared with those with white skin color/

Table 1 Coverage of cervical cancer screening according to sociodemographic variables and access to the healthcare services. Brazilian Health Survey, 2013[15]

Variables	Pap test within the past 3 years	Pap test more than 3 years ago	Never underwent Pap test
	Percentage (95%CI)	Percentage (95%CI)	Percentage (95%CI)
Civil status			
Married	83.6 (82.4–84.8)	10.47 (9.52–11.43)	5.89 (5.13–6.65)
Separated	71.9 (64.9–78.9)	17.62 (12.11–23.12)	10.51 (4.62–16.39)
Divorced	80.9 (77.4–84.4)	14.41 (11.08–17.74)	4.71 (3.21–6.20)
Widow	72.9 (69.0–76.9)	18.12 (14.87–21.37)	8.95 (6.56–11.34)
Single	74.9 (73.3–76.4)	11.08 (10.05–12.11)	14.06 (12.72–15.41)
Educational level			
No schooling or incomplete elementary school	72.1 (70.5–73.8)	15.82 (14.56–17.08)	12.04 (10.81–13.27)
Complete elementary school and incomplete high school	77.8 (75.2–80.3)	13.32 (11.23–15.40)	8.92 (7.28–10.56)
Complete high school and incomplete higher education	83.3 (81.8–84.8)	8.48 (7.40–9.57)	8.21 (7.03–9.38)
Complete higher education	88.7 (87.0–90.5)	7.11 (5.70–8.52)	4.14 (3.06–5.22)
Skin color or ethnicity			
White	82.6 (81.3–83.9)	10.31 (9.33–11.28)	7.05 (6.07–8.02)
Black	77.4 (74.1–80.8)	11.11 (9.02–13.20)	11.45 (8.39–14.51)
Brown	75.9 (74.4–77.4)	13.24 (12.15–14.32)	10.87 (9.78–11.96)
Place of residence			
Urban	80.1 (79.1–81.2)	11.52 (10.77–12.28)	8.34 (7.57–9.10)
Rural	74.1 (71.6–76.6)	12.10 (10.32–13.89)	13.82 (11.95–15.70)
Origin of the examination			
Brazilian Unified Healthcare System	83.6 (82.5–84.8)	16.37 (15.24–17.50)	–
Private	89.4 (87.8–91.0)	10.58 (8.95–12.21)	–
Healthcare insurance	93.4 (92.5–94.4)	6.56 (5.61–7.51)	–
Period it took the test result to arrive			
Within 1 month after the examination	88.7 (87.8–89.6)	11.27 (10.36–12.18)	–
Between 1 and 3 months after the examination	85.0 (83.5–86.6)	14.98 (13.41–16.54)	–
Between 3 and 6 months after the examination	83.7 (80.0–87.5)	16.25 (12.46–20.04)	–
More than 6 months after the examination	73.5 (61.8–85.2)	26.50 (14.78–38.23)	–
Has never received	71.4 (63.0–79.9)	28.57 (20.10–37.04)	–
Has never tried to get the result	57.6 (47.0–68.1)	42.44 (31.87–53.00)	–

Abbreviation: 95%CI, 95% confidence interval.

Table 2 Reasons mentioned for failure to undergo cervical cancer screening in Brazil. Brazilian Health Survey, 2013[15]

Reasons	Percentage (%) - 95% CI
Not thinking it is necessary	49.12 (45.33–52.91)
Being ashamed	10.5 (8.33–12.67)
Never being instructed to undergo the exam	22.32 (18.74–25.90)
Having financial difficulties	1.34 (0.71–1.97)
Had difficulty making an appointment	4.08 (2.80–5.37)
The waiting time in the healthcare service is too long	1.84 (1.06–2.62)
Others	10.8 (8.63–12.69)

Abbreviation: 95%CI, 95% confidence interval.

ethnicity (10.31%, 95%CI 9.33–11.28). There was no statistically significant difference with regard to the place of residence. There was a greater proportion of this inadequate coverage when the Brazilian Unified Healthcare System (SUS, in the Portuguese acronym) was the means of accessing the last examination (16.37%; 95%CI: 15.24–17.50). Most of these women reported they had never tried to get the result, or had never received it. In that group, 26.50% of the women received the result 6 months after the examination.

Never having performed the cytopathology examination was more prevalent among single women (14.06%; 95%CI: 12.72–15.41), those with no schooling or with incomplete elementary school (12.04%; 95%CI: 10.81–13.27), and among black women (11.45%; 95%CI: 8.39–14.51) compared with white women (7.05%; 95%CI: 6.07–8.02), and among those living in rural areas (13.82%; 95%CI: 11.95–15.70). The main reasons for not undergoing the test were: "not finding it necessary" (49.12%; 95% CI: 45.33–52.91) and "never being instructed to undergo the test" (22.32%; 95%CI: 18.74–25.90) (►**Table 2**).

Discussion

The results of the present study demonstrate that there is a marked regional and socioeconomic inequality in the coverage of the cytopathology examination in Brazil. They also show that the percentage of the coverage is below that which is recommended by the World Health Organization (WHO).

Despite this, some studies have reported a significant increase in the coverage rate of the exam in Brazil in the last decades. In a systematic review that described the Pap smear coverage in Brazil between the 1980's and 2000's, which was based on population-based cross-sectional studies, it was indicated that the coverage of the examination in Brazil ranged from 60 to 77%, regarding the execution of at least 1 test in the last 3 years prior to the survey.[18] A study performed in the state of Santa Catarina in 2009 recorded that the coverage rate of this exam was 86%.[19] A comparison between the coverage rate in the city of São Paulo in 1987 and 2002 showed a 24% increase in prevalence, which ranged from 68.8 to 85% along the years studied.[20] In the city of Boa Vista, in the state of Roraima, a cross-sectional study[13] based on a household survey reported a prevalence of 85.7% (95%CI: 82.5–88.5). The evolution of this indicator for Brazil can also be confirmed by comparing the results of the present study, which indicated a 79.4% coverage rate for the examination performed within the 3 years prior to the survey (IBGE, 2013),[15] to the data obtained in the National Household Sampling Survey (PNAD, in the Portuguese acronym) in 2003, which registered a 65.5% coverage rate among women aged between 18 and 69 years.[21]

The reduction in the mortality rate due to cervical cancer in Brazil in the last decades may be a consequence of the Pap test coverage expansion, since mortality is attenuated because of a better access to diagnostic and therapeutic measures. Barbosa et al[2] observed a downward trend in cervical cancer mortality rates in Brazil between 1996 and 2010, at the proportion of 1.7% per year, with the highest reduction rates observed for the South (annual percentage change [APC] = −3.9%), Southeast (APC = −3.0%) and Midwest (APC = -2.0%) regions. With similar results, the study by Girianelli et al[12] reported that, between 1980 and 2010, the drop in cervical cancer mortality occurred for all women in the Southeast and South, the most developed regions in the country, but reached only women living in the capitals of the North and Northeast regions. In several parts of the world, the incidence and risk of cervical cancer mortality has declined. In developed countries, the number of new cases has been reduced by ~ 80% because of an effective program for the detection and treatment of precancerous lesions.[22]

These results raise the hypothesis that, although there has been progress in the coverage rate of the cervical cancer screening test in Brazil, and a reduction in mortality rates for cervical cancer, the expansion of the Pap test coverage may not have developed in the same way among the Brazilian regions.

This hypothesis can be corroborated by the findings of the present study, which demonstrate that the states in the North and Northeast of Brazil recorded the lowest percentage of examinations performed within the last three years, in addition to the greater percentage of women who had never taken the test, which demonstrates the intense inequality in the Pap test coverage among the Brazilian regions.

In Brazil, the access of the population to different levels of healthcare is one of the meanings attributed to comprehensiveness. Even though the constitutional guarantee of universal access to healthcare has overcome formal barriers, difficulties related to the access and continuity of care remain in both basic care and specialized services. The organization based on spontaneous demand, a basic characteristic of the private healthcare model, is traditionally found in public healthcare services in the country.[23] Brazilian studies show that most women who undergo the Pap test do it spontaneously, and that emphasizes the relationship between opportunistic tracking and the low coverage rate of the examinations, often with excess examinations in some women, and the exclusion of others, probably the ones that would most benefit from the test.[11,13,24]

One of the factors that contribute the inefficiency of an unorganized program in Brazil is the difficulty related to diagnostic confirmation, follow-up and treatment of the

tracked cases. The information systems of the SUS are based on procedures and not on the person, as is the case with the Brazilian Cervical Cancer Information System (Siscolo, in the Portuguese acronym), which records the cytological exams with altered diagnoses performed in Brazil, but does not allow the screening history of these women to be recorded and, consequently, does not allow the identification of the ones who are not engaged in control or who underwent the test three or more years ago.[10]

In spite of the adequacy of the structure and work process of the basic care teams in Brazil in the prevention of cervical cancer, the results show that only half of all health units that compose the basic care network in Brazil has adequate structures for cervical cancer screening by means of cytopathology examination, and only 30% of the teams were classified with an adequate working process for the detection of cervical cancer.[25]

However, with the increased coverage of the cytological examination, two different phenomena, closely linked to differences in conditions of access, use and performance of health services, can be observed. On the one hand, there is the drop in the mortality rate in regions where social health conditions can ensure treatment and follow-up for all patients with altered exams, rendering possible the cure of the disease. On the other hand, there is the increased mortality rate in less developed regions, where cure cannot be guaranteed, or where the adherence of the target population is still limited, thus determining that part of the patients will only be cared for at an advanced stage of the disease, with few possibilities of cure.[26]

Therefore, it is important to recognize that, for the analysis of the reduction seen in cervical cancer incidence and mortality rates, other relevant points should be considered in conjunction with the Pap test coverage, such as the quality of the cervical cytology screening examinations that are performed, the access to services for biopsy and diagnostic confirmation, diagnostic examinations to stage confirmed cases, and access to cancer treatment: surgery, radiotherapy and chemotherapy.[14]

In the present study, undergoing the Papanicolaou test was closely related to the women's socioeconomic characteristics: those who underwent the examination more than 3 years prior to the survey and those who never underwent it were associated with women with lower levels of education, single or separated, and living in rural areas. These findings are similar to those described in several studies in Brazil, which found that women without a stable union, with low income and schooling limited to the elementary school presented higher odds of not having undergone the test.[13,27,28]

These findings reinforce the hypothesis that women living in worse socioeconomic conditions were more likely to be diagnosed with advanced cervical cancer.[29]

It is believed that women with low schooling have less power to pressure the healthcare services into providing quality care. Additionally, a low level of education can lead to a lower level of information and understanding, thus resulting in poor adherence to prevention strategies,[11] as it is evidenced that education increases the notion of the importance of regular health assessments and, therefore, the propensity to perform them; moreover, education can improve the understanding of the information, enhance the communication with the doctor, and improve the interpretation of the results.[30]

Other findings that stand out are related to marital status and failure to take the Pap test. It is said that, in general, the prevention measure is performed in conjunction with routine gynecological, obstetric or family planning activities, so that women living with their partners are more likely to use the healthcare services.[27,28,31]

The data also indicate that, for an important part of the population, especially the low-income population, the lack of knowledge about the need to undergo the exam and the lack of orientation toward its execution represent risk factors for the non-adherence to the preventive program. This fact raises the need for screening expansion, aiming at the most vulnerable groups in society, and for the development of comprehensive and effective preventive strategies that are aligned with local realities and consider education actions for the target audience in the context of primary healthcare.[13]

Conclusion

The present study verified that the coverage of the cervical cancer screening test for Brazilian women aged 25 to 64 years was close to the goal recommended by the BMH. However, lower coverage was observed in the less-favored social groups, indicating the strong influence of socioeconomic, demographic and healthcare disparities, as well as lack of continuity in healthcare and education actions for the prevention of cervical cancer.

Healthcare services should provide clinical and gynecological assistance, guidance on the control of sexually transmitted diseases and cervical cancer, and assistance in conception and contraception. The supply of such services is directly linked to the control of several factors related to cervical cancer. However, the barriers to its control are mainly related to failures in the screening programs and to the difficulty in accessing healthcare procedures.

In the present study, the cross-sectional design did not enable the use of temporality as a criterion of causality, since risk and outcome factors were measured at the same time, and the reverse causality bias cannot be eliminated, which constitutes one of the limitations of this study. The subject covered is personal and intimate, related to women's reproductive health, and this may have influenced the results. However, the sample size and the correct research procedures adopted strengthen the reliability of the data. Because this is a population survey, this study enables the identification of the actual coverage of the Papanicolaou test, and not just the number of exams performed in the public healthcare system.

References

1 Singh GK, Azuine RE, Siahpush M. Global inequalities in cervical cancer incidence and mortality are linked to deprivation, low socioeconomic status, and human development. Int J MCH AIDS 2012;1(01):17–30

2 Barbosa IR, Souza DLB, Bernal MM, Costa IdoC. Regional inequalities in cervical cancer mortality in Brazil: trends and projections through to 2030. Cien Saude Colet 2016;21(01):253–262
3 Tsu V, Jerónimo J. Saving the world's women from cervical cancer. N Engl J Med 2016;374(26):2509–2511
4 Manica ST, Drachler MdeL, Teixeira LB, et al. Socioeconomic and regional inequalities of pap smear coverage. Rev Gaucha Enferm 2016;37(01):e52287
5 Falcão GB, Ibiapina FLP, Feitosa HN, et al. Fatores associados à realização de citologia para prevenção de câncer do colo uterino em uma comunidade urbana de baixa renda. Cad Saude Colet 2014;22(02):165–172
6 Simard EP, Naishadham D, Saslow D, Jemal A. Age-specific trends in black-white disparities in cervical cancer incidence in the United States: 1975-2009. Gynecol Oncol 2012;127(03):611–615
7 Saslow D, Solomon D, Lawson HW, et al; ACS-ASCCP-ASCP Cervical Cancer Guideline Committee. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. CA Cancer J Clin 2012;62(03):147–172
8 Brasil. Instituto Nacional de Câncer José Alencar Gomes da Silva. Coordenação de Prevenção e Vigilância. Divisão de Detecção Precoce e Apoio à Organização de Rede. Diretrizes brasileiras para o rastreamento do câncer do colo do útero. Rio de Janeiro: INCA; 2016
9 World Health Organization. WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention. Geneva: WHO; 2013
10 Vale DBAP, Morais SS, Pimenta AL, Zeferino LC. Assessment of the cervical cancer screening in the Family Health Strategy in Amparo, São Paulo State, Brazil. Cad Saude Publica 2010;26(02):383–390
11 Ribeiro L, Bastos RR, Vieira MdeT, Ribeiro LC, Teixeira MTB, Leite ICG. Opportunistic screening versus missed opportunities: nonadherence to Pap smear testing in women attending prenatal care. Cad Saude Publica 2016;32(06):e00001415
12 Girianelli VR, Gamarra CJ, Azevedo e Silva G. Disparities in cervical and breast cancer mortality in Brazil. Rev Saude Publica 2014; 48(03):459–467
13 Navarro C, Fonseca AJ, Sibajev A, et al. Cervical cancer screening coverage in a high-incidence region. Rev Saude Publica 2015;49:17
14 Sousa AMV, Teixeira CCA, Medeiros SD, et al. [Cervical cancer mortality in the state of Rio Grande do Norte, Brazil, 1996-2010: time trends and projections up to 2030]. Epidemiol Serv Saude 2016;25(02):311–322 Portuguese
15 Instituto Brasileiro de Geografia e Estatística [Internet]. Pesquisa Nacional de Saúde: 2013: acesso e utilização dos serviços de saúde, acidentes e violências: Brasil, grandes regiões e unidades da federação. Rio de Janeiro: IBGE; 2015 [cited 2016 Jan 12]. Available from: http://biblioteca.ibge.gov.br/visualizacao/livros/liv94074.pdf
16 Souza-Júnior PRB, Freitas MPS, Antonaci GA, Szwarcwald CL. Desenho da amostra da Pesquisa Nacional de Saúde 2013. Epidemiol Serv Saúde. 2015;24(02):207–216
17 Damacena GN, Szwarcwald CL, Malta DC, et al. O processo de desenvolvimento da Pesquisa Nacional de Saúde no Brasil, 2013. Epidemiol Serv Saúde. 2015;24(02):197–206
18 Martins LFL, Thuler LCS, Valente JG. [Coverage of the Pap smear in Brazil and its determining factors: a systematic literature review]. Rev Bras Ginecol Obstet 2005;27(08):485–492 Portuguese
19 Gasperin SI, Boing AF, Kupek E. Cervical cancer screening coverage and associated factors in a city in southern Brazil: a population-based study. Cad Saude Publica 2011;27(07):1312–1322
20 Ozawa C, Marcopito LF. [Papanicolaou smear screening: coverage in two home surveys applied in the city of São Paulo in 1987 and 2001-2002]. Rev Bras Ginecol Obstet 2011;33(05):238–245 Portuguese
21 Novaes HMD, Braga PE, Schout D. Fatores associados à realização de exames preventivos para câncer nas mulheres brasileiras, PNAD 2003. Cien Saude Colet 2006;11(04):1023–1035
22 Forouzanfar MH, Foreman KJ, Delossantos AM, et al. Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. Lancet 2011;378(9801):1461–1484
23 Brito-Silva K, Bezerra AFB, Chaves LDP, Tanaka OY. Integrality in cervical cancer care: evaluation of access. Rev Saude Publica 2014; 48(02):240–248
24 Diniz AS, Xavier MB, Braga PP, Guimarães EAA. Assistência à saúde da mulher na atenção primária: prevenção do câncer do colo do útero. Rev APS. 2014;16(03):333–337
25 Tomasi E, Oliveira TF, Fernandes PAA, et al. Structure and work process in the prevention of cervical cancer in Health Basic Attention in Brazil: Program for the Improvement of Access and Quality. Rev Bras Saude Mater Infant 2015;15(02):171–180
26 Gamarra CJ, Valente JG, Azevedo e Silva G. Magnitude of mortality from cervical cancer in the Brazilian Northeast and socioeconomic factors. Rev Panam Salud Publica 2010;28(02):100–106
27 Albuquerque KM, Frias PG, Andrade CLT, Aquino EML, Menezes G, Szwarcwald CL. Pap smear coverage and factors associated with non-participation in cervical cancer screening: an analysis of the Cervical Cancer Prevention Program in Pernambuco State, Brazil. Cad Saude Publica 2009;25(Suppl 2):S301–S309
28 Borges MFSO, Dotto LMG, Koifman RJ, Cunha MdeA, Muniz PT. Prevalence of uterine cervical cancer testing in Rio Branco, Acre State, Brazil, and factors associated with non-participation in screening. Cad Saude Publica 2012;28(06):1156–1166
29 Müller EV, Biazevic MGH, Antunes JLF, Crosato EM. Socioeconomic trends and differentials in mortality due to cervical cancer in the State of Paraná (Brazil), 1980-2000. Cien Saude Colet 2011; 16(05):2495–2500
30 Arrossi S, Ramos S, Paolino M, Sankaranarayanan R. Social inequality in Pap smear coverage: identifying under-users of cervical cancer screening in Argentina. Reprod Health Matters 2008;16(32):50–58
31 Lage AC, Pessoa MC, Velásquez Meléndez JG. Fatores associados à não realização do Teste de Papanicolaou em Belo Horizonte, Minas Gerais, 2008. Rev Min Enferm. 2013;17(03):565–576

The Preference of Women and Men Regarding Female Genital Depilation

A preferência de mulheres e homens em relação à depilação genital feminina

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Abstract

Purpose To evaluate the preferences of women and men regarding female pubic hair depilation and identify possible reasons for these preferences.

Methods This is a cross-sectional study of men and women over 18 years old who were invited by the official blog of our institution to respond anonymously to an online and self-administered questionnaire made by the researchers. The analyses were made using the Statistical Analysis System (SAS, SAS Inc., Cary, NC, US) software, version 9.3, and contingency tables were used to verify the distribution of variables. The univariate statistical analysis was performed using the Pearson chi-squared test, and the differences for values of $p < 0.05$ were considered significant.

Results We obtained data from 69,920 subjects (52,787 women and 17,133 men). The mean age was 31.9 years for men, and 28.5 years for women. Most women (64.3%) and men (62.2%) preferred complete removal of female pubic hair, and this preference was more pronounced in younger women and men. Most women reported performing depilation at home (55.8%), with 44.4% using hot wax and 40.1% using a razor blade. About half of the women (44.7%) and men (50.1%) reported sexual activity, having intercourse 2 to 3 times per week. The frequency of intercourse and sexual satisfaction in women correlated with total pubic hair removal.

