Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 01, 2023

A Descriptive Study of Biochemical Changes as A Predictor of Severity of Preeclampsia And Associated Maternal And Fetal Outcome at Teritiary Care Centre

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Received: 05 December 2022 **Revised:** 18 January 2023 **Accepted:** 31 January 2023

ABSTRACT

Background: Approximately 1 in 2000 deliveries are complicated by eclampsia in developed countries; whereas the incidence in developing countries is estimated around 1 in 100 to 1 in 1700 cases. **Objective:** to find out the various risk factors of preeclampsia, clinical profile,to estimate level of biochemical markers in women with preeclampsia, to use this biochemical parameters as a marker for early detection of severity of preeclampsia.

Material and Methods: A Prospective cross-sectional study was conducted among all patients admitted in Department of Obstetrics and Gynecology of a tertiary care centre during January 2021 to June 2022.

Results: Majority of study participants were obese (BMI ≥25). PPH were the most common maternal complication. Of all maternal complications addressed, most of the maternal complications occurred in severe preeclampsia with deranged biochemical parameters. Premature births were seen in most of cases.Of all perinatal complications most of the complications were present in severe preeclampsia with deranged biochemical parameters.

Conclusion: Biochemical markers were significantly different between mild and severe groups of preeclampsia, and these biochemical markers can be utilized to predict and assess the severity of preeclampsia.

Keywords: Biochemical markers, Severity of Preeclampsia, Maternal andFetal Outcome.

INTRODUCTION

Globally each year, 5-7% of pregnancies are preeclampsia affected resulting approximately 70,000 maternal and 500,000 fetal deaths.[1] Preeclampsia adversely affects the mother and fetus causing some severe complications including fetal growth restriction (FGR), preterm delivery and perinatal death whereas, maternal complications are linked to hypertension, acute kidney damage, stroke, cardiomyopathy, liver failure, pulmonary edema and death.

There are various risk factors for preeclampsia such as previous history of preeclampsia, nulliparity, obesity, chronic hypertension, older age and diabetes mellitus.[2] Preeclampsia is specified by increased arterial blood pressure and proteinuria, whereas, eclampsia is characterized by convulsion, coma or both in preeclamptic patients.

Various changes in biochemical and haematological parameters are observed in preeclampsia as compare to the normal pregnancy.[3] Thus laboratory evaluation of pregnant women with hypertension is considered important to diagnosis and predict the occurrence of preeclampsia and its future consequences. The previous studies suggest that currently no individual marker is satisfactory for the prediction of preeclampsia occurrence and number of markers have been studied in search of the gold standard test that predict the severity of preeclampsia.[4]

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Eclampsia is defined as the development of convulsions and/or coma unrelated to other cerebral conditions during pregnancy or in the post-partum period in patients with signs and symptoms of pre-eclampsia after 20 weeks of gestation.[5]Eclampsia is an acute and life-threatening complication of pregnancy characterized by the appearance of tonic clonic seizures (convulsions), and or coma during pregnancy or labor or within 10 days of delivery, not due to epilepsy or other convulsion disorders associated with preeclampsia.[6]

In recent years, the new term "atypical preeclampsia-eclampsia" has been used to describe non-classical forms of hypertensive disorders arising during pregnancy.[7] Although there is no strict definition of atypical preeclampsia-eclampsia, it has come to include cases with minimal or no proteinuria, but with hypertension, or proteinuria with no or marginally elevated blood pressure (BP), or without hypertension or proteinuria.

Eclampsia includes convulsions and coma that happen during pregnancy but are not due to pre-existing organic brain disease.[7] Approximately 1 in 2000 deliveries is complicated by eclampsia in developed countries, whereas the incidence in developing countries varies from 1 in 100 to 1 in 1700 cases.[8] Although the incidence and mortality from eclampsia has fallen dramatically over the past decades due to better antenatal care, the associated maternal and fetal morbidity and mortality is still significant.[9]

Hypertensive disorders of pregnancy cause 14% of all maternal deaths globally, approximately 42,000 each year.[10] Nearly all of these deaths occur in low-resource settings (99%), with death in high-income settings being very rare.[11] Hypertensive disorders of pregnancy encompass chronic hypertension, gestational hypertension (newhypertension without proteinuria), pre-eclampsia (new hypertension with proteinuria or end-organ damage after 20 weeks of gestation and eclampsia.[11]

The majority of morbidity and mortality is associated with pre-eclampsia and eclampsia. It is estimated that the prevalence of preeclampsia globally is 4.6% (95% CI 2.7%–8.2%). [12] The prevalence of eclampsia globally is reported to be 0.3%.[13]

Very few studies conducted in Maharashtra regarding study of biochemical changes as a predictor of severity of preeclampsia and associated maternal and fetal outcome at tertiary care hospital. So I am interested to find out the various risk factors of preeclampsia, clinical profile, To estimate level of biochemical markers in women with preeclampsia, to use this biochemical parameters as a marker for early detection of severity of preeclampsia and to assess the maternal and fetal outcome.

