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Guruprasad

Assistant Professor, Department of
OBGY, Raichur Institute of
Medical Sciences, Raichur,
Karnataka, India

Dr. Sunitha HB

Associate Professor, Department of
OBGY, Gadag Institute of Medical
Sciences, Gadag, Karnataka, India

Correlation of preeclampsia related investigative parameters with the maternal outcome

Guruprasad and Dr. Sunitha HB

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Abstract

Background: Delaying this definitive management for severe preeclampsia to at least gain benefit of antenatal steroids and to organize resources for managing the anticipated complications is referred to as expectant management. Therefore, the present study was made attempt to study the maternal and perinatal outcome in severe preeclampsia.

Methods: The study was conducted in the Department of Obstetrics and Gynaecology, Kasturba Medical College, Manipal. One hundred and forty patients who had blood pressure $\geq 160/110$ mm of hg with proteinuria of any degree or Blood pressure $\geq 140/90$ mm of hg with proteinuria of $\geq 2+$ were included in the study. Statistical analysis was done by applying chi-square.

Results: Mean arterial pressure of >127 mm of Hg was found in 31.8% women with eclampsia and 18.2% with other complications. Hemoglobin $> 13g\%$ and total count > 11000 cells/cumm had no correlation with the maternal outcome related to severe preeclampsia. Platelets < 1 lakh/ml were found to have correlation with other complications related to preeclampsia but not with eclampsia. Serum uric acid $> 7U/l$ was found to have significant correlation with eclampsia as well as other complications related to preeclampsia. Serum creatinine $> 1.2mg/dl$ 35.2% had eclampsia and 52.9% had other complications.

Conclusion: Mean arterial pressure, uric acid, platelet count, serum creatinine were found correlate significantly with poor maternal outcome in women with severe preeclampsia. Prematurity and fetal growth restrictions are the main factors causing perinatal morbidity/ mortality. Timely cesarean delivery seems to improve perinatal outcome in settings with facilities for newborn care.

Keywords: Severe preeclampsia, blood pressure, maternal outcome, perinatal outcome

Introduction

Preeclampsia is the most challenging clinical entity affecting both mother and the fetus. It is one of the leading causes for maternal as well as perinatal morbidity/ mortality. In developing nations, the incidence of the disease is reported to be 4-18% with hypertensive disorders being the second most common obstetric cause of stillbirths and early neonatal deaths [1]. Approximately 1,00,000 women die worldwide per annum because of eclampsia. It is said that pre-eclampsia and eclampsia contribute to death of a women every 3 minutes worldwide. In India, incidence is 5-15% incidence being more in primigravida around 15% and multigravida around 10%.

Preeclampsia is mild in 75% of cases and severe in 25% of them [2]. In its extreme, the disease may lead to liver and renal failure, disseminated intravascular coagulopathy (DIC), and central nervous system (CNS) abnormalities. Besides placental insufficiency may cause fetal growth restriction and related perinatal complications; premature birth either spontaneous or induced for indications, is an important cause for perinatal morbidity/ mortality. Hemorrhage and hypertensive disorders together account for the largest proportion of maternal deaths in developing countries.

Contradicting reports are found in the literature regarding the role of investigative workups as indicators of severe disease that will direct to terminate pregnancy; also there are conflicting reports regarding the predictive role of these investigative parameters.

The present study is an attempt to analyze maternal and perinatal outcome in severe preeclampsia and to find the usefulness of the clinical and investigative work up as predictors of outcome.

Correspondence

Dr. Sunitha HB

Associate Professor, Department of
OBGY, Gadag Institute of Medical
Sciences, Gadag, Karnataka, India

Objectives

To study the maternal and perinatal outcome in severe preeclampsia and to find correlation of clinical, hematological and biochemical parameters in women with severe preeclampsia and maternal outcome.

