Prospective Study Of Obstetric And Perinatal Outcomes In Severe Preeclampsia With Altered Biochemical And Haematological Parameters Amongst Pregnant Women

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INTRODUCTION

Hypertensive diseases during pregnancy includes gestational hypertension (without proteinuria), preeclampsia (with proteinuria), and eclampsia (preeclampsia with convulsions). Pregnancy termination reverses the clinical manifestations of the disease, suggesting that trophoblastic invasion plays a central role in the pathogenesis of preeclampsia. A recent study revealed that excessive placental secretion of soluble fms-like tyrosine kinase-1 may contribute to endothelial dysfunction, hypertension, and proteinuria in preeclampsia.[2] In a multicenter study, approximately 30% of HDP cases were due to chronic hypertension, while 70% were due to gestational hypertension/preeclampsia.[3]

For the conceptus, the most common consequences associated with hypertensive diseases are the restriction of intra-uterine growth, low birth weight, prematurity, stillbirth and intrauterine death.[4,5] Predicting the onset of these complications could aid in timely interventions such as increased surveillance, treatment of symptoms, transfer to higher care facility and delivery when necessary, which could reduce morbidity and mortality from the HDPs.[6]

The most common immediate maternal complications are eclampsia, oligohydramnios, accidental hemorrhages, disseminated intravascular coagulation, and hemolysis, elevated liver enzymes and low platelets (HELLP) syndrome. Remote complications include residual hypertension, recurrent preeclampsia, and chronic renal failure[7]. Many hematological changes are seen in association with HDP, thrombocytopenia being the most common[8,9]. Changes are also seen in peripheral smear, coagulation profile, and liver enzymes. In such cases, definitive therapy can be initiated to prevent maternal and neonatal morbidity and mortality. From the standpoint of prevention, preeclampsia has remained a challenge for obstetricians. Various strategies have been proposed to reduce the perinatal effects of preeclampsia. This can be achieved by early diagnosis of preeclampsia simply via assessment of blood coagulation profile[10,11] , complete blood count, urine examination, and liver function tests performed to identify platelet abnormalities, red cell abnormality, and to detect progression to HELLP syndrome.

Thus, the present study is an attempt to analyse maternal and perinatal outcome in severe preeclampsia with altered biochemical and hematological parameters and to find the usefulness of these tests as predictors of maternal outcome. It will aid clinicians in early detection, monitoring, and management of cases with HDPs, especially severe preeclampsia.

DEFINATION

Blood pressure

- Systolic blood pressure of 140 mmHg or more or diastolic blood pressure of 90 mmHg or more on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure.
- Systolic blood pressure of 160 mmHg or more or diastolic blood pressure of 110 mmHg or more (Severe hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy).

Proteinuria

- 300 mg or more per 24 hour urine collection (or this amount extrapolated from a timed collection) or
- Protein/creatinine ratio of 0.3mg/dl or more or

- Dipstick reading of 2+(used only if other quantitative methods not available)

Or in the absence of proteinuria, new-onset hypertension with the new onset of any of the following:

- Thrombocytopenia: Platelet count less than 1 lakh/cumm
- Renal insufficiency: Serum creatinine concentrations greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease
- Impaired liver function: Elevated blood concentrations of liver transaminases to twice normal concentration
- Pulmonary edema
- New-onset headache unresponsive to medication and not accounted for by alternative diagnoses or visual symptoms

SEVERE FEATURES-

- Systolic blood pressure of 160 mmHg or more, or diastolic blood pressure of 110 mmHg or more on two occasions at least 4 hours apart (unless antihypertensive therapy is initiated before this time)
- Thrombocytopenia (platelet count less than 100,000 X 109/L)
- Impaired liver function as indicated by abnormally elevated blood concentrations of liver enzymes (to twice the upper limit normal concentration), and severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses
- Renal insufficiency (serum creatinine concentration more than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease)
- Pulmonary edema
- New-onset headache unresponsive to medication and not accounted for by alternative diagnoses
- Visual disturbances

METHODS

Purposive sampling of 200 severe preeclamptic women >32 weeks gestation was done attending the antenatal OPD of Sola Civil Hospital, Ahmedabad fulfilling the inclusion and exclusion criteria.