MATERIAL &METHODS

A Prospective cross-sectional study was conducted among 100 cases of preeclampsia admitted in Department of Obstetrics and Gynecology of a tertiary care centre during January 2021 to June 2022. Based on the inclusion and exclusion criteria, the subjects were selected.

Inclusion Criteria

1. Pregnant women with a singleton pregnancy.
2. Gestational age -all in the second and third trimester, the gestational period ranging from 20 weeks and above, calculated from the first day of the last menstrual period.
3. All diagnosed to have preeclampsia based on the development of hypertension (BP greater than 140/90mmHg) in the pregnancy for the first time , proteinuria with or without oedema.

Exclusion Criteria

1. Pregnancy with renal diseases
2. Gestational trophoblastic disease
3. Pregnancy with chronic hypertension
4. Pregnancy with heart disease
5. Pregnancy with diabetes or GDM

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6. Patients those who are not willing to participate in this study.

Approval for the Study

Written approval from Institutional Ethics committee was obtained beforehand. Written approval of OBGY and other related department was obtained. After obtaining informed verbal consent from all patients with the definitive diagnosis preeclampsia cases admitted to OBGY ward of tertiary care centre such cases were included in the study.

Sample Size: With reference to study by **Swain S et al (1993)** [14] He found that the 84% of preeclampsia cases developed eclampsia after delivery.

Formula for sample size = 4* P* Q / L2

Where P = 84%

Q = 100-84 = 16

L = Allowable error = 10% (Absolute error)

Sample size = 4 * 84*16/ 70.56 =76.19

Sample size Rounded to = 100

Sampling Technique

Convenient sampling technique used for data collection.

Methods of Data Collection and Questionnaire

Predesigned and pretested questionnaire was used to record the necessary information. Questionnaires included general information, such as age, sex, Medical history- chief complain, past history, general examination, systemic examination.

Menstrual history: LMP, EDD, Obstetrics history-marriage duration, parity,Mode of delivery, maternal complications, Type of eclampsia- antepartum, intrapartum, postpartum, No ANC visits, Gestational age at the time of admission, Mode of delivery, Maternal Outcome, ALT,ALP, total proteins, albumin and globulin levels, Maternal complications. All the procedures and investigations conducted under direct guidance and supervision of PG guide. Proforma of preeclampsia notes maintained.

Data Entry and Analysis

The data were entered in Microsoft Excel and data analysis was done by using SPSS demo version no 21 for windows. The analysis was performed by using percentages in frequency tables and correlation of preeclampsia. $P<0.05$ was considered as level of significance using the Chi-square test.

RESULTS

Majority of study participants were from 26-30 years age group e.g. 30 followed by 21-25,18-20,31-35 and > 35 years age group,29,18,16 and 7 cases respectively.

Majority of subjects were educated above 10th std contributing 76 (76%) followed by 16 (16%) upto secondary level (6th-10th) std and 8 cases (8%) upto primary (1^{st} - 5^{th}) std. respective

Majority of subjects were home makers contributing 57 (57%) followed by Labourer 13 (13%), Farmer 9 (9%), Employed 8(8%), Shop keeper 8(8%) and Sales woman 5(5%) respectively.

Most of study subjects are from lower socioeconomic class (III,IV,V) contributing 80 (80%) followed by 20 (20%) in upper classes (I,II).

Most of the study subjects were primiparous contributing 72 (72%) and 28 (28%) were multipara.

Majority of study participants were from 28-36 weeks of gestational age contributing 50 (50%) followed by ≥37 weeks 45 (45%) and <28 weeks 05(5%) respectively.

Most of study participants received inadequate ANC care as 70 (70%) cases with <4 visits whereas, 30 cases with ≥4 visits.

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Majority of study participants were obese (BMI ≥25) contributing 60 (60%) followed by 40 (40%) with BMI <25.

