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Risk factors for pre-eclampsia and its perinatal outcome

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ABSTRACT

Preeclampsia is a multiorgan, heterogeneous disorder of pregnancy associated with significant maternal and neonatal morbidity and mortality. The risk factors of pre-eclampsia and its maternal and fetal outcomes were investigated. This prospective observational study included 200 patients with pre-eclampsia and 100 patients with normal pregnancy. Significant risk factors of pre-eclampsia found in our study are primiparity, obesity, unbooked cases and positive family history of hypertension and teenage pregnancy. Headache was the common presenting complaint in 68.5% of severe pre-eclampsia cases. Abnormal Doppler findings were observed in 32.5% cases of severe pre-eclampsia cases, 11.7% of mild group and 6% of control. Caesarean section was the common mode of delivery for patients in pre-eclampsia (58%) and fetal distress was the common indication. More maternal and neonatal complications were encountered in women with pre-eclampsia when the pre-eclampsia was severe. The complications of severe preeclampsia could be prevented by more widespread use of prenatal care, prompt diagnosis of high-risk patients and timely intervention.

Keywords: Pre-eclampsia, pregnancy, eclampsia, and perinatal outcome**.**

INTRODUCTION

Pre-eclampsia is described as pregnancy specific syndrome, multifactorial, associated with reduced organ perfusion secondary to vasospasm and endothelial activation. The incidence of pre-eclampsia is commonly cited to be about 5%, although wide variation is reported. Pre-eclampsia once established is progressive till delivery[1]. Pre-eclampsia affects both the mother and fetus. Maternal complications include-abruptio, Acute renal failure (ARF), HELLP, convulsions, occipital lobe blindness, pulmonary edema and possible complications of caesarean sections. Fetal sequel of pre-eclampsia include-prematurity, fetal distress, intrauterine growth retardation, intrauterine death and still birth[2, 3].

Aggressive management and immediate delivery of foetus remote from term leads to high perinatal mortality and morbidity resulting from prematurity and growth restriction. Termination of pregnancy is the treatment par excellence. Fortunately, pre-eclampsia is a preventable disorder if only those at risk of developing it can be identified early in the antenatal period and managed appropriately. The paucity of studies that highlight the risk factors of pre-eclampsia in our local setting necessitated the conduct of present study.

The present study was undertaken to study the risk factors and feto-maternal outcome of pre-eclampsia.

MATERIAL AND METHODS

After obtaining informed and written consent, 200 cases singleton pregnancy of pre-eclampsia after 20 weeks of gestation of different parity, both booked and unbooked, were included in the study. The outcomes were compared with data from 100 cases of control group who were selected randomly with no history of hypertensive disorders of pregnancy. Patients with congenital fetal anomalies, chronic hypertension, diabetes, chronic obstructive pulmonary disease, renal failure and other medical risk factors complicating pregnancy were excluded from study.

Pre-eclampsia is defined by working group of the National High Blood Pressure Education Program as new onset of hypertension (BP >140 / 90 mmHg) associated with proteinuria ($\geq$ 0.3g / 24 hr of urine protein) after 20 weeks of gestation.

A detailed history was taken from all these patients including age, parity, and socioeconomic status, antenatal care, history of anaemia, family history, past obstetric history of PIH was recorded. The women's level of education and her husband's occupation were used to determine her social class. Signs and symptoms associated with pre-eclampsia were recorded. Both routine and specific investigations such as CBP, platelet count, LFT, blood urea, serum uric acid, serum creatinine, complete urine examination(including urine albumin), fundus examination, USG with BPP, Doppler flow studies were performed. Associated risk factors like IUGR were noted.

Patients having mild PE, with gestation age group > 37 weeks were induced and delivered, and < 37 weeks were advised in hospital or outpatient management depending on patient compliance.

All patients diagnosed as severe PE were admitted to hospital, managed according to gestational age, with the aim of preventing maternal and fetal complications. With in first 24 hours of admission, all patients with gestation < 34 weeks received 2 doses of Betamethasone, 12 mg each, 24 hours apart. In addition, patients with imminent eclampsia received Magnesium Sulphate prophylactically as per criteria laid down in MAGPIE trial, and were intensively monitored to prevent maternal and fetal complications[4]. For hypertension Methyldopa, Labetalol, Nifedepin were the commonly used, dose was adjusted accordingly to the severity of hypertension.

