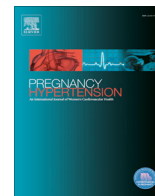




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Antenatal risk factors associated with need of postpartum antihypertensives in women with preeclampsia in South India: Case control study

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ABSTRACT

Objectives: To investigate the antepartum risk factors associated with the need for antihypertensive medication in the postpartum period in women with pre-eclampsia.

Methodology: Matched retrospective case control study was done in a tertiary center in south India between January 2016 and June 2016. We compared 100 preeclamptic women requiring antihypertensive medication in the postpartum period at discharge with 100 preeclamptic women who were not on antihypertensive medication at discharge, matched for age and parity at a ratio 1:1. Demographic data, maternal medical conditions, and delivery data were abstracted from maternal charts. Risk factors were evaluated using conditional logistic regression.

Results: Gestational age at delivery was comparable in both groups (34.3 vs. 35.6 weeks, $p = 0.220$). Cesarean section rates were higher in the cases compared to controls (53% vs. 32%, $p = 0.004$). After adjusting for age and parity women who had eclampsia, required prophylactic magnesium sulphate therapy and high peak antenatal systolic blood pressure were associated with postpartum antihypertensives. Using multivariate conditional logistic regression, mean systolic blood pressure (OR = 1.03, 95% CI 1.00–1.07), development of eclampsia (OR = 6.43, 95% CI 1.03–39.91) and need of prophylactic magnesium sulphate (OR = 5.02, 95% CI 2.02–12.47) were found to be associated with the need of postpartum antihypertensives.

Conclusions: In women with preeclampsia, development of eclampsia, use of prophylactic magnesium sulphate and high peak antenatal systolic blood pressure are more likely to require antihypertensives in postpartum period.

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1. Introduction

Pre-eclampsia affects 7–8% of the pregnancies and its associated with increased risk of maternal and perinatal morbidity [1]. Maternal complications include eclampsia, pulmonary edema, stroke, renal failure, disseminated intravascular coagulation and death. Postpartum course of preeclampsia is variable and the persistence of hypertension in the postpartum period is often a cause for concern. Hypertension can persist from pregnancy or present de novo in the postpartum period [2].

Abbreviation: HELLP, Hemolysis Elevated Liver enzymes Low Platelet count.

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There is limited literature on management of hypertension in the postpartum period as most studies have focused on the management of hypertension in antenatal period. Literature is also scarce regarding the antepartum risk factors associated with persistence of hypertension and the need of antihypertensives in the postpartum period [3–6]. Objective of this study was to investigate the antepartum risk factors associated with the need for antihypertensive medication in the postpartum period in women with pre-eclampsia.

2. Methodology

This was a matched retrospective case control study, involving south Indian women, conducted in the Women and children hospital, attached to the Jawaharlal Institute of Medical Education and Research, Puducherry, India between January 2016 and June

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2016. This facility is a tertiary care referral center which caters to the southeastern region of India with approximately 14,000 deliveries per year. Study population comprised of women who were admitted with a diagnosis of preeclampsia in the antenatal period by ACOG 2013 criteria and delivered in the institute [7]. Postnatal women who were on antihypertensive medication at discharge from hospital were the cases (group A) and those who did not require antihypertensive medication at discharge were included as controls (group B). Controls were matched with cases for age and parity at a ratio 1:1. Women with chronic hypertension and known cardiac problems were excluded.

Magnesium sulphate therapy following DHAKA regime used during labor and delivery in those with (1) severe hypertension, (2) HELLP syndrome and (3) those with convulsions [8]. Blood pressure was monitored during labor and delivery; those with records $\geq 160/110$ were managed following the ACOG protocol for severe hypertension using intravenous labetalol.[9]

Blood pressure was monitored three times a day following delivery in women with preeclampsia. During the monitoring if systolic blood pressure were ≥ 150 mmHg or diastolic blood pressure ≥ 100 mmHg, anti-hypertensive medications were started. Women were started on atenolol 25 mg once daily and titrated according to the blood pressure. Study was approved by the Institute Ethics Committee (Human studies).

From the medical records, the maternal age, parity, gestational age at diagnosis and delivery, highest antenatal, intrapartum and postpartum (within 24 h of delivery) systolic and diastolic BP recordings, presence of antenatally diagnosed HELLP syndrome, other medical comorbidities such as diabetes and various laboratory parameters like serum creatinine and complete blood counts were collected. Intra-partum antihypertensive requirements, use of prophylactic magnesium sulphate, mode of delivery and length of hospitalization after delivery were also noted. Neonatal data retrieved include birth weight, Apgar scores at 1 min and 5 min. Any maternal complications which occurred during hospital stay were also noted.

