



## A PROSPECTIVE STUDY FOR THE PREDICTION OF PREECLAMPSIA WITH SERUM PROLACTIN LEVEL

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**ABSTRACT** **Introduction:** Preeclampsia is a pregnancy-specific condition which is diagnosed based on the presence of the following clinical features: blood pressure (BP)  $\geq 140/90$  mmHg after 20 weeks of gestation and proteinuria  $\geq 300$  mg/24-hr or +1 with dipstick. Serum prolactin, being a vaso-inhibin precursor molecule and its anti-angiogenic activity may contribute to the pathophysiology of preeclampsia. So that Serum prolactin can be used as a new reliable parameter in early prediction of preeclampsia. **Material and Methods:** Prospective observational study carried out which included 139 pregnant women taken for study after pre-filling the inclusion and exclusion criteria, serum prolactin was done of every patient from 16-20 weeks then followed till delivery for the development of preeclampsia. **Results:** The preeclampsia incidence was seen to be 12.24% (17 patients) during the study duration. The mean serum prolactin levels were higher for the preeclampsia patients (382.41 vs 163.78) with a statistically significant difference ( $P < 0.001$ ). The sensitivity and specificity of the prolactin levels at cut off of 302 ng/ml was 94.12% and 90.16%. The PPV and NPV were 57.14% and 99.10%. **Conclusion:** Study concluded that there is an increased risk of development of Preeclampsia with an increased level of serum prolactin in early pregnancy. Early prediction of PE will offer a great potential to lower the rate of fetomaternal complications and provide a window for early intervention.

**KEYWORDS :** Preeclampsia, Pregnancy, Proteinuria, Hypertension, S. Prolactin.

### INTRODUCTION

Preeclampsia is a pregnancy-specific disorder defined as the emergence of hypertension and substantial proteinuria in a previously healthy woman after 20 weeks of gestation. In developing countries, HDP ranks second only to anemia with approximately 7-10% of all pregnancies complicated by some forms of hypertensive disorder and leads to various maternal and fetal complications<sup>1</sup>. Various biological markers implicated in the preeclampsia syndrome, have been measured to help predict its development.

Higher levels of circulating concentrations of soluble vascular endothelial growth factor receptor-1 (also known as soluble fms-like tyrosine kinase-1 [sFlt-1]) and soluble endoglin (sEng), as well as lower concentrations of placental growth factor (PlGF), are present at the time of preeclampsia diagnosis and have been linked to an increased risk of developing this condition for several weeks before the clinical manifestations<sup>2</sup>. Prolactin (PRL) is physiologically enhanced during normal pregnancy and has several effects other than reproduction and breastfeeding, including a prominent involvement in angiogenesis and antiangiogenesis<sup>3</sup>. Prolactin fragments that are formed due to proteolytic cleavage of monomeric prolactin are said to have antiangiogenic effects<sup>4</sup>.

Urinary prolactin excretion and its antiangiogenic prolactin fragments have been demonstrated in studies to be higher in preeclamptic women, increasing with the severity of the illness and the occurrence of poor outcomes<sup>5</sup>. Furthermore, antiangiogenic prolactin fragments are increased in preeclamptic women's serum, amniotic fluid, and placenta. These findings indicate that prolactin may have a role in the aetiology of preeclampsia and that disrupting this angiogenesis route may have a significant impact on the development of clinical symptoms and consequences.

**Study Design:** Prospective observational study.

**Sample Size And Mode Of Collection:** 139 antenatal patients, from 16-20 weeks period of gestation, were recruited from OPD in department of Obstetrics and Gynecology, and fulfilling the inclusion criteria formed the study population.

### Inclusion Criteria

- All pregnant women from 16 weeks to 20 weeks period of gestation irrespective of age and parity.

### Exclusion Criteria

- Chronic hypertension
- Type 1 & 2 Diabetes mellitus
- Multiple pregnancy

- Any chronic Thyroid disorders
- Patients with H/O galactorrhea
- Patients with H/O drug intake which affect serum prolactin such as neuroleptics, prokinetics, PPIs, H2 blockers.

### AIM AND OBJECTIVES

- To find out the incidence of preeclampsia in tertiary care unit
- To assess the correlation of S. Prolactin level during 16-20 weeks of gestation as a predictor for the development of preeclampsia

### METHODS

Pregnant women from 16-20 weeks Period of gestation attending the outpatient department of Obstetrics and Gynecology were explained about the study procedure in detail and their associated benefits in their own vernacular language and 139 consenting patients fulfilling the inclusion & exclusion criteria were considered for my study. General physical, systemic examination and obstetrical examination was done. Basic investigations were done. Complete blood counts, antenatal profile (if not done), urine routine and microscopy and serum prolactin. Under aseptic precautions, sampling was done by venepuncture, 2 ml of blood was drawn for serum prolactin which was done by which was done by ELISA method. The patients were followed up until delivery and assessed for the development of proteinuria, signs and symptoms of pre-eclampsia, IUGR and HELLP.

