

Maternal-fetal outcomes of women with hypertensive disorders of pregnancy

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SUMMARY

OBJECTIVE: The objective of this study was to determine adverse maternal and perinatal outcomes in pregnant women with hypertensive disorders of pregnancy.

METHODS: An analytical cross-sectional study was conducted on women admitted with hypertensive disorders of pregnancies to a university maternity hospital from August 2020 to August 2022. Data were collected using a pretested structured questionnaire. Variables associated with adverse maternal and perinatal outcomes were compared using multivariable binomial regression.

RESULTS: Of 501 women with pregnancies, 2, 35, 14, and 49% had eclampsia, preeclampsia, chronic hypertension, and gestational hypertension, respectively. Women with preeclampsia/eclampsia had significantly higher risks of cesarean section (79.4 vs. 65%; adjusted RR, 2,139; 95%CI, 1,386–3,302; $p=0.001$) and preterm delivery at <34 weeks' gestation (20.5 vs. 6%; adjusted RR, 2.5; 95%CI, 1.19–5.25; $p=0.01$) than those of women with chronic/gestational hypertension. Risks of prolonged maternal hospitalization (43.9 vs. 27.1%), neonatal intensive care unit admission (30.7 vs. 19.8%), and perinatal mortality (23.5 vs. 11.2%) were higher among women with preeclampsia/eclampsia.

CONCLUSIONS: Women with preeclampsia/eclampsia had a higher risk of adverse maternal and neonatal outcomes than those with chronic or gestational hypertension. This major maternity care center requires strategies for preventing and managing preeclampsia/eclampsia to improve pregnancy outcomes.

KEYWORDS: Hypertension, pregnancy-induced. Hypertension. Preeclampsia. Eclampsia.

INTRODUCTION

Hypertension is the most common medical disorder that occurs during pregnancy and complicates 5–10% of all pregnancies. Hypertensive disorders of pregnancy (HDP) are a critical threat to maternal and child health. Chronic hypertension is defined as high blood pressure before pregnancy. Gestational hypertension is characterized by high blood pressure after the 20th week of pregnancy (usually after 37 weeks), and this type of hypertension usually settles within 6 weeks after delivery¹⁻³.

Preeclampsia is defined as the identification of arterial hypertension in a previously normotensive pregnant woman, from the 20th week of pregnancy, with or without proteinuria. In the absence of proteinuria, preeclampsia is accompanied by systemic involvement or end-organ dysfunction,

such as thrombocytopenia, liver with or without right upper quadrant or epigastric abdominal pain, renal failure, pulmonary edema, and neurological complications, such as altered mental status, blindness, stroke, clonus, severe headaches, or persistent visual scotomata^{4,5}.

Eclampsia refers to the occurrence of generalized tonic-clonic seizures or coma (eclampsia sine eclampsia) in a pregnant woman with preeclampsia, which is a serious complication of the disease^{4,5}. HELLP syndrome is a form of preeclampsia in which endothelial dysfunction is manifested by the activation of coagulation and liver dysfunction, as detected through laboratory tests. Clinically, it is possible to present with normal blood pressure and without proteinuria. The latter is defined by an acronym that synthesizes the presence of hemolysis (H), the elevation of

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liver enzymes (elevated liver enzymes), and thrombocytopenia (low platelets). HELLP syndrome develops in 10–20% of pregnant women with preeclampsia/severe eclampsia⁶⁻⁸.

Almost all maternal deaths due to hypertensive syndromes occur in developing countries. A study reported that in more developed areas, the prevalence of eclampsia was estimated at 0.2%, with a maternal death rate of 0.8%, while in less favored regions, this prevalence rose to 8.1%, with a maternal death ratio of 22.0%. Thus, HDPs represent a problem of great interest in the scientific community owing to their frequency and maternal-fetal repercussions⁶⁻⁸.

Notably, while the principles of management of HDPs are the same across the world, the disproportionately high adverse pregnancy outcomes in resource-limited settings are primarily due to the challenges associated with the management and quality of care for HDPs in these settings^{3,4}.

Thus, even within the same countries, there are differences in pregnancy outcomes due to sociocultural differences and variations in the distribution and quality of healthcare¹. Moreover, the latter study aimed to determine the adverse maternal and perinatal outcomes among pregnant women admitted with HDP in the emergency room and directly compare the outcomes among women with preeclampsia or eclampsia and those with chronic or gestational hypertension.