Table 1: Distribution of study subjects as per BMI (kg/m^2)

BMI (kg/m^2)*	Frequency	Percentage
≥25	**60**	**60**
<25	**40**	**40**
Total	**100**	**100**

*****BMI (Body Mass Index) <25: Underweight and normal, BMI (Body Mass Index) ≥25: Obese

Proteinuria was present in 34% cases(1+ in 15% ,2+ in 10% ,3+ in 9%)Elevated liver enzymes (AST) was present in 18 % ,ALT in 8%cases,total bilirubin in 5% cases .KFT of 6% showed raised serum creatinine >100 µmol/L ,serum uric acid is raised in 6%and thrombocytopenia was seen in 16% of cases. LDH is increased in 11% cases.

Table 2: Distribution of study subjects as per laboratory investigations

Lab Investigation	Sub group	Frequency	Percentage
Urine protein	Nil	66	66
	1+	15	15
	2+	10	10
	3+	9	9
Total bilirubin	<0.8	95	95
	>0.8	5	5
AST(IU/L)	<70	82	82
	≥70	18	18
ALT(IU/L)	<70	92	92
	>70	8	8
LDH(IU/L)	<600	89	89
	600-800	6	6
	>800	5	5
Ser.Creatinine (µmol/L)	≤100	94	94
	>100	6	6
Ser.Uric acid(mg/dl	<10	94	94
	>10	6	6
Hb	>10	92	92
	<10	8	8
Platelets(10^3/mm^3)	≥100	84	84
	50-99	10	10
	<50	6	6

Out of 100 participants selected 34(34%) are having derranged laboratory investigations (as mentioned in table no.9)and 66(66%) are having normal lab investigations.

Table 3: Distribution of study participants based as per lab parameters (n=100)

Laboratory investigations (in table no 9)	Frequency	Percentage
Labs normal	66	66

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Labs abnormal	34	34
Total	100	100

Out of 100 preeclampsia patients 55% were with mild preeclampsia and 45 % were with severe preeclampsia

It was observed that out of 100 preeclampsia cases 45 (45%) were severe of which 30(30%) were having deranged laboratory investigations and rest 15(15%) were having normal laboratory investigations.

Also out of 55 mild preeclampsia cases 4 (4%) were having abnormal laboratory investigations and rest 51 % were having normal laboratory investigations.

Table 4: Distribution of preeclampsia based on severity as per blood pressure(n=100)

Severity of preeclmpsia	Frequency	Percentage
Mild (>140/90 mmhg<160/110 mmhg	55	55%
Severe (>160/110mmhg)	45	45%
Total	100	100%

Majority of subjects delivered through LSCS 59, followed by NVD 26 and AD 15 cases.

Out of 59 lscs 38 were with severe preeclampsia and rest 21 were mild preeclampsia.

Out of 26 NVD only 7(7%) severe preeclampsia patients delivered vaginally and 19(19%) mild preeclampsia delivered vaginally

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Out of 26 NVD only 7(7%) severe preeclampsia patients delivered vaginally and 19(19%) mild preeclampsia delivered vaginally

Postpartum hemorrhage most common complication in preeclampsia cases contributing 16 cases (16%) each followed by DIC (4%),HELLP syndrome (4%), CVA , trauma like tongue bite ,Pulmonary edema ,ARF in 2% cases each respectively and hypertensive crisis 1%.

Out of the 33 maternal complicated cases, it was observed that,25 cases were severe preeclampsia with deranged biochemical parameters ,5 cases were severe preeclampsia with normal biochemical parameters and rest 3 cases belongs to mild preeclampsia

Table 5: Maternal complications in preeclampsia cases

Complication	Frequency	Percentage
PPH	16	16
DIC	04	04
HEELP Syndrome	04	04
CVA	02	02
Trauma	02	02
Pulmonary oedema	02	02
ARF	02	02
Hypertensive Crisis	01	01

Prematurity were seen in 45%cases followed by full term live births without any neonatal complications 35%, RDS 15%, early neonatal death 3% and still birth in 2 cases respectively.