Monitoring was done depending on severity and gestational age, under the following headings

Patients were reviewed twice daily to assess the maternal and fetal conditions and the need for delivery. Labor was allowed to proceed in those patients who set into spontaneous labor. Need for delivery was classified on clinical grounds. If it was observed that delivery was to be effected in less than 4 hours, it was considered emergency. If delivery was indicated within 4-24 hours period, it was termed elective.

Mode of termination depended on period of gestation, favourability of cervix and urgency of termination. Cervical priming agents like PGE_2 gel or PGE_1were widely used if the cervix was found unfavourable. Labor was accelerated by artificial rupture of membranes and syntocinon whenever necessary. Caesarean section was performed for obstetric indications and when urgent termination was indicated for unfavourable cervix, failure of induction and fetal distress. The duration of labor, mode of delivery and indication for delivery was noted.

Fetal outcome was assessed by Apgar scores at birth. Birth weight was noted and any NICU admissions-indications and duration of admission was recorded. The outcome measures of the study were maternal and fetal outcome, mode of delivery caesarean section rate, maternal complications, period of NICU admission, and fetal morbidity and mortality.

Statistical analysis: Descriptive statistical analysis was carried out using Z test for proportions, for testing the differences in proportions between the groups. Statistical analysis was done by chi-square test using SPSS 15.0 version. All the statistical tests were considered statistically significant whenever $p< 0.05$.

RESULTS

Among the 200 cases of pre-eclampsia in our study conducted during one year period,111 cases (55.5%) were diagnosed as Mild pre-eclampsia as compared to severe Pre-eclampsia (89 cases,44.5%). Patient's clinical profile is shown in table1.

Table: 1. Parent characteristics

Variable		Pre -eclampsia		Control		pvalue
		Number	%	Number	%	
Socioeconomic status	Low	33	16.5	15	15	>0.05
	Middle	167	83.5	85	85	
Booking status	Booked	75	37.5	70	70	<0.01
	Unbooked	125	62.5	30	30	
Parity	Primi	133	66.5	42	42	< 0.01
	Multi	67	33.5	58	58	
BMI (kg/m²)	≤ 25	48	24	73	73	<0.01
	26-30	66	33	18	18	
	>30	86	43	9	9	
Family history of hypertension	Both parents	12	6	4	4	<0.01
	Father	11	5.5	2	2	
	Mother	37	18.5	7	7	
	None	140	70	87	87	

Maternal and fetal outcomes are depicted in table 2 & 3. In severe cases of PE, headache (68.5%), edema (65.2%) were the most common presenting complaints followed by 28% of cases with vomitings, 17.1% - decreased fetal movements and 12.3% each with epigastric pain and blurring of vision as compared to mild cases, who had minimal symptoms at presentation. 2 cases (2.25%) of severe PE had elevated creatinine levels (>1.2 mg/dl).All control group cases and mild PE cases had normal levels. Normal liver function tests were observed in majority of cases of pre-eclampsia, except for 7 severe cases who showed abnormal LFT and developed HELLP syndrome. None of the control group had abnormal LFT. Among 89 cases of severe PE, 7 cases (7.8%) had severe thrombocytopenia, which had HELLP syndrome. 15 cases (16.9%) moderate to borderline low platelet count. 67 cases (75.3%) had normal platelet count. Only 2 cases (1.8%) of mild pre-eclampsia had moderate degree of thrombocytopenia.All the control group cases had normal platelet count.

