

Comparison of Pregnancy Outcomes of Women with and Without Hypertension at the Latent Phase of Labor Who Were Under Medical Care for Preeclampsia

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ABSTRACT

OBJECTIVE: We explored the association between hypertension (>140/90) at the latent phase of labor (resistant hypertension) and the subsequent development of major maternal complications or adverse infant outcomes in women with preeclampsia under medical care.

STUDY DESIGN: We drew data from 824 women who were under follow-up at the Department of Perinatology of Health Sciences University Zeynep Kamil Women and Children's Health Training and Research Hospital with a diagnosis of preeclampsia. Women with and without resistant hypertension were compared in terms of major maternal complications and adverse infant outcomes.

RESULTS: Mean age and body mass index were similar between the two groups ($p>0.05$). The rate of preeclamptic complaints was significantly higher in groups with resistant hypertension (90.1% vs. 67.2%, $p<0.05$). Proteinuria was more frequent in the resistant hypertension group (78.7% vs. 66.8%, $p<0.001$). The newborn intensive care unit admission rate was significantly higher in the group with resistant hypertension (65.6% vs. 45.9%, $p<0.001$). Gestational age at delivery was significantly lower in the group with resistant hypertension compared to the normotensive group (34.6 vs. 32.9 weeks, $p<0.001$). There was a significant difference between the two groups in terms of the rate of preterm delivery (78.5% vs. 66.7%, $p=0.04$).

CONCLUSION: Resistant hypertension is associated with a higher rate of preeclamptic symptoms during labor and newborn intensive care unit admission.

Keywords: Hypertension, Pregnancy, Labor

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Introduction

Hypertensive complications of pregnancy have a wide range of presentations; therefore, it is accepted as a clinical syndrome (1). Clinical presentations include hypertension, proteinuria, platelet consumption, peripheral vasoconstriction, and hypovolemia, which have been considered to be secondary to placental insufficiency and generalized endothelial dysfunction (2,3). The main goal of managing preeclampsia is to keep the woman's blood pressure within the normal range with anti-hypertensive and to prevent the development of complications such as eclampsia. Delivery of the fetus and placenta is the only definitive treatment for preeclampsia. Treatment is largely symptomatic with monitoring of the development of complications. When blood pressure rises above a certain level, it can directly lead to vascular damage, which may result in life-threatening complications such as renal failure, stroke, and fetal distress (4). The primary goal of preeclampsia treatment should always be the safety of the mother. Although birth is always appropriate for the mother,

it may not be suitable for the fetus due to extreme prematurity. The decision between delivery and conservative management depends on fetal gestational age, maternal and fetal status during the initial evaluation, presence of labor or fetal membrane rupture, and the level of newborn and maternal services available. It is important to emphasize that hypertension is directly related to one of the most serious consequences for the mother, which may lead to focal neurological events including convulsions, cortical blindness, and even cerebral involvement such as cerebral hemorrhage, therefore the benefits of acute pharmacological control of severe hypertension before delivery are generally accepted (5). On the other hand, the significance of uncontrolled hypertension and strict blood pressure control during labor is still controversial.

We explored the association between hypertension at the latent phase of labor (resistant hypertension) and the subsequent development of major maternal complications or adverse infant outcomes in women with hypertensive complications of pregnancy under medical care.

Material and Method

We drew data from 824 women who were under follow-up at the Department of Health Sciences University Zeynep Kamil Women and Children's Health Training and Research Hospital with a diagnosis of preeclampsia. Women with and without resistant hypertension were compared in terms of major maternal complications and adverse infant outcomes. The study protocol was approved by the institutional ethics committee (2017/30) and the study was conducted under the Declaration of Helsinki.

Inclusion criteria were as follows; hypertension with or without proteinuria of ≥ 300 mg per 24 h or thrombocytopenia and if there is Hypertension plus proteinuria (i.e. in renal disease or class F Diabetes), worsening severe hypertension plus proteinuria and either new onset of symptoms, thrombocytopenia, or elevated liver enzymes. Singleton pregnancy with no previous cesarean delivery, age 18 years or older.

Exclusion criteria were as follows; eclampsia complicated by acute renal failure, HELLP syndrome (hemolysis, high liver enzymes, and low platelet count) or pulmonary edema, concomitant maternal diagnosis of renal disease and/or seizure disorder before labor starts, contraindication to Magnesium sulfate (MgSO₄) (e.g. drug hypersensitivity, myasthenia gravis, anuria or oliguria), any other anticonvulsant intake, age <17 years.

Participants were divided into two groups as a group with hypertension $\geq 140/90$ mmHg (resistant hypertension) and a group with blood pressure <140/90 mmHg at the latent phase of labor.

Preeclampsia was diagnosed in women with a new-onset

of hypertension and proteinuria or hypertension and significant end-organ dysfunction with or without proteinuria after 20 weeks of gestation in a previously normotensive woman. Eclampsia was diagnosed following the development of grand mal seizures in a woman with preeclampsia in the absence of other neurologic conditions that could account for the seizure. Antihypertensive medication was administered as methyldopa tablets 1-2 g per day in divided doses for blood pressure control blood pressure in cases with blood pressure >160/110 mmHg.

