Risk factors for hypertensive disorders of pregnancy in Southern Brazil

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Summary

Objective: The aim of the study was to identify the frequency of risk factors for hypertensive disorders in pregnancy in Southern Brazil. **Methods:** The study included 161 patients with hypertensive disorders and 169 control subjects matched by age and ethnicity. The frequency of the risk factors was compared by Fisher's exact test, chi-square and Student's *t* test. A multivariate logistic regression analysis assessed the independent role of clinical, social and demographic factors which were associated with occurrence of the hypertensive disease in pregnancy in the univariate analysis. **Results:** Patients enrolled in the study were predominantly Caucasian (73%) and the mean age was 29. In the multivariate analysis, the variables associated were: family history of preeclampsia (p = 0.001; OR = 3.88; 95% CI = 1.77-8.46), diabetes (p = 0.021; OR = 3.87; 95% CI = 1.22-12.27) and chronic hypertension (p = 0.002; OR = 7.05; 95% CI = 1.99-24.93). **Conclusion:** The risk factors associated with hypertensive disorders in pregnancy appear to be similar to those reported in other countries. The knowledge of the risk factors could be helpful in a prenatal care.

Keywords: Hypertension, pregnancy-induced; risk factors; Brazil.

Resumo

Fatores de risco para distúrbios hipertensivos durante a gravidez no Sul do Brasil

Objetivos: Identificar a frequência dos fatores de risco para distúrbios hipertensivos durante a gravidez na região Sul do Brasil. **Métodos:** O estudo incluiu 161 pacientes com distúrbios hipertensivos e 169 controles, compatíveis em idade e etnia. A frequência dos fatores de risco foi comparada a partir do teste exato de Fisher, teste qui-quadrado e teste *t* de Student. Uma análise logística multivariacional de regressão avaliou a influência de fatores clínicos, sociais e demográficos, associados com a ocorrência de doenças hipertensivas durante a gravidez na análise univariada. **Resultados:** Os pacientes envolvidos no estudo eram predominantemente caucasianos (73%) e a idade média foi 29 anos. Na análise multivariada as variáveis associadas foram: histórico de pré-eclâmpsia na família (p = 0,001; OR = 3,88; 95% IC = 1,77-8,46), diabetes (p = 0,021; OR = 3,87; 95% IC = 1,22-12,27) e hipertensão crônica (p = 0,002; OR = 7,05; 95% IC = 1,99-24,93). **Conclusão:** Os fatores de risco associados a distúrbios hipertensivos durante a gravidez parecem ser similares àqueles relatados em outros países. O conhecimento sobre os fatores de risco pode ser útil durante o acompanhamento pré-natal.

Unitermos: Hipertensão, induzida pela gravidez; fatores de risco; Brasil.

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Introduction

The hypertensive disorders of pregnancy affect up to 8% of all gestations and are the second leading cause, after embolism, of maternal mortality in United States, accounting for almost 15% of such deaths[1,2]. Expectant mothers with hypertension are predisposed toward the development of potentially lethal complications, mainly *abruptio placentae*, disseminated intravascular coagulation, cerebral hemorrhage, hepatic failure, and acute renal failure[3].

Hypertension during pregnancy, particularly preeclampsia, is one of the major obstetrical problems in less-developed countries and the causes of most cases remain unknown[4]. Obstetricians are attempting to early recognize and diagnose this complication. However, biophysical and biochemical tests have been suggested to identify women who are at increased risk of developing of this complication in the future. Unfortunately, some of these tests are invasive whereas others require expensive techniques or special expertise that preclude their utility in routine screening[4,5]. In addition, the results of the pooled data for the various tests studied suggest that many of them have poor sensitivity and poor predictive value[4,5].

Several risk factors have been described as predisponent to hypertensive disorders in pregnancy worldwide, such as: family history of preeclampsia[4], preeclampsia in a previous pregnancy[6,7], multifetal gestation[6,8,9], obesity[10], nulliparity[11], diabetes[11,12], chronic hypertension[6,12], and extremes of maternal age[4]. The knowledge of the most important risk factors in our population could be useful to identify the patients who have higher chances to develop the hypertensive disorders, and, subsequently, adequate prenatal care could contribute to decrease this mortality ratio. However, reports designed to identify risk factors for hypertensive disorders of pregnancy in our country are scarce[13,14]. Therefore, the aim of the present study was to identify the frequency of risk factors for hypertensive disorders in Southern Brazil.

Methods

A prospective case-control study was developed considering 161 patients with hypertensive disorders and 169 control subjects matched by age and ethnicity. Subjects were recruited in the maternity of a tertiary public hospital in Southern Brazil (Hospital Nossa Senhora Conceição) and they were followed until 90 days postpartum (late puerperium), since PE can occur after childbirth. The hypertensive disorders in pregnancy were classified according to the proposal of the ACOG[15]. The outcome was the occurrence of mild preeclampsia, severe preeclampsia, non-proteinuric gestational hypertension, chronic hypertension with mild preeclampsia superimposed and chronic hypertension with severe preeclampsia superimposed. At enrollment, a standardized questionnaire provided informations on age, weight, height, schooling (divided by levels and if completed or not), ethnicity, smoking habits, and known risk factors for hypertension in pregnancy. Body mass index (BMI) was calculated considering the values of weight and height obtained at the first appointment, and results were described as mean BMI. All subjects gave their written informed consent to be included in the study, and protocol was approved by the ethics committee of Grupo Hospitalar Conceição and by the National Research Ethics Committee.

