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ORIGINAL ARTICLE

Adverse pregnancy outcomes related to chronic arterial hypertension

Desfechos adversos gestacionais relacionados à hipertensão arterial crônica

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ABSTRACT

Objective: Evaluate adverse perinatal outcomes related to previous systemic arterial hypertension (SAH). **Methods:** This is a case-control study conducted at Darcy Vargas Maternity Hospital, in Joinville, SC, Brazil, from August to December 2020. A sample composed of patients older than 18 years old who have recently given birth was interviewed. Patients were divided into two groups, patients with and without previous SAH. In the adjusted odds ratio calculation (OR), a 95% confidence interval (95%CI) was used. **Results:** Two groups were analyzed: one with previous SAH (n=110/6.5%) and one without previous SAH (n=1,560/93.4%). Regarding maternal characteristics, patients with SAH were older, more obese, had more previous pregnancies, caesarean sections, abortions, prenatal appointments, gestational diabetes mellitus (GDM), pregnancy induced hypertension (PIH), and previous diabetes mellitus (DM). About the characteristics of the newborns of mothers with SAH, lower gestational age at birth, higher incidence of caesarean section, prematurity, low birth weight and neonatal intensive care unit (ICU) were observed. After calculating the adjusted odds ratio, it was found that pregnant women with SAH had higher chance of GDM (CR=2.157; 95%CI 1.373-3.390), PIH (CR=2.739; 95%CI 1.619-4.663), and prematurity (CR=2.552; 95%CI 1.090-5.979). **Conclusion:** The presence of previous SAH increased the chance of GDM by 2.1 times, PIH by 2.7 times and prematurity by 2.5 times.

Keywords: Hypertension; Pregnancy, High-risk; Hypertension, Pregnancy-induced.

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RESUMO

Objetivo: Avaliar desfechos adversos perinatais relacionados à hipertensão arterial sistêmica (HAS) prévia. **Métodos:** Trata-se de um estudo de caso controle realizado na Maternidade Darcy Vargas, Joinville/SC, entre agosto e dezembro de 2020. Entrevistou-se uma amostra composta de puérperas maiores de 18 anos que foram divididas em dois grupos: pacientes com e sem HAS prévio. No cálculo de razão de chance (RC) ajustado, utilizou-se o intervalo de confiança de 95% (IC95%). **Resultados:** Analisou-se dois grupos: puérperas com HAS prévio (n=110/6,5%) e sem HAS prévio (n=1.560/93,4%). Quanto às características maternas, puérperas com HAS tiveram maior idade, eram mais obesas, tiveram mais gestações anteriores, cesarianas prévias, abortos, fizeram mais consultas pré-natal e tiveram mais diabetes mellitus gestacional (DMG), doença hipertensiva específica da gravidez (DHEG) e diabetes mellitus (DM) prévio. Em relação aos recém-nascidos de mães com HAS, observaram-se menor idade gestacional ao nascimento, maior incidência de cesariana, prematuridade, baixo peso ao nascer e unidade de terapia intensiva (UTI) neonatal. Após o cálculo de razão de chance ajustado, verificou-se que gestantes com HAS tiveram maior chance de DMG (RC=2,157; IC95% 1,373-3,390), DHEG (RC=2,739; IC95% 1,619-4,663) e prematuridade (RC=2,552; IC95% 1,090-5,979). **Conclusão:** A presença de HAS prévia aumentou a chance de DMG em 2,1 vezes, DHEG em 2,7 vezes e de prematuridade em 2,5 vezes.

Palavras-chave: Hipertensão; Gravidez de alto risco; Hipertensão induzida pela gravidez.

Introduction

Chronic systemic arterial hypertension (SAH) during pregnancy is defined by persistently high blood pressure (BP), with systolic BP ≥140mmHg and/or diastolic BP ≥90mmHg, before the pregnancy or up to 20 weeks of pregnancy[1]. Its prevalence may be estimated in 0.6% in the United States, getting higher over the years, and very much related to advanced age and racial inequalities[2]. The weight gain between women and the more advanced maternal age during pregnancy are the main reasons to the gradual increase of chronic hypertension during pregnancy[2,3].

Its occurrence is among the most important causes of maternal and fetal morbimortality in the United States[4], with significant impact in obstetric outcomes during pregnancy[5].

Many studies have pointed out important maternal occurrences towards chronic systemic arterial hypertension[5-7], and the risk of developing serious hypertension and pre-eclampsia is directly related to the BP control and the use of antihypertensive drugs[8]. Among the maternal outcomes associated to previous hypertension, there are pre-eclampsia[5-7], acute renal failure[7], pulmonary edema[7] and caesarian section[5,6]. Gestational diabetes mellitus (GDM) is also related to chronic SAH during pregnancy[5].

