

**ORIGINAL RESEARCH ARTICLE****CAN SERUM PROLACTIN BE A RELIABLE MARKER FOR PREECLAMPSIA? A HOSPITAL BASED STUDY ON NEPALESE MOTHERS**S Timalcina<sup>1\*</sup>, P Gyawali<sup>2</sup><sup>1</sup> Department of Biochemistry, Chitwan Medical College, Bharatpur-13, Chitwan.<sup>2</sup> PhD Scholar, Charles Sturt University, School of Community Health, Australia.*\*Correspondence to: Dr. Santosh Timalcina, Chitwan Medical College, Bharatpur-13, Chitwan, Nepal Email: santoshtim10@iom.edu.np***ABSTRACT**

Preeclampsia is a pregnancy specific complication characterized by hypertension, proteinuria and oedema. It has remained as a major cause of maternal and perinatal morbidity and mortality worldwide. The major function of prolactin is its role in lactation during pregnancy, but many authors have claimed that this hormone is also involved in angiogenesis, thus linking it with the pathogenesis of preeclampsia. In this context, our study aims to compare the serum prolactin level between preeclamptic and healthy pregnancies and correlate with the severity. A total of 54 pregnant women diagnosed with preeclampsia and 60 age and gestational weeks matched healthy pregnant women were recruited in this case control study. Preeclampsia was defined as per Australasian Society Consensus Statement research definition. Among 54 preeclamptic women, 41 had mild preeclampsia and 13 had severe preeclampsia. The mean age and the gestational weeks of the preeclamptic cases and pregnant controls were not significantly different. This study showed that the median concentration of prolactin was significantly higher in preeclampsia than in normal pregnancies (156.6 vs. 129.8 ng/mL,  $P=0.012$ ). Though the median concentration of prolactin was higher in severe preeclampsia in comparison to mild one, the difference did not reach the significant level (228.3 vs. 152.9 ng/mL,  $P=0.061$ ). No significant correlation of prolactin was found with mean arterial pressure and 24h UTP. Due to poor correlation with established markers of severity, serum prolactin is not a reliable marker of preeclampsia.

**Key words:** *Preeclampsia, Pregnancy, Prolactin.*<http://dx.doi.org/10.3126/jcmc.v4i4.11955>**INTRODUCTION**

Preeclampsia is a pregnancy specific complication characterized by onset of hypertension, proteinuria and oedema after 20 week of gestation. De novo preeclampsia (not considering superimposed preeclampsia) complicates 5-6% of all the pregnancies and remains a major cause of maternal and perinatal morbidity and mortality worldwide.<sup>1</sup> In Nepal, the incidence of preeclampsia or eclampsia was 20 cases to one thousand hospital deliveries.<sup>2</sup> Poor placentation coupled with excessive maternal intravascular inflammatory response has been suggested as its cause.<sup>3</sup>

The role of prolactin in the pathogenesis of preeclampsia has been a subject of much controversy. Besides functioning primarily as a “lactation hor-

monone”, some of the authors have claimed that its osmoregulatory and hypertensive properties could play an important role in the pathogenesis of preeclampsia. There is also evidence that prolactin causes renal retention of fluid and electrolytes, elevation of arterial pressure and potentiation of the effects of the pressor agents.<sup>4</sup>

Although a high serum level of prolactin has been shown to be associated with preeclampsia elsewhere, studies from Nepal are lacking. The aim of this study is to compare the maternal serum prolactin level between preeclamptic and healthy pregnancies and correlate it with mean arterial pressure (MAP) and 24 hour-urinary total protein (24h UTP).

## MATERIALS AND METHODS

This non-randomized case-control study was conducted from May 2010 to August 2011 in Institute of Medicine, Tribhuvan University Teaching Hospital (IOM, TUTH), Nepal. A total of 54 preeclamptic cases were studied after the ethical approval from institutional review board of IOM. Preeclampsia was defined as per Australasian Society Consensus Statement research definition.<sup>5</sup> Further subdivision of the cases into mild and severe type was done based on the available guidelines. Primigravid women diagnosed to have preeclampsia were explained about the study and were enrolled from maternity ward of the hospital. Age and gestational week matched pregnant controls were selected from women who visited Antenatal checkup (ANC) clinic.

Serum and urine samples from the cases were col-

lected within 24 h of diagnosis. Serum prolactin was measured using sandwich Chemiluminiscent Assay (CLIA), Bio-Ekon, Beijing.

Data analyses included standard descriptive statistics using SPSS v. 20, with variables expressed as mean  $\pm$  SD or medians as appropriate. Unpaired t-test or Mann-Whitney U test was used for comparison of means and medians respectively. A p-value of  $< 0.05$  was considered statistically significant.

## RESULTS

A total of 54 cases and 60 controls were enrolled in the study. Out of them, 41(75.9 %) had mild preeclampsia and 13 (24.1 %) had severe preeclampsia.