METHODS

An analytical cross-sectional study was conducted according to the STROBE statement⁹. This study was conducted between August 2020 and August 2022 at a *Januário Cicco* Maternity School, a university maternity hospital for high-risk pregnancies in a region of northeastern Brazil with an HDI of 0.684. The study population included pregnant women older than 18 years who were at least in their 20th week of pregnancy and were admitted to the emergency room with a diagnosis of HDP. Women with other morbidities, smokers, or drug users were excluded. Those who could not respond to the questionnaire or were admitted without complete antenatal care were also excluded.

The sample size was calculated using EpiInfoTM version 7.1.1.14, with a sample power of 80% and a confidence interval (CI) of 95%. In eclampsia/eclampsia (76.7%), like the proportions of hypertensive disorders observed by Crenstil et al., an estimated sample size of 437 was adequate to detect a 15% difference in adverse maternal or fetal outcomes between women with preeclampsia/eclampsia and those with chronic/gestational hypertension, using a 5% contingency allowance, and the estimated sample size was 459.

Data were analyzed using Stata 11.0 (Stata Corporation, Texas, USA). Categorical variables were compared using the

chi-square (χ^2) or Fisher's exact tests, as appropriate, while continuous variables were compared using Student's t-tests. The risk factors associated with adverse maternal and perinatal outcomes were examined using binomial regression with a log-link function to estimate crude and adjusted relative risks (RRs) with 95%CI. The variables for the regression models were selected based on biological plausibility, literature evidence, and invariable analysis results. To directly compare the outcomes in women with preeclampsia/eclampsia and those with chronic/gestational hypertension, crude and adjusted RRs were calculated for preeclampsia/eclampsia relative to chronic/gestational hypertension. Statistical significance was set at probability values <0.05.

Ethics

The study followed the ethical and legal norms recommended by Resolution 466/12 of the National Health Council and was approved by the Research Ethics Committee (CAAE:38143320.2.0000.5537). All participants signed a consent form to participate in this study. The study was conducted in accordance with the Declaration of Helsinki and its modifications.

RESULTS

Sociodemographic and reproductive characteristics

Altogether, 501 pregnant women with HDP were included: 316 with hypertension and 185 with preeclampsia or eclampsia. The mean and standard deviation ages of the hypertensive and preeclampsia/eclampsia groups were 32.19 ± 6.59 years and 27.57 ± 6.72 years. Regarding educational background, 181 (57.3%) patients received primary education in the hypertension group and 99 (53.5%) in the preeclampsia/eclampsia group. Regarding marital status, the results showed that 201 (63.6%) patients were married or cohabiting in the hypertension group and 121 (65.4%) in the preeclampsia/eclampsia group. Most patients were not primiparous, 185 (58.5%) in the hypertension group and 105 (56.7%) in the preeclampsia/eclampsia group. Concerning parity, 176 (55.7%) patients in the hypertension group had 1–4 deliveries compared with 100 (54.0%) in the eclampsia/eclampsia group. The estimated gestational age at diagnosis was >27 weeks for the hypertension group 310 (98.1%) and preeclampsia/eclampsia group 176 (95.1%). There were no significant differences between all variables regarding sociodemographic and reproductive characteristics.

In the eclampsia/eclampsia group, 12(6.5%) patients developed HELLP syndrome.

No statistically significant difference was found in both groups for the number of consultations: the hypertension group (mean±standard deviation) 6.7±0.68 and the eclampsia/eclampsia group 6.5±0.73.

Comparison of adverse maternal and perinatal outcomes

Concerning the adverse maternal outcomes, women with preeclampsia/eclampsia had significantly higher risks of cesarean section (79.4 vs. 65%; adjusted RR, 2.139; 95%CI, 1.386–3.302; $p<0.001$). Term labor at <34 weeks of gestation (20.5 vs. 6%; adjusted RR, 2.505; 95%CI, 1.194–5.257; $p=0.015$) was significantly higher among women with preeclampsia/eclampsia than women with chronic/gestational hypertension (Table 1).