Conclusion Most Brazilian women and men prefer the complete removal of female pubic hair, especially those who are younger and more sexually active. Women who are satisfied with the appearance of their own genitalia have a stronger preference for complete removal of pubic hair.

Keywords
- depilation
- hair removal
- genitalia
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- internet
- sexual behavior

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Resumo

Objetivos Avaliar a preferência de mulheres e homens em relação à depilação genital feminina, e identificar possíveis razões envolvidas nessa preferência.

Método Estudo transversal em que homens e mulheres com mais de 18 anos foram convidados por meio do blog oficial de nossa instituição a responder anonimamente a um formulário on-line e autoadministrado de autoria dos pesquisadores. As análises foram realizadas no programa Statistical Analysis System (SAS, SAS Inc., Cary, Carolina do Norte, EUA), versão 9.3, e tabelas de contingência foram construídas para verificar a distribuição entre as variáveis. A análise estatística univariada foi realizada com o teste qui-quadrado de Pearson, e foram consideradas significativas as diferenças para $p < 0,05$.

Resultados Foram obtidos dados de 69.920 indivíduos (52.787 mulheres e 17.133 homens). A idade média dos indivíduos foi de 31,9 anos entre os homens, e de 28,5 entre as mulheres. A maioria das mulheres (64,3%) e dos homens (62,2%) preferiram a genitália feminina completamente depilada, e essa preferência foi mais pronunciada em mulheres e homens mais jovens. A maioria das mulheres afirmaram se depilar em casa (55,8%), e 44,4% delas usam cera quente, e 40,1% utilizam lâmina de barbear. Quase metade das mulheres (44,7%) e metade dos homens (50,1%) alegaram ter frequência sexual de 2 a 3 vezes por semana. A frequência sexual das mulheres e a satisfação com sua própria genitália foram positivamente relacionadas com a preferência pela remoção total dos pelos pubianos.

Conclusões A maioria das mulheres e dos homens brasileiros preferem a remoção completa dos pelos genitais femininos, o que é ainda mais pronunciado nos indivíduos mais jovens e sexualmente ativos. As mulheres satisfeitas com a aparência de sua própria genitália tendem a preferir a remoção completa dos pelos pubianos.

Palavras-Chave

- depilação
- remoção de pelos
- genitália
- sexualidade
- internet
- comportamento sexual

Introduction

Women have increasingly removed hair from their pubic regions since the second half of the twentieth century.[1] There are many techniques used for this practice, including hot or cold wax, scissors or clippers, razors, depilatory creams, laser treatment, and electrolysis.[2] Depilation in the pubic region may be related to sexual activity. Moreover, many additional factors may be related to pubic hair depilation, so this subject requires further investigation.

Giraldo et al[3] studied 364 Brazilian college women, and reported that more than 90% practiced pubic hair removal; 57.6% reported partial removal, and 36.8% reported complete removal. In women from the United States, the extent of pubic hair removal appears to be associated with age and physical, social, and economic parameters. DeMaria and Berenson,[4] in particular, collected data from 1,677 women, and reported that the habit of shaving was associated with being white, young (aged between 21–30 years), and at or below normal weight, and with having an annual household income greater than $30,000 and 5 or more sexual partners over the lifetime.[4] This study also reported the main reasons women removed their pubic hair were to achieve a cleaner appearance of the pubic region, and the belief that pubic hair is unattractive.[4]

Another study in the United States reported that women remove their pubic hair for hygienic reasons, comfort, and increased sensation during sex.[5] Women may also remove their pubic hair to improve their sexual attractiveness. For example, in a study with 235 Australian women, Tiggermann and Hodgson[6] observed that 60% of the subjects removed some pubic hair, and that 48% removed most or all of their pubic hair.

Butler et al[7] evaluated the practices and preferences of pubic hair depilation in 1,110 men and women from two universities in the United States. They found that 95% of the subjects removed their pubic hair at least once every 4 weeks; women were more likely to report their status as completely depilated, and men were more likely to prefer sexual partners with completely depilated genitalia.[7] In line with these results, a recent cross-sectional study in the United States examined 3,316 women, and found that most subjects (62%) performed total pubic hair removal, and that older women were less likely to shave their pubic hair.[8] Likewise, a study by Herbenick et al[9] with 2,451 women from the United States observed that complete removal of pubic hair was associated with younger age.

An internet-based study aimed to characterize male preferences regarding vulvar appearance, and found that the subjects preferred the vulva partially (39%) or completely (24%) depilated, and that younger males were more likely to prefer complete hair removal.[10] Schick et al[11] analyzed 647 photos from Playboy magazine published between 1953 and 2007, and 185 photos from this magazine published between 2007 and 2008. They found that the women had significantly less pubic hair over the years.[11] Together, these observations

indicate that the pornography industry has influenced female hair removal habits, because younger people who were exposed to this trend of hair removal for longer periods of their lives tend to show higher rates of complete pubic hair removal compared with older people.

Overall, these previous studies of preferences regarding female pubic hair removal indicate possible relationships with different sociodemographic parameters. However, more studies are needed to examine the factors related to female and male preferences regarding female pubic hair removal to evaluate the reproducibility of previously identified relationships, and to identify additional factors related to preferences. Additionally, most studies on female pubic hair depilation examined individuals from the United States. Studies in other countries can help to establish parallels between different cultures, and identify parameters that globally or locally influence the preference for female pubic hair depilation. Therefore, the aims of this study were to evaluate the preferences of Brazilian men and women regarding female pubic hair removal, and to identify the factors associated with different preferences.

Methods

This cross-sectional internet-based study recruited men and women from Brazil who were at least 18 years-old to fill out an online self-administered survey, without time limitation, entitled "Preference on Female Genital Depilation" from April 30, 2015 to August 31, 2015.The participants were invited via the official blog of the Clinic for Human Sexuality Research, from the Department of Gynecology & Obstetrics of Ribeirão Preto Medical School. This study was broadly publicized in all regions of Brazil via radio interviews, television programs, and an online Brazilian newspaper. The survey form was developed by the researchers based on a previous pilot study (performed between September 18, 2014 and October 18, 2014) that aimed to make the vocabulary of the questionnaire simple and accessible (data not shown). The variables were: sex, age, educational level, region of residence within Brazil, type of female pubic hair depilation preferred, motivation for this preference, sexual orientation, relationship status, weekly intercourse frequency, method and location from which pubic hair is removed, and satisfaction with the appearance of the genital region. This survey is part of a larger study, and contained 22 questions: 12 directed to both sexes, and 10 for women only. The necessary guidelines to understand and address the issues were in the statements of the survey and in each question, and there was no need for additional explanations. All participants were Brazilian men or women, who were at least 18 years old, and had internet access. The participants were excluded if they did not answer all the questions.

The survey used in this research project was approved by the Department of Gynecology & Obstetrics Research Committee and the Ethics Committee of our institution (under protocol number 8497/2014).

The answers of all subjects were viewed through a spreadsheet generated by Google Drive (Google, Inc., Mountain View, CA, US), and stored as Microsoft Excel (Microsoft Corporation, Redmond, WA, US) spreadsheets. The data in the spreadsheets were then imported into the Statistical Analysis System (SAS, SAS Inc., Cary, NC, US) software, version 9.3. Absolute and relative frequencies were estimated by the PROC FREQ procedure. Contingency tables were used to examine the variables of interest, and to determine frequency distributions. The univariate statistical analysis was performed using the Pearson chi-square test, and a $p < 0.05$ was considered significant.

Results

We received responses from 86,187 individuals (66,365 women and 19,822 men). A total of 13,578 women and 104 men were excluded because they were younger than 18 years old and/or due to failure to answer 1 or more questions. Thus, we analyzed data from 69,920 subjects (52,787 women and 17,133 men) (►**Table 1**).

Most women were between 18 and 35 years old (82.14%), and similar proportions were 18–25 years old (42.22%) and 26–35 years-old (39.92%). A smaller percentage of women were older than 36 years old (17.86%). Most men were also between 18 and 35 years old (71.09%), and 28.91% were older than 36 years old. However, a significantly greater portion of the men were 26–35 years old (41.5%) compared with those who were 18–25 years old (17.91%). Most men and women reported having incomplete undergraduate education, complete undergraduate education, or complete postgraduate education. Smaller numbers reported only having incomplete high school or complete high school degrees. Most participants were from the southeastern region of Brazil (women: 49.78%, men: 54.81%).

Most women preferred to use hot wax (44.4%) or a razor blade (40.1%) to remove their pubic hair, and the remainder subjects reported the use of a variety of other methods (15.5%). Most women performed depilation at home (55.8%), and 30.5% had it performed in a beauty salon (►**Table 1**).

Extent of Depilation and Reasons for Preferring Depilation

Most women (64.3%) and men (62.2%) preferred complete depilation of the pubic region; 31.9% of women and 31.4% of men preferred partial depilation; and 2.6% of women and 4.3% of men preferred no depilation. Among women, the main reasons for pubic hair removal were hygiene ($n = 13,120$; 24.8%), a combination of beauty, hygiene, and sexual relations ($n = 12,890$; 24.4%), and hygiene and sexual relations ($n = 7,800$; 14.8%). Among men, the main reasons were beauty ($n = 3,728$; 21.7%), and a combination of beauty, hygiene, and sexual relations ($n = 4,578$; 26.7%). Thus, 37,205 (70.5%) women considered hygiene one of the reasons for their depilatory practice, and 12,488 (72.9%) men considered beauty as one of the reasons for their preference for pubic hair removal.

Table 1 Characteristics of the study participants (52,787 women and 17,133 men)

Variable	Women n (%)	Men n (%)
Age (in years):		
18–25	22,288 (42.22)	5,069 (29.59)
26–35	21,070 (39.92)	7,111 (41.50)
36–45	7,458 (14.13)	3,068 (17.91)
> 45	1,971 (3.73)	1,885 (11)
Level of education:		
Postgraduate	11,569 (21.92)	4,194 (24.48)
Undergraduate (complete)	13,763 (26.07)	5,399 (31.51)
Undergraduate (incomplete)	15,976 (30.27)	4,659 (27.19)
High school (complete)	9,540 (18.07)	2,416 (14.10)
High school (incomplete)	1,565 (2.96)	380 (2.22)
Other	374 (0.71)	85 (0.50)
What region of Brazil are you from?		
Midwest	5,098 (9.66)	1,725 (10.07)
Northeast	9,551 (18.09)	3,037 (17.73)
North	2,393 (4.53)	504 (2.94)
Southeast	26,277 (49.78)	9,390 (54.81)
South	9,468 (17.94)	2,477 (14.46)
What kind of female genital depilation do you prefer?		
Complete	33,927 (64.27)	10,655 (62.19)
Partial	16,835 (31.89)	5,376 (31.38)
None	14,01 (2.65)	730 (4.26)
Other	624 (1.18)	372 (2.17)
What is the reason for your preference?		
Beauty	4,451 (8.43)	3,728 (21.76)
Hygiene	13,120 (24.85)	711 (4.15)
Sexual relations	5,353 (10.14)	2,663 (15.54)
Beauty and hygiene	3,395 (6.43)	1,106 (6.46)
Beauty, hygiene and sexual relations	12,890 (24.42)	4,578 (26.72)
Beauty and sexual relations	2,131 (4.04)	3,076 (17.95)
Hygiene and sexual relations	7,800 (14.78)	572 (3.34)
Other	3,647 (6.91)	699 (4.08)
Sexual orientation:		
Heterosexual	49,313 (93.42)	16,707 (97.51)
Homosexual	11,45 (2.17)	175 (1.02)
Bisexual	2,248 (4.26)	238 (1.39)
Other	81 (0.15)	13 (0.08)
Relationship status:		
None	11,579 (21.94)	2,530 (14.77)
Dating exclusively	20,198 (38.26)	6,536 (38.15)
Married	21,010 (39.80)	8,067 (47.08)
How often do you have sex?		
No sexual activity	4,813 (9.12)	557 (3.25)
Up to once per month	214 (0.41)	51 (0.30)
Up to once per week	13,076 (24.77)	3,482 (20.32)
Two to three times per week	23,589 (44.69)	8,593 (50.15)
More than three times per week	11,095 (21.02)	4,450 (25.97)
You prefer to depilate with:		
Hot wax	23,427 (44.38)	*
Cold wax	671 (1.27)	*
Razor blade	21,168 (40.10)	*
Depilatory cream	1,557 (2.95)	*
Laser	3,029 (5.74)	*
Electric razor	1,807 (3.42)	*
Other	1,128 (2.14)	*
Where do you depilate?		
Home	29,456 (55.80)	*
Beauty Salon	16,115 (30.53)	*
Clinic	6,677 (12.65)	*
Other	539 (1.02)	*
Are you satisfied with the appearance of your genital area?		
Dissatisfied	1,683 (3.19)	*
Slightly satisfied	9,260 (17.54)	*
Satisfied	29,654 (56.18)	*
Very satisfied	12,190 (23.09)	*

Note: * Questions that were exclusive to women.

Preferences in Different Age Groups

Our analysis of different age groups indicated that complete removal of pubic hair was preferred by most women who were between 18 and 25 years old (74.26%) and 26 to 35 years old (60.47%), and this preference gradually declined with age (►**Table 2**). In contrast, the women's preference for partial depilation increased with age, and this preference was reported by 48.96% of women who were older than 45 years old. Among men, the preference for complete depilation also decreased with age, and the preference for partial depilation increased with age. Among all age groups, only a small number of men and women preferred no depilation, although this preference also increased with age.

Table 2 Preferences for extent of female pubic hair removal in different age groups of women and men

		Preferred extent of female pubic hair removal					
	Age group, years	Complete	Partial	None	Other	Total	*p*
Women n (%)	18–25	16,551 (74.26)	4,900 (21.98)	617 (2.77)	220 (0.99)	22,288 (100)	< 0.0001
	26–35	12,741 (60.47)	7,609 (36.11)	476 (2.26)	244 (1.16)	21,070 (100)	
	36–45	3,766 (50.5)	3,361 (45.07)	215 (2.88)	116 (1.56)	7,458 (100)	
	> 45	869 (44.09)	965 (48.96)	93 (4.72)	44 (2.23)	1,971 (100)	
Men n (%)	18–25	3,499 (69.03)	1,320 (26.04)	146 (2.88)	104 (2.05)	5,069 (100)	< 0.0001
	26–35	4,485 (63.07)	2,253 (31.68)	240 (3.38)	133 (1.87)	7,111 (100)	
	3–45	1,689 (55.05)	1,146 (37.35)	161 (5.25)	72 (2.35)	3,068 (100)	
	> 45	982 (52.10)	657 (34.85)	183 (9.71)	63 (3.34)	1,885 (100)	

Preferences for Pubic Hair Removal and Sexual Orientation

Most of the men (97.5%) and women (93.4%) were heterosexual (►**Table 1**). The majority of women who were heterosexual (64.5%), homosexual (62.4%), and bisexual (60.2%) all preferred complete removal of pubic hair (►**Table 3**). Similarly, most men who were heterosexual (62.27%), homosexual (61.71%), and bisexual (57.56%) also preferred complete removal of pubic hair.

Preferences on the Extent of Pubic Hair Removal and Frequency of Intercourse

We found that most women (44.7%) and men (50.1%) reported having intercourse 2 to 3 times per week, and smaller percentages (~ 22%) of women and men reported a frequency of up to once per week or more than 3 times per week. Significantly fewer men and women reported having no intercourse or a frequency of once per month (►**Table 1**).

Regardless of the frequency of intercourse, total removal of pubic hair was preferred by most women and men (►**Table 4**). The percentage of women and men who preferred total removal of pubic hair increased with the frequency of intercourse, and was greatest for women (72.2%) and men (65.8%) who reported having intercourse more than 3 times per week. Similar percentages of men and women who preferred partial pubic hair removal reported no intercourse up to intercourse 2–3 times per week, and the lowest percentage of preference for partial depilation was among women and men who declared a sexual frequency of more than 3 times per week. Very few women and men preferred no pubic hair removal in all intercourse frequency groups, but there was a trend for a decline in this preference with an increase in the frequency of intercourse.

Preferences for the Extent of Pubic Hair Removal and Satisfaction with Genital Appearance

A total of 56.2% of women reported being satisfied, and 23.1% were very satisfied with the appearance of their genitalia (►**Table 1**). A total of 20.7% of women reported being dissatisfied or only slightly satisfied with the appearance of their genitalia.

Most women preferred complete removal of their pubic hair, irrespective of the extent of their satisfaction with the appearance of their genitalia (►**Table 5**). The highest and lowest percentages of women who preferred complete depilation were those who reported being very satisfied (68.6%) and dissatisfied (60.6%) respectively. The percentage of women who reported a preference for partial hair removal

Table 3 Preferences regarding the extent of female pubic hair removal in men and women with different sexual orientations

		Preferred extent of female pubic hair removal					
	Sexual orientation	Complete	Partial	None	Other	Total	*p*
Women n (%)	Heterosexual	31,823 (64.53)	15,849 (32.14)	1,116 (2.26)	525 (1.06)	49,313 (100)	< 0.0001
	Homosexual	714 (62.36)	351 (30.66)	61 (5.33)	19 (1.66)	1,145 (100)	
	Bisexual	1,354 (60.23)	620 (27.58)	203 (9.03)	71 (3.16)	2,248 (100)	
	Other	36 (44.44)	15 (18.52)	21 (25.93)	9 (11.11)	81 (100)	
Men n (%)	Heterosexual	10,404 (62.27)	5,250 (31.42)	698 (4.18)	355 (2.12)	16,707 (100)	< 0.0001
	Homosexual	108 (61.71)	52 (29.71)	6 (3.43)	9 (5.14)	175 (100)	
	Bisexual	137 (57.56)	73 (30.67)	24 (10.08)	4 (1.68)	238 (100)	
	Other	6 (46.15)	1 (7.69)	2 (15.38)	4 (30.77)	13 (100)	

Table 4 Preferences for the extent of female pubic hair removal and frequency of sexual intercourse in women and men

		Preferred extent of female pubic hair removal					
	Sexual frequency	Complete	Partial	None	Other	Total	*p*
Women n (%)	No sexual activity	2,774 (57.64)	1,716 (35.65)	248 (5.15)	75 (1.56)	4,813 (100)	< 0.0001
	Up to once per month	120 (56.07)	74 (34.58)	10 (4.67)	10 (4.67)	214 (100)	
	Up to once per week	7,842 (59.97)	4,717 (36.07)	368 (2.81)	149 (1.14)	13,076 (100)	
	02 to 03 times per week	15,184 (64.37)	7,590 (32.18)	546 (2.31)	269 (1.14)	23,589 (100)	
	> 03 times per week	8,007 (72.17)	2,738 (24.68)	229 (2.06)	121 (1.09)	11,095 (100)	
Men n (%)	No sexual activity	314 (56.37)	186 (33.39)	35 (6.28)	22 (3.95)	557 (100)	< 0.0001
	Up to once per month	27 (52.94)	18 (35.29)	4 (7.84)	2 (3.92)	51 (100)	
	Up to once per week	2,071 (59.48)	1,188 (34.12)	155 (4.45)	68 (1.95)	3,482 (100)	
	02 to 03 times per week	5,315 (61.85)	2,748 (31.98)	362 (4.21)	168 (1.96)	8,593 (100)	
	> 03 times per week	2,928 (65.8)	1,236 (27.78)	174 (3.91)	112 (2.52)	4,450 (100)	

was similar in the 4 groups who reported different levels of satisfaction with their genital appearance (~ 32%). A significant minority of women in all four groups preferred no depilation.

Discussion

This study evaluated the preferences of Brazilian women and men regarding female pubic hair removal by women, and the relationships of different preferences with sociodemographic parameters and factors related to sexual activity. Our self-administered and online survey has data from 69,920 subjects, the largest sample size so far reported among studies on female pubic hair depilation.

Our analysis indicated that 64.3% of women and 62.2% of men preferred female genitalia with no hair at all. Moreover, the complete removal of female pubic hair was preferred by women and men in all regions of Brazil. These findings are in line with the results of multiple studies conducted in the US.[7,8,11] However, our findings differ from those of Giraldo et al[3] in Brazil, Herbenick et al[9] in the USA, and Tiggermann and Hodgson[6] in Australia, who reported that women preferred partial removal of pubic hair, and from those of Mazloomdoost et al,[10] who reported that men from the US preferred partial depilation. These differences may be due to cultural differences. Furthermore, comparisons of studies of the same population indicated that the preference for complete pubic hair removal has increased over time.