Material and methods

A prospective study was conducted in the Department of Obstetrics and Gynaecology, Kasturba Medical College, Manipal from July 2009 to July 2011. 140 patients who had blood pressure $\geq 160/110$ mm of hg with proteinuria of any degree or Blood pressure $\geq 140/90$ mm of hg with proteinuria of $\geq 2+$ were included in the study. Institutional ethics committee approval was taken before starting the study. Women with severe preeclampsia- eclampsia were evaluated and managed as per the hospital protocol. Blood pressure of patient was measured in supine position after 10 minutes of rest using mercury sphygmomanometer with appropriate cuff size tied at heart level. The women were monitored clinically as well as by investigative work up. Proteinuria was estimated daily by dip stick method. Serum analysis of uric acid was done by urease method and serum creatinine was done by jaffe rate blanked method to check renal function, liver function tests was done by using automated analyzer. Platelet count and protein estimates in 24 hour urine (biuret method) were done at admission and as indicated by the clinical disease behavior. Peripheral smear was done to look for spherocytosis, schizocytosis, reticulocytosis, anisocytosis, triangular cells, helmet cells and burr cells for screening for HELLP syndrome. Fundus oculi was examined using Ophthalmoscope for hypertension induced changes and the findings were graded as per Keith, Wagner and Barker (1939) classification. Sonographic estimation of fetal growth, weight and amount of liquor was carried out. Fetal condition was monitored by fetal heart rate auscultation and fetal heart rate tracings, Doppler analysis and modified biophysical profile.

Women were put on antihypertensive drugs- Alpha methyl dopa (maximum dose up to 2g/day)/ labetalol (800mg/day)/ amlodipine and/ or Nifedipine (up to 30mg); dose adjustments or treating with additional drugs was done as per individual requirement. Two doses of intramuscular dexamethasone 12 mg, 12 hours apart was given for preterm salvageable pregnancies.

Women on expectant management were asked to report if they had headache or epigastric pain or vomiting or visual disturbances, those with eclampsia received magnesium sulfate (Pritchard regime) with standard monitoring for magnesium toxicity.

Pregnancy was terminated for eclampsia, uncontrolled hypertension in spite of being on maximum dose of antihypertensives, persisting/ progressively deteriorating clinical symptoms or the biochemical markers, occurrence of complications such as placental abruption, eclampsia, renal failure and indication of non-reassuring fetal status. The decision regarding the route of delivery was based on estimated fetal weight, salvage ability, gestational age, amniotic fluid index, fetal status and cervical score. The neonates were managed by the specialist neonatology team.

Outcome measures

All women who were referred or diagnosed here as severe preeclampsia were monitored and investigative parameters were compared with the maternal outcome. Investigative parameters are as follows mean arterial pressure cutoff of 129 was taken, random urine protein above 2+, 24 hour urine protein values were divided $<3g$ and 3-5g, hemoglobin 11gm% and total count 11000 cu/mm cutoff was taken, platelets less than 100000 cells/ml, serum uric acid cutoff 7 mg/dl, serum creatinine 1.2 mg/dl. These were compared with various adverse maternal outcome. The maternal outcome was divided in to three categories.

1. Normal outcome
2. Eclampsia
3. Other complications (Abruption, HELLP, renal failure, pulmonary edema, cardiomyopathy, cerebral hemorrhage).

Analysis was done to find the total number of live births, still births, neonatal deaths and IUGR for severe preeclampsia and eclampsia. Perinatal outcome was noted after delivery, babies admitted in NICU and there outcome was observed. Preterm deliveries divided according to period of gestation 28 to 34 weeks and 34 to 37 weeks. Birth weight was divided in to 4 groups less than 1kg. 1.1 to 1.5 kg, 1.51kg to 2.5kg and more than 2.51 kg. For these groups outcomes were noted and total babies survived for each group was observed.

Statistical analysis

Descriptive statistics such as mean, SD and percentage was used. Relationship between variables was done by applying chi-square test. A p-value less than 0.05 were considered as significant.

Results

Table 1: Patient profile

Patient characteristics		Observation
Mean age (years)		26 (18-38)
Parity (Number)	Primigravida	86 (61.4%)
	Multigravida	54 (38.5%)
Previous history [Number (%)]	Preeclampsia	12 (8.5%)
	BOH	5 (3.5%)
	Chronic hypertension	6 (4.2%)
Associated medical disorder	SLE	2
	Pheochromocytoma	2
Gestational age (weeks)	At diagnosis	30 (20-39.3)
	At delivery	33 (20-40)
Antenatal Booking [Number (%)]	Booked	21 (15%)
	Referred	119 (85%)
Vaginal delivery		35 (25%)
Caesarean delivery		105 (75%)

Mean age of women with severe preeclampsia was 26 years. Eleven were above 35 years and 6 were teenage pregnancies. Two third of the group (61.4%) was primigravida. Previous history of preeclampsia, bad obstetric history and chronic hypertension was seen in 25 women. Associated medical disorder systemic lupus erythematosus and pheochromocytoma was seen in 4 women. Outside (85%) and only 15% were booked with us. Due to maternal or fetal indications emergency

cesarean delivery was done in 105(75%) and 35(25%) had vaginal delivery. Three women had cesarean delivery outside before referral here. Among vaginal deliveries 4 had spontaneous onset of labor and 25 had induced preterm delivery. It was observed that mean gestational age at diagnosis of severe preeclampsia was 30 weeks and gestational age at delivery was 33 weeks. Most of them were referred from outside.