Regarding the adverse fetal outcomes, the neonatal intensive care unit (NICU) admission (22.7 vs. 6.0%; adjusted RR, 2.567; 95%CI, 1.296–5.088; $p=0.007$) and perinatal mortality (5.4 vs. 2.2%; adjusted RR, 0.423; 95%CI, 0.101–1.770; $p=0.239$) were significantly higher among women with preeclampsia/eclampsia than women with chronic/gestational hypertension. Apgar (<7) at 1 min (15.1 vs. 8.8%, adjusted

RR, 1.967; 95%CI, 1.112–3.477; $p=0.020$) and Apgar (<7) at 5 min (7.0 vs. 2.5%, adjusted RR, 3.683; 95%CI, 1.500–9.356; $p=0.006$) were significantly higher among women with preeclampsia/eclampsia (Table 2).

In the initial analysis, prolonged maternal hospital stay was associated with preeclampsia/eclampsia ($p=0.04$). However, after calculating the adjusted risk, this association was not confirmed ($p=0.556$).

DISCUSSION

Hypertension during pregnancy is a major contributor to maternal and perinatal mortality^{10,11}. We found that women with preeclampsia/eclampsia had a higher risk of cesarean section. It is crucial to point out that preeclampsia is not an indication for cesarean delivery, as expected, because of the severe complications arising from this condition. However, although pregnant women with preeclampsia can undergo vaginal delivery, most women choose to undergo cesarean section^{12,13}.

In this sample, the prevalence of preterm labor was 20.5 and 6% in the preeclampsia/eclampsia and chronic gestational hypertension

Table 1. Adverse maternal outcomes of women with chronic hypertension compared to women with preeclampsia/eclampsia.

Maternal outcomes	Chronic gestational hypertension (n=316) n (%)	Preeclampsia/eclampsia (n=185) n (%)	Crude RR (95%CI)	p-value	Adjusted RR (95% CI)	p-value
Term labor <34 weeks	19 (6.0)	38 (20.5)	4.041 (2.251–7.254)	<0.0001	2.505 (1.194–5.257)	0.015
Term labor >37 weeks	107 (33.9)	96 (51.9)	2.106 (1.454–3.053)	<0.0001	1.152 (0.980–2.361)	0.061
Cesarean section ^a	206 (65.2)	147 (79.4)	2.065 (1.35–3.160)	0.001	2.139 (1.386–3.302)	0.001
Prolonged maternal hospital stay ^b	159 (50.3)	110 (59.4)	1.448 (1.003–2.091)	0.048	1.126 (0.757–1.677)	0.556

RR: relative risk; CI: confidence interval. ^aAdjusted for the stage of pregnancy at admission. ^bAdjusted for estimated gestational age (EGA) at diagnosis, EGA at delivery, and stage of pregnancy at admission.

Table 2. Adverse fetal outcomes of women with chronic hypertension compared to women with preeclampsia/eclampsia.

Maternal outcomes	Chronic/gestational hypertension (n=316) n (%)	Preeclampsia/eclampsia (n=185) n (%)	Crude RR (95% CI)	p-value	Adjusted RR (95%CI)	p-value
Prematurity birth<34 weeks	19 (6.0)	38 (20.5)	4.041 (2.251–7.254)	<0.001	2.505 (1.194–5.257)	0.015
Apgar (<7) at 1 min ^a	28 (8.8)	28 (15.1)	1.835 (1.049–3.207)	0.033	1.967 (1.112–3.477)	0.020
Apgar (<7) at 5 min	8 (2.5)	13 (7.0)	2.909 (1.183–7.159)	0.020	3.683 (1.500–9.356)	0.006
NICU admission	19 (6.0)	42 (22.7)	4.591 (2.577–8.179)	<0.001	2.567 (1.296–5.088)	0.007
Perinatal mortality ^b	7 (2.2)	10 (5.4)	2.522 (0.943–6.745)	0.065	0.423 (0.101–1.770)	0.239

RR: relative risk; CI: confidence interval; NICU: neonatal intensive care unit. ^aAdjusted for EGA at diagnosis and stage of pregnancy at admission. ^bAdjusted for parity (before delivery), EGA at diagnosis; the number of antenatal visits, and stage of pregnancy at admission.

groups, respectively. Worse results were previously observed in the poorest regions such as Ethiopia, Tigray region (40.8%)¹⁴, Nekemte (41.2%)¹⁵, Ghana (21.7%)¹⁶, and India (24.6%)¹⁷. On the other hand, better results were found in the United States (17.4%)¹⁸ and São Paulo city (10.6%)¹⁸. The discrepant findings can be explained due to the quality of antenatal care service and different management guidelines used across the countries¹⁹.