Out of 100 preeclampsia cases selected, 55% were mild preeclampsia and 45% severe preeclampsia (table no.). Of 55 mild preeclampsia cases, 15 had prematurity, 6 had RDS, 1early neonatal death was observed. Of 45%severe preeclampsia cases, 30 had prematurity, 9 had RDS, 2 early neonatal death and 2 still birth

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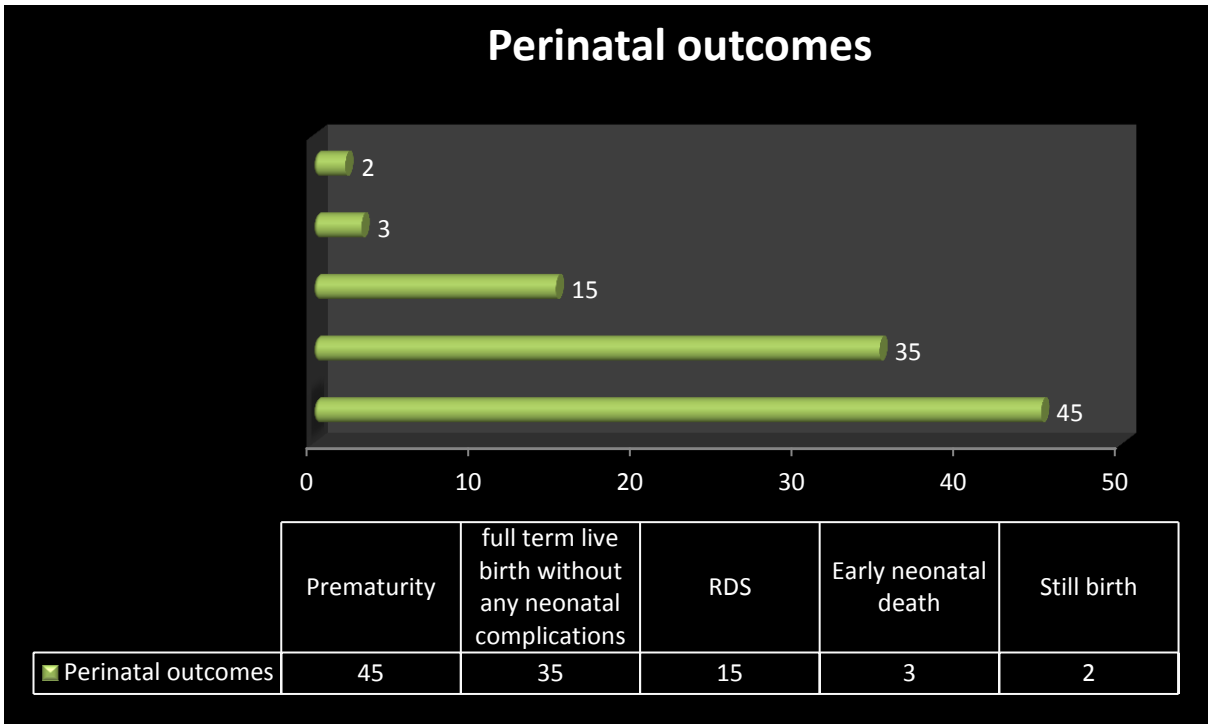

Figure 1: Perinatal outcomes in preeclampsia cases

RDS: Respiratory distress syndrome.

DISCUSSION

In present study, majority of study participants were from 26-30 years age group e.g. 30 followed by 21-25, 18-20,31-35 and > 35 years age group,29,18,16 and 7 cases respectively**.** Similar result found in the study conducted by **Rebahi H et al (2018)**[15]A study by **Sarma HK et al**[16] found that, most (60 %) of the patients were between 20 – 25 years.

Most of the subjects were educated above 10thstd contributing 76 (76%) followed by 16 (16%) upto secondary level (6th-10th) std and 8 cases (8%) upto primary (1st - 5th) std. respectively. Similar result observed by **Sarma HK et al**[16] found that, majority of women with eclampsia were having low literacy status.

Most of study subjects are from lower socioeconomic class (III,IV,V) contributing 80 (80%) followed by 20 (20%) in upper classes (I,II).Similar result found in the study conducted by **Sarma HK et al(2014)**[16] found that, majority of the patients (41.67%) were from upper lower class and lower class (55 %). Poverty, illiteracy are some important factors which prevent woman in from seeking antenatal advice during pregnancy.

Most of the study subjects were primiparous contributing 72 (72%) and 28 (28%) were multipara. A study by **Sarma HK et al(2014)**[16] found that, most of the preeclamptic patients were primigravida (85%).Findings of present study are comparable with studies by **Shiraz's et al**[17], **Dutta et al**[18].

In current study Majority of study participants were from 28-36 weeks of gestational age contributing 50 (50%) followed by ≥37 weeks 45 (45%) and <28 weeks 05(5%) respectively. A study by **Kaur P (2012)**[19] revealed that, Maximum number of patients presented in third trimester of pregnancy (96%) except 4% who had gestation < 28 weeks.