Table 2: Disease profile

Clinical parameter		Number (%)
Systolic BP(mm of Hg) n = 140	≤ 140	35(25)
	140 - 160	63(45)
	>160	42(30)
Diastolic BP(mm of Hg) n = 140	90 - 110	118(84.3)
	>110	22(15.7)
Impending eclampsia (n=26)	Severe headache	10(38.4)
	Epigastric or upper right quadrant pain	5(19.2)
	Persistent visual symptoms	6(23.07)
	Oliguria	5(19.2)
Eclampsia (n = 140)		29(20.1)
ICU admission		4(2.85)

Systolic blood pressure was >160 mm of Hg only in 42(30%) of the group. The remaining 70% of them though the systolic BP was not in the range of severe PE, had other criteria of severe preeclampsia. Similarly only 22 women (15%) had diastolic BP more than 110 mm of Hg. Blood pressure (both systolic and diastolic) ≥ 160/110 mm of Hg was seen in 44(31.4%).

Signs of impending eclampsia were seen in 26 women with severe preeclampsia. Twenty nine (20%) women had eclampsia. Four women required ICU admission: Two had renal failure and one each had HELLP and disseminated intravascular coagulation.

Table 3: Investigation profile

Investigations	Cut off values	Number (%)
Urine protein	1+	14 (10)
	≥2+	126 (90)
24 hr urine protein (n=42)	<3 g	33 (23.5)
	3-5 g	9 (6.4)
Serum creatinine(mg/dl)	≤1.2	123 (87.8)
	>1.2	17 (12.1)
Serum uric acid(mg/dl)	≤7	106 (75.7)
	>7	34 (24.2)
AST(I/U)	≤70	119 (85)
	>70	17 (12.1)
ALT(I/U)	≤70	123 (87.8)
	>70	17 (12.1)
LDH(I/U)	≤600	96 (68.5)
	>600	44 (31.4)
Platelets (lakh/ml)	≤1	25 (17.8)
	>1	115 (82.1)

Abnormal value above cut-off to define severe PE was found commonly for proteinuria (90%). Other investigations had values in the severe PE range only in 12-34% of the group.

Table 4: Maternal complications

Complication	Frequency (Number)	%
Eclampsia	29	20.7
Abruption	5	3.57
HELLP	6	4.28
Renal failure	9	6.42
Pulmonary edema	4	2.85
Cardiomyopathy	1	0.71
Cerebral haemorrhage	1	0.71
Discharged against medical advice	2	1.4
Maternal mortality	Nil	

Out of 140 women studied 20.7%(29) had eclampsia, abruption 3.5%(5), HELLP 4.28%(6), renal failure 6.42%(9), pulmonary edema 2.85%(4), cardiomyopathy 0.71%(1), cerebral hemorrhage 0.71%(1). 17 women had more than 1 complication (HELLP, eclampsia, pulmonary edema, cerebral infarct, renal failure). Two women were discharged against medical advice

one with renal failure with pulmonary edema and the other with HELLP. There was no maternal mortality among 140 women studied.

Among 29 women with eclampsia, 25 women had antepartum eclampsia at the time of arrival and 2 each had antepartum and postpartum eclampsia after admission.

Table 5: Perinatal outcome

Perinatal outcome	Preterm (n=117)		Term (n=23)	
	n	%	N	%
Stillbirth	29	27.4	4	50
Live birth	88	75	19	82.6
Neonatal death	7	6.6	1	12.5
NICU admissions	64	60.3	4	50
Respiratory distress syndrome	23	21.7	3	37.5
Sepsis	2	1.9	0	
IVH	1	0.9	0	
Hyperbilirubinemia	9	8.5	5	62.5
NEC	2	1.8	0	
Survivors	81	69	18	78

Among the 140 women, 114 had perinatal complications [stillbirth 33, neonatal morbidity 81(neonatal deaths 8)]. Of the 114 with perinatal complications 106 were preterm and 8 were term babies. In the preterm group 81(69%) babies survived; of the 88 live newborns the survival was 92%. Among term babies

4(50%) were still births(1 due to abruption, 2 were due to severe IUGR and oligoamnios and 1 due to severe oligoamnios). there was one neonatal death due to severe respiratory distress syndrome.