Inclusion criteria:

Pregnant women who had Blood pressure ≥ 160/110 mmHg after 32 week of gestation with proteinuria.

Exclusion criteria:

o BP <160/110 mmHg
o W eeks of gestation <32 weeks.
o Chronic hypertension
o Women with other co-morbid conditions- Diabetes, chronic hypertension etc. o IUD
o Women who declined consent.

On admission, detailed history regarding age, parity, period of gestation, signs and symptoms, obstetric and family history was recorded from the patient or patient's attendant, as appropriate. After that, general physical, abdominal and pelvic examination was carried out. Investigations like complete hemogram, absolute platelet count, liver function tests, renal function tests, coagulation profile, fundoscopy and 24 hours urine for protein were performed in all the patients.

Blood pressure of study subjects was measured by using mercury sphygmomanometer with appropriate cuff size tied at heart level. The women were evaluated clinically as well as by investigative work up. Proteinuria was estimated daily by dipstick method. Complete blood count with platelets and serum analysis of uric acid, creatinine, and renal and liver function tests was done by using automated analyser. A peripheral smear was done for screening for HELLP syndrome

After the initial workup, the study population was divided into two groups:

GROUP-I (CASE): Severe preeclampsia with altered biochemical and hematological parameters.

Criteria for putting the severe preeclamptic patients in case group (minimum one criteria should be fulfilled)-

1. Platelet count <1.5 lakh/cumm
2. S. Bilirubin >1.2 mg/dl
3. S. LDH >600 IU/L
4. S. Uric acid >6 mg/dl

5. S. Creatinine > 1.1 mg/dl

GROUP-II (CONTROL): Severe preeclampsia with normal biochemical and hematological parameters.
Women were put on antihypertensive drugs and dose was adjusted or treatment with additional drugs was done as per individual requirement. Two doses of intramuscular betamethasone 12 mg, 24 hours apart was given for preterm salvageable pregnancies. Repeat investigations were done after 72 hours, according to the hospital protocol.
If the blood pressure was controlled on the antihypertensive regime and the laboratory parameters did not deteriorate after 72 hours, the patients were kept on expectant management under which they were regularly followed up biweekly for assessing the maternal condition, repeat investigations, and fetal wellbeing via MBBP and USG Doppler until 38 weeks after which the labour was induced if she did not go into spontaneous labour. Stripping of membranes was done according to the hospital protocol. Women on expectant management were asked to report if they have headache or epigastric pain or vomiting or visual disturbances.
Pregnancy was terminated for uncontrolled hypertension in spite of being on maximum dose of antihypertensive, persisting/progressively deteriorating clinical symptoms or the biochemical/hematological markers, occurrence of complications such as placental abruption, eclampsia, renal failure and indication of non-reassuring fetal status. The decision regarding the delivery was based on estimated fetal weight, salvage ability, gestational age, amniotic fluid index, fetal status and Bishop's score. The neonates were managed by pediatric team at neonatal intensive care unit if needed. All the subjects were monitored, and the investigative parameters were compared with various maternal and fetal outcome.

