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To Study the Role of Maternal Serum Beta hCG at 13 - 20 Weeks of Gestation in Prediction of Pre-Eclampsia

Dr. Vanitha.V	MD, DGO., Senior Assistant Professor ., Institute of Obstetrics and Gynaecology., Madras Medical College
Dr. Shanthi.S	MD, DGO, Senior Assistant Professor ., Institute of Obstetrics and Gynaecology., Madras Medical College
Dr. S. Usha Rani	MD., DGO, Professor, Institute of Obstetrics and Gynaecology. Madras Medical College

ABSTRACT

AIM :To study the role of maternal serum beta hCG for the prediction of pre-eclampsia by measuring at 13 - 20 weeks of gestation.

MATERIALS AND METHODS: This is a population based cohort study conducted in a tertiary government hospital, Chennai in 200 antenatal women attending OPD. Patients were selected based on the inclusion and exclusion criteria. A detailed clinical history and clinical examination was done. All basic laboratory investigation was done and maternal serum beta hCG was estimated by ELISA technique. Early obstetrics ultrasound and reliable menstrual history dates were used to calculate gestational age. The study subjects were followed till delivery and observed for development of pre eclampsia.

RESULTS OF THE STUDY: There was statistical significance with occurrence of pre-eclampsia with respect to age group (more in teenage and elderly women), parity (more in primi gravida's) and BMI (more in overweight women)

There was no statistically significant correlation between occurrence of pre eclampsia with socio economic status and Gestational diabetes.

The beta HCG value of more than 71220 mIU/ml can be considered as marker for predicting pre – eclampsia in the early second trimester of pregnancy.

CONCLUSION: This study showed that measuring serum beta hcg in early second trimester at (13-20weeks) is a useful indicator to identify women who are likely to develop pre-eclampsia in the same pregnancy. The beta HCG value of more than 71220 mIU/ml can be considered as marker for predicting pre – eclampsia in the early second trimester of pregnancy. Also higher levels are associated with increased severity of pre-eclampsia.

KEYWORDS   Pre eclampsia, Beta HCG, predicting preeclampsia

Introduction –

Pre-eclampsia is a multi-system disorder of unknown etiology unique to pregnancy with onset after 20 weeks gestation occurring in 3- 8% of pregnancy.[1] Pre-eclampsia predisposes to many lethal complications like HELLP syndrome, abruptio placentae, disseminated coagulopathy, eclampsia, acute renal failure and of preterm birth, IUGR,

and perinatal mortality. Therefore it is utmost necessary to diagnose it early. Intensive management of pre-eclampsia can prevent many maternal and fetal complications.

The initiating event in the process of developing pre-eclampsia was considered to be the abnormal placentation[2]. Immunological changes occurring in the trophoblasts during mid trimester results in secretary response and it is seen as rise in serum beta hCG levels. In pre-eclampsia, focal cellular necrosis occurs in the syncytiotrophoblast and there is increased mitotic activity with proliferation of the cytotrophoblast [3, 4]. In severe pre-eclampsia there is rapid transformation of the proliferating trophoblast into syncytiotrophoblast[5]. The insufficient trophoblast migration into the spiral arteries and subsequent placental hypoxia results in elevated hCG production[6] by hyperplasic cytotrophoblastic cells of the placenta [7,8,9]. There is a relationship between pre -eclampsia and increased maternal serum beta-HCG levels2, which indicates that there is an abnormal secretory function of the placenta in patients with pre eclampsia.

Berg and colleagues(2003) reported that pre-eclampsia complications accounts for about 16% of maternal deaths and more than half of it are preventable. Therefore prediction of preeclampsia in early gestation is of utmost importance to de-

tect and to intervene in the management of high risk pregnancies much earlier to reduce the maternal death and fetal mortality and neonatal morbidity.

Materials and Methods –

This is a population based cohort study. This study included a total number of 200 antenatal women attending ANC clinic in a government tertiary care institute. This study was conducted from March 2013 to December 2013.

Inclusion criteria :

Pregnant normotensive, non-proteinuric women were randomly selected from the gestational age of 13 to 20 weeks of pregnancy irrespective of parity.