Table 6: Correlation of Mean arterial pressure, Serum creatinine, Serum uric acid, Platelet count with maternal outcome

	Maternal Outcome		
	Normal	Eclampsia	Other complications
Mean arterial pressure			
<127 mm of Hg (n=96)	70(72.9%)	15(15.6%)	13(13.5%)
>127 mm of Hg (n=44)	23(52.3%)	14(31.8%)	8(18.2%)
p-value		0.042	0.646
Serum creatinine			
<1.2mg/dl (n=123)	88(71.5%)	23(18.6%)	12(9.7%)
>1.2mg/dl (n=20)	5(29.4%)	6(35.2%)	9(52.9%)
p-value		0.819	0.025
Serum uric acid			
<7mg/dl (n=106)	82(77.3%)	13(12.2%)	11(10.3%)
>7mg/dl (n=37)	11(32.3%)	16(47.1%)	10(29.4%)
p-value		0.001	0.010
Platelet count			
<1 lakh/ml (n=28)	10(40%)	9(36%)	9(36%)
≥ 1 lakh/ml (n=115)	83(72.1%)	20(17.3%)	12(10.4%)
p-value		0.626	0.003

The table shows that of the 44 women who had mean arterial pressure >127 mm of Hg 31.8% women had eclampsia and this had significant correlation (p=0.042).

Out of 140 women who had severe preeclampsia 20 had serum creatinine more than 1.2 mg/dl. Among them 5 had normal outcome, 6 had eclampsia and 9 had other complications. Statistically significant correlation was seen between serum creatinine and maternal complications (p=0.025).

37 women who had severe preeclampsia had serum uric acid more than 7 mg/dl. Among them 11 had normal outcome, 16 had eclampsia and 10 had other complications. There was statistically significant correlation between serum uric acid >7mg/dl and both eclampsia (p=0.001) and other maternal complications (p=0.01).

Out of 140 women with severe preeclampsia 28 had platelets less than one lakh. Among them 10 women had normal outcome, 9 had eclampsia and 9 had other complications. There was correlation between low platelets and maternal

complications other than Eclampsia (p=0.003).

Discussion

The maternal and perinatal morbidity and mortality due to preeclampsia has come down dramatically in developed countries. This has been achieved by improvements in antenatal care and early hospitalization and proper maternal and fetal surveillance. In developing countries preeclampsia-eclampsia still stands as one of the major complications of pregnancy.

It has been observed that preeclampsia is more common in young or elderly primigravidas and it is reported that maternal age > 35 years was significantly associated with preeclampsia and attributed this to the fact that progressive vascular endothelial damage occurs with aging [3]. In a study by Abuheja AT had a still higher age preponderance (45 – 46 years) of the preeclampsia⁴. However in our study the mean age of the women with preeclampsia was 26 years probably because in India the age of primigravidas is mostly between 20-30 years.

It is shown that nulliparous women are at an increased risk which is related to maternal first exposure to chorionic villi [5]. The majority of women in this study were also primigravida (61.4%).

In the present study, 15% were booked case and 85% were referred cases. All with eclampsia were unbooked in our study similar to 80-90% of the eclampsia being unbooked cases in the studies Zuspan [5]. However Sibai BM reported that one-third of women with regular prenatal care had abrupt onset of severe preeclampsia/eclampsia without prior positive clinical or laboratory findings [6].

In this study, the most common maternal complication was eclampsia 20.7%, followed by renal failure (6.42%), HELLP syndrome (4.28%), placental abruption (3.5%) and pulmonary edema (2.8%). Also there were preeclampsia associated rare complications such as cerebral hemorrhage and cardiomyopathy. This was comparable with the various studies [7].

In present study 4 (2.8%) women required ICU admission because of renal failure, HELLP and pulmonary edema. There was no maternal death in this study. The most common cause of death are intracranial bleeding and acute renal failure secondary to abruption placentae. It was comparable with the other studies where the ICU admissions in there study were due to HELLP, renal failure, abruption and DIC [8]. The greatest risk of maternal death is when eclampsia develops before 28 weeks of gestation [6]. In this study there were no early onset eclampsia case seen.

Babies born to severe preeclampsia and eclampsia mothers are mainly low birth weight (<2.5kg) which may be due to preterm delivery or intrauterine growth restriction. In present study, of 107 (93%) live newborns were low birth weight (<2.5 kg). In this group 93 babies survived; and among the very low birth weight (<1000g) newborns the survival rate was 66%.