About newborn complications, studies have demonstrated that the presence of chronic SAH is associated to a higher newborn mortality, when compared to pregnant women without this disease[5,6]. In addition, the presence of chronic SAH is related to premature births[6], low birth weight[6], small infant for gestational age[5,9], and admission to neonatal intensive care unit (ICU)[6].

Considering the important relation between the presence of previous chronic SAH and so many adverse gestational and perinatal outcomes, more investigations about this pathology during pregnancy are relevant. Then, this study intended to examine perinatal outcomes associated to previous chronic SAH during pregnancy.

Methods

This is a case-control study focused on the impact of previous SAH in the adverse perinatal outcomes. The

interviews contemplated socioeconomic aspects, life habits, familiar and obstetric history, besides information about the current pregnancy. They were applied to a random and stratified sample composed of patients older than 18 years old who have given birth at Darcy Vargas Maternity Hospital, in Joinville, SC, Brazil, and whose complete prenatal assistance was through the Unified Health System, in Joinville, as well.

The data gathering was performed from August to December 2020, after approval of the Research Ethics Committee, and all the information was obtained through a qualified-hearing interview and the Electronic Records of Darcy Vargas Maternity Hospital 48 hours after the birth.

The project was approved under the number CAAE 28786020.5.0000.5363 by the Research Ethics Committee of Hans Dieter Schmidt Regional Hospital, Joinville, SC, Brazil, and it followed all the criteria defined by Resolution 466/2012. All the pregnant women have signed the Informed Consent Form in person.

Through interviews, maternal data like age, body mass index (BMI), weight gain, race, education level, remuneration, and marital status were analyzed. In addition, information about familiar and obstetric history, life habits (smoking, alcoholism, and other drugs), the presence of previous diseases (diabetes mellitus and SAH) or the ones developed during pregnancy (gestational diabetes mellitus - GDM, pregnancy induced hypertension - PIH), as well as the number of prenatal appointments at the High-Risk Sector at Darcy Vargas Maternity Hospital, were evaluated. Chronic arterial hypertension was defined as systemic arterial hypertension diagnosed before pregnancy or before 20th weeks of gestation.

Through the patient's record, the newborn's characteristics were examined, like Capurro score, birth weight, adequacy of birth weight for gestational age, Apgar score at 1 and 5 minutes, mode of delivery, necessity of neonatal ICU, besides adverse outcomes, like prematurity, low birth weight, laceration, and episiotomy. Newborns weighing below the 10% percentile were classified as small for gestational age; those who were between the 10th and 90th percentile were classified as adequate for gestational age and newborns above the 90% percentile were classified as large for gestational age. NBs weighing <2.5kg were classified as having low birth weight and those weighing >4kg were defined as macrosomic.

According to the World Health Organization (WHO), body mass index (BMI) was classified as underweight when below 18.5, normal weight in the interval of 18.5 to 24.9 and pre-obesity between 25.0 to 29.9. For obesity, values between 30.0 to 34.9 were classified as class I, 35.0 to 39.9 class II and above 40 were classified as class III obesity.

The classification of gestational weight gain was determined by the Institute of Medicine considering the pregnant women's BMI, which denotes that in underweight mothers it should be between 12.5 and 18kg and normal weight in the interval of 11 and 16kg, whereas the weight gain should be between 7 and 11.5kg, and 5 to 9kg and in pre-obese and obese women, respectively.

The inclusion criteria were: an only-fetus pregnant women who were assisted during prenatal care in Health Units of the Unified Health System, in Joinville, whose deliveries have happened at Darcy Vargas Maternity Hospital, and who have decided voluntarily to participate of the investigation, through the agreement by the Informed Consent Form. The exclusion criterion was: pregnant women who have refused to participate of the investigation after the beginning of the questionnaire.

At the same time, the data were inserted in an electronic database with double entry, in order to check the agreement and possible typing mistakes. The Statistical Package for the Social Sciences (SPSS), version 21.0, was used to analyze the data statistically. All the variables were analyzed descriptively, and the continuous variables were examined by means and standard deviation. To qualitative variables, absolute and relative frequencies were calculated. To check the equality hypothesis between the groups' means, the Student's t-test was used, if the distribution was normal, or the Mann-Whitney non-parametric test for non-normal distributions. The normality test used was Kolmogorov-Smirnov's. To confirm the groups' homogeneity towards the proportions, Chi-squared test or Fisher's exact test were used, for frequencies below 5.