The frequencies of risk factors were compared between groups by Fisher's exact test, chi-square and Student's *t* tests. A multivariate logistic regression analysis was performed by a backward conditional procedure to assess the independent role of clinical, social and demographic variables which were significantly associated with hypertensive disease in pregnancy in the univariate analysis, using the SPSS package. The variables tested in the univariate analysis included the family and the previous history of preeclampsia, multifetal gestation, BMI, nulliparity, diabetes, chronic hypertension, smoking (current smoker × non-smoker), schooling (women with at least complete fundamental level, according to Brazilian educational system, were considered as having high schooling) and prenatal care. The continuous variable (BMI) was entered as a linear factor after being tested for nonlinearity, using the SPSS package. The p-values < 0.05 were considered statistically significant.

Results

Patients enrolled in this study were predominantly Caucasian (73%) and the mean age was 29 years (13-48 years). The frequency of cases of hypertensive disorders complicating pregnancy was the following: 58 mild preeclampsia (36.0%), 51 severe preeclampsia (31.7%), 3 eclampsia (1.9%), 7 gestational hypertension (4.3%), and 42 chronic hypertension with preeclampsia superimposed (26.1%).

Table 1 shows the demographical, clinical and social risk factors for hypertensive disorders. The family history of preeclampsia (PE), previous PE history, high BMI, diabetes, chronic hypertension, schooling and prenatal were demonstrated to be more frequent in hypertensive disorders in pregnancy when compared to normotensive women. Regarding nulliparity, multifetal gestation (even so higher in the patients group) and smoking habits, there were no significant differences between patients and controls.

Table 2 provides the characteristics of women with hypertensive disorders in pregnancy compared to normotensive women (with risk estimates calculated by the univariate logistic regression analysis). The family and previous history of PE, high BMI, nulliparity, diabetes, chronic hypertension, schooling and prenatal were

significantly associated with hypertensive disease in pregnancy while multifetal gestation, and smoking habits were not associated with this disorder. In the multivariate analysis, the association with the following variables remained statistically significant: family history of PE, diabetes, and chronic hypertension (Table 3).

Table 1 – Risk factors for hypertensive disorders in pregnancy

Characteristic	Hypertensive disorders n = 161	Control n = 169	p
Family history of PE	44%	20%	< 0.001
Previous PE history	57%	7%	< 0.001
Multifetal gestation	6%	3%	0.530
BMI (kg/m²)*	32.9 ± 6.1	28.2 ± 4.6	< 0.001
Nulliparity	27%	22%	0.300
Diabetes	26%	6%	< 0.001
Chronic hypertension	30%	5%	< 0.001
Smoking	18%	23%	0.327
Schooling	34%	57%	0.003
Prenatal	88%	97%	0.007

PE, preeclampsia; BMI, body mass index; *Data are presented as mean ± SD or %.

Table 2 – Characteristics of women with hypertensive disorders in pregnancy compared to normotensive women (univariate analysis)

Characteristic	Odds ratio (95% CI)	p
Family history of PE	3.21 (1.77-5.83)	< 0.001
Previous PE history	17.81 (7.79-40.69)	< 0.001
Multifetal gestation	1.67 (0.54-5.32)	0.370
BMI (kg/m²)	1.19 (1.12-1.27)	< 0.001
Nulliparity	2.07 (1.14-3.77)	0.017
Diabetes	4.57 (1.92-10.84)	0.001
Chronic hypertension	8.86 (3.97-19.77)	< 0.001
Smoking	0.71 (0.40-1.25)	0.707
Schooling	0.38 (0.20-0.70)	0.002
Prenatal	0.24 (0.08-0.75)	0.014

PE, preeclampsia; BMI, body mass index.

Table 3 – Characteristics of women with hypertensive disorders in pregnancy compared to normotensive women (multivariate analysis)

Characteristic	Odds ratio (95% CI)	p
Family history of PE	3.88 (1.77-8.46)	0.001
Diabetes	3.87 (1.22 -12.27)	0.021
Chronic hypertension	7.05 (1.99-24.93)	0.002

PE, preeclampsia.

Discussion

The causes of hypertensive diseases in pregnancy are still uncertain, thus the effective primary prevention is not available in this stage[4]. However, several risk factors have been identified and modification of some of these risk factors might result in the decreasing of its frequency.

In our data, family history of PE, previous PE history, high BMI, nulliparity, diabetes, and chronic hypertension were significantly more frequent in patients when compared to the control group. In addition, schooling was less frequent in cases than in controls. Our results are similar to other studies in different populations[3,11,12,16-19]. Moreover, the frequency of eclampsia and chronic hypertension with superimposed preeclampsia are according to other reports that investigated women with hypertensive diseases in pregnancy in a Brazilian population[13,20,21].