We observed that women and men of similar age, educational level, relationship status, and frequency of intercourse had similar preferences regarding the removal of pubic hair in general, and regarding the extent of pubic hair removal. This indicates a positive feedback between women and men regarding their preferences for female pubic hair depilation. Moreover, there is a possibility that the preferences of men and women with similar characteristics are influenced by the same external (unmeasured) factors that determine their preferences regarding female pubic hair removal.

The present study indicated that younger men and women were more likely to prefer complete pubic hair removal in women, but older men and women were more likely to prefer partial depilation. These observations are in accordance with other studies[4,7–10,12] and with the recent trend for complete removal of female pubic hair reported by Schick et al.[11]

Our analysis of the reason for preferring female pubic hair depilation indicated that hygiene was the major reason in women, and beauty was the major reason in men. Even though the presence of body hair in general is not associated with poor hygiene, many people apparently believe that pubic hair can accumulate debris and complicate genital cleaning, and thereby facilitate the acquisition of infections.

Table 5 Preferences for the extent of female pubic hair removal in women who reported different levels of satisfaction with the appearance of their genitalia

		Preferred extent of female pubic hair removal					
	Satisfaction with genital appearance	Complete	Partial	None	Other	Total	*p*
Women n (%)	Dissatisfied	1,020 (60.61)	555 (32.98)	92 (5.47)	16 (0.95)	1,683 (100)	< 0.0001
	Slightly satisfied	5,761 (62.21)	3,178 (34.32)	231 (2.49)	90 (0.97)	9,260 (100)	
	Satisfied	18,778 (63.32)	9,914 (33.43)	650 (2.19)	312 (1.05)	29,654 (100)	
	Very satisfied	8,368 (68.65)	3,188 (26.15)	428 (3.51)	206 (1.69)	12,190 (100)	

This may explain why women considered hygiene as the major reason for removal of pubic hair. Other studies also reported associations between female pubic hair depilation and hygiene.[4,5,7,8]

The results of this study are consistent with previous studies that reported that consuming pornography and erotica can influence preferences for pubic hair removal, as reported by Desruelles et al[13] and Ramsey et al.[14] However, this influence must be further investigated in order to evaluate this relationship more directly. Besides, more studies are needed to analyze the influence of the media in general and of the internet and social media on the increasing preference for pubic hair depilation.

We also evaluated preferences for different types of female pubic hair removal in women and men with different sexual orientations. Interestingly, most women and men who defined themselves as heterosexual, homosexual, and bisexual preferred complete removal of female pubic hair. These observations suggest that the same factor(s) may influence the preferences of subjects with different sexual orientations.

Our study also indicates that women and men who have intercourse with greater frequency were more likely to prefer complete removal of female pubic hair. This may be related to our observation that men view hairless genitalia as more attractive, and women view hairless genitalia as more hygienic. Other studies also reported associations of the preference for complete depilation and greater sexual activity.[9,12,15] In line with these observations, we also found that, in general, subjects who preferred no depilation had lower frequencies of intercourse.

The results of the present study indicate that women who are less satisfied with the appearance of their own genitalia were less likely to perform complete pubic hair removal, and had a greater preference for no removal of pubic hair. Likewise, women who reported being satisfied with the appearance of their own genitalia were more likely to prefer complete depilation. Thus, a woman who is dissatisfied with the appearance of her own genitalia may not remove her pubic hair, simply because it conceals her genitalia.

All relationships examined in this work had p-values much lower than the proposed level of significance ($p < 0.05$). A major strength of this study is that it is the largest study of Brazilian people to evaluate the preferences of women and men regarding the removal of female pubic hair. Our study identified several sociodemographic and other factors related to the preference for hair removal. As a whole, our findings provide an important basis to understand the motivations for the now widespread practice of female pubic hair depilation.

Limitations

A limitation of this study is that we recruited participants via the internet, and there were therefore biases inherent to the use of convenience sampling. All participants filled out the forms anonymously and privately, and we have no evidence regarding their understanding of the questions or the accuracy of their answers. However, due to the large number of participants, we expect that any intentionally or unintentionally inaccurate answers would be overwhelmed by the larger number of accurate answers. In addition, we used a pilot study to assure the adequacy of the language used in the survey. All participants were literate and had access to the internet, so we excluded those who were illiterate and had no internet access. Internet access in Brazil does not cover urban and rural areas equally, and is not available to many individuals from lower socioeconomic strata, so this may have biased our results. However, we believe these limitations, which are inherent to the use of the internet to recruit subjects, are overwhelmed by the several advantages provided by using the internet, such as the ability to recruit a very large sample, the absence of biases introduced by the physical presence of researchers during the interview, and the minimal expenses needed to conduct large surveys. The possibility of a non-representative sample, a limitation inherent to convenience sampling, may have been overcome by our extensive publicity of the survey, so that Brazilians from all regions, of all ages, and with all educational levels, were aware of the study.

Conclusions

This study found that Brazilian women and men prefer female genitalia without any hair, and that this preference was stronger for younger people. This preference may be due to the influence of recent trends in beauty, aesthetics, eroticism, and pornography. Women reported the main motivation for the removal of female pubic hair is hygiene, and men reported the main reason for this preference is beauty. Men and women who have more frequent intercourse are more likely to prefer complete depilation, and women who are more satisfied with the appearance of their own genitalia are more likely to prefer complete depilation.

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Conflicts of Interest

The authors have no conflicts of interest to declare.

References

1 Glass AS, Bagga HS, Tasian GE, et al. Pubic hair grooming injuries presenting to U.S. emergency departments. Urology 2012;80(06): 1187–1191

2 Dendle C, Mulvey S, Pyrlis F, Grayson ML, Johnson PD. Severe complications of a "Brazilian" bikini wax. Clin Infect Dis 2007;45 (03):e29–e31

3 Giraldo PC, Polo RC, do Amaral RL, Reis VV, Beghini J, Bardin MG. [Habits and traditions of female college students related to intimate clothing, genital adornments, genital hair removal and sexual practices]. Rev Bras Ginecol Obstet 2013;35(09):401–406 Portuguese

4 DeMaria AL, Berenson AB. Prevalence and correlates of pubic hair grooming among low-income Hispanic, Black, and White women. Body Image 2013;10(02):226–231

5 DeMaria AL, Sundstrom B, McInnis SM, Rogers E. Perceptions and correlates of pubic hair removal and grooming among college-aged women: a mixed methods approach. Sex Health 2016;13 (03):248–256

6 Tiggermann M, Hodgson S. The hairlessness norm extended: reasons for and predictors of women's body hair removal at different body sites. Sex Roles 2008;59(11):889–897

7 Butler SM, Smith NK, Collazo E, Caltabiano L, Herbenick D. Pubic hair preferences, reasons for removal, and associated genital symptoms: comparisons between men and women. J Sex Med 2015;12(01):48–58

8 Rowen TS, Gaither TW, Awad MA, Osterberg EC, Shindel AW, Breyer BN. Pubic hair grooming prevalence and motivation among women in the United States. JAMA Dermatol 2016;152 (10):1106–1113

9 Herbenick D, Schick V, Reece M, Sanders S, Fortenberry JD. Pubic hair removal among women in the United States: prevalence, methods, and characteristics. J Sex Med 2010;7(10):3322–3330

10 Mazloomdoost D, Crisp CC, Westermann LB, Benbouajili JM, Kleeman SD, Pauls RN. Survey of male perceptions regarding the vulva. Am J Obstet Gynecol 2015;213(05):731.e1–731.e9

11 Schick VR, Rima BN, Calabrese SK. Evulvalution: the portrayal of women's external genitalia and physique across time and the current barbie doll ideals. J Sex Res 2011;48(01):74–81

12 Herbenick D, Hensel D, Smith NK, et al. Pubic hair removal and sexual behavior: findings from a prospective daily diary study of sexually active women in the United States. J Sex Med 2013;10 (03):678–685

13 Desruelles F, Cunningham SA, Dubois D. Pubic hair removal: a risk factor for 'minor' STI such as molluscum contagiosum? Sex Transm Infect 2013;89(03):216

14 Ramsey S, Sweeney C, Fraser M, Oades G. Pubic hair and sexuality: a review. J Sex Med 2009;6(08):2102–2110

15 Bercaw-Pratt JL, Santos XM, Sanchez J, Ayensu-Coker L, Nebgen DR, Dietrich JE. The incidence, attitudes and practices of the removal of pubic hair as a body modification. J Pediatr Adolesc Gynecol 2012;25(01):12–14

Preeclampsia*
*Pré-eclâmpsia**

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Abstract

The authors review hypertensive disease during pregnancy with an academic and practical view, and using the best evidence available. This disease, which is the most important clinical disease in Brazilian pregnant women, may have its incidence reduced with prevention through the use of calcium and aspirin in pregnant women at risk. Previously, it was a disease that presented with *hypertension with proteinuria,* but it has now been classified with new clinical parameters besides proteinuria. Morbidity and mortality should be reduced in a continental country such as Brazil using protocols for the early treatment of complications by calculating severe outcomes in preeclampsia. The early treatment of acute hypertension, use of magnesium sulfate and early hospitalization in cases of preeclampsia are concepts to pursue the reduction of our pregnant women's mortality.

Keywords
- pregnancy arterial hypertension
- preeclampsia
- HELLP syndrome
- high risk pregnancy
- pregnancy complications

Resumo

Os autores revisam a doença hipertensiva na gestação com uma visão acadêmica e prática, utilizando as melhores evidências disponíveis. A doença clínica mais importante na gestante brasileira pode ter sua incidência diminuída com a prevenção por meio do uso de cálcio e aspirina em gestantes de risco. Antes uma doença que apresentava hipertensão *arterial com proteinúria,* agora vem sendo classificada com novos parâmetros clínicos além da proteinúria. A morbidade e mortalidade devem ser diminuídas, em um país continental como o Brasil, utilizando-se protocolos para o tratamento precoce de suas complicações mediante o cálculo de desfechos graves em pré-eclâmpsia. O tratamento precoce da hipertensão arterial, o uso do sulfato de magnésio e a internação precoce em casos de pré-eclâmpsia são conceitos para perseguirmos a diminuição da mortalidade de nossas gestantes.

Palavras-chave
- hipertensão arterial na gestação
- pré-eclâmpsia
- síndrome HELLP
- gestação de alto risco
- complicações na gravidez

Highlights

- New concepts of diagnosis and risk for preeclampsia;
- Guidelines for preeclampsia prevention treatment;
- Prediction model of severe maternal outcomes in preeclampsia (fullPIERS) 12.

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Introduction

The hypertensive syndromes that occur during pregnancy, especially preeclampsia (PE), result in real risk and significant impact on indicators related to maternal and child health. These syndromes are causal factors related to maternal and perinatal death, and they cause definitive limitations to maternal health and serious problems resulting from associated elective prematurity. In Brazil, PE is the main cause of elective prematurity.

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There is no accurate information on the incidence of preeclampsia worldwide, but it is estimated to occur in 3–5% of pregnancies. Specifically in Brazil, a systematic review identified an incidence of 1.5% for PE and of 0.6% for eclampsia.[1] Certainly, information concerning Brazil is still underestimated, and definitely varies according to the country's regions. A Brazilian study[2] reports that the estimated prevalence of eclampsia is of 0.2% in the most developed areas, with a maternal death rate of 0.8%, whereas in less favored regions this prevalence rises to 8.1%, with a maternal mortality rate corresponding to 22.0%.

The aim of this text is to sensitize health providers about the magnitude of the problem, recognize local specificities, and adopt interventions based on the best scientific evidence available to develop strategies for prevention, early detection of the disease, and reduction of maternal and perinatal harm.

Pathophysiological Foundations

Some evidence supports the hypothesis of maternal immune system involvement in the disease. In case there are problems of immunological adaptation to the trophoblast, there will be problems in trophoblast perfusion, with consequent hypoxia. These primary alterations would trigger a series of local hypoxia phenomena, and reoxygenation could amplify the local effects, such as the formation of oxygen-reactive species, activation of the maternal inflammatory system, and acceleration of cellular apoptosis processes that would limit the establishment of normal placentation and imbalance between pro-angiogenic factors, such as the vascular endothelial growth factor (VEGF) and the placental growth factor (PlGF), and soluble anti-angiogenic factors such as the soluble fms-like tyrosine kinase-1 (sFLT-1), with predominance of the latter, resulting in generalized activation of the maternal inflammatory system, universal endothelial dysfunction, and limited placental vascularization.[3,4]

Universal arteriolar spasm due to endothelial activation results in an insidious and progressive process, culminating in multiple organ insufficiency. Preeclampsia should be interpreted as a chronic disease with potential for progressive multiple organ failure. This evolutionary character must be taken into account, as well as its unpredictability and clinical instability in decisions. Endothelial activation basically determines: vasoconstriction and consequent increase in peripheral resistance; changes in capillary permeability, which are responsible for edema; and activation of the coagulation system.

The kidneys suffer from anatomopathological patterns (glomerular endotheliosis and focal sclerosis), with consequent proteinuria and impairment of the glomerular filtration. In the liver, ischemia occurs with varying intensity, leading to dysfunction with elevated levels of transaminases. Focal or confluent edema and/or hemorrhage distend the capsule, and may result in hepatic rupture with massive bleeding.

Vasospasm hinders the uteroplacental blood flow with varying intensity, depending on the moment of the process and on the existence of a chronic pre-existing injury. Regarding coagulation, there is activation and consumption of platelets with progressive consumption and disseminated coagulation. The brain can be affected by ischemia aggravated by diffuse edema, resulting in seizure (eclampsia) or stroke. Patients presenting severe conditions, particularly eclampsia, should receive differentiated care, given the progressive functional limitation of multiple organs.

Definitions of Hypertensive States during Pregnancy

The expansion of pathophysiological knowledge has resulted in the expansion of clinical possibilities to define PE. However, the recommendations adopted by the International Society for the Study of Hypertension in Pregnancy (ISSHP)[5] remain. According to such recommendations, arterial hypertension is characterized when the systolic blood pressure (SBP) is $\geq$ 140 mm Hg and/or the diastolic blood pressure (DBP) is $\geq$ 90 mm Hg, considering the fifth Korotkoff sound (silence). For the measurement, the patient should sit and place one of the forearms at the height of the atrium (half of the external bone); the measurement should be repeated in one or two five-minute intervals. The usually available cuffs are used for readings in arms with perimeter around 30 cm. Obese patients need appropriate cuffs or correction tables according to their brachial perimeter.

Protein loss of 300 mg or more in 24-hour urine specimen collection should be considered for the definition of proteinuria. For more agility in the diagnosis, evaluations in an isolated sample of urine with proteinuria/creatininuria (P/C) ratio (both in mg/dL) $\geq$ 0.3 are considered adequate. In the absence of such diagnostic possibilities, proteinuria with at least 1+ reagent tape may be considered as long as the quality of the method is assured. Differently from previous recommendations, the intensity of the proteinuria should no longer be associated with the maternal prognosis, nor be the only aspect to guide decisions.

Preeclampsia is defined as arterial hypertension identified for the first time after the 20th week associated with proteinuria, and it may overlap with another hypertensive state. Taking into account the current concept of PE syndrome, rigid concepts have been abandoned.[6] Thus, in the absence of proteinuria, the diagnosis of PE may be based on the presence of headache, visual turbidity, abdominal pain or altered laboratory tests, such as thrombocytopenia (less than 100,000/mm^3), hepatic enzyme elevation (double the basal), renal impairment ($>$ 1.1 mg/dL or double the baseline), or pulmonary edema and visual or brain disorders such as headache, scotomas, or convulsions.

These criteria should be adopted for patients with preexisting hypertension (arterial hypertension preceding pregnancy or identified before 20 weeks), with worsening of baseline blood pressure (BP), and the onset of proteinuria, suggesting PE overlap. Hence, concerning the diagnosis,

Table 1 Severe complications of preeclampsia

Affected organic system	Adverse conditions	Severe complications indicating termination of pregnancy
Central nervous system	Headache; visual symptoms	Eclampsia; PRES; cortical blindness; Retinal detachment; Glasgow scale < 13; TIA; stroke; RND.
Cardiorespiratory	Chest pain; dyspnea; saturation O_2 < 97%	Severe uncontrolled hypertension (for a 12-hour period despite maximum doses of hypotensive agents); SO_2 < 90%, need for O_2 > 50% for > 1 hour, intubation, support with vasoactive drugs; pulmonary edema; myocardial ischemia or infarction.
Hematological	Leukocytosis; thrombocytopenia; high INR PTT	Platelets < 50.000/dL;* need for transfusion of any blood product.
Renal	Elevated creatinine and uric acid	ARF (creatinine > 1.5 mg/dL without previous renal disease); need for dialysis (without previous CRF).
Hepatic	Nausea; vomiting epigastralgia; URQ pain; SGOT; SGTP; LDH; elevated bilirubin; low plasma albumin	Hepatic impairment (INR > 2 in absence of DIC or use of warfarin); hepatic hematoma with or without rupture.
Fetoplacental	Non-reactive CTG; Oligohydramnios; IUGR; Doppler of umbilical artery with absent or reversed diastolic flow	PA; reversed a-wave in ductus venous; fetal death.

Abbreviations: ARF, acute renal failure; CRF, chronic renal failure; CTG, cardiotocography; DIC, disseminated intravascular coagulation; INR; IUGR, intrauterine growth restriction; LDH, lactate dehydrogenase; PA, placental abruption; PPT, prothrombin time; PRES, posterior reversible encephalopathy syndrome; RND, reversible neurological deficit; SGOT, serum glutamic oxaloacetic transaminase; SGTP, serum glutamic pyruvic transaminase; TIA, transient ischemic attack; URQ, upper right quadrant of the abdomen.
Note: *Platelets < 100.000 are considered as indication of interruption of pregnancy.
Adapted from: Magee LA, Pels A, Helewa M, Rey E, von Dadelszen P; Canadian Hypertensive Disorders of Pregnancy (HDP) Working Group (2014).[8]

preeclampsia is considered hypertension after the twentieth week and one of the following criteria:

1. Significant proteinuria (P/C ratio > 0.3; > 1.0 g/L on reagent tape);
2. Maternal organic dysfunctions;
   - Loss of renal function (creatinine > 1.02 mg/dL);
   - Hepatic dysfunction (increase of transaminases by > 2 times the normal upper limit; epigastralgia);
   - Neurologic complications (altered mental state; blindness; hyperreflexia with clonus, scotomas, visual blurring, diplopia, Doppler of maternal ophthalmic artery with peak ratio > 0.78);
   - Hematologic complications (thrombocytopenia, disseminated intravascular coagulation [DIC] < hemolysis);
   - Antiangiogenesis status (PlGF < 36 pg/mL or sFlt-1/PlGF ratio > 85).
3. Uteroplacental dysfunction (asymmetric intrauterine growth restriction [IUGR]; altered umbilical Doppler, especially if the Doppler is altered in both maternal uterine arteries).

When PE occurs in pregnant women with chronic hypertension, it is considered overlapping preeclampsia. Severe preeclampsia is defined as PE associated with severe enough maternal-fetal complications to pose imminent risk of maternal-fetal impairment. Persistent SBP ≥ 160 mm Hg or DBP ≥ 110 mm Hg or presence of any of the criteria listed in ►**Table 1** characterize a pregnant woman as having severe PE. In general, pregnant women with signs or symptoms of severe PE have a decompensated disease that may rapidly progress to maternal and perinatal morbidity and mortality. Proteinuria levels should not be considered criteria of severity in PE.[7,8] The presence of PE, regardless of its severity, entails increased fetal and maternal risk. Eclampsia is the occurrence of generalized motor seizures (grand mal seizures) in pregnant women with PE that are not caused by coincident neurological disease and may occur in the prepartum period (50%), during delivery (20%), and in the postpartum period (between 11 and 44%).

Classification

There are several classifications described for hypertensive disorders in pregnancy. In 2014, the ISSHP reviewed the classification of hypertensive disorders during pregnancy (►**Table 2**).[5]

Significant Proteinuria

It is the excretion of 300 mg or more of proteins in a 24-hour urine collection. The 24-hour collection is subject to many collection and storage errors, and should not be used for clinical purposes unless 24-hour creatinine clearance is also

Table 2 Classification of hypertensive disorders of pregnancy

Classification
1. Chronic hypertension
2. Gestational hypertension
3. Preeclampsia with or without overlapping chronic hypertension
4. White coat hypertension

Adapted from: Tranquilli et al (2014).[5]

measured to assess the adequacy of the collection.[5] The measurement of the P/C ratio in the urine sample has been of clinical utility, and values ≥ 0.3 demonstrate a good correlation with significant proteinuria. A P/C ratio in an isolated sample of urine ≥ 0.3 corresponds to significant proteinuria 92% of times, and a ratio ≥ 0.5 corresponds to significant proteinuria 100% of times.[9] The presence of 1.0 g/l or more of proteins on the reagent tape strongly suggests significant proteinuria.