Table: 2. Maternal and fetal out comes

Variable		Mild Pre -eclampsia		Severe Pre -eclampsia		Control	
		Number	%	Number	%	Number	%
Total patients		111	55.5%	89	44.5	100	100
Headache		6	5.4	61	68.5	0	0
Reduced fetal movements		5	4.5	16	17.1	0	0
Epigastric Pain		0	0	11	12.3	2	2
Blurring of Vision		0	0	11	12.3	0	0
Edema		48	43.2	58	65.2	21	21
Increased serum creatinine		0	0	2	2.25	0	0
Abnormal LFT		0	0	7	7.9	0	0
Low platelet count (<1 lakh/mm^3)		0	0	7	7.8	0	0
Fundoscopy Grades	0	107	96.4	44	49.4	100	100
	1	4	3.6	37	41.6	0	0
	2	0	0	7	7.9	0	0
	3	0	0	1	1.1	0	0

Table: 3. Maternal and fetal out comes

Variable		Mild Pre -eclampsia		Severe Pre -eclampsia		Control	
		Number	%	Number	%	Number	%
Doppler findings	Diastolic notch	7	6.3	18	20.2	5	5
	↑resistance	2	1.8	8	8.9	1	1
	Absent diastolic flow	2	1.8	3	3.4	0	0
	Reverse flow	2	1.8	0	0	0	0
	Normal findings	98	88.3	60	67.5	94	94
Oligohydramnios		20	18	20	22.5	8	8
$MgSO_4$ prophylaxis		0	0	32	35.9	0	0
Caesarian section		60	54	56	62.9	40	40
Abruptio placentae		3	2.7	9	10.1	0	0
Eclampsia		0	0	11	12.3	0	0
PPH		12	10.8	9	10.1	3	3
HELLP		0	0	7	7.8	0	0
ARF		0	0	1	1.1	0	0

The association of eclampsia as complication of severe PE is statistically significant with p value being <0.01. Regarding PPH as maternal complication, 12 cases (10.8%) were seen in mild pre-eclampsia and 9 cases (10.1%) in severe group. 3 cases (3%) were also observed in the control group.

There is statistically significant association between PPH and PE. (p value 0.007). 9 cases (10.1%) of Abruptio were observed in severe PE patients and 3 cases (2.7%) in mild PE. Severe PE patients had 7 cases (7.8%) of HELLP, single case each of Acute Renal Failure and Blindness as maternal complication. Neonatal mortality in severe PE group was 21.3% as compared to mild PE group 8.1% and 1% in control group. This analysis suggested that gestation age at delivery and severity of pre-eclampsia was responsible for the difference in neonatal outcome in both the groups**.**

CAUSES OF EARLY NEONATAL DEATH	11 Cases
Respiratory distress syndrome	5
Necrotising enterocolitis	2
Septicaemia	1
Asphyxia	1
Meconium aspiration syndrome	1
Intraventricular hemorrhage	1

DISCUSSION

The present study is an observational case-control study of 200 cases of pre-eclampsia aimed at analysing the feto-maternal outcome and compare with 100 cases of control group with normal BP. In our study group, most of the cases (83.5%) belonged to middle socioeconomic status, having common environmental background with sedentary life style. Most of the cases in our study group were unbooked with incidence of 62.5% as compared to 30% of control group (criteria of booking in our study: was a minimum of 4 visits during antenatal period). Severe pre-eclampsia was commonly observed in unbooked cases, who received minimal or no antenatal care. Study by Anthony M et al established the significance and impact of antenatal care in reducing the fetal and perinatal morbidity and mortality[5]. In our study, primigravidas accounted for 66.5% in pre-eclampsia groups as compared to multigravidas, which accounted for 33.5%. In our study, 24% cases of pre-eclampsia and 73% of controls had BMI less than 25 kg/m² BMI, 33% of pre-eclampsia and 18% cases of control group had BMI between 26-30. 43% cases of pre-eclampsia group and 9% of controls had BMI >30 kg/m² suggesting an increased risk of pre-eclampsia in cases with BMI >30 kg/m². Studies conducted by Lee CJ et al.,[6] and Stone JL et al.,[2], have suggested that the risk of pre-eclampsia doubles with an increased in body mass index.