Multinomial logistic regression models were utilized to analyze the relation between previous SAH and adverse perinatal outcomes (GDM, PIH, caesarean section, prematurity, low birth weight, and neonatal ICU). Then, the relevance of the effect of the variables was estimated according to the adjusted *odds ratio* (OR) calculation and the confounding factors, using a 95% confidence interval (95%CI). The confounding factors used were age, previous caesarean section, smoking, alcoholism, and other drugs. The values were considered significant when $p<0.05$.

Results

Due to the high prevalence of complications associated to SAH in the maternal-fetal pregnancy, it is important to analyze the maternal characteristics that imply this event, thinking about an association between the variables that lead to the development of this disease. This way, in this study, 1,670 women who have given birth were evaluated in the public obstetric service of Darcy Vargas Maternity Hospital in Joinville, SC. Among the patients, 110 (6.5%) had SAH before the pregnancy, while 1,560 (93.4%) did not have the disease.

Regarding the characteristics that were significant in the present study, they were different towards the age, being the patients with previous SAH older in average than the pregnant women without the disease, and the weight, more specifically about the pregestational BMI. Higher BMI was noticed among the hypertensive mothers, as well as obesity, that was more prevalent between them too.

Considering the previous pregnancies among the patients, the group with previous SAH had more prior pregnancies, more prior caesareans, and more miscarriages, as well as more prenatal appointments. In addition, both groups had differences according to the number of complications. The group with previous SAH demonstrated more GDM and more prevalence of PIH. Besides, the patients of this group had more prevalence of previous DM. All these results are synthetized in detail in Table 1.

About the newborns' characteristics, the children of mothers with previous SAH had lower mean gestational age at birth and were more premature, with higher prevalence of deliveries before 37 weeks among this group. In relation to the delivery mode, the number of caesareans between the women with previous SAH was higher. Moreover, the low-birth-weight index was higher in this group too.

In terms of these variables, it was possible to expect that the number of neonatal ICU hospitalizations between newborns of mothers with previous SAH would be higher, what in fact occurred. The study pointed out there was higher percentage of babies of these mothers submitted to intensive therapy, when compared to newborns of mothers without previous hypertension. These data are in Table 2.

After calculating the adjusted odds ratio to women who have given birth with or without previous SAH, it was found that pregnant women with SAH had higher chance of GDM (CR=2.157; 95%CI 1.373-3.390), PIH (CR=2.739; 95%CI 1.619-4.663), and prematurity (CR=2.552; 95%CI 1.090-5.979), what did not interfere in caesarean section, low birth weight or neonatal ICU, according to Table 3.

Discussion

This study is important because it analyzed the impacts of SAH and its outcomes during pregnancy in a significant number of pregnant women from the same maternity hospital. It observed that patients with SAH have more chances of developing GDM. Besides, patients with this disease tend to present PIH. Regarding the newborn, pregnant women with SAH have more probability of premature birth. However, the relation between patients with SAH and a higher quantity of caesarean sections, low weight at birth, and the number of neonatal hospitalizations was not significant.

In this study, 1,670 patients were analyzed, and 110 (6.5%) had SAH. Comparing this information with the literature, an article has examined many former studies that evidenced the number of patients with SAH was about 1 to 5%[6]. In another study, whose population consisted of 109,932 pregnant women, only 1.3% had SAH [5]. Another analysis, made in south Brazil, had an incidence of 5.5% of the disease[10]. In this perspective, our study presented higher prevalence in comparison to that of the literature. Then, we concluded it occurred because of some factors, as mean maternal age and obesity, both being risk factors to SAH[6], since in our study the mean maternal age was 30.9 years old, and most pregnant women with SAH were obese. Furthermore, this higher prevalence of SAH may also be explained by the study being conducted in a maternity for high-risk reference in our region.

Considering the characteristics of pregnant women with SAH, this study observed that the disease is more frequent in older and obese women, who have had previous pregnancies, higher BMI and higher number of miscarriages and caesarean sections. Other investigations confirm the maternal characteristics that were identified, that is, pregnant women with SAH have more probability of being older and having higher BMI[5,11]. Literature also points out SAH is more common between pregnant women who have presented miscarriage, caesarean, and metabolic problem[5], and the ones who have had more than one pregnancy[12].

In agreement with our results, a similar study observed that patients with SAH have more chances of developing GDM[13]. Both GDM and SAH are related to resistance to insulin, oxidative stress, poor immune system, and inflammatory processes[14]. The referred study achieved OR for GDM developing of 2.1, while another study pointed out 2.07[15].