Outcome: Maternal complications that were assessed during database screening included; acute renal failure (urine output <25 mL/hour), pulmonary edema, cerebrovascular accident (stroke), cardiac arrest, liver failure, coagulopathy, adult intensive care unit admission, complications of delivery (placental abruption, retained placenta, postpartum hemorrhage), length of hospital stay, and maternal death.

Neonatal: APGAR scores at first and fifth minutes and need for Neonatal Intensive Care Unit (NICU) admission.

MgSO₄ was administered with the standardized protocol as a loading dose of 6 grams of magnesium sulfate over 30 minutes, followed by a maintenance dose of magnesium sulfate of 2grams/hour when indicated.

For this study, latent phase was defined as painful irregular or regular contractions without rest in the presence of a cervical dilatation of less than <6 cm (6).

Statistical analyses were carried out with SPSS Version 12.0 (SPSS Inc., Chicago, Ill., USA). To test the normality assumption, variables were assessed by Kolmogorov–Smirnov test. Statistically significant differences were determined using the Student t-test. Categorical variables were compared by the Chi-square test. Statistical significance was defined as $p < 0.05$. Multivariate regression analysis was performed to find independent predictors of neonatal intensive care unit admission.

Results

Mean age and body mass index were similar between the two groups (Table I). There were 52 (18.4%) women with more than 3 previous pregnancies in the group with resistant hypertension, whereas there were 118 (21.8%) participants with more than 3 previous pregnancies in the group with normotension ($p=0.262$). Postpartum persistent hypertension was diagnosed in 6 (2.1%) women in the group with refractory to antihypertensive medication, whereas 9 (1.7%) patients had persistent postpartum hypertension in the group with normotension ($p=0.634$). The rate of preeclamptic complaints was significantly higher in groups with resistant hypertension (90.1% vs. 67.2%, $p < 0.05$). Retinopathy rates were similar between the two groups (0.9% vs. 1.8%, $p=0.290$). Proteinuria

was more frequent in the resistant hypertension group (78.7% vs. 66.8%, $p<0.001$). The liver enzymes were found to be significantly increased in the persistent hypertensive group when compared to control (Table II).

Table I: Comparison of some demographic characteristics of groups with and without hypertension at the latent phase of labor

		N	Mean	Std. Deviation	p
Age (Years)	NT	542	30.057	6.3	0.109
	HT	282	29.330	5.9	
BMI (Kg/m ²)	NT	542	30.788	5.5	0.614
	HT	282	30.996	5.8	

NT: Normotensive, HT: Hypertensive, BMI: Body mass index

Table II: Comparison of some serum biochemical analysis results of groups with and without hypertension at the latent phase of labor

		Mean	Std. Deviation	p
BUN (mg/dL)	NT	10.04	3.8	0.239
	HT	10.5	3.9	
Creatinine (mg/dL)	NT	1.5	0.9	0.861
	HT	1.6	0.9	
ALT (mg/dL)	NT	34.4	4.2	0.003
	HT	44.5	5.1	
AST (mg/dL)	NT	37.5	4.2	0.013
	HT	46.1	5.3	
LDH (U/L)	NT	256.1	19.7	0.253
	HT	274.2	24.7	

NT: Normotensive, HT: Hypertensive, BUN: Blood urea nitrogen, ALT: Alanine transferase, AST: Aspartate transferase, LDH: Lactate dehydrogenase

Approximately half of the pregnant women were required to undergo labor induction (54.2% vs. 48.9%, $p=0.148$). Eclamptic seizures were observed in 3.5% of cases in the groups with resistant hypertension; whereas there were 12 (2.2%) cases in the group with normotension ($p=0.260$). Antihypertensive medication was needed in 94% of cases in the hypertensive groups; whereas 58.9% cases in the group with normotension ($p<0.001$) before labor. MgSO₄ infusion was indicated in 95.4% of cases in the group with hypertension; whereas 70.1% of cases in the group with normotension ($p<0.001$) during labor. The newborn intensive care unit admission rate was significantly higher in the group with resistant hypertension compared to the normotensive (65.6% vs. 45.9%, $p<0.001$). Gestational age at delivery was significantly lower in the group with resistant hypertension compared to the normotensive group (32.9±3.4 vs. 34.6±4.3 weeks, $p<0.001$). There was a significant difference between the two groups in terms of the rate of preterm delivery (78.5% vs. 66.7%, $p=0.04$). Birth weight was significantly lower in

the group with resistant hypertension (2467g vs. 2104g, $p<0.001$). The multivariate regression model MgSO₄ therapy, preterm delivery, presence of preeclamptic symptoms, proteinuria, and resistant hypertension at the latent phase of labor were included in the model, prematurity was found to be a significant factor for newborn intensive care unit admission after adjustment for other confounders [OR:19.5, 95%CI (6.5-58), $p<0.001$]. No significant difference was determined in terms of the duration of hospital stay between the two groups (3.8 vs. 3.9 days, $p=0.525$). Again no difference was found between the two groups in terms of first and fifth minutes APGAR scores ($p=0.374$ and $p=0.340$, respectively). Cesarean delivery rates were similar between the two groups (79.2% vs. 84.4%, $p=0.07$).