In our group there were 75.5% of preterm babies and 5.7% were term babies. Sixty percent of preterm newborns and 50% of term newborns required NICU admission, the common neonatal complication in preterm newborns was respiratory distress syndrome 23 (21.7%) and in term newborns was hyperbilirubinemia 5 (62.5%). Survival among preterm and term newborns was 92% and 95% respectively. It has been estimated that of all pregnancies among women suffering from severe preeclampsia and eclampsia, 11.5% to 30% end up as still births or perinatal deaths⁹. In the present study stillbirths were 23.5% and perinatal deaths were 29%. All still births were referred cases.

In our study we considered mean arterial pressure (MAP) as one of the measures to study the correlation with the outcome. We noted that women had eclampsia or other preeclampsia related complications even at blood pressures- systolic or diastolic or both-not at a level beyond the cut off of 160/110 mm Hg for severe preeclampsia. When we considered MAP more than 127mm Hg, 31.8% had eclampsia, 18.2% had other maternal complications, 52.3% had normal outcome and one women had cerebral hemorrhage for her MAP was > 127 mm of Hg. Studies by Menzies J and Zang J have reported that there is no relation between blood pressure and adverse maternal outcome [10, 11]. However Martin Jr. found correlation between systolic blood pressure more than 160 mm of hg and stroke [12]. Systolic blood pressure also had a significant ($p < 0.05$) influence on perinatal deaths in the study by Dhananjay BS among women with eclampsia [13].

Proteinuria was always thought to be a good indicator of the severity of preeclampsia. In present study random urine protein more than 2+ was seen in 129 patients; 22.2% had eclampsia and 15.8% had other complications. Twenty four hour urinary

protein testing could be done only for 42 women. In other cases decision to terminate pregnancy had to be taken immediately, hence there was no time for 24 hour analysis. Seventy seven percent of women whose 24 hour urine protein was 3 to 5 grams had normal outcome. Chan P *et al.* and Thangaratnam S *et al.* have found that no level of proteinuria could be defined to predict outcomes and is a poor predictor of either maternal or fetal outcome [14, 15].

There is elevation of hemoglobin and hematocrit caused by decrease in plasma volume. It is known that haemoconcentration is a hallmark of eclampsia, because of haemoconcentration there is decreased regional perfusion and leads to altered cerebral autoregulatory function which can in turn lead to PRES [10]. In present study one women had hemoglobin more than 13g% and 21.4% had between 11 to 13 g% had eclampsia. HELLP syndrome was seen in women with hemoglobin 11 to 13 g% in 4 and more than 13 g% in two women. One study showed that increased hemoglobin/hematocrit reflects the severity of preeclampsia. So hemoglobin/hematocrit are not good predictors of eclampsia [16].

Preeclampsia is a proinflammatory state caused by placental hypoperfusion. In this study 105 women had total count more than 11000/cc., 4 patients with HELLP had total count more than 11000/cc. A study by Magann EF found that there was significant elevation of total WBC count than platelet count [17]. Platelet count varied inversely with WBC counts and the finding of an association between increasing leucocytosis and worsening thrombocytopenia early in the course of HELLP syndrome supports the hypothesis that it may represent an inflammatory state. But it is not a good predictor for maternal outcome in sever preeclampsia.

It is also seen that women with serum uric acid more than 7 mg/dl, 47.1% had eclampsia and 29.4% had other maternal complications. This was comparable with the studies by Parrish M *et al.* [18] and Menzies *et al.* [10]. In present study Women who had uric acid less than 7 mg/dl 12.2% had eclampsia and 10.3% had other severe preeclampsia related complications.

In the present study it was found that women who had serum creatinine more than 1.2 mg/dl was found to have more other maternal complications like abruption, renal failure etc. Women who had serum creatinine less than 1.2mg/dl, was found to have 18.6% eclampsia and 9.7% other maternal complications. Other studies have also found that serum creatinine>1.2 mg/dl is associated with adverse maternal outcome [18, 19].

Platelet count less than 100×10^9 was associated with maternal complications other than eclampsia. This was comparable with the studies Brown MA *et al.* [19].

Conclusion

Maternal and perinatal morbidity is still high among women with severe preeclampsia. Mean arterial pressure >126 mm of Hg, uric acid >7mg/dl, platelet count <1,00,000 cells/cc, serum creatinine>1.2 mg/dl were found correlate significantly with poor maternal outcome in women with severe preeclampsia. Prematurity and fetal growth restrictions are the main factors causing perinatal morbidity/ mortality. Timely cesarean delivery seems to improve perinatal outcome in settings with facilities for newborn care.

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