Chronic Arterial Hypertension

Chronic arterial hypertension in pregnancy is the occurrence of systemic arterial hypertension (SAH) preceding pregnancy. As there often are no records of BP measurements before gestation, SAH is considered chronic when observed in the first trimester of gestation or, at most, up to the 20th week. In most cases, chronic hypertension refers to essential hypertension, usually associated with family history of hypertension, and often accompanied by overweightness or obesity. More rarely, secondary hypertension may occur. Given the age range of the pregnant women, the presence of secondary hypertension is usually due to underlying parenchymal renal diseases, such as glomerulonephritis and reflux nephropathy.

Gestational Hypertension

Gestational hypertension is defined as arterial hypertension arising for the first time after the 20th week of gestation without being accompanied by any signs, symptoms or laboratory abnormalities that characterize preeclampsia.

White Coat Hypertension (Syndrome)

About 25% of people with increased BP measurements in medical consultations have white coat hypertension. The diagnosis can be confirmed by serial measurements (preferably taken by nurses) or ambulatory BP monitoring (ABPM). There are few studies on the repercussion of this type of disorder in pregnancy, some suggesting that up to 50% of these cases evolve to gestational hypertension or PE.[5]

Preeclampsia diagnosis should be presumed in pregnant women with arterial hypertension and significant proteinuria occurring after the 20th week of gestation (except in cases of hydatidiform mole, when PE can occur before the 20th week). If the increase in BP and proteinuria occurs after the 20th week in a primigravida with family history (mainly sister or mother) of PE or eclampsia, the probability of correct PE diagnosis will be greater than 90%.

Even in the absence of significant proteinuria, the occurrence of hypertension after the 20th week should translate into a PE diagnosis if there are signs of maternal or placental dysfunction (sFLT-1/PlGF ratio > 85, PlGF < 36 pg/mL, creatinine > 1.02 mg/dL; increased transaminase levels by > 2 times the upper limit of normal; epigastralgia; altered mental status; blindness; hyperreflexia with clonus, scotomas, visual disturbance, diplopia, maternal ophthalmic artery Doppler with peak ratio > 0.78; thrombocytopenia $< 150{,}000$/dL, DIC, hemolysis; asymmetric IUGR, umbilical Doppler with decrease or absence of diastolic flow, reverse diastolic flow in umbilical, especially if it is a Doppler with a protodiastolic notch in both maternal uterine arteries).

Serum uric acid increases early in PE, and has a positive correlation with placental bed atheromatosis injuries, lower birth weight infants,[10] degree of hemoconcentration[11] and severity of glomerular endotheliosis.[12] Uric acid levels > 4.5 mg/dL are abnormal in gestation.[13]

The decreased activity of antithrombin III (AT III, $< 70\%$) correlates with renal glomerular endotheliosis, and its measurement may be important in the differential diagnosis with chronic hypertension.[14] Calciuria is decreased in PE, and may also be useful in the differential diagnosis with chronic hypertension. A 24-hour calciuria below 100 mg suggests PE.[15]

In patients at high risk for PE (►**Table 1**), it is prudent to perform baseline tests at the beginning of pregnancy for further comparison. This evaluation should be restricted to the measurement of platelets, creatinine, uric acid, and a search for basal proteinuria (that is, a P/C ratio in the urine sample). In these patients, a precise dating of the gestational age (GA) through ultrasonographic examination in the first trimester is fundamental. A Doppler evaluation of the uterine arteries after the 23rd week of GA is useful to evaluate the presence of an adequate placental implantation or not. Uterine arteries with normal resistance indices indicate low probability of occurrence of PE during pregnancy (high negative predictive value).[16,17] However, pulsatility indices above the 95th percentile for GA and presence of bilateral protodiastolic notch beyond 27 weeks are signs of deficient trophoblastic invasion and consequent increased risk of PE and/or IUGR.

Differential Diagnosis between Preeclampsia and Chronic Systemic Arterial Hypertension

The first onset of hypertension and proteinuria in a primigravida after the 20th week of gestation easily leads to the diagnosis of PE. Likewise, pregnant women with high BP levels before the 20th week or even before the beginning of pregnancy should be diagnosed as having chronic hypertension. However, the differential diagnosis can become difficult when the pregnant woman is seen for the first time after the 20th week with arterial hypertension and cannot inform her previous blood pressure levels accurately. If the pregnant woman is not a primigravida, her serum uric acid level is < 4.5 mg/dL, and the 24-hour calciuria > 100 mg, the diagnosis of chronic hypertension is more likely.

Prediction of Preeclampsia

Advances in the knowledge of the pathophysiology of PE have resulted in the adoption of prediction methods. Through epidemiological data, it is possible to recognize women more likely to develop the disease[18] (►**Table 1**), and develop a differentiated prenatal follow-up strategy. In addition to the clinical features, the literature is rich in publications suggesting prediction methods. Among the several alternatives, the use of Doppler of the uterine arteries and detection of plasmatic substances, such as proteins of placental origin or resulting from angiogenic imbalance, stand out.

The uterine artery Doppler performed in the first or second trimesters has limited accuracy, presents difficulties in assuring the standardization and qualifications in its measurement, and the equipment is costly. The various alternatives of plasma markers also lack the accuracy that justifies their adoption in the clinical practice. The use of plasma markers related to angiogenesis/antiangiogenesis imbalance has been described in the literature as a promising tool for the early detection of PE. However, additional studies are needed to define uniform methods of quantification and evaluate their accuracy before recommending the use in the clinical practice. Despite the large number of 'predictive factors,' there is no consistent evidence identifying the impact of these methods on maternal and perinatal prognosis. Thus, there is no consistent evidence to adopt universal screening in the clinical practice besides the identification of clinical risk.

Due to the high incidence and severity of PE, several attempts have been made to identify the patients at greatest risk of developing it. Preeclampsia in a previous pregnancy poses an average risk of around 15% for PE recurrence, and of 22% for gestational hypertension. Recurrence is more likely if the previous PE had early onset, was severe, or complicated by eclampsia or HELLP syndrome. A high BMI during the previous PE increases the risk of recurrence.[8] Among the several tests proposed to predict the occurrence of PE, the most used currently is the Doppler flowmetry of the uterine arteries.

The Doppler study of the uterine arteries in patients at risk for PE showing persistent protodiastolic incisions beyond the 23rd week of gestation identifies high-resistance placental circulation that usually results from this deficiency of vascular invasion by the trophoblast and consequent increased risk of PE and/or IUGR in the current pregnancy. In a systematic review including 74 studies with 79,547 patients, it was concluded that the 24-week uterine artery Doppler study is the best predictor of PE. The Doppler should be considered positive in the presence of an altered pulsatility index (above the 95th percentile for GA) in combination or not with the persistence of a bilateral protodiastolic notch in the uterine arteries.[19] The presence of these alterations in the velocimetry test is not a diagnosis of PE, but in patients with clinical risk, it shows a greater chance of having pregnancy-specific hypertensive disease and/or IUGR in the current gestation. The greatest usefulness of this Doppler evaluation is its high negative predictive value. Thus, if a patient at high clinical risk for PE (that is, mother and sister with positive history of PE) has a Doppler flowmetry test indicating good diastolic flow in the uterine arteries after the 25th week, her risk of developing PE decreases. In pregnant women at low clinical risk for PE and IUGR, there is no use for a Doppler evaluation of the uterine arteries, since this test cannot identify an increased risk in this population of pregnant women.

Prevention

Only the use of calcium and low-dose aspirin are recommended and considered effective in the clinical practice. Calcium supplementation (calcium carbonate, 1,000–2,000 mg/day) and the use of small daily doses (50–170 mg) of aspirin for at-risk groups are the only alternatives that have shown some degree of effectiveness in randomized clinical trials (Grade A of recommendation).

Antiplatelet Agents

Since 1985, several studies have been published analyzing the effects of using low doses of aspirin for PE prevention. A systematic review published in the Cochrane Library[20] included 37,560 pregnant women at moderate and high risk for preeclampsia. The authors concluded that low-dose aspirin (50–150 mg/day) reduces by 17% the risk of developing PE (risk ratio [RR]: 0.83) with a number needed to treat (NNT) of 72 pregnant women.

Roberge et al[21] reviewed 42 randomized clinical trials (27,222 women) comparing groups using acetylsalicylic acid (ASA, 50–150 mg once a day) with controls. When compared with controls, the groups using ASA initiated before 16 weeks compared with initiation after the 16th week was associated with: a large reduction in perinatal mortality (RR: 0.41, 95% confidence interval [95%CI]: 0.9–0.92 versus RR: 0.93, 95%CI: 0.73–1.19); PE (RR: 0.47, 95%CI: 0.36–0.62 versus RR = 0.78, 95%CI: 0.61–0.99); severe PE (RR: 0.18, 95%CI: 0.08–0.41 versus RR: 0.65, 95%CI: 0.40–1.07); IUGR (RR: 0.46, 95%CI: 0.33–0.64 versus RR: 0.98, 95%CI: 0.88–1.08); and preterm birth (RR: 0.35, 95%CI: 0.22–0.57 versus RR = 0.90, 95%CI: 0.83–0.97).

A critical analysis of the various studies enables the conclusion that although there is no benefit in prescribing aspirin for patients at low risk for PE, its use in the high-risk population can bring benefits. For pregnant women at risk (of PE, eclampsia or hemolysis, elevated liver enzymes and low platelet count [HELLP] syndrome in the previous gestation, recurrent fetal loss or antiphospholipid antibody syndrome), aspirin should be administered prophylactically at low doses (75–170 mg) once a day in the evening (before going to sleep), and initiated before the 16th week. Although it can be maintained until delivery, suspension after the 36th week is rational, as it would avoid potential risks of increased bleeding during delivery.

Based on the current evidence, the use of low molecular weight heparin (enoxaparin 40 mg/day) or sodium heparin (10,000 15,000 IU/day) is not indicated for PE prevention in any patient group.

Supplementation with Calcium

The use of calcium is based on the relationship between a diet with little calcium and increased incidence of eclampsia. Furthermore, in low-income populations with calcium-rich diets, there is lower incidence of PE and eclampsia. There are several studies correlating calcium supplementation and the ingested amounts of calcium in the diet with BP levels and PE.

According to a Cochrane Library review,[22] in 12 studies involving 15,206 pregnant women, calcium supplementation reduced the risk of PE (RR: 0.7) and hypertension (RR: 0.48). This effect is higher among pregnant women at high risk for PE and among those on a low-calcium diet. There was no increase in maternal or fetal adverse events in the population studied. The largest study on calcium supplementation performed with low-risk pregnant women did not show decreased PE frequency,[23] while the majority of randomized controlled trials with pregnant women at high risk for PE have shown a significant decrease of the disorder.[24] The use of calcium (1 g/day) is recommended from the 12th week of gestation, and only for pregnant women at high risk for PE development, especially those on a low-calcium diet.

Screening

The main risk factors for the development of PE are first pregnancy, previous or family history of PE, chronic hypertension, diabetes, collagenosis, black ethnicity, obesity and thrombophilia (►**Table 3**).[25,26] Special attention must be paid during the prenatal care of these patients to perform the diagnosis of preeclampsia as early as possible.

The evaluation of biomarkers for PE has been the subject of numerous studies, and may be useful in the early diagnosis of PE. Ideally, the biomarker evaluation should be easy to perform, low-cost, and enable the detection of pregnancy-specific hypertensive disease as early as possible, preferably in the first trimester of pregnancy, before the onset of hypertension. Recent reviews show that, to date, none of the available clinical trials has achieved an ideal sensitivity level ($>$ 90%) for the prediction of PE. Only the Doppler

Table 3 Risk factors for PE

Risk factors	Risks
Strong evidence	
Prestimoniário	2.4 (2.1–2.7, 95%CI)
Diabetes mellitus	RR: 2–3 and higher if decompensated DM
Twin pregnancy	RR: 3 (2–4.2, 95%CI)
Sister with PE	RR: 3.3 (1.5–7.5, 95%CI)
Sister, mother or grandmother with eclampsia	Respectively 37%, 26% and 16% of PE
Chronic SAH	25% of developing PE overlap
PE in previous pregnancy	25% of PE recurrence
Fetal hydrops (non-immune)	RR: 10
Molar pregnancy	RR: 10
New paternity	Similar risk to first pregnancy
APS	Increases risk
Medium or weak evidence	
BMI $\geq$ 25.8	RR: 2.3–2.7
Maternal age $>$ 40 years	RR: 3–4
Use of contraceptive barrier method	Increased risk
Longer duration of sexual activity	Decreased risk
Prior abortion $<$ 10 weeks with the same father	Decreased risk
Excessive weight gain	Increased risk
Artificial insemination	Increased risk
'Risk man' (previous partner had PE)	RR: 1.8 (1.2–2.6)
Pregnant woman born with low birth weight	Increases the risk
Bleeding in 1st trimester	Increases the risk

Abbreviations: APS, antiphospholipid syndrome; BMI, body mass index; PE, preeclampsia; RR, relative risk; PA, placental abruption; SAH, systemic arterial hypertension.

Notes: Medium or weak evidence, some studies have demonstrated the association; strong evidence, several studies have shown risk.

Adapted from: Magee et al & Canadian Hypertensive Disorders of Pregnancy (HDP) Working Group (2014)[8] , Corrêa Júnior et al (2009)[25] and Sibai et al (2005).[26]

performed between 20–24 weeks showed sensitivity > 60% for PE detection, particularly if performed in pregnant women at increased risk in the 2nd trimester, and to predict severe PE of early onset.[19,27–30]

Using a mathematical model and taking into account the relative risk regarding the maternal age, nuchal translucency procedure, beta-human chorionic gonadotrophin (β-HCG) and pregnancy-associated plasma protein A (PAPP-A) dosing, Nicolaides classifies pregnant women as being at high risk (> 1/50), intermediate risk (1/51–1,000) and low risk (<1/1000) of having preeclampsia. Therefore, low-risk pregnant women are advised to undergo only three prenatal consultations, while high-risk pregnant women are advised to undergo more visits. This structure of prenatal care has been criticized because when classified as low-risk, many pregnant women could have a delayed PE diagnosis, especially those with later onset of PE. This prenatal care model to predict preeclampsia must be effectively tested.[31]

Model to Predict Severe Maternal Outcomes

Von Dadelszen et al[32] have developed an interesting and practical model to predict severe maternal outcomes (►**Fig. 1**). This model was developed in four countries (Canada, New Zealand, Australia and the United Kingdom) and externally validated.[33] It can assist clinicians to assess the patients' percentage of risk of having a fatal outcome or a severe complication within the following seven days. For its use, simply access the fullPIERS calculator website (available in four languages) and find a risk calculator (►**Fig. 1**), insert the data on GA, presence or absence of dyspnea or chest pain, O_2 saturation, dosage of creatinine, platelets, serum glutamic oxaloacetic transaminase (SGOT) or serum glutamic pyruvic transaminase (SGPT), and obtain the percentage of occurrence of severe complications.

Complications

Systemic arterial hypertension during pregnancy can generate several complications (►**Table 4**) that will invariably require careful evaluation and management by the medical staff.

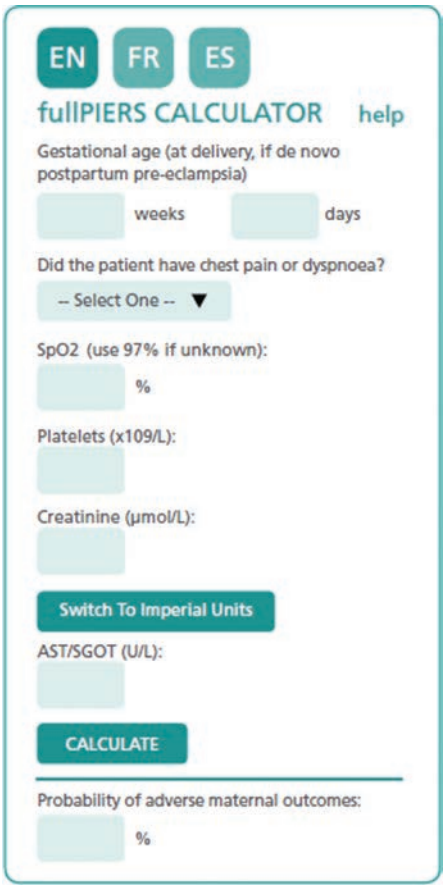

Fig. 1 Risk calculator. **Source:** von Dadelszen, Payne (2011).[32]

Renal Insufficiency

Renal capillary glomerular endotheliosis was considered the characteristic injury of PE for many years. Some authors only considered the PE diagnosis to be accurate in the presence of this renal injury. Damage to the glomerular membrane causes renal dysfunction, and the glomerular filtration rate and renal plasma flow are decreased in relation to healthy pregnant women. There is hyperuricemia in PE, but the elevation of uric acid plasma is transient (dependent on the contraction of plasma volume), and the levels return to

Table 4 Complications of SAH in pregnancy

Affected system	Disorder
Cardiovascular	Severe SAH, pulmonary edema, pulmonary embolism, vascular accidents
Renal	Oliguria, ARF
Hematological	Hemolysis, thrombocytopenia, DIC
Neurological	Eclampsia, cerebral edema, stroke, PRES
Ophthalmologic	Amaurosis, retinal hemorrhages, exudates, papilledema
Hepatic	Dysfunction, ischemia, hematoma, capsular rupture
Placental	Ischemia, thrombosis, PA, fetal hypoperfusion

Abbreviations: ARF, acute renal failure; DIC, disseminated intravascular coagulation; PRES, posterior reversible encephalopathy syndrome; PA, placental abruption; SAH, systemic arterial hypertension.

normal figures after childbirth. Acute renal failure (ARF) is an uncommon event in PE. In general, bilateral cortical necrosis is associated with bleeding and excessive hypotension.[34]

Oliguria in PE has a pre-renal cause most of the times. Therefore, when the urine output drops < 25 mL/h, 1,000 mL of saline solution should be administered within 30 minutes. If the urinary output does not normalize, central hemodynamic monitoring is indicated. Normal or increased pulmonary capillary pressure (PCP) and increased urinary concentration mean that oliguria is caused by intrinsic renal arteriolar spasm caused by angiospasm. At other times, oliguria may be a consequence of decreased ventricular function. In general, these patients have very high PCP and incipient pulmonary edema.

Pulmonary Edema

Most pulmonary edema cases in pregnant women are associated with difficult-to-control hypertension. In PE, pulmonary edema occurs more frequently after delivery, associated with excessive fluid infusion.

The etiology of pulmonary edema in PE appears to be multifactorial. The reduction in colloid osmotic pressure (COP), increase in capillary permeability, and elevation in vascular hydrostatic pressure produce extravasation of fluids in the interstitium and alveolar space. In non-pregnant patients, the decrease in COP/PCP gradient has been correlated with pulmonary edema development. Gestation induces decreased COP, and this decrease is accentuated in PE.

The diagnosis and treatment of pulmonary edema in PE is similar to those of non-pregnant patients: oxygen therapy, water restriction, intravenous (IV) furosemide (80 mg initially) and central hemodynamic monitoring. Reduction in afterload is obtained with the use of vasodilators (hydralazine, nifedipine).

Coagulopathy

Patients with PE frequently have abnormalities in the coagulation system. Reduction in AT III activity (< 70%), increase in factor VIII consumption, and elevation of platelet factor IV can be detected before the clinical manifestations.[13] Although there are changes in the coagulation system since the onset of the disease, in patients with PE, most blood coagulability changes occur due to HELLP syndrome (thrombocytopenia and hepatic dysfunction) and not to DIC.

Management of Preeclampsia

Regardless of the severity of the clinical picture, every patient diagnosed with PE should be hospitalized for follow-up in a high-risk gestational unit. Any patient with PE apparently with a benign condition may suddenly develop complications severe enough to result in maternal and/or fetal death.