**Table 1. Serum Prolactin Values In Non Pregnant And Pregnant Female**

Unit	Non Pregnant female	First Trimester	Second Trimester	Third Trimester
ng/ml	0-20	36-213	110-330	137-372
µg/L	0-20	36-213	110-330	137-372
pmol/L	0-859	1,565-9,261	4,783-14,347	5,957-16,174

### RESULTS

A total of 139 patients were included in this study. Pre-eclampsia was seen in 17 patients (12.24%) in the study. The pre-eclampsia incidence was seen to be 12.24% during the study duration.

**Table 2. Frequency Distribution Of Cases According To Development Of Pre-eclampsia**

Pre-eclampsia Status	Number	Percentage
No Pre-eclampsia	122	87.76
Pre-eclampsia present	17	12.24
Total	139	100.00

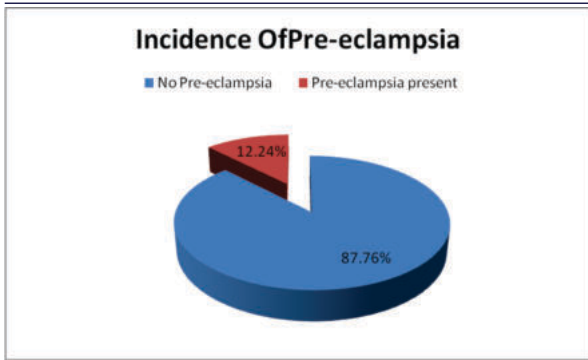


Figure 1: Incidence Of Pre-eclampsia

The mean serum prolactin levels were higher for the pre-eclampsia patients (382.41 vs 163.78) with a statistically significant difference (P<0.001).

Table 3. Comparison Of Values Of Serum Prolactin In Pre-eclampsia And No Preeclampsia Cases.

Serum prolactin and pre-eclampsia	Pre-eclampsia -	Pre-eclampsia +	Overall	P value
Number of patients	122	17	139	<0.001
Mean	163.78	382.41	190.52	
Std dev	88.17	61.05	111.43	
Min	23.00	278.00	23.00	
Max	377.00	489.00	489.00	

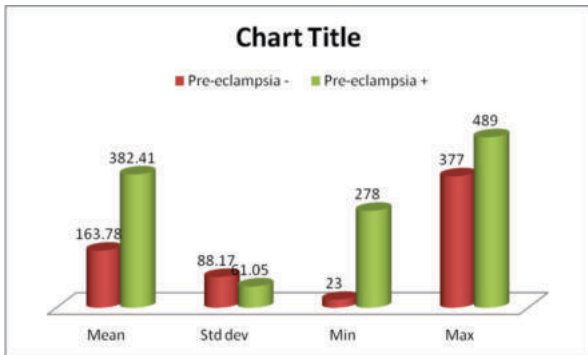


Figure 2. Bar Charts Showing Value Of Serum Prolactin Level In Preeclampsia And No Pre-eclampsia In Study Population

Serum prolactin levels in the study were used to assess the status of PE in the patients. The diagnostic efficacy of Pre-eclampsia was high as reflected by the high AUC (area under the curve) score of 97.2% . The results were significant statistically (P<0.0001).

Table 4. Area Under Curve Analysis

Pre-eclampsia and Serum prolactin	
AUC	0.972
P value	<0.0001
95% CI	0.946-0.997

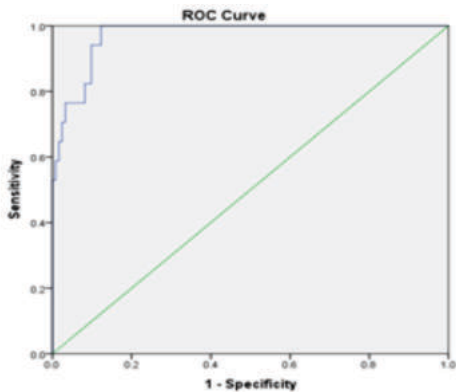


Figure 3. ROC Analysis

The serum prolactin levels based on the above ROC analysis was seen to be 302 ng/ml.

Table 5. Contingency Table For Preeclampsia And Prolactin Cut Off

Cut off – 302	Pre-eclampsia +	Pre-eclampsia -	Grand Total
Prolactin >302	16 (94.11%)	12 (9.83%)	28
Prolactin 302 or less	1 (5.89%)	110 (90.16%)	111
Grand Total	17	122	139

It was seen that 94.11% of the pre-eclampsia patients were having a prolactin level of >302ng/ml. 90.16% of the patients without PE had prolactin level of 302ng/ml or less. The results were significant statistically (P=0.0001).