As expected, multivariate analysis showed that family history of PE, diabetes and chronic hypertension are independent risk factors for hypertensive diseases in pregnancy. The family and the previous history of PE increased the risk for this complication in our patients. These data have been reported in other studies[12,19,21-23]. Indeed, the genetic component in pathophysiological abnormalities of preeclampsia has been suggested[24-26]. Preeclampsia was reported to be more common in daughters of preeclamptic women[27] and in pregnancies fathered by sons of preeclamptic women[28]; this data suggest the involvement of both maternal and fetal genes in the syndrome. Pregnant women with this history should be carefully monitored in the prenatal care and postpartum[5].

High BMI was prevalent in both groups; however, the mean BMI was higher in hypertensive women, and it is a definite risk factor for developing pregnancy-induced hypertensive disorders, including preeclampsia[10]. Risk increases with BMI[4,10], and the possible explanation is the increased shear stress due to hyperdynamic circulation associated with obesity[3]. The worldwide increase in obesity is likely to raise the frequency of preeclampsia[4]. Our result is in agreement with other Brazilian reports: Nucci et al.[14] who showed that overweight nutritional status (obesity and pre-obesity) was associated with an increased risk for preeclampsia, Gaio et al.[13] who identified obesity as a risk factor for preeclampsia/eclampsia and chronic hypertension, and Assis et al.[29] who demonstrated that obesity is a risk factor for gestational hypertension and for preeclampsia superimposed on chronic hypertension. Actions in public health could prevent and/or treat obesity and, consequently, could prevent hypertensive disorders.

With regard to diabetes, Schmidt et al.[30] confirmed that gestational *diabetes mellitus* is independently associated with preeclampsia in Brazilian women, and preexisting diabetes *mellitus* is also a risk factor for preeclampsia[11]. Women with preexisting chronic hypertension also have an increased risk of preeclampsia[8,9,12,23,29].

In the present study, diabetes, and particularly, preexisting chronic hypertension were risk factors for preeclampsia in Southern Brazilian women. Thus, actions in the public health focused to prevent these diseases are important to also prevent preeclampsia.

Generally, PE is regarded as a disease of first pregnancy and its frequency ranges between 2% and 7% in healthy nulliparous women[31]. Nulliparity is well established as a risk factor for hypertensive disorders in pregnancy[3,11]. In this study, nulliparity was confirmed as a risk factor in the conditional logistic regression analysis. Nulliparous women have a two-fold increase in the risk of developing hypertensive disorders in pregnancy.

On the other hand, there were no significant differences in multifetal gestation and smoking habits, characteristics that were described in some reports as risk factors[3,11,32,33]. Multiple pregnancy doubles the risk of preeclampsia[11,17]; however, in our findings this association was not established, likely due to low number of cases in both groups of subjects associated with a reduced sample size as a whole. Extremes of maternal age cannot be demonstrated as a risk factor in our study since our sample is matched by age; nevertheless, it is an established risk factor for PE[3]. A curious but consistent finding is that women who smoke cigarettes have a lower risk of PE than women who do not smoke[27]. However, this benefit is cancelled out by the substantial negative effect of smoking on fetal growth, risk of placental abruption, and general health. In our population, this "protective" effect was not observed.

Regardless of the indicator of social deprivation, we found that low educational level was significantly more frequent in the group of cases. Haelterman et al.[33] showed that the burden of PE is concentrated in socially disadvantaged women, thus health services should be more responsive to the specific needs of these women. In our study, we found the protective effect of the prenatal care and its importance cannot be refuted. In the prenatal care the following factors are analyzed, among others: schooling, familiar and previous history of hypertension and diabetes, number of pregnancies, and smoking. Some of these factors were demonstrated to influence the development of hypertensive disorders in pregnancy. Women who are adequately assisted can detect earlier these possible risk factors; therefore, they can assume preventive actions, decreasing the chance of developing the disease. Our results show that women who do not received prenatal care have a four-fold increase in the risk of developing hypertensive disorders in pregnancy. To our knowledge, this is the first study which reported this association in Brazil. A previous study realized in a Brazilian population revealed that low degree of schooling and socioeconomic status are factors that hinder access to prenatal care[31,34]. Investments in public health intended to improve the prenatal access, mainly in the group of women with low schooling and socioeconomic status, can decrease the levels of hypertensive disorders of pregnancy in our population.

Conclusion

In conclusion, the present study confirmed that family and previous history of PE, high BMI, diabetes and chronic hypertension are more frequent in patients with hypertensive disorders in pregnancy. Their frequencies appear to be similar to those reported in North American[3] and European[11] women, and our results reflect behavioral factors whereby women may be predisposed to increased risk of PE. Hypertensive disorders and their complications are the most common cause of maternal death in Latin America and Caribbean[37-39]. The knowledge of important risk factors in our population could be useful to help the clinician to detect pregnant women who will develop preeclampsia. Prevention of hypertensive diseases in pregnancy would mean a huge step forward in prenatal care and, assuming that effective prenatal is available, it may have greater potential in the treatment of these diseases.

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