There was no significant difference between cases and the controls in terms of age and gestational age, suggesting a good match.

Table 1. Clinical characteristics of the study population

	Total preeclamptic cases	Pregnant Controls	P-value
Mean age $\pm$ SD	26.4 $\pm$ 3.23	26.13 $\pm$ 3.35	0.66
Mean gestational weeks $\pm$ SD	32.01 $\pm$ 3.08	31.21 $\pm$ 2.92	0.16
Median prolactin level (ng/ml)	156.6	129.8	0.01

The median concentration of prolactin was significantly higher in the preeclamptic cases (156.6 vs. 129.8 ng/mL,  $P=0.01$ ). The median concentration of prolactin, although higher in severe preeclampsia in comparison to mild one, did not reach the level of significance (228.3 vs. 152.9 ng/mL,  $P=0.06$ ). No significant correlation of prolactin was found with MAP and 24h UTP.

## DISCUSSION

Prolactin is a polypeptide hormone primarily secreted by the anterior pituitary that rises physiologically during pregnancy. Apart from the biological function of lactation, this hormone has been linked with angiogenesis.<sup>6</sup> This may have an important implication as abnormal angiogenesis is an essential component in the pathogenesis of preeclampsia.

The present study showed a higher prolactin level in preeclamptic pregnancies compared to age and gestational-week matched normal pregnancies. A study by Marlettini MG et al, also have reported higher plasma prolactin levels in women with pregnancy induced hypertension (PIH) at 39 weeks of gestation when compared to controls.<sup>7</sup> Similarly, Hayashi RH et al have reported the significant elevation of prolactin in

PIH group in comparison to normal pregnancy only at the 37 to 39 gestational weeks interval but the difference did not reach the significant level when the overall value of 16-42 gestational weeks was compared.<sup>8</sup>

Pre-eclampsia is a placenta dependent disease exemplified by the fact that all the symptoms disappear after delivery. Placental expression of anti-angiogenic factors such as soluble fms-like tyrosine kinase 1 (sFlt-1) in response to placental ischemia/hypoxia has been identified to have central role in its pathophysiology. These placental factors, after getting into the maternal circulation are supposed to cause endothelial dysfunction resulting in hypertension and proteinuria, characteristic of this disease.<sup>9</sup>

Explanations for the higher prolactin levels in the preeclamptic pregnancies have been sought after. A reduced prolactin clearance may be one of plau-

sible explanation for the higher prolactin levels in preeclampsia, as early kidney involvement occurs in this condition. The disturbed anterior pituitary functions, as evidenced by rise in ACTH and TSH in preeclampsia,<sup>10</sup> has also been proposed as the likely explanation.

The cross sectional nature of our study didn't allow us to establish the association of the elevated prolactin levels with birth outcomes. A large scale study by Brown MA et al has shown a significant association of hyperuricemia and proteinuria with a higher rate of maternal and fetal complications,<sup>11</sup> but not so with prolactin. The interest in the association between prolactin levels and adverse pregnancy outcomes in preeclampsia has been renewed by the discovery of vasoinhibins, which have anti-angiogenic and vasoconstrictive effects. They have been found to be enhanced in the serum and urine of preeclamptic women and interestingly, are supposed to be derived from the cathepsin D-mediated cleavage of prolactin in the affected placenta.<sup>12</sup> Notably, these vasoinhibins have been associated with the endothelial cell dysfunction and compromised birth weight that characterize preeclampsia

Though it has been proposed that prolactin causes rise in MAP based on rabbit studies,<sup>13</sup> the same might not hold true for humans as evidenced by poor correlation between MAP and serum prolactin in our study. This is in agreement with one of the studies that have shown a non-significant relationship between the blood pressure and the prolactin levels.<sup>7</sup> In this regard, serum prolactin is not a good indicator of severity of disease, based on its poor correlation with MAP and 24h UTP, which are established markers of the severity of the disease.

Urinary prolactin (uPRL) normalized for creatinine excretion, however, has been studied and has been shown to have a high discrimination power to identify the presence of preeclampsia, as uPRL excretion in normal subjects is virtually undetectable. The uPRL excretion had a good correlation with the severity of preeclampsia, regardless of the degree of proteinuria, gestational age and serum prolactin levels.<sup>14</sup> But, the low sensitivity of the technique for detecting prolactin in urine samples would be a major hindrance in it being used as a reliable marker for preeclampsia in

Nepalese population

## CONCLUSION

The present study demonstrates a significant difference in serum prolactin levels in preeclamptic mothers compared to normal pregnant controls, suggesting the idea of possible role of prolactin in the pathogenesis of preeclampsia. However, it has poor correlation with the severity of preeclampsia and with the established markers of its severity such as MAP and 24h-UTP. Therefore, serum prolactin can't be used currently as a reliable marker of preeclampsia. Urinary prolactin, if sensitive and low cost assays developed, could be a better and reliable marker for the disease condition.

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