2.1. Sample size

It was calculated using the nMaster2.0 software(CMC vellore, India); based on the study by Peterson et al. [6], with proportion of chronic hypertension in those women with pre-eclampsia requiring antihypertensive medication in the postpartum was 6.6%. Using an 2 sided alpha error of 5%, power of 90% and an anticipated odds ratio of 4.0, we required to study 96 cases and 96 controls. We studied 200 women with preeclampsia with 100 cases who were discharged on antihypertensive medication in postpartum and 100 controls in this study.

2.2. Statistical analysis

Data analysis was done using STAT 13.1 (StataCorp, Texas, USA). Association of the various factors with use of antihypertensive in the post-partum period were assessed using chi-square test for categorical variables or Student's *t* test for continuous variables. Conditional logistic regression analysis was done to assess the independent association of various risk factors with use of antihypertensive in the post-partum period. A *p* value of <0.05 was considered as significant.

3. Results

Of the 8438 deliveries during the study period, 336 women (3.98%) were admitted with pre-eclampsia. Of 336 women 22 women with chronic hypertension and 9 with heart disease were

excluded. From the remaining 305 women with preeclampsia, we included 100 consecutive preeclamptic women who required antihypertensive at the discharge from the hospital following delivery as cases (group A) and 100 women matched for age and parity as controls (group B). There were only 9 women with diabetes in the index pregnancy; so they were not assessed for association in the study. Mean gestational age at diagnosis of preeclampsia was higher in those without requirement of antihypertensive in the postpartum period however this difference was not found to be statistically significant (33.6 ± 5.2 vs. 32.3 ± 4.8 weeks, $p = 0.071$) and the women with proteinuria 2+ or more on spot urine examination was comparable (92% vs. 86%, $p = 0.17$). Gestational age at delivery was comparable in both the groups (34.3 ± 3.3 vs. 35.6 ± 4.1 weeks, $p = 0.220$). More women in group A were delivered by cesarean section compared to group B (53% vs. 32%, $p = 0.004$). Postnatal hospital stay was longer in women who required postpartum antihypertensives (13.0 ± 7.7 vs. 9.8 ± 6.2 days, $p = 0.002$). There were no maternal deaths in the study population. Pulmonary edema occurred in one patient among women who required postpartum antihypertensives and the occurrence of acute renal failure was similar in both the groups (11% vs. 13%, $p = 0.663$).

There were six (6%) still births among compared to ten (10%) in the control group. Among the live born babies ($n = 184$), birth weight of the babies was lower in group A (1737.3 ± 696.3 vs 2013.8 ± 814.7 , $p = 0.01$) whereas APGAR score <7 at 5 min (9.6% vs 12.2%, $p = 0.56$) and neonatal death (6.4% vs. 6.7%, $p = 0.94$) was comparable in both groups. Admission to neonatal ICU was higher in women who required antihypertensives in the postpartum period. (66.0% vs 43.3%, $p = 0.002$)

Table 1 shows the characteristics of the cases and controls along the crude odds ratio adjusted for age and parity. Peak systolic blood pressure was higher in women who required postpartum antihypertensives compared to the diastolic blood pressure in the antenatal period. After adjusting for age and parity, development of eclampsia, systolic blood pressure in the antenatal period, use of prophylactic magnesium sulphate were found to be associated with the need of antihypertensive in the postpartum period.

Multivariate analysis showed 3 significant independent risk factors viz, eclampsia, mean peak antenatal systolic blood pressure and use of prophylactic magnesium sulphate to be associated with need of antihypertensive therapy in postpartum (Table 2). Women who required prophylactic magnesium sulphate have odds of 5.0 times and those with eclampsia have odds of 6.4 times for the need of antihypertensives in the postpartum. Each mm Hg rise in the peak systolic blood pressure in the antenatal period increased the odd by 3% for the need of antihypertensive in the postpartum period.

4. Discussion

Among women with preeclampsia, peak antenatal systolic blood pressure, development of eclampsia and the need of prophylactic magnesium sulphate were associated with the need of antihypertensives in the postpartum period, after adjusting for age, parity and other parameters in the study. Hospital stay following delivery was significantly higher in women who required postpartum antihypertensives.

Identification of women based on antenatal risk factors for hypertension in the postpartum period will help us to follow up these women with better monitoring and institution of timely therapy. This can be helpful in prevention of the complications secondary to hypertension such as stroke, renal failure or pulmonary edema. Higher rates of perinatal mortality were noted in the study population. This may be explained by the large number of referral we receive from the neighboring areas with pre-eclampsia having

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