Discussion

In this study, we aimed to explore the association between hypertension at the latent phase of labor and the subsequent development of major maternal complications or adverse infant outcomes in women with hypertensive complications of pregnancy under medical care. Our data analysis revealed that hypertension at the latent phase of labor is associated with a higher rate of preeclamptic symptoms during labor, a higher rate of premature delivery, and newborn intensive care unit admission.

Hypertension in pregnancy is associated with high perinatal morbidity and mortality, especially premature delivery, fetal growth restriction, and hypoxemia due to placental insufficiency. Mortality and morbidity increased on the maternal side and the incidence of cardio and cerebrovascular events and long-term complications have been reported. Most complications are associated with severe preeclampsia (7). Additionally, the previous meta-analysis showed that the presence of chronic hypertension was also associated with a risk of preeclampsia, cesarean delivery, preterm birth, low birth weight, neonatal intensive care admission, and perinatal mortality (8).

Maternal complications are related to the severity of the disease. On the other hand, periodic events are associated with placental insufficiency and prematurity. Therapeutic pregnancy terminations in cases of severe hypertension or fetal distress are the main cause of preterm delivery. On the other hand, in an uncontrolled hypertension scenario, delivery delays put both mother and fetus at risk. Treatment of hypertension in pregnancy has been associated with worse fetal outcomes, such as intrauterine growth restriction and preterm labor (9,10). In these cases, it is not clear whether this poor outcome following antihypertensive medication is related to teratogenicity or decreased blood pressure and following impaired placental perfusion. On the other hand, the hypertensive disease itself may be responsible for placental and fetal deterioration, especially when preeclampsia is present (11,12).

Most guidelines recommend pharmacological treatment in patients with severe hypertension (13-16). In the case of mild or moderate hypertension, treatment targets, as well as treatment, have been questioned (11). In patients with chronic hypertension, the ACOG statement recommends the preservation of drugs initiated before pregnancy to keep systolic blood pressure and diastolic blood pressure between 120/160 mmHg and 80/105 mmHg respectively (13).

More recently, the CHIPS study (17) compared “strict control (target DPB 85 mmHg) versus less strict control (target DPB 100 mmHg)” of blood pressure for perinatal and maternal events. The primary outcome was a loss of a pregnancy or a high level of neonatal survival longer than 48 hours in the first 28 days, and a secondary outcome was severe maternal complications until hospital discharge or the end of the puerperium. It was reported that there was no significant difference in perinatal events between the two groups. Another entity has been introduced in the literature, which is defined to be labor onset hypertension, however, the pathophysiology of labor onset hypertension is still unclear.

Lao et al. suggested that labor onset hypertension represents a late manifestation of the preeclampsia process (18). They reasoned that labor onset hypertension patients had lower blood pressure in pregnancy and were not identified until the intrapartum elevation of blood pressure. However, although the pathophysiology of labor onset hypertension is still unknown, preeclampsia is currently considered to arise from endothelial dysfunction during pregnancy (19-21). This disorder, preeclampsia itself causes fetal disturbances including fetal growth restriction, immaturity of organs, and non-reassuring fetal status via placental dysfunction (21).

In addition to hypertension, another clinical finding that is frequently encountered in cases with preeclampsia is proteinuria, according to the previous studies, 8–10% of eclamptic patients had proteinuria without hypertension, additionally, 50% of women with new-onset proteinuria were shown to develop preeclampsia within 3 weeks (22). Several different related outcomes have been introduced for both proteinuria and hypertension separately, for example; the major threat of hypertension during labor is stroke, which is associated with extremely significant risks for both the mother and child (23). Pregnancy-related strokes were shown to be encountered in 20–25/100 000 deliveries (24) which resulted in a 9–38% maternal mortality rate (23). This subject is further complicated by the labor itself because some significant impacts of labor on systemic tension have been shown. Hypertension was not observed before labor onset in 53% (10/19 cases) of cases of eclampsia during labor (25). Additionally, in another study, it was reported that three out of eight eclamptic episodes occurred during labor (26). Furthermore 27% of eclamptic episodes involved patients who displayed elevated blood pressure at delivery without any prior symptoms of hyperten-

sion or proteinuria (27). Several other studies considered hypertension that initially develops during labor to be a physiological change and reported this change to have positive outcomes (28). Further studies suggested that the greater fetal demand and reduced placental blood flow during labor might be the main underlying mechanism of labor onset hypertension (29), which may be accepted to be a compensatory mechanism. Therefore, tension control during labor may deteriorate placental perfusion by interfering with this compensatory mechanism.

All these aforementioned data showed us that both approaches, controlling hypertension or not strictly controlled hypertension during labor, may lead to an unfavorable outcome for the mother or the fetus. Therefore, further clinical assessments seem to be mandatory while determining the target tension during labor.

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