The fetuses of mothers with PE who remain hospitalized have half the risk of death compared with fetuses of mothers who are not hospitalized. In addition, hospital-based patients with PE have newborns with more advanced GA at delivery and greater birthweight.[35]

Antihypertensive Therapy in Preeclampsia

Severe systolic hypertension is an independent factor for stroke in pregnancy.[36] The goal of the antihypertensive treatment is to protect the pregnant women from stroke (stroke, rupture of hepatic hematoma). In 2011, the World Health Organization (WHO) strongly recommended the antihypertensive treatment for severe preeclampsia with the aim of reducing maternal morbidity and mortality.[37] Moderate hypertensive pregnant women with long-term SAH and those with secondary SAH and/or repercussion in target organs should be treated with antihypertensive medication to remain normotensive. The CHIPS study demonstrated that strict control of arterial hypertension with initiation of antihypertensive treatment from pressure levels of 140/90 mm Hg improves fetal weight, decreases prematurity rates, the diagnosis of severe SAH, and cases of thrombocytopenia and transfusion. This study advises the initiation of the hypertension treatment earlier than we had previously indicated.[38]

Acute Hypertension

Nifedipine administered orally is the first drug of choice for the treatment of a hypertensive crisis (►**Table 5**). Alternatively, hydralazine can be used intravenously or intramuscularly with similar success as nifedipine.[39] However, the meta-analysis of Magee et al[40] showed that the use of hydralazine for hypertensive crisis control presented disadvantages compared with nifedipine and labetalol, demonstrating increased risk of maternal hypotension (RR: 3.29), placental abruption (PA; RR: 4.17), fetal adverse events and fetal bradycardia (RR: 2.04). Labetalol is an effective alternative for the treatment of acute hypertension during pregnancy, even though it is not commercially available in Brazil. Sodium nitroprusside should be reserved for cases of hypertensive encephalopathy or hypertensive crisis not responsive to other treatments, and the dose should always be > 4 µg/kg/min per infusion pump.[16,39,41,42] Angiotensin-converting-enzyme inhibitors, angiotensin inhibitors or blockers, diazoxide and propranolol should not be used in PE because they pose too much risk to the health of the fetuses.[40,43]

Anticonvulsive Preventive Therapy

Magnesium sulfate ($MgSO_4$) is the drug of choice for preventing eclampsia, and the only drug with proven preventive effects against eclamptic seizures. Randomized clinical trials demonstrate that $MgSO_4$ is superior to hydantoin, diazepam, and placebo for the prevention of eclampsia and its recurrent seizures. The treatment with $MgSO_4$ should be used during labor, prior to cesarean section, or whenever there are signs/symptoms consistent with imminent eclampsia. Magnesium sulfate reduces the risk of eclampsia by 57%, and decreases the risk (RR: 0.55) of maternal death without deleterious effects on the fetus.[44]

Magnesium sulfate should be used for up to 24 hours postpartum in cases of eclampsia and severe PE. Magnesium sulfate is not a risk-free drug, and its administration should be monitored. When administered intravenously, an infusion pump with strict nursing control to avoid the risks of

Table 5 Treatment of acute hypertension (BP > 160/110 mm Hg)

1. Position the patient in left lateral decubitus.
2. Infuse 5% glucose serum into the peripheral vein.
3. Administer nifedipine 10 mg orally and repeat 10 mg every 30 minutes if necessary.
If there is no adequate response, administer IV hydralazine 5 mg.* If BP is not controlled, repeat 5–10 mg every 20 minutes.
4. Check maternal BP every 5 minutes for 20 minutes after medication administration.
5. Evaluate fetal cardiac frequency (cardiotocography) for at least 20 minutes after medication administration.
6. Repeat medication if necessary (BP > 155/105 mm Hg), up to the maximum dose of 30 mg for each drug.
7. Maintain BP < 160/110 mm Hg and > 135/85 mm Hg.
8. Other options:
A. Labetalol 20 mg IV bolus and, if necessary, repeat 40 mg in 10 minutes, and up to two doses of 80 mg every 10 minutes up to a maximum dose of 220 mg. Do not use in asthmatics patients or in those with heart failure.
B. Sodium nitrate 0.25 µg (kg/min) up to maximum of 4 µg (kg/min) and do not use for more than 4 hours.

Abbreviations: BP, blood pressure; IV, intravenous.
Note: *Dilute 1 ampoule (20 mg 2 mL) in 3 mL of distilled water: each milliliter will have 5 mg of hydralazine.
Adapted from: Report of the National High Blood Pressure Education Program (2000).[15]

depression and respiratory arrest due to overdosage should be used.

Although $MgSO_4$ therapy has been more effective than placebo for the prevention of eclampsia, even in mild PE cases, and its use has not been associated with unfavorable maternal fetal outcomes,[44,45] the use in patients with mild PE is controversial, given the low incidence (0.6%) of eclampsia in these patients. In patients with mild PE, the NNT for the prevention of 1 case is 129, while in patients with severe PE it is 36. The rational use of $MgSO_4$, avoiding routine use in the group known to have mild PE, has a lower cost.

The use of a low-dose $MgSO_4$ infusion (0.6 g/h) after a standard 4 g IV attack dose was as effective as the traditional 4 g intramuscular (IM) regimen of 4/4 hours, with 3.3% recurrence in patients with IM $MgSO_4$, and 2% in patients with IV infusion of 0.6 g/h.[46] Therefore, continuous IV infusion at a low dose (0.6 g/h) may be an alternative, especially in patients with higher incidence of side effects or even impaired renal function. The preferred treatment is IV therapy in infusion pump at a concentration of 1 g/h. Schemes for the use of $MgSO_4$ are shown in ►**Tables 6** and **7**.

The degree of maternal and fetal impairment should be assessed simultaneously with the treatment of severe hypertension and prevention of eclampsia. If there is intense and persistent epigastralgia, mainly associated with very high BP levels, there may be distension of the hepatic capsule by subcapsular hemorrhage. In this situation, it is important to evaluate the liver with an ultrasound or tomography. The confirmation of a hematoma implies the necessity of strict BP control and the indication of cesarean section, because there

Table 6 Prevention of convulsions with magnesium sulfate heptahydrate ($MgSO_4$ $7H_2O$)

I. Attack dose: 4 g of $MgSO_4$ (8 mL of 50% $MgSO_4$ 7H2O diluted in 12 mL of distilled water) IV in 5–10 minutes.
II. Maintenance dose IV: 0.6–2 g/h IV (dilute 10 mL of 50% $MgSO_4$ 7H2O in 240 mL of saline solution and infuse at a rate of 50 mL/hour (1 g/hour) or 100 mL/hour (2 g/hour) continuously. Every 120 minutes, check if diuresis is preserved (> 25 mL/hour) and if tendon reflexes are present.
III. Maintenance dose IM:* 10 mL at 50% in the upper outer quadrant of the buttock every 4 hours (alternating buttocks). Evaluate diuresis (> 25 mL/hour) and patellar reflexes before each application.

Abbreviations: IM, intramuscular; IV, intravenous.
Note:* Especially useful for transporting patients in ambulance and in ambulatories, situations in which IV infusion control is precarious.

Table 7 Magnesium sulfate therapy: special situations

I. If there is a lapse ≥ 6 hours between maintenance doses and diuresis is ≥ 25 mL/hour, restart treatment with the attack dose.
II. If renal function is impaired (serum creatinine ≥ 1.3 mg/dL): Apply half the maintenance dose. Measure the serum magnesium level before each new dose 4–7 mEq/L: therapeutic levels 8–10 mEq/L: inhibition of tendon reflexes > 10 mEq/L: risk of cardiorespiratory arrest.
III. Respiratory function impairment: Respiratory depression: 1 g intravenous calcium gluconate and oxygen therapy. Respiratory arrest: *besides calcium gluconate*, endotracheal intubation and assisted ventilation.

Table 8 Laboratory evaluation in PE

Suspected diagnosis	Initial evaluation	Follow-up
Proteinuria/creatininuria ratio or proteinuria in reagent tape	Pulse oximetry Hemogram Creatinine Platelets Serum glutamic oxaloacetic transaminase or lactate dehydrogenase	Platelets Serum glutamic oxaloacetic transaminase or lactate dehydrogenase

may be hepatic rupture during the expulsive period. In addition, laboratory tests should be requested to evaluate renal and hepatic functions and possible hematological changes (►**Table 8**).

Management in Pregnancy at Gestational Age > 36 Weeks or with Proven Fetal Lung Maturity

The cure of PE occurs only after the removal of the placenta; thus, the clinical management depends basically on a balance between the severity of the disease and the GA. Aimed at reducing maternal and fetal complications, patients should be referred to tertiary services where pre-established protocols are followed. These measures lead to a reduction from 5.1% to 0.7% in the occurrence of combined maternal adverse events.[47] In addition, delivery before 37 weeks is an independent factor that protects against the recurrence of PE in the next gestation.[48] Koopmans et al[49] randomized 756 patients with mild PE or gestational hypertension for expectant management (watchful waiting) or induction of labor from the 36th week. In the induction group, fewer maternal complications occurred, with no difference in the rates of cesarean or perinatal complications. The planned induction in PE with mature fetuses significantly reduces the morbidity of PE with a significant decrease in care costs.

The existence of a mature fetus is sufficient reason for the definitive treatment of the disease (birth). Therefore, the management of pregnant women with fetuses close to term (GA ≥ 36 weeks) and PE (even mild PE) should be based on the following parameters:

a. Patient hospitalization in an obstetric center.
b. Treatment of acute arterial hypertension episodes (►**Table 5**).
c. Prevention of severe forms of convulsions with $MgSO_4$ (►**Tables 6** and **7**).
d. Evaluation of the degree of maternal and fetal impairment.
e. Interruption of the gestation, preferably by inducing labor.

Management in Pregnancy at Gestational Age > 33 Weeks and < 36 Weeks

Pregnant women with PE and a preterm fetus should be admitted to a hospital obstetrical center with neonatal and maternal intensive care unit (ICU) facilities for evaluation and treatment. The goal of the management is to reach a GA closer to term without this posing too much risk for the pregnant woman and the concept.

Initially, antihypertensive and anticonvulsant therapies should be used as described before (►**Tables 5**, **6** and **7**). The $MgSO_4$ treatment will be discontinued if the conservative management is adopted. The use of hypotensive drugs (methyldopa) is reserved for cases in which the BP exceeds safe levels (SBP > 160 mm Hg or DBP > 110 mm Hg) and in the presence of other risk components indicating immediate cessation of pregnancy.

The assessment of the maternal involvement by physical examination (BP, diuresis, state of consciousness, O_2 saturation), laboratory evaluation (►**Table 8**), and fetal impairment screening are indicated.

After the first 24 hours of observation and evaluation, it is necessary to decide for conservative conduct or interruption of gestation. The definition of the best moment to interrupt the pregnancy depends on several individual factors, neonatal ICU conditions, and the degree of maternal and/or fetal impairment. As a general rule: 1) if the PE is classified as mild, that is, without imminent risk to maternal and fetal health, the interruption should be postponed, if possible, up to the 36th week; and 2) if the PE is classified as severe (►**Table 9**), the pregnancy should be interrupted.

By adopting the conservative approach, pregnant women should remain hospitalized with restricted physical activity (avoid resting restricted to the bed because it does not contribute to the stabilization of the clinical picture and increases the risk of thrombosis). The diet can be unrestricted and normosodic. The pregnant woman's weight should be recorded every two days, and the vital signs should be evaluated only during the waking period, avoiding waking the patient up during sleep. Weekly or in a shorter term, in case of clinical necessity, a laboratory evaluation should be performed (►**Table 8**). The fetus should be auscultated every day, with observation of the daily rate of fetal movement. In patients with mild PE, it is advisable to evaluate the fetal well-being once a week, and whenever any changes in the maternal state occur. Ultrasonography to check fetal development and assessment of fetal-maternal hemodynamics (Doppler flowmetry) should be performed at the time of PE diagnosis.

To monitor fetal development, an ultrasound should be repeated at least in ten-day intervals due to the high incidence of IUGR. The evaluation of placental circulation by the Doppler study of the umbilical arteries is the only fetal evaluation test with level 1 of evidence that has proven to decrease perinatal mortality in pregnant women with SAH and IUGR.[16] Therefore, ideally, patients with PE in conservative management should undergo at least one weekly

Table 9 Maternal and fetal indications of termination of pregnancy in severe preeclampsia < 34 weeks[39]

Maternal	Fetal
HELLP syndrome	Fetal growth below percentile 5
Eclampsia	Repeated late fetal decelerations on cardiotocography
Pulmonary edema or O_2 saturation < 94%	Vein Doppler with pathological a-wave
BP without control despite medications	Fetal death
Serum creatinine > 1.5 mg/dL or oliguria (< 500 mL/ mL/24 hours)	Suspected PA, ROM or onset of labor
Suspected PA, ROM or onset of labor	

Abbreviations: BP, blood pressure; HELLP, hemolysis, elevated liver enzymes and low platelet count; PA, placental abruption; ROM, rupture of membranes.
Adapted from: Sibai, Barton (2009).[53]

Doppler evaluation. Antepartum cardiotocography and fetal biophysical profile may be used complementarily when the Doppler examination is altered in preterm gestations, and when there is need or possibility of prolonging gestation. During labor, cardiotocography with continuous or intermittent monitoring of the fetal heart rate is the test of choice for fetal surveillance.

The induction of fetal lung maturity with corticosteroids can be performed in pregnancies < 34 weeks in which the birth is predicted for the next the 24 or 48 hours.[16] If an elective cesarean is indicated (without labor) for a pregnant woman at < 39 weeks, the use of corticosteroids for pulmonary maturation brings benefits by reducing the need for hospitalization in the neonatal ICU for the newborn's mechanical ventilation.[50,51] When pregnancy interruption is indicated and the fetus is < 36 weeks of GA, the patient has to be hospitalized or transferred to a tertiary-level healthcare hospital.

Management in Pregnancy at Gestational Age < 33 Weeks

In pregnant women at GA < 33 weeks and stable fetal maternal condition, we can opt for conservative management with assiduous management of all parameters of maternal and fetal well-being. By choosing the expectant management, one should be alert to any signs of clinical decompensation. Particular attention should be paid to the degree of maternal thrombocytopenia, which is an important indicator of morbidity and mortality. Patients with PE and platelets between 150,000 and 100,000 cells/mm^3 already have an increase in fetal and maternal morbidity and mortality, which will be greater the lower the platelet count.

Conservative Management of Severe Preeclampsia

The prevalence of severe PE is of ~ 1% of pregnancies, and is associated with progressive deterioration of the fetal-maternal picture.[52,53] All pregnant women with severe PE should be hospitalized, and the initial management should include administration of $MgSO_4$ and antihypertensive drugs (SBP ≥ 160 mm Hg or DBP ≤ 110 mm Hg).[52] In the presence of eclampsia, pulmonary edema, coagulopathy and non-reactive fetal evaluation, labor should be performed even before the completion of the corticosteroid therapy for fetal maturity. ►**Table 4** shows the main parameters for the interruption of gestation.

Several studies[52,53] describe the complications in the conservative management of severe PE < 34 weeks, namely: PA (16–39%); perinatal death (up to 17%); small fetuses for GA (up to 70%); presence of nonreactive fetal tests (26–74%); pulmonary edema (up to 8%); eclampsia (up to 5.6%); HELLP syndrome (4–27%); and renal failure (up to 17%). The main reason for gestational discontinuation in this group of pregnant women is the worsening of the fetal status; therefore, fetal and maternal evaluation should be performed daily, using the various methods available. If the pregnancy is ≤ 32 weeks, but there is risk of maternal and/or fetal death, PA, HELLP syndrome, DIC, eclampsia, severe uncontrollable hypertension (≥ 160/110 mm Hg) or hepatic hematoma, the choice should be interruption of pregnancy.

The prospective fullPIERS study[32] assessed the occurrence of severe maternal outcomes (maternal death and life-threatening complications) in 2,023 pregnant women with PE admitted to tertiary-level hospitals for follow-up in four countries (Canada, New Zealand, Australia and the United Kingdom) in. There were severe complications in 261 women (5%). The predictors for these complications were: GA < 34 weeks, chest pain, dyspnea, low O_2 saturation, thrombocytopenia, increased serum creatinine and altered hepatic transaminases (SGOT). The authors also showed that requiring lactate dehydrogenase (LDH) measurement when the liver enzymes are normal is redundant and should be avoided. It is only necessary to titrate one of the liver enzymes (SGOT or SGPT), and it is not necessary to request coagulation tests.

Some authors recommend trying the conservative management in women with severe PE who received betamethasone only up to the 32nd week on the grounds that the risk of serious maternal complications is not compensated by the additional gain in fetal maturity.[54]

HELLP Syndrome

The acronym HELLP stands for hemolysis, elevated liver enzymes and low platelet count (►**Table 10**). The

Table 10 Diagnosis of HELLP syndrome

	Exam	Parameter
Hemolysis Peripheral blood smear (schistocytosis, anisocytosis, echinocytosis, poikilocytosis)	Bilirubin	$>$ 1.2 mg/dL
	Lactate dehydrogenase	$>$ 600 U/L
Hepatic impairment	Serum glutamic oxaloacetic transaminase	$>$ 70 U/L
Thrombocytopenia	Platelets	$<$ 100,000/mm^3

Abbreviation: HELLP, hemolysis, elevated liver enzymes and low platelet count.
Source: Sibai et al (1986).[55]

pathophysiology of this disease is unclear, but the hepatic hematologic involvement of PE can be considered. Hemolysis, elevated liver enzymes and low platelet count syndrome develops in 0.1 to 0.8 of all pregnancies, and in 10–20% of pregnant women with severe PE/eclampsia. About a third of HELLP syndrome diagnoses are performed in the postpartum period. In patients with antepartum diagnosis, 10% of diagnoses were performed before the 27th week, 20% after the 37th week, and 70% between the 27th and 37th weeks.[55,56]

Hemolysis, elevated liver enzymes and low platelet count syndrome is related to microangiopathic hemolytic anemia and vasospasm in the maternal liver. The symptomatology is usually poor, and may include malaise, epigastralgia, nausea and headache. The degree of clinical suspicion of HELLP syndrome cases is very important. In the presence of thrombocytopenia in a patient with PE, HELLP syndrome should be strongly considered. Many cases go through days with a vague symptom of malaise and the patient reporting nonspecific symptoms, similar to a cold, with generalized pain, nausea and epigastric pain. Some studies point to a varying prevalence of the main symptoms, such as malaise (50 to 90%), pain in the right hypochondrium or epigastralgia (30 to 90%), and nausea and vomiting (20 to 50%); proteinuria may be absent.[57,58]

The diagnostic confirmation of HELLP syndrome is by laboratory tests (►**Table 10**), using the laboratory parameters described by Sibai.[55] Thrombocytopenia is the main and earliest laboratorial modification found. The appearance of coagulation abnormalities, such as change in prothrombin time, partial thromboplastin time, and fibrinogen, is uncommon. When thrombocytopenia is severe ($<$ 50,000/mm^3), products of fibrin degradation and activation of AT III appear, indicating the initiation of an intravascular coagulation process. Eventually, patients with HELLP syndrome have hemorrhagic diastasis with bleeding at multiple sites (hematuria, hematemesis, surgical wound bleeding). Red cell fragmentation is present in HELLP syndrome, and although the amount of fragmentation is not associated with the severity of multiple organ dysfunction, it represents the involvement of the endothelial system in the microcirculation. Fragmentation is a result of the passage of red blood cells through small damaged vessels. Hepatic dysfunction can be measured by various parameters, such as increased LDH and transaminases (SGOT and SGPT). Renal dysfunction will depend on the severity of the condition, and it can be diagnosed in up to 46% of HELLP syndrome cases.[59] After hepatic and renal dysfunction, the patient may present pulmonary damage with DIC, characterizing a multiple organ dysfunction. In less than 2% of HELLP syndrome cases, a hepatic hematoma is formed. The diagnosis can be made by ultrasonography, and the treatment varies from conservative therapy to surgical management in cases of hepatic rupture.[60] If there is hepatic hematoma without rupture, a cesarean section is indicated, and surgical exploration should not be performed given the risk of rupture at that time.

Differential Diagnosis

Differential diagnosis between HELLP syndrome and other pathologies (especially hemorrhagic and hepatic pathologies) that may occur in the puerperal cycle is fundamental. Among the main pathologies, the following stand out: acute hepatitis, cholecystitis, pancreatitis, lupus, fatty liver of pregnancy, thrombocytopenic purpura, hemolytic-uremic syndrome, and septic or hemorrhagic shock, among others. Severe complications of HELLP syndrome occur with hemorrhage (central nervous system, liver, operative wound, PA).