Headache was the predominant symptom in severe (68.5%cases) pre-eclampsia group, followed by vomiting seen in 28% of severe cases, epigastric pain and blurring of vision in 12.3% cases. In our study, 7.8% cases of severe pre-eclampsia group had platelet count < 1 lakhs/mm^3,16.9% cases of severe and 1.8% cases of mild pre-eclampsia group had platelet count in between 1-1.5 lakhs/cu.mm. Study by S. Mohaptra[7] concluded that there is inverse relationship between severity of PIH and platelet count.

In our study, the incidence of abnormal Doppler in pre-eclampsia was 22.1%. 32.5% cases of severe pre-eclampsia group and 11.7% of mild cases had abnormal Doppler as compared to 6% in control group. In cases which showed diastolic notch, 6 cases had oligohydramnios, 9 had IUGR, 11 cases were preterm and perinatal mortality was observed in 3 cases. Groom et al.,[8] in their studies showed diastolic notch as predictor of pre-eclampsia.

Increased resistance on Doppler was seen in 10 cases of pre-eclampsia when compared to single case of control group. Absent diastolic flow was observed in 5 cases of pre-eclampsia, of which 2 cases had oligohydramnios, 2 had IUGR, 2 cases were premature and single case was still birth. 2 cases had early neonatal death and 2 cases were admitted to NICU. There were 2 cases of reverse flow on Doppler. Both the cases had evidence of oligohydramnios and IUGR and ultimately resulted in intra uterine deaths. This data shows the significance of abnormal Doppler findings in relation to perinatal morbidity and mortality in pre-eclampsia and the need for early termination of pregnancy in high risk cases managed through abnormal Doppler. Incidence of oligohydramnios in our study was 20% of pre-eclampsia cases as compared to 8% in control group. Cases with long duration pre-eclampsia were seen to develop severe oligohydramnios.

In our study, magnesium sulphate was given was given to 32 cases of severe pre-eclampsia group who presented with imminent signs of eclampsia and among them 9 cases developed seizures before receiving magnesium sulphate and among remaining 23 cases were given magnesium sulphate as prophylaxis for imminent eclampsia and no case developed seizures i.e incidence of seizures was 0% after magnesium sulphate prophylaxis. MAGPIE trial[4] reported 0.8% incidence of seizures in patients who received prophylaxis

In our study incidence of abruption was 12.8% - of which 10.1% was seen in severe and 2.7% in mild pre-eclampsia. It was managed by terminating the pregnancy. In our study, PPH was common complication with incidence of 10.4% in whom many cases of severe PPH required blood transfusions. The incidence of PPH is similar in both mild-10.8% and in severe-10.1% compared to control of 3%. Our findings are comparable with the study by Ben hmid R[9], who observed 35.4% incidence.

In our study, 42.4% of babies in severe pre-eclampsia group and 24.3% of mild group required admission for various conditions such as RDS, birth asphyxia, MAS. This difference in incidence is because of more number of LBW and preterm deliveries as seen in severe pre-eclampsia group with increased perinatal morbidity and mortality. In our study, the overall incidence of NICU admission was 32.5% when compared to study by Attiya Ayaz et al.,[10] with 26% incidence. In our study perinatal mortality rate is 14%; 8.1% in mild, 2.1.3% in severe and 1% in control. Among 7 (3.5%) babies with still birth in pre-eclampsia, abruption was the cause in 5 cases and placental insufficiency associated with oligo and IUGR was the cause in remaining 2 cases. Among 6 cases (3%) of IUFD, 4 cases were seen in mild pre-eclampsia group compared to 2 cases of severe pre-eclampsia. Abruptio was the cause in a single case of IUFD and the remaining 5 cases were associated with oligohydramnios, IUGR and abnormal Doppler. Gestational age at delivery and severity of preeclampsia was related to poor neonatal outcome in preeclampsia.

CONCLUSION

Significant risk factors of pre-eclampsia found in our study are primiparity, obesity, unbooked cases and positive family history of hypertension and teenage pregnancy. This study emphasise the importance of antenatal steroids, magnesium sulphate prophylaxis for severe preeclampsia and the importance of USG - Doppler in antenatal period for good fetal results. The present study also indicated that early onset pre-eclampsia cases had poor perinatal outcome associated with IUGR, oligohydramnios, abnormal Doppler and prematurity.

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