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Gynaecology

FIRST TRIMESTER SCREENING BY BIOCHEMICAL MARKERS FOR PREDICTION OF PREECLAMPSIA

Dr.Veena Gupta Professor, Department of Obs and Gynae, MLN Medical College, Prayagraj.

Dr.Divya Gupta* Junior Resident, Department of Obs and Gynae MLN Medical College, Prayagraj. *Corresponding Author

Dr.Nidhi Sachan Assistant Professor, Department of Obs and Gynae MLN Medical College, Prayagraj.

Dr Kumari Shweta Junior Resident,Department of Obs and Gynae MLN Medical College, Prayagraj.

ABSTRACT **Aim:** To correlate biochemical markers in antenatal patients with subsequent development of preeclampsia. **Material Method:** 131 pregnant women, in first trimester of pregnancy were investigated for their serum βHCG, PAPP-A, PIGF. These patients were followed uptill term for the development of preeclampsia. **Results:** Out of 131 antenatal cases 20.61% developed preeclampsia. βHCG levels <10th percentile (<0.56 MoM) with mean 0.783±0.285MoM (p<0.001), predicted preeclampsia with sensitivity of 22.22% and specificity of 85.58%. While PAPP-A level < 10th Percentile (<0.58 MoM) with mean 0.969±0.59M (p value 0.0001) predicted preeclampsia with sensitivity of 29.6% and specificity of 88.46%. PlGF levels <10th percentile(<0.6 MoM) with mean 0.54±0.158MoM (p value<0.0001) predicted preeclampsia with sensitivity of 66.6% and specificity 94.4%. **Conclusion:** Maternal serum βHCG, PAPPA, PlGF vary between normal pregnancies and those that subsequently developed preeclampsia . Thus our study concludes that biochemical markers especially PlGF in first trimester have high predictive value in detection of preeclampsia.

KEYWORDS : PIGF, β HCG, PAPP-A, Preeclampsia

INTRODUCTION

Preeclampsia is a syndrome that manifests clinically in the second half of pregnancy (usually after 20 weeks) as a new onset hypertension arterial pressure exceeding 140/90 mmHg on 2 occasions, atleast 4 to 6 hours apart with associated proteinuria ≥ 300mg per 24 hours of urine collection or with any one of the following features of end organ damage i.e, platelet count<1Lac/mm3, serum creatinine>1.1mg/dl, raised liver enzymes twice the normal, evidence of pulmonary oedema and cerebrovascular symptoms.

Preeclampsia is the major contributor to maternal and perinatal mortality and morbidity worldwide **(McIntrie et al.,1999)**. According to World Health Organization 16 percent of maternal deaths are attributed to hypertensive disorders**(Khan, 2006)** and 5 fold increase in perinatal mortality with iatrogenic prematurity being main culprit. Pre-eclampsia is a multi organ disease, which presents with varying degree of severity. The prevention of preeclampsia remains a considerable challenge in obstetrics. Although the symptoms of preeclampsia generally manifest in second to third trimester of pregnancy, their underlying pathology takes place in first trimester between 9 - 13 weeks **(Kaufmann et al.,2003)**. Numerous pathophysiological mechanisms, alone or in combination, have been suggested to be responsible for diverse subsets of pre-eclampsia. They include impaired vascular remodeling of the maternal fetal interface, excessive immune response to paternal antigens, maternal inflammatory response, very low density lipoprotein toxicity, increased trophoblastic apoptosis and imbalance of angiogenic factors all these process being modulated by genetic and environmental parameters. Maternal serum biochemical markers screening in identification and use of first trimester markers for preeclampsia were chosen on the basis of specific pathophysiological abnormalities that have been found in association with pre-eclampsia like **Human Chorionic Gonadotropins, Pregnancy associated plasma protein A, Placental Growth Factor.** These are markers of placental dysfunction, endothelial cell activation and dysfunction, coagulation activation, angiogenesis and markers of systemic inflammation.

MATERIALSAND METHODS

The present study was done in Swaroop Rani Nehru Hospital and Kamla Nehru Hospital, in the Department of Obstetrics and Gynaecology, Moti Lal Nehru Medical College Prayagraj on 131 pregnant women, attending outpatient department and indoor cases in first trimester of pregnancy (9 to 13 weeks 6 days of gestation) over a period of twelve months(September 2019-August 2020). All women included in this study were investigated for their serum PAPPA, βHCG, PIGF at 9 to 13 weeks of gestation.