Poor neonatal results can be related to chronic SAH due to superimposed pre-eclampsia[14]. Pre-eclampsia is more common when the blood pressure presents a sudden increase, or when there is the urgent need of using anti-hypertensive medicines in order to control the blood pressure. In addition, the development of proteinuria or its sudden increase are also associated to chronic SAH among women with pregestational proteinuria or proteinuria that developed at the beginning of pregnancy. This means the study[14] is in accordance with our investigation, as both concluded chronic SAH interferes in the increase of PIH prevalence. This study presents OR of 1.6, similar to the 2.7 value our study has found[14].

Regarding the increase of the prevalence of caesarean sections among patients with SAH in comparison to patients with no SAH, there are controversies, because some studies affirm there is a significant number[11,12], while other ones say there is not[5]. The difference seen in the found results points out there is alteration in the number of caesarean sections, and it can be explained according to our study due to the considerable difference in the sampling size, as the first one analyzed 795,221 pregnant women, and the second one 1,670.

About the characteristics of newborns to mothers with SAH, our study observed that children to mothers with previous SAH presented lower mean gestational age at birth. Also, there was more prevalence of caesareans among patients with SAH, besides higher index of prematurity, low weight at birth, and higher number of hospitalizations in neonatal ICU. Moreover, other studies confirm these particularities between newborns to mothers with SAH, as prematurity, low weight at birth, and higher number of hospitalizations in neonatal ICU[6].

The increase of the premature birth index among pregnant women with SAH was seen in similar studies[11,12]. SAH is responsible to restricted blood flow

Table 1. Maternal characteristics towards systemic arterial hypertension (SAH)*.

	Patients without SAH (n=1,560)	Patients with SAH (n=110)	*p*
Age	27.1 (6.1)	30.9 (6.3)	0.000
Pregestational BMI	25.8 (5.4)	31.9 (6.4)	0.000
Obesity	323 (20.7)	59 (53.6)	0.000**
Weight gain	12.8 (7.1)	11.4 (8.3)	0.039
Excessive weight gain	651 (41.7)	60 (54.5)	0.009**
Race			0.870**
White	1,264 (81.1)	87 (79.1)	
Black	64 (4.1)	5 (4.5)	
Brown	230 (14.8)	18 (16.4)	
Schooling			0.838**
Primary	392 (25.1)	29 (26.4)	
Secondary	964 (61.8)	65 (59.1)	
Higher	204 (13.1)	16 (14.5)	
Previous pregnancies	2.3 (1.4)	2.9 (1.9)	0.001
Previous normal childbirths	1.3 (1.3)	1.4 (1.7)	0.180
Previous caesarians	0.7 (0.9)	1.1 (1.1)	0.000
Miscarriages	0.2 (0.6)	0.4 (0.9)	0.046
Remunerated activity	689 (44.2)	50 (45.5)	0.793**
Marital status			0.458
Married	465 (29.8)	35 (31.8)	
Single	917 (58.8)	61 (55.5)	
Stable union	152 (9.7)	10 (9.1)	
Divorced	26 (1.7)	4 (3.6)	
Number of prenatal appointments	8.5 (3.2)	11 (4.7)	0.000
Adequation to MH	1,320 (84.6)	97 (88.2)	0.313**
Adequation to WHO	1,015 (65.1)	74 (67.3)	0.638**
High-risk prenatal DVM	420 (26.9)	81 (73.4)	0.000**
GDM	294 (18.8)	51 (46.4)	0.000**
PIH	119 (7.6)	32 (29.1)	0.000**
Previous DM	13 (0.8)	7 (6.4)	0.000**
Smoking	119 (7.6)	6 (5.5)	0.402**
Alcoholism	35 (2.2)	3 (2.7)	0.735***
Other drugs	10 (0.6)	0 (0.0)	1.000***

Legend: *Mean and standard deviation, absolute numbers, and percentage; **Chi-squared test; ***Fisher's exact test; BMI = Body mass index; GDM = Gestational diabetes mellitus; DM = Diabetes mellitus; PIH = Pregnancy induced hypertension; WHO = World Health Organization; MH = Ministry of health; DVM = Darcy Vargas Maternity Hospital. Source: Elaborated by authors.

to the placenta. This reduction in the blood volume causes placental insufficiency, being necessary the premature birth[16]. Our study concluded that the OR to the occurrence of premature birth was 2.5, while a similar study achieved OR of 1.6[12].