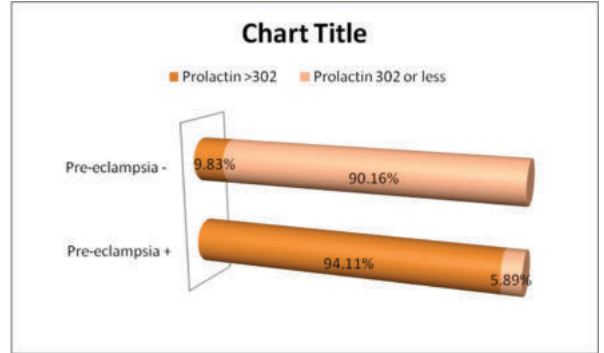


Figure 4. Chart Showing Distribution Of Pre-eclampsia Cases On The Basis Of Prolactin Cut Off 302 Ng/ml

The overall accuracy of the serum prolactin levels (at cut off levels of 302) in accurately diagnosing the Pre-eclampsia status was 90.65%. The sensitivity and specificity of the prolactin levels at cut off of 302 was 94.12% and 90.16%. The PPV and NPV were 57.14% and 99.10%.

Table 6. Diagnostic Test Evaluation

Diagnostic test evaluation	Value	95% CI
Sensitivity	94.12%	71.31% to 99.85%
Specificity	90.16%	83.45% to 94.81%
Positive Likelihood Ratio	9.57	5.52 to 16.59
Negative Likelihood Ratio	0.07	0.01 to 0.44
Disease prevalence	12.23%	7.29% to 18.86%
Positive Predictive Value	57.14%	43.47% to 69.80%
Negative Predictive Value	99.10%	94.26% to 99.86%
Accuracy	90.65%	84.54% to 94.93%

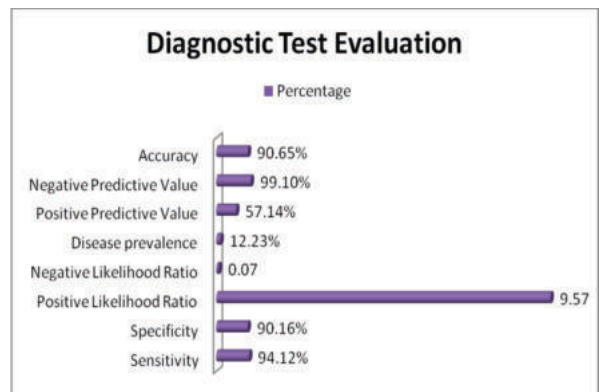


Figure 5. Chart For Diagnostic Test Evaluation

**CONCLUSION**

Early prediction of pre-eclampsia will offer a great potential to lower the rate of fetomaternal complication and provide a window for early intervention. In our study, 139 antenatal patients were included and outcomes analysed. A diagnostic test evaluation done for prolactin revealed that serum prolactin levels of 302ng/ml and above are highly predictive of pre-eclampsia. The sensitivity and specificity was high along with high levels of accuracy. The study proved the utility of serum prolactin as an effective marker for the pre-eclampsia prediction.

**REFERENCES**

- [1] Tejal P, Astha D. Relationship of serum uric acid level to maternal and perinatal outcome in patients with hypertensive disorders of pregnancy. *Gujarat Med J.* 2014 Aug;69(2):1-3.
- [2] Levine RJ, Maynard SE, Qian C, Lim KH, England LJ, Yu KF, Schisterman EF, Thadhani R, Sachs BP, Epstein FH, Sibai BM. Circulating angiogenic factors and the risk of preeclampsia. *New England journal of medicine.* 2004 Feb 12;350(7):672-83.
- [3] Struman I, Bentzien F, Lee H, Mainfroid V, d'Angelo G, Goffin V, Weiner RI, Martial JA. Opposing actions of intact and N-terminal fragments of the human prolactin/growth hormone family members on angiogenesis: an efficient mechanism for the regulation of angiogenesis. *Proceedings of the National Academy of Sciences.* 1999 Feb 16;96(4):1246-51.
- [4] Clapp C, Thebault S, Jeziorski MC, Martinez De la Escalera G. Peptide hormone regulation of angiogenesis. *Physiological reviews.* 2009 Oct;89(4):1177-215.
- [5] González C, Parra A, Ramírez-Peredo J, García C, Rivera JC, Macotela Y, Aranda J, Lemini M, Arias J, Ibarguengoitia F, de la Escalera GM. Elevated vasoinhibins may contribute to endothelial cell dysfunction and low birth weight in preeclampsia. *Laboratory investigation.* 2007 Oct 1;87(10):1009-17.
- [6] Kratz A. Case records of the Mas-Kratz A, Ferraro M, Sluss PM. Case records of the Massachusetts General Hospital: laboratory values. *N Engl J Med.* 2004;351(15):1549-63.
- [7] Abbassi-Ghanavati M, Greer LG, Cunningham FG. Pregnancy and laboratory studies: a reference table for clinicians. *Obstetrics & Gynecology.* 2009 Dec 1;114(6):1326-31.