Exclusion criteria

1. Multifetal pregnancy
2. Congenital foetal malformations
3. Chromosomal disorders in foetus,
4. Previously known medical disorder complicating pregnancy
5. Molar pregnancy
6 Gestational age < 13 and > 20 weeks

A detailed history was taken. Her name, age, address, height, pre pregnancy weight, socioeconomic class ,obstetric score, past history of preeclampsia and family history of preeclampsia. Thorough clinical examination was done. Laboratory investigation was done, includes basic haematological investigations, urine albumin and maternal serum beta hCG was estimated by ELISA technique. Informed consent was obtained from all subjects. Early ultrasound measurement of crown-

rump length of the foetus and reliable menstrual history dates were used in gestational age calculation.

The study subjects were followed once a month till 28 weeks of gestation, once a fortnight till 36 weeks, and once a week till delivery and observed for development of pre-eclampsia. During each visit she was examined thoroughly including blood pressure, urine albumin, pedal edema and foetal well-being was assured.

Quantitative determination of beta hCG is done by Enzyme Immunoassay method [10].

Results –

As 'p' value is 0.000,there is statistically significance between pre-eclampsia cohort and normal cohort with regard to age group. Pre - eclampsia is more common in teenage and in elderly gravida. (Table 1)

Age Group (yrs)	Pre-eclampsia cohort		Normal cohort	
	No of Cases	%	No of Cases	%
< 20	16	36.4 %	18	11.5 %
21 - 25	8	18.2 %	73	46.8 %
26 - 30	8	18.2 %	45	28.8 %
> 30	12	27.3 %	20	12.8 %
Table 1				

PERCENTAGE DISTRIBUTION OF PREECLAMPSIA AMONG

PRIMI GRAVIDA AND MULTI GRAVIDA

OBSTETRIC SCORE	PRE-ECLAMPSIA COHORT		NORMAL COHORT	
	NO OF CASES	%	NO OF CASES	%
1	32	72.7 %	80	51.3 %
2	10	22.7 %	70	44.9 %
3	2	4.5 %	6	3.8 %
Table 2				

As the p value is 0.029, there is statistical significance between

parity and occurrence of pre-eclampsia. pre-eclampsia is more common in primi gravida than in multigravida. (Table 2)

BMI – DISTRIBUTION OF PREECLAMPSIA

BMI	PRE ECLAMPSIA COHORT		NORMAL COHORT	
	NO OF CASES	%	NO OF CASES	%
1	2	4.5 %	86	55.1 %
2	14	31.8 %	51	32.7 %
3	23	52.3 %	12	7.7 %
4	5	11.4 %	7	4.5 %

Table 3
1- Healthy weight 2- over weight   3- Moderate obesity 4- Severe obesity.

As p< 0.0001, there is statistical significance between, pre-eclampsia cohort and normal cohort, with regard to BMI. Pre eclampsia is found more common in overweight women. (Table 3)

Statistics
Area Under a Receiver Operating Characteristic Curve (ROC):

Total area under ROC curve is used as a single index for measuring the performance a test. When the AUC is larger, the better is overall performance of the medical test to correctly identify diseased and nondiseased subjects.

When the AUCs of two tests are equal, it represents similar overall performance of tests but this does not necessarily mean that both the curves are identical. It indicates that they may cross each other.

ROC CURVE - b hCG
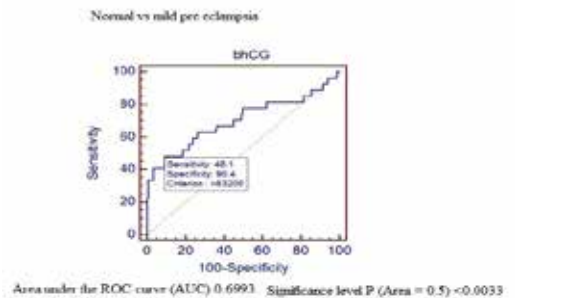### Normal vs mild pre eclampsia

Fig 1
From Fig 1 ROC, we infer that in the prediction of mild pre eclampsia for the cut off value >63200 mIU/ml, the Area Under the RO curve(AUC) is 0.6993, Sensitivity is 48.1 and specificity is 90.4.
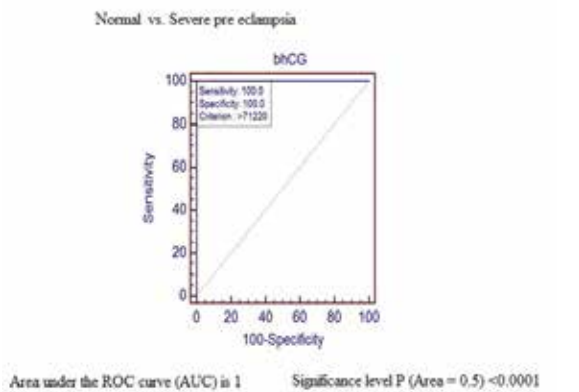
Normal vs. Severe pre eclampsia