Regarding the relation between pregnant women's SAH and newborns' low weight at birth, similar studies disagree with our results, since they have observed mothers with chronic hypertension have more chances of having small for gestational age (SGA) newborns[5,11], which can be partly explained due to premature births and placental outcomes[16]. The divergence between the results of our article and the similar studies is probably because of the difference of the sampling size.

Table 2. Newborns' characteristics towards systemic arterial hypertension (SAH)*.

	Patients without SAH (n=1,560)	Patients with SAH (n=110)	*p*
Birth weight	3,303.9 (525.0)	3,138.7 (753.4)	0.098
Birth GA	38.7 (1.8)	37.7 (2.6)	0.000
Weight adequacy			0.069**
SGA	118 (7.6)	14 (12.7)	
AGA	1,214 (77.8)	76 (69.1)	
LGA	228 (14.6)	20 (18.2)	
Macrosomic	112 (7.2)	7 (6.4)	0.748**
Delivery mode			0.000**
Normal birth	920 (59.0)	43 (39.1)	
Caesarian	640 (41.0)	67 (60.9)	
Laceration	525 (33.7)	24 (21.8)	0.011**
Episiotomy	116 (7.4)	2 (1.8)	0.012***
Apgar at 1 minute	7.7 (0.9)	7.6 (1.1)	0.602
Apgar at 5º minute	8.8 (0.6)	8.8 (0.8)	0.790
Prematurity	104 (6.7)	20 (18.2)	0.000**
Low weight at birth	84 (5.4)	16 (14.5)	0.000**
Neonatal ICU	116 (7.4)	18 (16.4)	0.001**

Legend: *Mean and standard deviation, absolute numbers, and percentage; **Chi-squared test; ***Fisher's exact test; GA = Gestational age; SGA = Small for gestational age; AGA = Appropriate for gestational age; LGA = Large for gestational age; ICU = Intensive care unit. Source: Elaborated by authors.

Table 3. Odds ratio calculation (CR) of adverse outcomes towards systemic arterial hypertension (SAH).

	p	CR	95%CI
GDM	0.001	2.157	1.373-3.390
PIH	0.000	2.739	1.619-4.663
Caesarian	0.180	1.985	0.729-5.403
Prematurity	0.031	2.552	1.090-5.979
Low weight at birth	0.744	1.203	0.397-3.640
Neonatal ICU	0.857	0.927	0.407-2.112

Legend: GDM = Gestational diabetes mellitus; PIH = Pregnancy induced hypertension; ICU = Intensive care unit; 95%CI: 95% confidence interval; *Confounding factors: age, previous caesarean section, pregestational BMI, excessive weight gain, previous diabetes mellitus, smoking, alcoholism, and other drugs. Source: Elaborated by authors.

Opposing our study, the referred article concluded that chronic SAH increases the prevalence of hospitalizations in neonatal hospitalizations[6], while our study reports that chronic SAH did not present significant influence in this outcome, although it has presented a higher number of hospitalizations. This divergence possibly occurred due to the considerable difference in the sampling size, which is very higher in comparison to the one we pointed out here and contemplates many countries.

In order to better contextualize, our institution assists approximately 6,000 deliveries per month. Although our study analyzed a sample of pregnant women in the same institution, the investigation could be longer, what would increase the number of samples as well as the diversity of patients. Moreover, our analysis was carried out using a data base from our institution, in which the sample size was calculated aiming to evaluate another variable. Therefore, the 6 months period of data collection may not reflect an adequate sample size for the analysis of chronic SAH. With the results from this study, it was possible to conclude that the attention and care of hypertensive pregnant women must be intensified and considered at prenatal assistance. These findings must be analyzed with caution and may not be extrapolated to other populations, due to the retrospective nature of the study. For future investigations, we suggest prospective studies that analyze the impacts of SAH in gestational outcomes, with a sampling size calculation directed to this variable.

Conclusion

Through the present investigation, it was possible to conclude that previous SAH increases the chance of GDM by 2.1 times, PIH by 2.7 times and prematurity by 2.5 times. However, the chances of a caesarean, of having a newborn with low birth weight and the need of neonatal ICU between pregnant women with previous SAH are not significantly different, when compared to women without the disease.

Authors' Contributions

Pedro Bonilauri Ferreira, Felipe Farah, Guilherme Schroder Stepic and Mateus de Miranda Gauza contributed to the writing of the work. Rodrigo Ribeiro e Silva for the statistical analysis of the work. Jean Carl Silva coordinated the study and reviewed the work.

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