Thrombocytopenia $<$ 50,000/mm^3 is associated with the occurrence of DIC and a strong indicator of hemorrhagic complications. The presence of headache, visual changes and epigastralgia significantly increases the risk of eclampsia. In a Brazilian study[61] performed with 105 patients with HELLP syndrome, the main complications found were bleeding (34%), oliguria (47%), acute renal failure (20%), acute pulmonary edema (7%), need for blood transfusion (33%), and maternal death (4%). These data confirm the severity of this syndrome and the importance of the management at a tertiary center with experienced teams. The most important factor for the reduction of maternal morbidity and mortality is the early diagnosis, which should be made in the asymptomatic phase through laboratory investigation of thrombocytopenia, hemolysis and hepatic alterations in all patients with PE. Although the main cause of jaundice in pregnancy is hepatitis, if it occurs, the presence of HELLP syndrome with advanced hemolysis should always be ruled out.

Management in HELLP Syndrome

As it happens with eclampsia, HELLP syndrome should be regarded as an obstetric emergency requiring immediate care. The treatment is based on the prevention of hemorrhagic complications and eclampsia, control of SAH and the onset of labor.

The timing of interruption can be programmed depending on the severity of each case and the GA. In pregnancies > 34 weeks, labor induction should start immediately, with simultaneous control of the hypertensive crisis by using $MgSO_4$ and blood products when indicated. In pregnant women at GA< 34 weeks, in the absence of serious complications, such as hepatic hematoma, severe thrombocytopenia and eclampsia, corticosteroid therapy should be performed for pulmonary maturation before the interruption of pregnancy. O'Brien et al[62] propose fundamental steps for the care of HELLP syndrome, as follows:

1. Have high diagnostic suspicion in pregnant women with PE;
2. Perform laboratory tests and differential diagnosis;
3. Evaluate maternal and fetal conditions;
4. Control blood pressure;
5. Stabilize the clinical picture: venous access; administration of $MgSO_4$ and antihypertensive drugs;
6. Consider the use of corticosteroids for fetal maturity;
7. Hemotherapy if necessary;
8. Check if there is need for hepatic imaging (epigastralgia);
9. If cesarean section is indicated, evaluate with the anesthesiologist the technique to be adopted;
10. Actively manage labor or plan the cesarean section with the proper technique;
11. Plan for care in maternal and neonatal ICUs if necessary;
12. Perform laboratory evaluation every 6–24 hours, depending on the severity of the condition, until stabilization;
13. Maintain the use of antihypertensive and $MgSO_4$ in the puerperal period; and
14. Counseling for future pregnancies.

As the management of patients with HELLP syndrome should be performed in tertiary centers with maternal and neonatal ICUs, suspected cases should be transferred immediately in an adequate ambulance in the presence of a life-saving physician after contact with the reference maternity. The patient should be on IV $MgSO_4$, and if an infusion pump is not available, the attack dose should be administered intravenously, avoiding IM administration if thrombocytopenia $< 100{,}000/mm^3$ due to the risk of gluteal hematoma. Magnesium sulfate should be started immediately, and maintained for up to 24 hours postpartum, with control of diuresis, tendon reflexes, and respiratory rate (►**Table 10**).

Fetal conditions, GA and uterine cervix (Bishop score) are fundamental in deciding the route of birth. If < 30 weeks, in absence of labor, and Bishop score < 5, elective caesarean section is recommended after initiating $MgSO_4$.[6] In pregnant women with < 32 weeks and fetuses with restricted growth, and alteration of the umbilical artery Doppler, it is preferable to perform a cesarean section, except in cases already in labor.[61] The other patients may be submitted to labor induction. Anesthesia of the pudendal nerve should be avoided due to the risk of hematoma. Caesarean sections should be performed by experienced professionals using the best surgical technique and with attention to intraoperative hemostasis. In the presence of thrombocytopenia ($< 100{,}000/mm^3$), infraumbilical median laparotomy is recommended to reduce the risk of hematomas in the aponeurotic detachment. If thrombocytopenia is $< 75{,}000/mm^3$, epidural or subdural anesthesia should be avoided, and general anesthesia should be performed. The use of an aspiration drain is recommended in the most severe patients, especially in those with DIC, facilitating postoperative control. The Portovac (Howmedica, Toronto, Ontario, Canada) drain (polyethylene with closed drainage system) or the Blake (Ethicon, Somerville, NJ, US) drain (silicone, soft, continuous drainage) can be used. The latter has the advantage of continuous drainage, and since it does not have a closed drainage system, it causes less obstruction problems due to small clots. These should be removed 24 to 48 hours after the cesarean section, depending on the evolution of the patient's surgical clinical status and the amount of drainage. Care should be taken with puerperal blood loss and the risk of uterine hypotonia. Thus, the prophylactic use of IV oxytocin and misoprostol (rectal or intrauterine) is extremely valuable.

Use of Corticosteroids for Thrombocytopenia Rescue

Corticosteroids have been used for the treatment of women with HELLP syndrome, especially those with platelets $< 50{,}000/mm^3$. The mechanism of action includes reduction of platelet adhesion, reduction in platelet removal by the spleen, and increase in platelet activation. Currently, a Brazilian study (COHELLP) is underway to verify the efficacy of dexamethasone in patients with HELLP and thrombocytopenia < 50,000.

Some centers use dexamethasone 10 mg intravenously every 12 hours before delivery and after birth until laboratory recovery. Some studies have demonstrated an improvement in thrombocytopenia and other laboratory tests with this practice, as well as a decrease in the need for transfusions, hypertension and the use of antihypertensive drugs, presenting a postpartum recovery with lower morbidity.[63] However, this finding has not been reported in other studies.[64] We still lack more consistent evidence on the benefit of corticosteroid therapy in maternal morbidity and mortality. In a recent systematic review of the Cochrane Library, the conclusion is that there is insufficient evidence for the routine use of steroids in HELLP syndrome, and that their use may be justified in special situations in which platelet increase is important.[65] Intravenous dexamethasone may be used if platelets are < 50,000/dL. This recommendation may open a window of opportunity, rescuing thrombocytopenia even temporarily, enabling, for example, the use of blockade anesthesia in a caesarean section.

Blood and Platelet Transfusion

In the presence of abnormal bleeding and HELLP syndrome, or in the presence of severe thrombocytopenia ($<$ 20,000 platelets), even without bleeding, transfusion of platelet concentrate is always indicated. If the patient underwent a cesarean section, the transfusion of platelets is recommended when the count is $<$ 50,000/mm^3. Each platelet concentrate unit elevates the platelets by $\sim$ 5,000 mm^3 to 10,000 mm^3 in an adult weighing 70 kg.[62]

Postpartum Management

The postpartum period remains extremely critical. In general, in the first 24 hours of the puerperal period, there is a transient worsening of the clinical picture due to consumption of platelets and coagulation factors. This worsening is more pronounced when the birth occurs by caesarean section. Therefore, we should not base on the postoperative process of preeclampsia. Many maternal deaths have occurred in the postpartum period because of hemorrhagic complications and some degree of little importance given to care in that period. Even if the patient does not have clinical parameters for an ICU admission yet, she must be admitted to this type of unit for immediate control of any kind of postpartum change. Laboratory control will be performed using the same parameters of diagnosis (platelets, LDH, SGOT, bilirubin). Diuresis should be controlled and maintained above 25 mL/hour. Hypertension should be maintained below 160/100 mm Hg. If there is spontaneous diuresis above 25 mL/hour, normal creatinine, LDH decrease, improvement in platelet levels and hepatic transaminases, we can consider the disease entered remission.

Preeclampsia Delivery Route

The preferred route of delivery in PE is vaginal, with no contraindication for cervical maturation procedures (Foley catheter, prostaglandin analogues), and cesarean section is reserved for usual obstetric indications. There should be constant monitoring of the fetal heart rate (FHR) during the first or second periods of childbirth. The presence of uterine hyperactivity, increased uterine tone, vaginal bleeding or pathological decelerations of the fetal heart rate should be seen as signs of possible PA.

For the cesarean section, epidural or subdural anesthesia may be used. In this situation, the patient should be hydrated with an infusion of 1,000 mL lactated ringer or saline before sympathetic block to avoid severe hypotension with decreased tissue perfusion of vital organs (kidneys and placenta).

In addition, while the patient remains supine during cesarean section, a cushion should be placed under the pregnant woman's right flank, thereby reducing the compression of the uterus on the large vessels of the abdomen. If severe hypotension still occurs, liquid infusion will be necessary to fill the dilated vascular space, avoiding the use of vasopressor substances. In emergency situations or when there is a complicated pregnancy-specific hypertensive disease (eclampsia, HELLP syndrome, DIC), general anesthesia is the preferred option. In this eventuality, it is important to alert the anesthesiologist about the use of $MgSO_4$, because its sedative action may be dangerous in conjunction with succinylcholine.

In general, the hypertensive picture disappears or improves substantially in the first 24 hours of the puerperal period, although the symptoms may remain up to six weeks after childbirth. If BP is $<$ 150/100 mm Hg, the patient may be discharged without antihypertensive therapy and undergo a weekly evaluation in an outpatient setting until PE signs disappear.

Management in Gestational Age $<$ 24 Weeks

The presence of severe PE in the second trimester, and especially $<$ 25 weeks, is associated with high rates of perinatal mortality (up to 83%) and maternal complications (27 to 71%), including maternal death.[52,66] Immediate delivery is associated with a lower chance of fetal survival, while prolongation of the pregnancy may somewhat increase the chance of fetal survival, but it adds an important risk of maternal morbidity and mortality. In these cases, the ideal management is not established yet, and is the reason for numerous studies and discussions in the literature. Some authors[52–54] recommend the interruption of pregnancy in these cases after discussing with the couple and obtaining signed informed consent. When the option is for expectant management, fetal and maternal evaluations should be performed daily, controlled in centers with obstetricians, neonatologists and intensivists experienced in high-risk obstetrics.

Persistent Postpartum Hypertension

Chronic hypertensive patients may develop hypertensive encephalopathy, pulmonary edema and cardiac insufficiency in the puerperal period. These events are more frequent in patients with overlapping PE, previous cardiac or renal disease, PA, or with difficult to control BP. In patients who remain hypertensive, drugs for its control should be administered orally. In the other patients, BP can be controlled weekly for a month, then at intervals of three to six months for one year.

When prescribing antihypertensive medication, it is necessary to bear in mind that the vast majority is excreted in human milk and can be absorbed by the newborn. Although there is a lack of good studies on the use of antihypertensive drugs in lactation, the recommendation to avoid diuretics seems reasonable, given their potential to suppress lactation. Neonatal exposure to methyldopa, labetalol, captopril and nifedipine is considered safe, and, therefore, a good option in the breastfeeding period.

Atenolol and metoprolol should be avoided because of their higher concentration in the breast milk, with potential effects on the newborn.[67] In patients with severe PE, but not

in those with mild or overlapping PE, the use of furosemide 20 mg/day after delivery improves BP control and decreases the need for antihypertensive drugs.[68]

Postpartum Counseling and Prognosis

Patients should be followed up in the puerperal period and, if they remain hypertensive, for at least 12 weeks. Persistent hypertension after this period should be considered as chronic hypertension. Patients with PE before the 30th week of pregnancy have a 10% chance of recurrence in the next gestation. The rate may be greater in black women. The recurrence rate of the HELLP syndrome is $\sim$ 5% of times. The recurrence of PE is also higher among multiparous women than among those who had the disease in the first pregnancy, especially if there is a change of partner in the next pregnancy.

Apparently, human pregnancy is an excellent cardiovascular stress test, and the occurrence of PE, especially if early onset PE ($<$ 32 weeks), means a failure in the cardiovascular capacity of the pregnant woman. The literature has an increasing number of studies with long-term follow-up in which the data point to a positive relationship between PE/eclampsia and hypertension, cardiovascular disease, ischemic stroke and early mortality in the future.[47]

A population study[69] demonstrated an association between the occurrence of chronic renal failure (CRF) and previous history of PE. The occurrence of PE in the first pregnancy was associated with a 4.7-fold higher risk (3.6–6.1, 95%CI) of developing CRF, and this risk was even greater (15.5 times) in women who had developed PE in 2 or 3 pregnancies. The study concluded that PE is a marker of risk for future development of CRF. In another population-based study in Norway, Irgens et al[68] confirmed that patients with preeclampsia have a 20% higher risk of death from cardiovascular disease (RR = 1.2 [1.02–1.37, 95%CI]) than the population without PE and, when it occurs at younger GAs associated with prematurity, the risk is almost 8 times higher (RR = 8.12 [4.31–15.33, 95%CI]). Patients with a history of PE for more than ten years had DBP and body mass index (BMI) higher than the controls.[71]

For these reasons, after the hospital discharge of patients who had PE, especially if diagnosed before the 32nd week, the women should always be advised to maintain healthy lifestyles from the cardiovascular and metabolic points of view. In these patients, more than in all others, guidelines on avoiding smoking, obesity, hyperglycemia and hypercholesterolemia, as well as the prescription of physical exercises and diet, are a medical obligation.

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References

1 Abalos E, Cuesta C, Grosso AL, Chou D, Say L. Global and regional estimates of preeclampsia and eclampsia: a systematic review. Eur J Obstet Gynecol Reprod Biol 2013;170(01):1–7 Review
2 Giordano JC, Parpinelli MA, Cecatti JG, et al. The burden of eclampsia: results from a multicenter study on surveillance of severe maternal morbidity in Brazil. PLoS One 2014;9(05):e97401
3 de Oliveira LG, Karumanchi A, Sass N. Preeclampsia: oxidative stress, inflammation and endothelial dysfunction. Rev Bras Ginecol Obstet 2010;32(12):609–616
4 Smets EM, Visser A, Go AT, van Vugt JM, Oudejans CB. Novel biomarkers in preeclampsia. Clin Chim Acta 2006;364(1-2):22–32
5 Tranquilli AL, Dekker G, Magee L, et al. The classification, diagnosis and management of the hypertensive disorders of pregnancy: A revised statement from the ISSHP. Pregnancy Hypertens 2014; 4(02):97–104
6 American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol 2013;122(05):1122–1131
7 Martins-Costa SH, Vettorazzi J, Valério E, et al. Protein creatinine ratio in random urine sample of hypertensive pregnant women: maternal and perinatal outcomes. Hypertens Pregnancy 2011; 30(03):331–337
8 Magee LA, Pels A, Helewa M, Rey E, von Dadelszen P; Canadian Hypertensive Disorders of Pregnancy (HDP) Working Group. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. Pregnancy Hypertens 2014;4(02):105–145 Review
9 Ramos JG, Martins-Costa SH, Mathias MM, Guerin YL, Barros EG. Urinary protein/creatinine ratio in hypertensive pregnant women. Hypertens Pregnancy 1999;18(03):209–218
10 Ramos JG, Martins-Costa S, Edelweiss MI, Costa CA. Placental bed lesions and infant birth weight in hypertensive pregnant women. Braz J Med Biol Res 1995;28(04):447–455 https://www.ncbi.nlm.nih.gov/pubmed/8520542
11 Beaufils M, Uzan S, DonSimoni R, Brault D, Colau JC. Metabolism of uric acid in normal and pathologic pregnancy. Contrib Nephrol 1981;25:132–136
12 Pollak VE, Nettles JB. The kidney in toxemia of pregnancy: a clinical and pathologic study based on renal biopsies. Medicine (Baltimore) 1960;39:469–526
13 Chesley LC. Hypertensive disorders in pregnancy. New York: Appleton Century Crofts; 1978
14 Weiner CP. Disseminated intravascular coagulopathy associated with pregnancy. In: Clark SL, DB Cotton DB, Hankins GD, Phelan FP, editors. Critical care obstetrics. 2nd ed. Oxford: Blackwell Scientific; 1991:180–199
15 Ramos JG, Martins-Costa SH, Kessler JB, Costa CA, Barros E. Calciuria and preeclampsia. Braz J Med Biol Res 1998;31(04):519–522
16 Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol 2000;183(01):S1–S22
17 Yu CK, Papageorghiou AT, Parra M, Palma Dias R, Nicolaides KH; Fetal Medicine Foundation Second Trimester Screening Group. Randomized controlled trial using low-dose aspirin in the prevention of pre-eclampsia in women with abnormal uterine artery Doppler at 23 weeks' gestation. Ultrasound Obstet Gynecol 2003; 22(03):233–239
18 Duckitt K, Harrington D. Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies. BMJ 2005; 330(7491):565 Review
19 Grill S, Rusterholz C, Zanetti-Dällenbach R. Potentialmarkers of preeclampsia–a review. Reprod Biol Endocrinol 2009;7:70
20 Duley L, Henderson-Smart DJ, Meher S, King JF. Antiplatelet agents for preventing pre-eclampsia and its complications. Cochrane Database Syst Rev 2007;(02):CD004659 Review

21 Roberge S, Nicolaides KH, Demers S, Villa P, Bujold E. Prevention of perinatal death and adverse perinatal outcome using low-dose aspirin: a meta-analysis. Ultrasound Obstet Gynecol 2013;41(05): 491–499

22 Hofmeyr GJ, Lawrie TA, Atallah AN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev 2010;(08): CD001059

23 Levine RJ, Hauth JC, Curet LB, et al. Trial of calcium to prevent preeclampsia. N Engl J Med 1997;337(02):69–76

24 Norwitz ER, Robinson JN, Repke JT. Prevention of preeclampsia: is it possible? Clin Obstet Gynecol 1999;42(03):436–454 Review

25 Corrêa MD Júnior. Aguiar, RA, Corrêa MD. Fisiopatologia da préeclâmpsia: aspectos atuais. Femina 2009;37(05):247–253

26 Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. Lancet 2005;365 (9461):785–799 Review

27 Cnossen JS, ter Riet G, Mol BW, et al. Are tests for predicting pre-eclampsia good enough to make screening viable? A review of reviews and critical appraisal. Acta Obstet Gynecol Scand 2009;88 (07):758–765

28 Giguère Y, Charland M, Bujold E, et al. Combining biochemical and ultrasonographic markers in predicting preeclampsia: a systematic review. Clin Chem 2010;56(03):361–375

29 Myatt L, Clifton RG, Roberts JM, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units (MFMU) Network. First-trimester prediction of preeclampsia in nulliparous women at low risk. Obstet Gynecol 2012;119(06):1234–1242

30 Verlohren S, Galindo A, Schlembach D, et al. An automated method for the determination of the sFlt-1/PlGF ratio in the assessment of preeclampsia. Am J Obstet Gynecol 2010;202 (02):161.e1–161.e11

31 Nicolaides KH. Turning the pyramid of prenatal care. Fetal Diagn Ther 2011;29(03):183–196

32 von Dadelszen P, Payne B, Li J, et al; PIERS Study Group. Prediction of adverse maternal outcomes in pre-eclampsia: development and validation of the fullPIERS model. Lancet 2011;377 (9761):219–227

33 Akkermans J, Payne B, von Dadelszen P, et al. Predicting complications in pre-eclampsia: external validation of the fullPIERS model using the PETRA trial dataset. Eur J Obstet Gynecol Reprod Biol 2014;179:58–62

34 Barron WM. Hypertension. In: Barron WM, Lindheimer MD. Medical disorders during pregnancy. 2nd ed. St. Louis: Mosby; 1995. Cap. 1. p. 1–36.