RESULTS:

Table 1: demographic distribution among patients between two groups

	Group–I (CASE) (n=100)	**Group–II(CONTROL) (n=100))**	**P Value**	**Result**
Age distribution (in years)				
≤20year	10	4	0.1854	NS
21–25year	60	55		
26–30year	27	3		
31–40year	3	6		
Gravida				
Primigravida	68	65	0.399	NS
multigravida	32	35		
POG (Period of gestation) on admission (weeks)				
<34	28	20	0.1187	NS
34-36	52	48		
>36	20	32		
POG (Period of gestation) (weeks) of delivery				
<34	8	2	0.0028	Significant
34-36	36	20		
>36	56	78		

Most of the patients belonged to the age group of 21-25 years (60 in Group-I and 55 in Group-II), followed by 26-30 year age group (27 in Group-I and 35 in Group-II). Comparing the cases in the present study with other

studies, we found that the mean age in Maged et al[12] and Nagar et al's[13] study were 26.1+5.1 years and 25.9+4.3 years respectively, which is similar to our study (25+3.09 years).
Maximum patients were primigravida, in both case group and control group. This goes in accordance to the notion that preeclampsia is a disease of first pregnancy. In the study of Maged et al[12], they observed that 60% patients were primigravida as compared to 40% multigravida. Nagar et al[13] reported 57% primigravida and 43% multigravida. This is consistent with our study (68% primigravida, 32% multigravida)
Majority of the patients belonged to 34-36 weeks (52 in Group-I and 48 in Group-II). shows the distribution of period of gestation at the time of delivery. Our mean gestational age at delivery was 36.4+1.52 wks, which is consistent with Maged et al's[12] study (35.5+1 wks).
Most of the patients were delivered at term in both of groups. This was because of the regular follow up of the patients with control of blood pressure, and repeat investigations done biweekly that we were able to do expectant management till term. Foetal surveillance was done in each visit.

Table 4: Comparison of mean blood pressure between the two groups

MEAN + S.D.	Group 1 (CASE) (n=100)	Group –II (CONTROL) (n=100)	P Value	Results
Systolic BP	182+11.9	174.7 +12.46	<0.0001	Significant
Diastolic BP	123.5+7.43	119.42 +6.39	<0.0001	Significant

The blood pressure was higher in preeclamptic patients with altered hematological and biochemical parameters, and the result being statistically significant. (<0.05)
Maged et al[12] and Nagar et al[13] observed in their study that the mean SBP in cases was 175+14 mmHg and 148±3.8 mmHg respectively and the mean DBP was 116+14 mmHg and 95±1.4 mmHg respectively.

Table 2: Comparison of mean values of biochemical and haematological parameters between two groups.

Mean + S.D.	Group–I (CASE) (n=100)	Group –II (CONTROL) (n=100)	P value	Results
LDH (U/L)	559.76 + 128.2	446 + 72.86	<0.0001	Significant
S.Bilirubin (mg/dl)	0.8+0.28	0.55+0.14	<0.0001	Significant
S.Uric acid (mg/dl)	6.524+1.44	4.87 + 0.66	<0.0001	Significant
S.Creatinine (mg/dl)	0.997+0.28	0.85+0.1	<0.0001	Significant
Hemoglobin (g/dl)	10.71+1.45	10.67+1.46	0.3312	NS
Platelet count (lakh/cumm)	1.38+0.34	1.99+0.28	<0.0001	Significant

The statistical difference was significant (p<0.05) for the mean values of uric acid, LDH, serum bilirubin, creatinine and platelet count.
The most common altered parameter was platelet count (66%), followed by serum uric acid (54%), serum LDH (18%), serum creatinine (14%) and lastly, serum bilirubin (10%).
Manged et al[12] reported the mean values of S. bilirubin(0.53±0.27),S. uric acid(6.0±1.17),S. Creat(0.97±0.35),Hb(13.0±1.90) and platelet count(1.13±0.36).

Table 3: Comparison of mode of delivery between two groups.

Mode of delivery	Group–I (CASE) (N=100)	Group –II(CONTROL) (N=100)	P Value	Results
Vaginal delivery (VD)	78	85	0.2024	NS
Caesarean section (LSCS)	22	15		

In Case Group, 22 patients had LSCS and 78 patients had VD respectively. In Control Group, 15 patients had LSCS and 85 patients had VD respectively, the result being statistically non-significant (p>0.05). We followed our departmental protocol where trial of labour was given to every patient, provided the maternal and fetal conditions remained stable.