Most of study participants received inadequate ANC care as 70 (70%) cases with <4 visits whereas, 30 cases with ≥4 visits. Also it was revealed that, proportion of antepartum eclampsia was significantly higher (85.71%) in women who had <4 visits as compared to

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 01, 2023

those with **≥4 visits** during Antenatal period.(50%). Similar study by**Rebahi H et al (2018)**[15]observed that**,** inadequate prenatal care was associated with eclampsia ($\chi 2$=11.62, p=0.001)

In current study Majority of study participants were obese (BMI ≥25) contributing 60 (60%) followed by 40 (40%) with BMI <25. Proportion of antepartum eclampsia in present study was significantly higher (83.33%) in obese women with BMI **≥25 Kg/m2.** A similar study by**Ganesh KS et al (2010)**[20]revealed that, prepregnancy BMI of ≥25 is significant risk factor for preeclampsia. Findings of present study are comparable with various other studies.[21,22]

Proteinuria was present in 34% cases(1+ in 15% ,2+ in 10% ,3+ in 9%)Elevated liver enzymes (AST) was present in 18 % ,ALT in 8%cases,total bilirubin in 5% cases .KFT of 6% showed raised serum creatinine >100 μmol/L ,serum uric acid is raised in 6%and thrombocytopenia was seen in 16% of cases. LDH is increased in 11% cases.

Out of 100 participants selected 34(34%) are having derranged laboratory investigations and 66(66%) are having normal lab investigations.

In current study out of the study participants (100) 55 % belongs to mild preeclampsia and 45 % belongs to severe preeclampsia(based on blood pressure).

It was observed that out of 100 preeclampsia cases 45 (45%) were severe of which 30(30%) were having deranged laboratory investigations and rest 15(15%) were having normal laboratory investigations.

Also out of 55 mild preeclampsia cases 4 (4%) were having abnormal laboratory investigations and rest 51 % were having normal laboratory investigations.

Our findings are in accord with the study conducted by **Martin et al**[23] that found the importance of selected parameters in assessing the risks of patients for significant maternal morbidity. The researchers found that the serum lactate dehydrogenase, aspartate aminotransferase (AST), ALT, uric acid, creatinine and 4+ urinary protein were able to distinguish the preeclamptic patients with greater severity.

In another study by **Mei-Dan et al**[24], higher ALT and AST levels in initial trimesters were associated with increase disease severity during later stages of pregnancy; evidencing the importance of liver enzymes in predicting the severity of preeclampsia and its application in prevention of significant morbidity and mortality.

It was observed that serum ALT levels were significantly raised in severe preeclampsia as compare to the mild group.[25] In previous studies it has been observed that the serum total protein and albumin were significantly lowered whereas hyperbilirubinemia though not common but may rise in severe forms of preeclampsia.[26]

In accordance to the previous studies our study findings illustrated the significant rise in ALP levels in severe preeclampsia than mild preeclampsia.[66-68] However, in contrast to the study by **Hazari et al**[26] that found higher levels of GGT in severe preeclampsia than mild group, no differences were observed between both groups in this study.

In the study by **Al Ghazali et al**[27] highest levels of serum albumin were found in normal pregnant women (4.076±1.448 gm/dl) as compare to the gestational hypertension (3.500±0.386 gm/dl), mild preeclampsia (3.155±0.293 gm/dl) and severe preeclampsia (2.618±0.328 gm/dl) groups (p-value<0.001), demonstrating the positive correlation between preeclampsia severity and serumalbumin..

Postpartum hemorrhage most common complication in preeclampsia cases contributing 16 cases (16%) each followed by DIC (4%),HELLP syndrome (4%), CVA , trauma like tongue bite , Pulmonary edema ,ARF in 2% cases each respectively and hypertensive crisis 1%.

Out of the 33 maternal complicated cases,it was observed that,25 cases were severe preeclampsia with deranged biochemical parameters ,5 cases were severe preeclampsia with

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 01, 2023

normal biochemical parameters and rest 3 cases belongs to mild preeclampsia,similar result reported by **Ganesh KS et al (2010)**[20]

Of 45%severe preeclampsia cases,30 had prematurity,9 had RDS,2 early neonatal death and 2 still birth. Eclampsia not only kills mother but also kills fetus. A study by **Akhtar R et al (2011)**[28]showed that, among neonatal outcome 18 % baby were still born and 9 % were early neonatal death.

CONCLUSION

The current study findings suggest that biochemical markers were significantly different between mild and severe groups of preeclampsia, and these biochemical markers can be utilized to predict and assess the severity of preeclampsia.

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