Fig 2
From Fig 2 ROC,we infer that in the prediction of severe pre eclampsia for the cut off value > 71220 mIU/ml ,the Area Under the ROC curve(AUC) is 1. Sensitivity is 100 and specificity is 100. It indicates that b hCG is the good indicator for prediction of severe preeclampsia
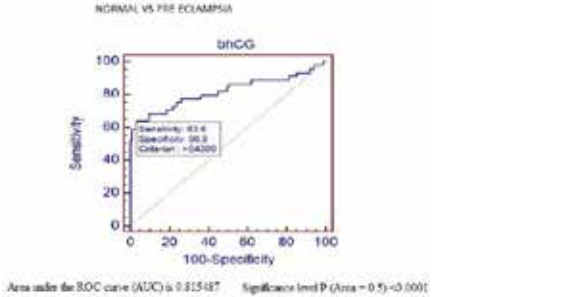
NORMAL VS PRE ECLAMPSIA

Fig 3
- From Fig 3 ROC, we infer that in the prediction of preeclampsia for the cut off value > 64399 mIU/ml , the Area Under the ROC curve (AUC) is 0.815487. Sensitivity

is 63.6 % and specificity is 96.8 %.
- It indicates that b hCG is good in predicting severe pre eclampsia than mild pre eclampsia.
- Regarding b hCG values, in predicting mild pre eclampsia with the cut off value more than 63200 mIU/ml the Sensitivity is 48.1% and specificity is 90.4%.
- In predicting severe pre eclampsia with the cut off value more than 71220 mIU/ml , the sensitivity is 100 % and specificity is 100%.
- In predicting pre eclampsia with the cut off value > 64399 mIU/ml , Sensitivity is 63.6% and specificity is 96.8% .
- It indicates that b hCG is a good predictor of pre eclampsia, but it is a better predictor of severe pre eclampsia than mild pre eclampsia.

Discussion
- In this study we found that serum b hcg were elevated in pre eclampsia, more significantly elevated in severe pre eclampsia when compared with controls. This indicates that there exists an abnormal secretory functions of the placenta in cases of pre eclampsia.
- In our study among 200 women 44 developed preeclampsia with the cut off value of b hCG value > 63200 mIU/ml the Sensitivity is 48.1% and specificity is 90.4% for predicting pre eclampsia .
- With the cut off value of b hCG > 71220 mIU/ml the sensitivity is 100 % and specificity is 100% for predicting pre eclampsia . It has good sensitivity and specificity in predicting severe pre eclampsia.
- Our study was supported by desai and rao[11,12] , 62 cases out of 90 (68.9%) with value > 2 mom developed pre eclampsia against 21 cases out of 130 (16.5%) who had beta hcg < 2mom. The difference was statistically significant.[13]
- Study conducted by Roiz Hernandez et al[14,15] showed that with the cut off value of 2 mom for serum beta hcg in multigravida and primigravida during second trimester , the area below roc curve was 0.96 and 0.95, respectively , its sensitivity was 88.5% and 100% respectively . The positive predictive value was 0.45 and 0.25.
- There was statistical significance with occurrence of pre-eclampsia with respect to age group (more in teenage and elderly women), parity (more in primi gravida's) and BMI (more in overweight women)
- There was no statistically significant correlation between occurrence of pre eclampsia with socio economic status and Gestational diabetes.
- The beta HCG value of more than 71220 mIU/ml can be considered as marker for predicting pre – eclampsia in the early second trimester of pregnancy.

Conclusion –
This study showed that measuring serum beta hcg in early second trimester at (13-20weeks) is a useful indicator to identify women who are likely to develop pre-eclampsia in the same pregnancy. The beta HCG value of more than 71220 mIU/ml can be considered as marker for predicting pre – eclampsia in the early second trimester of pregnancy. Also higher levels are associated with increased severity of pre-eclampsia.

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