Additionally, we found that preterm delivery was more observed in the preeclampsia/eclampsia group. Approximately 75% of preterm births result from spontaneous preterm labor and may be associated with a history of pregnancy-induced hypertension²⁰.

The risk of prolonged maternal hospitalization was significantly higher among women with preeclampsia/eclampsia. According to Goes et al., the latter results have been associated with the incorrect use of antihypertensive drugs during pregnancy²¹.

NICU admission and perinatal mortality were higher among women with preeclampsia/eclampsia. Preeclampsia, when it presents itself in a severe form or when not treated early, can complicate pregnancy, increasing the risk of death to the mother and newborn, as observed in our results²².

Despite the importance of the number of antenatal consultations, Interestingly, we did not find a statistically significant difference in both studied groups: the hypertension group (mean±standard deviation) 6.7±0.68, and the eclampsia/eclampsia group 6.5±0.73. Although the minimum number of prenatal consultations is being reached in both groups, perhaps the quality of these consultations can be questioned, considering the high prevalence of unfavorable neonatal outcomes in this population.

Another critical point that must be considered is a postpartum follow-up of these patients. In the past, it was believed that hypertensive diseases of pregnancy were self-limiting, and the resolution of pregnancy was considered a cure. However, the literature demonstrated that HDP increase the risk of cardiovascular diseases throughout a woman's life. However, this is the most neglected moment in medical care, and a lack of adequate care during the puerperium can result in significant health problems, predisposing considerable maternal death rates. The College of Obstetricians and Gynecologists (ACOG) released guidelines proposing a longitudinal action that was not restricted to just one consultation in the sixth postpartum week. Therefore, an adequate assessment should encompass physical health, breastfeeding, contraception, mental health, social support, and any specific assessment, depending on risk factors and comorbidities^{23,24}.

Hypertension during the gestational period has a course of development that still needs clarification as maternal hypertension and prematurity are events of multicausal origin and

behave in a complex way. The number of children, antenatal consultations, hospitalization, and high-risk antenatal care were associated with prematurity²³. These results highlight the importance of early hospital referral for women with preeclampsia and eclampsia. A health system approach focused on the availability of qualified professionals with training in emergency obstetric and neonatal care, as well as the preparation of facilities to measure blood pressure, adequate blood pressure control, and close monitoring throughout pregnancy, with timely referrals, can contribute to the reduction of maternal (and newborn) deaths²⁵.

A limitation of this study was its cross-sectional nature. Therefore, despite the high number of patients, our results cannot be generalized to the entire global population. Despite this limitation, our data indicate that preeclampsia and eclampsia are public health concerns with a negative impact on perinatal outcomes.

CONCLUSION

Women with HDPS have a higher risk of adverse maternal and neonatal outcomes. Women with preeclampsia/eclampsia had an increased risk of cesarean section and preterm delivery compared to those with chronic/gestational hypertension.

Strategies for improving pregnancy outcomes among women with HDPs, especially preeclampsia/eclampsia, are needed. Including a health system approach focused on the availability of qualified professionals with training in emergency obstetric and neonatal care, as well as the preparation of facilities to measure blood pressure, adequate blood pressure control, and close monitoring throughout pregnancy, with timely referrals (minimum of six quality appointments), can contribute to the reduction of maternal (and newborn) deaths in low-income regions.

Finally, some simple objective strategies could be adopted to reduce adverse events, such as at least five good-quality prenatal consultations. The early diagnosis and management of gestational hypertension could decrease unfavorable maternal-fetal outcomes. The improvement of prenatal in primary care could impact the rates of gestational hypertension and its consequences.

AUTHORS' CONTRIBUTIONS

IMX: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Supervision, Visualization, Writing – original draft. **APFC:** Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization. **KSM:** Conceptualization, Supervision, Validation.

YEB: Conceptualization. **AKG:** Conceptualization, Methodology, Project administration, Supervision, Validation, Visualization, Writing – review & editing. **ACZS:** Data curation, Formal Analysis, Investigation, Writing – original draft. **RO:** Data

curation, Formal Analysis, Investigation, Software, Writing – original draft. **HK:** Validation, Writing – review & editing. **ACAS:** Methodology, Supervision, Visualization, Writing – original draft.

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