35 Barton JR, Witlin AG, Sibai BM. Management of mild preeclampsia. Clin Obstet Gynecol 1999;42(03):455–469 Review

36 Martin JN Jr, Thigpen BD, Moore RC, Rose CH, Cushman J, May W. Stroke and severe preeclampsia and eclampsia: a paradigm shift focusing on systolic blood pressure. Obstet Gynecol 2005;105 (02):246–254

37 World Health Organization (WHO). WHO recommendations for prevention and treatment of preeclampsia and eclampsia. Geneva: World Health Organization; 2011

38 Magee LA, von Dadelszen P, Rey E, et al. Less-tight versus tight control of hypertension in pregnancy. N Engl J Med 2015;372(05): 407–417

39 Martins Costa S, Ramos JG, Barros E, Bruno RM, Costa CA, Goldin JR. Randomized, controlled trial of hydralazine versos nifedipine in preeclamptic women with acute hypertension. Clin Exp Hypertens B 1992;11(01):25–44

40 Magee LA, Cham C, Waterman EJ, Ohlsson A, von Dadelszen P. Hydralazine for treatment of severe hypertension in pregnancy: meta-analysis. BMJ 2003;327(7421):955–960

41 Montán S. Drugs used in hypertensive diseases in pregnancy. Curr Opin Obstet Gynecol 2004;16(02):111–115 Review

42 Sibai BM. Treatment of hypertension in pregnant women. N Engl J Med 1996;335(04):257–265 Review

43 Paula LG, Martins Costa S. Tratamento anti-hipertensivo na gestação e lactação. Femina 2003;31(09):803–808

44 Altman D, Carroli G, Duley L, et al; Magpie Trial Collaboration Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Lancet 2002;359(9321):1877–1890

45 Livingston JC, Livingston LW, Ramsey R, Mabie BC, Sibai BM. Magnesium sulfate in women with mild preeclampsia: a randomized controlled trial. Obstet Gynecol 2003;101(02):217–220

46 Chowdhury JR, Chaudhuri S, Bhattacharyya N, Biswas PK, Panpalia M. Comparison of intramuscular magnesium sulfate with low dose intravenous magnesium sulfate regimen for treatment of eclampsia. J Obstet Gynaecol Res 2009;35(01):119–125

47 von Dadelszen P, Magee L. What matters in preeclampsia are the associated adverse outcomes: the view from Canada. Curr Opin Obstet Gynecol 2008;20(02):110–115

48 Bhattacharya S, Campbell DM, Smith NC. Pre-eclampsia in the second pregnancy: does previous outcome matter? Eur J Obstet Gynecol Reprod Biol 2009;144(02):130–134

49 Koopmans CM, Bijlenga D, Groen H, et al; HYPITAT study group. Induction of labour versus expectant monitoring for gestational hypertension or mild pre-eclampsia after 36 weeks' gestation (HYPITAT): a multicentre, open-label randomised controlled trial. Lancet 2009;374(9694):979–988

50 Stutchfield P, Whitaker R, Russell I; Antenatal Steroids for Term Elective Caesarean Section (ASTECS) Research Team. Antenatal betamethasone and incidence of neonatal respiratory distress after elective caesarean section: pragmatic randomised trial. BMJ 2005;331(7518):662

51 Royal College of Obstetricians and Gynaecologists. Antenatal corticosteroids to reduce neonatal morbidity and mortality [Internet]. London: Royal College of Obstetricians and Gynaecologists; 2010. (Green-top Guideline no 7). [cited 2017 Feb 12]. Available from: www.rcog.org.uk/

52 Sibai BM, Barton JR. Expectant management of severe preeclampsia remote from term: patient selection, treatment, and delivery indications. Am J Obstet Gynecol 2007;196(06):514.e1–514.e9

53 Haddad B, Sibai BM. Expectant management in pregnancies with severe pre-eclampsia. Semin Perinatol 2009;33(03):143–151 Review

54 Bombrys AE, Barton JR, Nowacki EA, et al. Expectant management of severe preeclampsia at less than 27 weeks' gestation: maternal and perinatal outcomes according to gestational age by weeks at onset of expectant management. Am J Obstet Gynecol 2008;199 (03):247.e1–247.e6

55 Sibai BM, Taslimi MM, el-Nazer A, Amon E, Mabie BC, Ryan GM. Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe preeclampsia-eclampsia. Am J Obstet Gynecol 1986;155(03): 501–509

56 Martin JN Jr, Macann EF, Blake PG, Martin RM, Pwry KG Jr, Roberts WE. Analysis of 454 pregnancies with severe preeclampsia/eclampsia HELLP syndrome using the 3 class system of classification. [abstract] Am J Obstet Gynecol 1993;168(01):386

57 Haddad B, Barton JR, Livingston JC, Chahine R, Sibai BM. Risk factors for adverse maternal outcomes among women with HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome. Am J Obstet Gynecol 2000;183(02):444–448

58 Cavkaytar S, Ugurlu EN, Karaer A, Tapisiz OL, Danisman N. Are clinical symptoms more predictive than laboratory parameters for adverse maternal outcome in HELLP syndrome? Acta Obstet Gynecol Scand 2007;86(06):648–651

59 Ramos JG, Martins-costa S, Vettorazzi-Stuczynski J, Brietzke E. Morte materna em um hospital terciário do Rio Grande do Sul – Brasil: um estudo de 20 anos. Ver Bras Ginecol Obstet. 2003;25 (06):431–436

60 Wicke C, Pereira PL, Neeser E, Flesch I, Rodegerdts EA, Becker HD. Subcapsular liver hematoma in HELLP syndrome: Evaluation of

diagnostic and therapeutic options–a unicenter study. Am J Obstet Gynecol 2004;190(01):106–112
61 Katz L, Amorim MM, Miranda GV, Pinto e Silva JL. Clinical and laboratorial profile and complications of patients with HELLP syndrome admitted in an obstetric intensive care unit. Rev Bras Ginecol Obstet 2008;30(02):80–86
62 O'Brien JM, Barton JR. Controversies with the diagnosis and management of HELLP syndrome. Clin Obstet Gynecol 2005; 48(02):460–477 Review
63 Martin JN Jr, Thigpen BD, Rose CH, Cushman J, Moore A, May WL. Maternal benefit of high-dose intravenous corticosteroid therapy for HELLP syndrome. Am J Obstet Gynecol 2003;189(03): 830–834
64 Fonseca JE, Méndez F, Cataño C, Arias F. Dexamethasone treatment does not improve the outcome of women with HELLP syndrome: a double-blind, placebo-controlled, randomized clinical trial. Am J Obstet Gynecol 2005;193(05):1591–1598
65 Woudstra DM, Chandra S, Hofmeyr GJ, Dowswell T. Corticosteroids for HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome in pregnancy. Cochrane Database Syst Rev 2010;(09): CD008148 Review
66 Ganzevoort W, Sibai BM. Temporising versus interventionist management (preterm and at term). Best Pract Res Clin Obstet Gynaecol 2011;25(04):463–476
67 Podymow T, August P. Hypertension in pregnancy. Adv Chronic Kidney Dis 2007;14(02):178–190 Review
68 Ascarelli MH, Johnson V, McCreary H, Cushman J, May WL, Martin JN Jr. Postpartum preeclampsia management with furosemide: a randomized clinical trial. Obstet Gynecol 2005;105(01):29–33
69 Vikse BE, Irgens LM, Leivestad T, Skjaerven R, Iversen BM. Preeclampsia and the risk of end-stage renal disease. N Engl J Med 2008;359(08):800–809
70 Irgens HU, Reisaeter L, Irgens LM, Lie RT. Long term mortality of mothers and fathers after pre-eclampsia: population based cohort study. BMJ 2001;323(7323):1213–1217
71 Canti IC, Komlós M, Martins-Costa SH, Ramos JG, Capp E, Corleta Hv. Risk factors for cardiovascular disease ten years after preeclampsia. Sao Paulo Med J 2010;128(01):10–13

Acute Abdomen Secondary to Ruptured Epithelial Ovarian Cancer during Pregnancy: The Relevance of Teamwork

Abdome agudo secundário à ruptura do câncer do ovário epitelial durante a gravidez: a importância do trabalho em equipe

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Abstract

Acute abdomen secondary to epithelial ovarian cancer rupture during pregnancy is a rare event. Our aim is to present how the work of a coordinated multidisciplinary team in a case of ruptured epithelial ovarian cancer during pregnancy is feasible to obtain the best results possible. A 34-year-old woman during the 37th week of her first gestation presented with an acute abdomen. During laparotomy, a ruptured 16.5-cm left ovarian tumor was detected; the tumor was extirpated and sent to pathologic evaluation. In the meantime, a Kerr cesarean section was performed, and a healthy female neonate was born. The tumor was diagnosed as a cystadenocarcinoma; therefore, the family and the combined surgical team (obstetricians and a surgical oncologist) decided to complete a definitive radical ovarian cancer surgery: hysterectomy, right salpingo-oophorectomy, lymphadenectomy, omentectomy and appendectomy. The patient's postoperative evolution was uneventful, and she was sent to adjuvant chemotherapy.

Keywords

- acute abdomen
- epithelial ovarian cancer
- ovarian cancer
- pregnancy
- ruptured epithelial ovarian cancer

Resumo

O abdome agudo secundário à ruptura do câncer do ovário epitelial durante a gravidez é um evento raro. Nosso objetivo é apresentar como o trabalho de uma equipe multidisciplinar coordenada em um caso de ruptura do câncer de ovário epitelial durante a gravidez é viável para obter os melhores resultados possíveis. Uma mulher de 34 anos de idade, durante a 37ª semana de sua primeira gestação, apresentou um

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Palavras-chave
- abdome agudo
- câncer de ovário epitelial
- cancro do ovário
- gravidez
- ruptura do câncer

abdome agudo. Durante a laparotomia, foi detectado um tumor ovariano esquerdo com ruptura de 16,5 cm; O tumor foi extirpado e enviado para avaliação patológica. Enquanto isso, uma cesariana de Kerr foi feita, e uma recém-nascida saudável nasceu. O tumor foi diagnosticado como um cistoadenocarcinoma; então, a família e a equipe cirúrgica combinada (obstetras e oncologista cirúrgico) decidiram concluir uma cirurgia radical definitiva do câncer de ovário: histerectomia, salpingo-ooforectomia direita, linfadenectomia, omentectomia e apendicectomia. A evolução pós-operatória da paciente foi sem intercorrências, e ela foi enviada para quimioterapia adjuvante.

Introduction

When an acute abdomen occurs during pregnancy, it poses a huge challenge.[1] However, an acute abdomen caused by a ruptured epithelial ovarian cancer during pregnancy is an exceptional disorder.[2,3] Our aim is to present how the work of a coordinated multidisciplinary team in a case of ruptured epithelial ovarian cancer during pregnancy is feasible.

Case Description

A 34-year-old woman during the 37th week of her first gestation called her obstetrician because she felt an acute abdominal pain. The patient stated that the pain was sharp, and its intensity increased until it became incapacitating; her physician recommended that she presented to an emergency room immediately. In the meantime, the obstetrician called the surgical oncologist to inform that the patient was in the 37th week of her first gestation and, additionally, she had a big-papillary left ovarian tumor, discovered during her last abdominal ultrasound. Both physicians agreed to evaluate the patient; in the emergency room, the patient presented an evident acute abdomen, and the physicians decided for an immediate laparotomy. Using epidural anesthesia, during the laparotomy, a ruptured 16.5-cm left-ovarian tumor, with intraperitoneal spillage of its inner

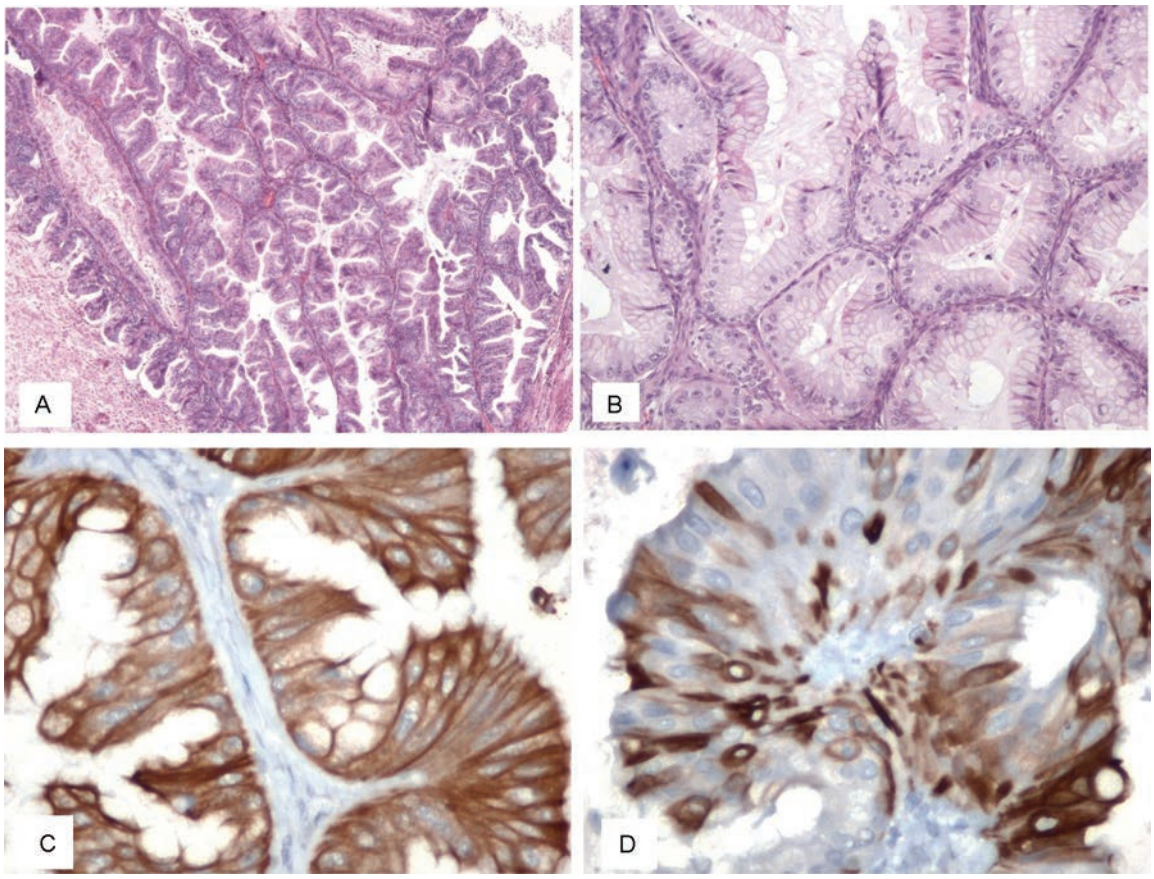

Fig. 1 (A) Photomicrograph of a hematoxylin and eosin-stained section (4x) showing abundant tumor papillae; (B) photomicrograph of a hematoxylin and eosin-stained section (10x) showing goblet cells with nuclear stratification; (C) photomicrograph of cytokeratin CK7 immunohistochemistry (40x); (D) photomicrograph of cytokeratin CK20 immunohistochemistry (40x).

liquid, was recognized; through the broken tumor wall, many big papillae were observed. A sample from the liquid was taken, and a left salpingo-oophorectomy was completed, and both specimens were sent to the pathology department (at 1 am) for a transoperatory examination. In the meantime, a Kerr cesarean section was performed, and a healthy female neonate weighing 2.35 kg was born. The pathologist diagnosed a ruptured cystadenocarcinoma. With this diagnosis, the patient's husband and the combined surgical team (obstetricians and a surgical oncologist) decided to complete an ovarian carcinoma routine: hysterectomy, right salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, infracolic omentectomy and appendectomy, with no gross residual tumor; the patient's postoperative evolution was uneventful. The definitive pathologic report was a ruptured moderately differentiated mucinous cystadenocarcinoma (►**Fig. 1**), without tumor capsule invasion and with no metastases to the other surgical specimens. The patient received 6 cycles of carboplatin plus paclitaxel; by the end of the treatment, the patient was well, without tumor recurrence 15 months later.

Discussion

To our best knowledge, after an extensive literature review (in the PubMed, Google Scholar, LILACS, and Scopus databases), this is the first case of a ruptured epithelial ovarian cystadenocarcinoma during pregnancy favorably resolved in the primary surgery with a cesarean section and a radical surgical procedure. There are two previous reports, one of an endometrioid ovarian carcinoma, and the other of a mucinous cystadenocarcinoma, of cases that presented with rupture during pregnancy[4,5], and in both cases, definitive diagnosis and surgical radical treatment for ovarian cancer were performed after the emergency was solved.[4,5]

Acute abdominal pain during pregnancy entails a huge challenge,[1] and when indicated according to specific clinical features, laparotomy is the best way to preserve the lives of the mother and the fetus.[1] However, oncologic procedures during pregnancy are an enormous challenge.

It is well known that, among non-pregnant women, radical surgical cyto-reduction and adjuvant chemotherapy are the standard of care for epithelial ovarian cancer.[6,7] However, these tumors during pregnancy are rare, and due to their infrequency, a lot of questions regarding the treatment are pending. Thus, each case of epithelial ovarian cancer during pregnancy needs to be treated individually.[6,7] According to some authors, due to increasing maternal age rates worldwide, an increase in the prevalence of cancers complicating pregnancies is soon expected.[2,3,8] Considering the product well-being, a complete radical surgery for ovarian cancer during pregnancy in the primary surgery has not been previously reported.[7]

Conclusion

A multidisciplinary team working closely in the management of ovarian cancer during pregnancy is of paramount importance to obtain the best possible results[7,9], like in the case presented in this study.

Ethical Standards

Disclosure of potential conflicts of interest: the authors have no conflicts of interest to declare.

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Informed Consent

Informed consent was obtained from the patient.

Contributions

All of the manuscript authors made substantial contributions to the conception, design, development, and draft of the article, and all read and agreed with the manuscript's final version submitted to RBGO.

References

1 Nair U. Acute abdomen and abdominal pain in pregnancy. Curr Obstet Gynaecol 2005;15(06):359–367
2 Salani R, Billingsley CC, Crafton SM. Cancer and pregnancy: an overview for obstetricians and gynecologists. Am J Obstet Gynecol 2014;211(01):7–14
3 Goh W, Bohrer J, Zalud I. Management of the adnexal mass in pregnancy. Curr Opin Obstet Gynecol 2014;26(02):49–53
4 Gottheil S, McGee J. Endometrioid ovarian carcinoma during pregnancy presenting with acute rupture. J Obstet Gynaecol Can 2013;35(11):1020–1022
5 Malhotra N, Sumana G, Singh A, Deka D, Mittal S. Rupture of a malignant ovarian tumor in pregnancy presenting as acute abdomen. Arch Gynecol Obstet 2010;281(05):959–961
6 Grimm D, Woelber L, Trillsch F, Keller-v Amsberg G, Mahner S. Clinical management of epithelial ovarian cancer during pregnancy. Eur J Cancer 2014;50(05):963–971
7 Blake EA, Kodama M, Yunokawa M, et al. Feto-maternal outcomes of pregnancy complicated by epithelial ovarian cancer: a systematic review of literature. Eur J Obstet Gynecol Reprod Biol 2015;186:97–105
8 Saeed Z, Shafi M. Cancer in pregnancy. Obstetrics, Gynaecol Reprod Med 2011;21(07):183–189
9 Cooke L, Shafi MI. Cancer in pregnancy. Obstetrics, Gynaecol Reprod Med 2013;23(10):317–319

Uterine Extramedullary Plasmacytoma as a Primary Manifestation of Multiple Myeloma

Plasmocitoma extramedular uterino como manifestação primária de mieloma múltiplo

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Abstract

The association between plasmacytomas and multiple myeloma (MM) is well-described, and in about one third of the cases of plasmacytoma the additional study will lead to the diagnosis of MM. The finding of plasmacytomas in the genital tract is extremely rare, with sparse cases described in the literature, and these cases pose a challenge regarding the optimal guidance and treatment. This paper describes a case of uterine extramedullary plasmacytoma in a 79-year-old woman with complaints of postmenopausal abnormal uterine bleeding. The complementary study led to the diagnosis of uterine plasmacytoma and, subsequently, of MM. Despite the unfavorable outcome of this case, we consider pertinent to report it because it constitutes a differential diagnosis to be taken into account in the approach of pelvic masses.

Keywords
- plasmacytoma
- multiple myeloma

Resumo

A associação entre plasmocitomas e mieloma múltiplo (MM) encontra-se bem demonstrada, e em cerca de um terço dos casos de plasmocitoma o estudo adicional conduzirá ao diagnóstico de MM. O achado de plasmocitomas no trato genital é extremamente raro, havendo um número muito limitado de casos descritos na literatura, o que dificulta concluir sobre a melhor forma de orientação e tratamento destes casos. O presente trabalho descreve um caso de plasmocitoma extramedular uterino em mulher de 79 anos estudada por queixas de hemorragia uterina anômala pós-menopáusica. O estudo complementar levou ao diagnóstico de plasmocitoma uterino e, posteriormente, de MM. Apesar do desfecho desfavorável do caso, consideramos pertinente o seu relato por se tratar de um diagnóstico diferencial a levar em consideração na abordagem de massas pélvicas.