Inclusion Criterion- All pregnant women of 9 to 13 weeks 6 days giving consent

Exclusion Criterion-

- Not giving consent
- Twin pregnancy
- Missed abortion
- Chronic hypertension

Interpretive unit is MOM (Multiple of Median)which takes into account variables such as gestational age (USG), maternal weight, race, multiple gestation, IVF, smoking, previous history of pre-eclampsia. β HCG<0.56 MoM, PAPP A<0.58 MoM and PIGF <0.60 MOM i.e, less than 10th percentile of reference range were considered as high risk cases.

OBSERVATION AND RESULT

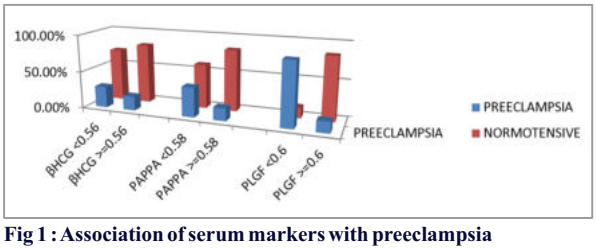

Fig 1 : Association of serum markers with preeclampsia

Out of total number of antenatal cases **16.03%** had βHCG levels <10thpercentile (<0.56MoM) of them 28.57% developed preeclampsia while 19% of cases with normal levels developed preeclampsia. **15.26%** of antenatal cases had PAPPA levels <10th percentile (<0.58 MoM) of them 40% developed preeclampsis while 17% with normal levels developed preeclampsia and **26.9%** of antenatal cases had PlGF levels <10th percentile (<0.6MoM) of them 85.7% developed preeclampsia while 15% with normal levels developed preeclampsia.

In the present study the mean levels of Serum βHCG, PAPPA and PlGF in women who developed preeclampsia were found to be decreased than those who remained normotensive [0.783+0.285 MoM vs 1.489+-1.033 MoM] with (p value 0.001) ,[0.969+-0.59MoM vs 1.29+0.63MoM] with (p value 0.0184) and [0.54+0.158MoM vs 1.55+-0.619MoM] with (p value<0.0001)respectively.

Table 1 : Comparision of Sensitivity, Specificity, PPV and NPV of First Trimester Markers (βHCG, PAPPA, PlGF) And Ultrasonographic Markers In Prediction of Preeclampsia

Parameters	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
βHCG	22.22%	85.58%	14.62%	90.83%

PAPPA	29.63%	88.46%	22.20%	91.88%
PlGF	66.67%	94.44%	57.14%	91.67%
Biochemical Markers (BHCG+PAPPA)	44.44%	72.88%	18.25%	92.66%

DISCUSSION

Decreased level of βHCG was found in cases who developed preeclampsia in comparison to those who remained normotensive (p value 0.001). Similar to study done by **Ong et al** in 2000 with (p value <0.001)

PAPPA level was reduced in cases who developed preeclampsia than those who remain normotensive with statistically significant association (p value 0.0184) Comparative figures of association between decreased PAPPA levels antenatal patients and development of preeclampsia in different studies had similar findings

STUDIES	YEAR	P- VALUE
Poon et al	2010	0.001
Saxena et al	2013	0.02
Leslie Myatt	2013	0.04
Kuc et al	2013	0.016
Scazzocchio et al	2013	>0.05
Ozdamar et al	2014	<0.001
Present study	2020	0.0184

PlGF level was decreased in cases who developed preeclampsia and those who remain normotensive (p value<0.0001). Comparative figures of association between decreased PlGF levels antenatal patients and development of preeclampsia in different studies had similar findings

Studies	Year	P-value
Mauro Parra et al	2013	<0.05
Leslie Myatt	2013	<0.001
Boutin et al	2019	<0.01
Present Study	2020	<0.0001

CONCLUSION

Our study thus concludes that integrated first trimester screening by biochemical markers shows a prediction in detection of preeclampsia. Maternal serum βHCG, PAPPA and PlGF levels vary between normal pregnancies and those that subsequently developed preeclampsia. Their levels were significantly reduced in preeclampsia group compared to normotensive group . Hence measuring βHCG, PAPPA and PlGF levels in first trimester may be useful in prediction of preeclampsia.

The findings of my study are similar to the previous studies which revealed that in pregnancies developing preeclampsia the Maternal serum βHCG, PAPPA and PlGF levels are reduced.

A large population based study evaluating algorithms combining multiple markers are needed, if screening approaches are to be eventually implemented. High cost of these tests can be a limiting factor in implementation of these test as a screening modality in general population.

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