Singhal et al[14] reported 65% vaginal delivery and 32.6% Caesarean section ,they had 2% hysterotomy rate.

Table 4: Indication of caesarean section between two groups.

Indication of caesarean section	Group 1 (CASE) (n=22) (%)	Group 2 (CONTROL) (n=15) (%)	P value	Result
Failure of induction	7 (31.8%)	6 (40%)	0.45	NS
Fetal distress/ Doppler changes	6 (27.2%)	3 (20%)		
NPOL	4 (18.1%)	5 (33.3%)		
Deteriorating maternal condition (no trial given)	5 (22.7%)	1 (6.6%)		

in cases, the caesarean rates were marginally increased because of deteriorating maternal (where trial of labour could not be given) and fetal condition (more IUGR in cases than controls). Other causes like NPOL or induction failure were nearly in the same numbers in both the groups.

Table 5: Comparison of type of maternal complications between two groups.

Maternal Complications	Group–I (CASE) (N=100) (%)	Group –II (CONTROL) (N=100) (%)	P value	Result
Abruption	10	3	0.044	Significant
Eclampsia	6	2	0.14	NS
Renal dysfunction/failure	7	1	0.03	Significant
DIC	5	1	0.09	NS
HELLP	8	0	0.0039	Significant
Pulmonary edema	4	1	0.174	NS
PPH	4	1	0.174	NS
Maternal mortality	3	0	0.081	NS
Nil	67	92	<0.0001	Significant

In the Case Group, 10 patients had Abruption, 6 patients had Eclampsia, 6 patients had ARF, 5 patients had DIC, 8 patients had HELLP, 4 patients had pulmonary oedema, 4 patients had PPH and mortality was seen in 3 patients

In control Group, the incidence of maternal complications were seen in a lesser number,their clinical manifestations were less severe when compared to those with altered parameters.

Amongst all the complications, abruption, renal dysfunction/ARF and HELLP were found statistically significant (p<0.05) while the others were not statistically significant (p>0.05).

Dr Rajni Priyanka et al[15] reported 7.85% abruption, 10.71% ARF, 3.57% HELLP, 2.85% pulmonary edema and 13.57% DIC in their study.

Maged et al[12] observed 13.30% eclampsia and 8.90% HELLP.

Table 6: Comparison of type of perinatal complications between two groups.

Perinatal complications	GROUP 1 (CASE) (N=100)	GROUP 2 (CONTROL) (N=100)	P value	Result
Prematurity	44	22	0.0009	Significant
SGA/IUGR	24	11	0.0156	Significant
NICU admission	20	10	0.0477	Significant
Stillbirth	0	0	-	-
BIRTH WEIGHT (kgs)				
<2	15	4	*0.0012*	*Significant*
2-2.5	38	23		
2.5-3	34	55		
>3	13	18		
APGAR score		)		
<7	16	10	0.207	NS
>7	84	90		

The most common neonatal outcome was prematurity (44% in Group-I and 22% in Group-II). The high incidence of preterm delivery was attributed to the early intervention.

Maged et al[12] showed in their study that low birth weight was seen in 68.8% with 71.40% neonates being preterm. NICU admissions, neonatal deaths and stillbirths was more in babies of severe preeclamptic mothers which is consistent with present study.

In Case Group, 24 neonates had SGA/IUGR. There were 20 NICU admissions, 2 neonatal deaths. In Control Group, 11 (11%) neonates had SGA/IUGR. There were 10 NICU admissions and 1 neonatal death. Total 3 deaths were observed (2 in cases and 1 in control).

More neonates in Group-I had APGAR scores <7. Conditions leading to this were prematurity leading to respiratory distress syndrome, fetal distress, birth ashypxia or hypoxia.

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