

# Biochemical Markers for Detecting Severity of Preeclampsia

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## ABSTRACT

**Background:** Preeclampsia is the hypertensive pregnancy with hallmark of proteinuria. Assessment of various biochemical markers is important to differentiate and predict the severity of preeclampsia.

**Methodology:** This was a comparative cross sectional study that recruited 125 pregnant women diagnosed with preeclampsia. There were 30 patients with mild and 95 with severe preeclampsia. The serum total bilirubin, alanine transaminase (ALT), gamma glutamyl transferase (GGT), alkaline phosphatase (ALP), total proteins and albumin levels were measured.

**Results:** There were significant differences in gestational age, ALT, ALP, total proteins, albumin and globulin levels between mild and severe preeclampsia ( $P < 0.05$ ). However, significant association was not observed for age, serum total bilirubin and GGT between two groups.

**Conclusion:** The serum ALT, ALP, total proteins and albumin may provide sensitive measurement for the prediction of severity of preeclampsia.

**Key words:** Mild, Preeclampsia, Pregnant women, Severe

## INTRODUCTION

Globally each year, 5-7% of pregnancies are preeclampsia affected resulting approximately 70,000 maternal and 500,000 fetal deaths.<sup>1</sup> 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.<sup>2,3</sup>

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.<sup>4</sup> 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.<sup>5</sup> The present study investigated the utility of serum total bilirubin, alanine transaminase (ALT), gamma glutamyl transferase (GGT), alkaline phosphatase (ALP), total proteins and albumin levels as the biochemical markers for detecting the severity of preeclampsia.

## MATERIALS AND METHODS

It was a comparative cross sectional study conducted at the Liaquat University of Medical and Health Sciences, Jamshoro between years 2015 to 2017, after Ethical Committee Review approval. Total  $n=125$  pregnant women diagnosed with preeclampsia were recruited and further grouped into, mild ( $n=30$ ) and severe ( $n=95$ ) preeclampsia. Mild preeclampsia was defined as blood pressure  $\geq 140/90$  mmHg and proteinuria ( $\geq 0.3g/24h$ , or  $\geq 1+$  by dipstick); after 20th weeks gestation without previous history of

hypertension. Severe preeclampsia included pre-eclamptic patients with one of the features of blood pressure  $\geq$  than 160/110 mmHg, proteinuria  $\geq 5g/24h$  urine specimen (or  $\geq 3+$  by dipstick), oliguria, cerebral/visual symptoms, pulmonary edema, cyanosis, epigastric/right upper quadrant pain, hemolysis, eclampsia, elevated liver enzymes and low platelets (HELLP) syndrome and FGR.<sup>6</sup> Blood samples from patients were collected at the admission before getting medications. Patients with history of chronic or systemic and endocrine disorders were excluded. The serum total bilirubin, ALT, GGT, ALP, total proteins and albumin levels were measured on Roche Modular system auto analyzer. The data was analyzed on SPSS-20. The means were compared by independent sample t-test and  $P < 0.05$  was considered as significant.

## RESULTS

Thirty women had mild preeclampsia whereas 95 had severe preeclampsia. The mean age and gestational age of the pregnant women with mild preeclampsia were  $26.73 \pm 4.97$  years and  $38 \pm 3.26$  weeks, respectively and with severe preeclampsia were  $26.38 \pm 4.91$  years and  $36 \pm 4.52$  weeks, respectively. No significant association was observed for age, serum total bilirubin and GGT between mild and severe preeclampsia groups. However significant differences were noted for gestational age, ALT, ALP, total proteins, albumin and globulin levels between both groups ( $P < 0.05$ ) (Table I).

Table I: Variables among mild and severe preeclamptic women

Variable	Severity of Preeclampsia	Mean $\pm$ SD	P-Value
Age (years)	Mild	26.73 $\pm$ 4.97	0.73
	Severe	26.38 $\pm$ 4.91	
Systolic blood pressure (mmHg)	Mild	141.66 $\pm$ 6.48	<0.001
	Severe	162.79 $\pm$ 18.5	
Diastolic blood pressure (mmHg)	Mild	97.33 $\pm$ 8.68	<0.001
	Severe	110 $\pm$ 15.91	
Gestational age (weeks $\pm$ days)	Mild	38 $\pm$ 3.26	0.03
	Severe	36 $\pm$ 4.52	
Total bilirubin (mg/dL)	Mild	0.53 $\pm$ 0.34	1.31
	Severe	0.66 $\pm$ 0.42	
Alanine transaminase(IU/L)	Mild	22.87 $\pm$ 7.05	<0.001
	Severe	41.19 $\pm$ 39.61	

Gamma glutamyl transferase (IU/L)	Mild	14.93±9.67	0.53
	Severe	13.65±9.67	
Alkaline phosphatase (IU/L)	Mild	346.8±126.28	<0.001
	Severe	491.91±289.82	
Total proteins (grams)	Mild	7.1±1.32	0.001
	Severe	6.18±1.24	
Albumin (grams)	Mild	3.61±0.56	0.001
	Severe	3.21±0.56	
Globulin (grams)	Mild	3.5±0.94	0.010
	Severe	2.97±0.93	

## DISCUSSION

The current study findings suggest that serum ALT, ALP, total proteins and albumin levels 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. Our findings are in accord with the study conducted by Martin et al<sup>7</sup> 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<sup>8</sup>, 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. In various studies, liver function tests were found sensitive in predicting the unfavorable fetomaternal outcomes. It was observed that serum ALT levels were significantly raised in severe preeclampsia as compare to the mild group.<sup>9,10</sup>

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.<sup>11</sup> These findings are consistent with our study, as we also found decreased levels of total protein and albumin in severe preeclampsia, however in our study no difference was noted in serum total bilirubin between both groups, showing lower sensitivity of total bilirubin levels in predicting severity of preeclampsia. In the similar study, serum AST and ALT were found increased in severe preeclampsia as compare to mild and normal pregnant women. In accordance to the previous studies our study findings illustrated the significant rise in ALP levels in severe preeclampsia than mild preeclampsia.<sup>11-13</sup> However, in contrast to the study by Hazari et al<sup>11</sup> 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<sup>14</sup> 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. Further Gojnic et al<sup>15</sup> proposed the hypoalbuminemia as an early sign of preeclampsia and its correlation with disease severity.

## CONCLUSION

We found that serum ALT, ALP, total proteins and albumin may provide sensitive measurement of preeclampsia severity. These biochemical markers may be helpful in predicting and assessing the severe consequences of preeclampsia.

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