Palavras-chave
- plasmocitoma
- mieloma múltiplo

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Introduction

Plasma cells dyscrasias refer to a group of neoplasms that is characterized by the proliferation of a monoclonal population of plasmocytes that secretes monoclonal immunoglobulins. These neoplasms may present in single or multiple lesions (solitary plasmacytomas or multiple myeloma respectively). The association between plasmacytomas and multiple myeloma (MM) is well-established,[1] and in about one third of the cases the additional study of a plasmacytoma will lead to the diagnosis of MM.[2] These tumors can appear in the bone or in different organs, and are classified as bone or extramedullary plasmacytomas respectively.[3] Extramedullary plasmacytomas in the female genital tract are quite rare, either as solitary plasmacytomas or as part of a disseminated MM. There are few cases described in the literature,[3–7] considering that 80% of extramedullary plasmacytomas arise in the head or neck, mostly in the superior respiratory and digestive tracts.

Case Report

We present a case of a 79-year-old woman, bedridden and totally dependent on other people to perform her daily activities, with a past history of breast cancer at 54 years old treated with conservative surgery followed by radiotherapy. She had no other relevant personal antecedents, made no chronic use of medications, and had no smoking or drinking habits. Her menarche occurred at 11 years old, and she had regular cycles and 1 pregnancy (with a vaginal delivery at 27 years old). There was no history of use of hormonal contraceptives, and she had spontaneous menopause at 41 years without hormonal therapy.

The patient arrived to the emergency department with complaints of postmenopausal abnormal uterine bleeding (AUB) since the previous month, with no other symptoms. Upon physical examination, there were no signs of hemodynamic instability. Upon the speculum examination, a moderate amount of necrotic tissue and blood with fetid odor was found in the vagina and through the external cervical orifice; they were sent for a histological test. The blood work was normal, with a hemoglobin level of 11.7 g/dL. The pelvic ultrasound showed a heterogenic endometrial thickening of 21 mm, atrophic ovaries, and no adnexal masses. The histological study revealed a neoplasm with diffuse infiltration of atypical plasma cells, suggestive of myeloma. Immunohistochemistry: CD138 and CD56 positive, cytokeratins, S100, estrogen receptors, actin, desmin, CD20 and CD79a negative (►**Fig. 1**). The kappa and lambda light chain analysis was inconclusive. She had an antigen Ki-67 level of 60%.

Shortly after, the patient returned to the emergency with a history of severe pain and functional disability of the right arm after brushing her teeth. Radiography identified a supracondylar pathological fracture of the right humerus, which reinforced the diagnosis hypothesis of MM. Additionally, she maintained the

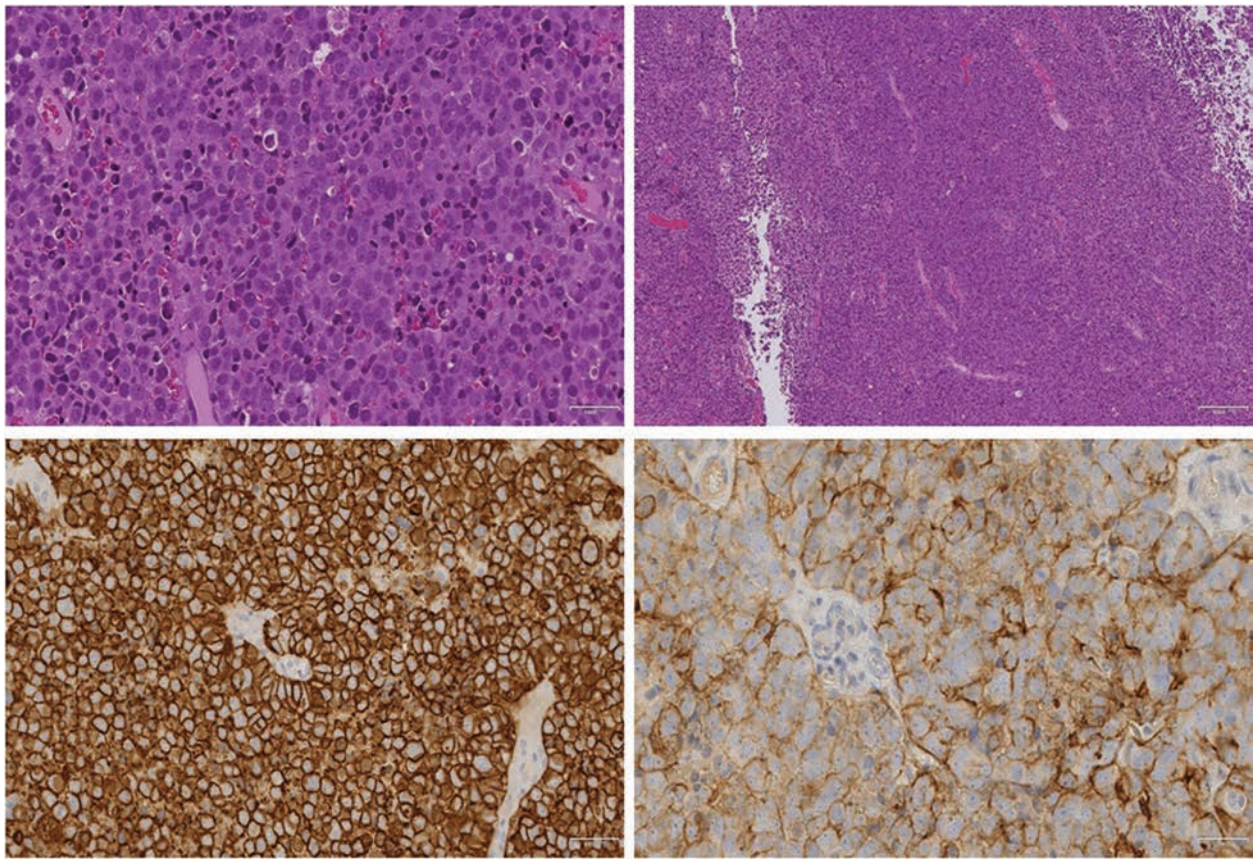

Fig. 1 Histological study of fragments of the endometrium. (**A** and **B**) Hematoxylin-eosin (HE). Immunohistochemistry with positivity for CD56 (**C**) and CD138 (**D**) antibodies.

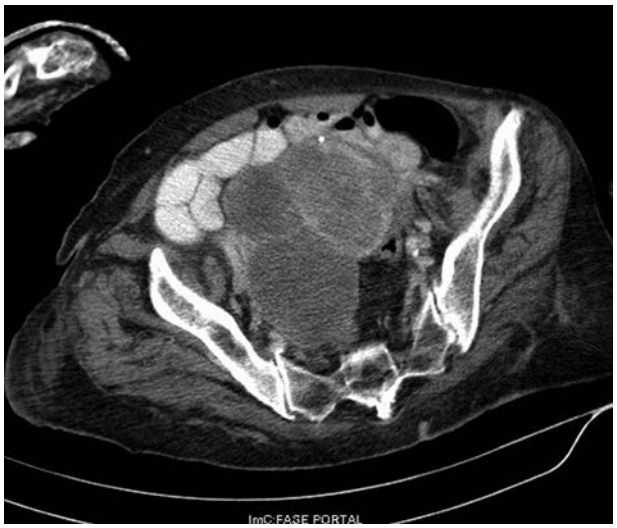

Fig. 2 Enlarged uterus with a heterogeneous uterine lesion of macrolobulated contours and intense contrast-enhanced, of probable neoformative origin.

AUB, but with associated anemia (hemoglobin level of 7.2 g/dL). The patient was then admitted to the Department of Orthopedics. During hospitalization and a complementary study, a rise in the β-2-microglobulin and kappa chain levels was noted. Computed tomography (CT) showed diffuse osteopenia and two expansive lesions: one with 6.9 × 7.9 cm, solid and heterogeneous, well-delimited, with moderate contrast-enhanced, located on the left hypochondrium, between the diaphragmatic cupula, stomach, pancreas and spleen, with apparent cleavage plan with adjacent structures; the other lesion measured 10 × 11 × 9 cm, and was heterogeneous, with macrolobulated contours, and intense contrast-enhanced, located on the pelvis, probably of neoformative origin, and was responsible for an increase in the uterine volume (►**Fig. 2**).

Conservative treatment for the fracture was decided, and the patient was referred to a Hematology-Oncology appointment. In the follow-up, the diagnosis of MM was assumed, considering that the patient had a histologically-confirmed plasmacytoma, bone lesion of target organ and increase in biomarkers. However, as the patient was totally dependent, bedridden, without conditions for intensive chemotherapy regimens and presented progressive worsening of the general condition with performance status 4 at the time of the appointment, we decided to immediately start a treatment with melphalan combined with prednisolone, without waiting for other tests, namely the bone biopsy.

The patient maintained a gradual worsening of the general condition, and only had a chemotherapy cycle before dying shortly after, in a palliative care unit.

Discussion

The extramedullary and bone plasmacytomas correspond to localized forms of plasma cells neoplasms,[8] and result from the proliferation of monoclonal plasma cells.[9]

The mean age of onset of these lesions is 55 years, with a predominance of females,[1] and the most common location of extramedullary plasmacytomas is the upper respiratory and digestive tracts (82%), followed by the gastrointestinal tract, the urogenital tract, the skin, the lung and the breast.[10] The initial form of presentation may correspond to the finding of one or more localized swellings and/or the onset of nonspecific symptoms related to its location.[11]

The association between plasmacytomas, especially bone plasmacytomas, and MM has been well-described.[11] Extramedullary involvement, however, is less frequent, and it generally presents in more advanced stages of the disease.[12] Not only is there a risk of progression of solitary plasmacytomas to MM, but plasmacytomas may occur in naturally as secondary forms of MM.[13]

In less than 5% of patients with a plasma cell dyscrasia, the onset of the disease is the detection of a plasmacytoma with no manifestations of systemic disease.[14] The incidence of extramedullary plasmacytomas at the time of the diagnosis of MM is around 7–18%, and 6–20% of patients will develop this type of tumor during the MM follow-up,[15] with a better survival prognosis in the latter situation.[1]

The diagnosis of primary plasmacytoma (bone or extramedullary) differs from MM because there is a histological confirmation but no evidence of plasma cells involving the bone marrow, with no evidence of lytic lesions in the bone study, and absence of hypercalcemia, anemia or insufficiency associated renal disease.[10]

Due to its important association with MM and prognosis implications,[10] the initial investigation of patients with extramedullary plasmacytoma should include a detailed study to confirm or exclude this diagnosis.[8] Similarly, the follow-up of patients with the diagnosis of plasmacytoma should include adequate surveillance to allow the early detection of MM, although the duration and frequency of such follow-up have not yet been well-established.[8]

The occurrence of plasmacytomas in the female genital tract is rare, with few cases described.[3–7,14,16,17] Due to the scarcity of available information, the optimal follow-up and treatment are also to be clarified.

Regarding the treatment, the distinction between primary plasmacytoma and MM is essential, as the approaches are quite different. While the former has a good response to radiotherapy (the first-line treatment), in the latter, the systemic treatment is the choice.

We describe a rare diagnosis of a uterine extramedullary plasmacytoma detected by postmenopausal AUB. In this case, although the complementary study was not concluded due to the rapid worsening of the general health state, the finding of bone lesions and histologically-confirmed plasmacytoma led to the diagnosis of MM. This report is relevant because it constitutes a differential diagnosis to be presented in the study of pelvic masses with important management and prognosis implications.

Conflicts to Interest

The authors have no conflicts of interest to declare.

References

1 Schols SE, Tick LL. Recurrent extramedullary plasmacytoma in asymptomatic multiple myeloma: a case report. J Med Case Reports 2015;9:37

2 Ruiz Santiago F, Tello Moreno M, Martín Castro A, Guzmán Alvarez L, Navarrete González P. Soft tissue extramedullary plasmacytoma. Case Rep Med 2010;2010:307902

3 Fischer EG, Bocklage TJ, Rabinowitz I, Smith HO, Viswanatha DS. Primary plasmacytoma arising in an endocervical polyp with detection of neoplastic cells on papanicolaou test. A case report and review of the literature. Arch Pathol Lab Med 2003;127(01):e28–e31

4 Mondal SK, Chatterjee S, Mandal S, Bhattacharjee D. Primary extramedullary plasmacytoma of ovary: Report of a rare neoplasm. J Cancer Res Ther 2015;11(04):923–924

5 Zhong YP, Zhang JJ, Huang XN. Multiple myeloma with rupture of ovarian plasmacytoma. Chin Med J (Engl) 2012;125(16):2948–2950

6 Emery JD, Kennedy AW, Tubbs RR, Castellani WJ, Hussein MA. Plasmacytoma of the ovary: a case report and literature review. Gynecol Oncol 1999;73(01):151–154

7 Shakuntala P, Praveen S, Shankaranand B, Rajshekar K, Umadevi K, Bafna U. A rare case of plasmacytoma of the ovary: a case report and literature review. Ecancermedicalscience 2013;7:288

8 Pinto JA, Sônego TB, Artico MS, Leal CFA, Bellotto S. Extramedullary plasmacytoma of the larynx. Int Arch Otorhinolaryngol 2012; 16(3):410–413

9 Kilciksiz S, Karakoyun-Celik O, Agaoglu FY, Haydaroglu A. A review for solitary plasmacytoma of bone and extramedullary plasmacytoma. Sci World J 2012;2012:895765

10 Ooi GC, Chim JC, Au WY, Khong PL. Radiologic manifestations of primary solitary extramedullary and multiple solitary plasmacytomas. AJR Am J Roentgenol 2006;186(03):821–827

11 Guo SQ, Zhang L, Wang YF, et al. Prognostic factors associated with solitary plasmacytoma. Onco Targets Ther 2013;6:1659–1666

12 Huang H, Bazerbachi F, Mesa H, Gupta P. Asymptomatic multiple myeloma presenting as a nodular hepatic lesion: a case report and review of the literature. Ochsner J 2015;15(04):457–467

13 Park YM. Imaging findings of plasmacytoma of both breasts as a preceding manifestation of multiple myeloma. Case Rep Med 2016;2016:6595610

14 Huang CC, Liu MT, Pi CP, Chung CY. Primary plasmacytoma of the uterine cervix treated with three-dimensional conformal radiotherapy. Singapore Med J 2008;49(12):e361–e364

15 Bladé J, de Larrea CF, Rosiñol L. Extramedullary involvement in multiple myeloma. Haematologica 2012;97(11):1618–1619

16 Johansen B, Ahlbom G, Ostergård B. Extramedullary solitary plasmocytoma at the uterine cervix as a cause of postcoital bleeding. Acta Obstet Gynecol Scand 1989;68(03):279–280

17 Sun N, Wang L, Li W. A case of extramedullary solitary plasmacytoma arising at the uterine cervix. Eur J Gynaecol Oncol 2012; 33(04):423–424

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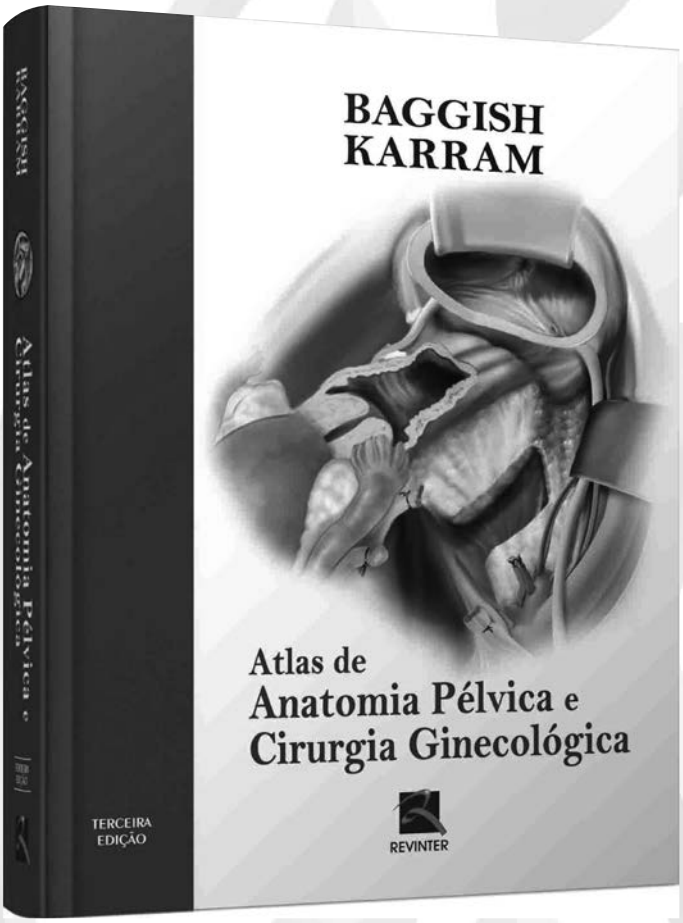

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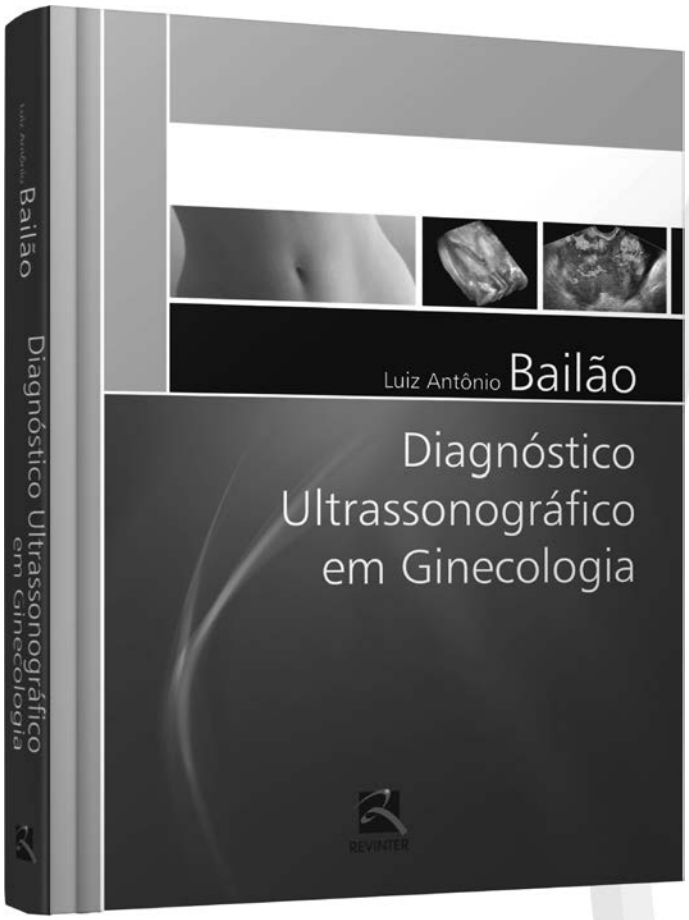

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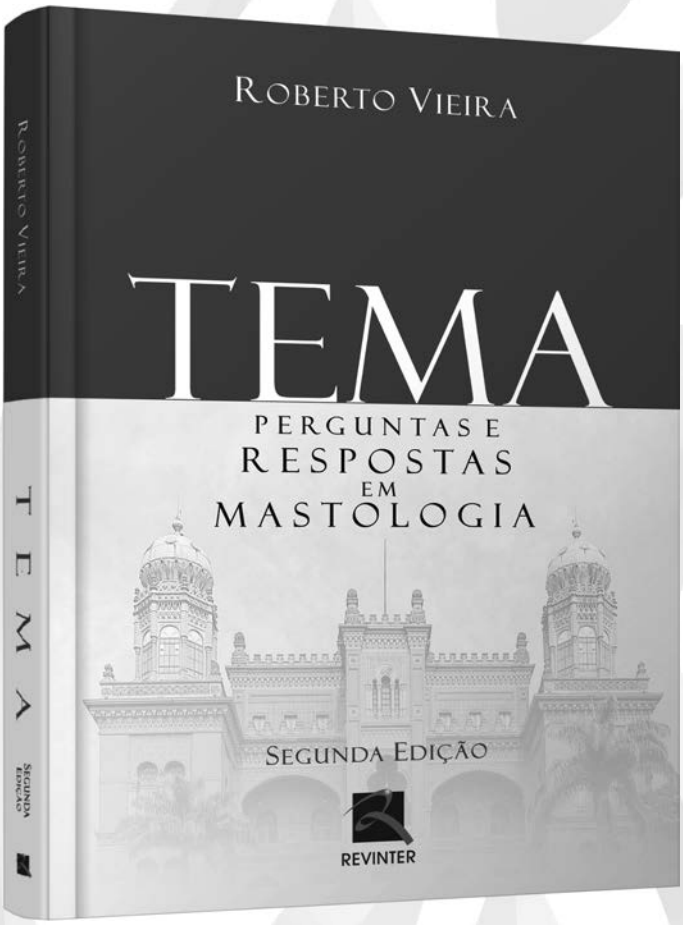

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