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Original Article

Role of Second Trimester Maternal Serum Markers as Predictor of Preeclampsia

Dayal Meena[1], Gupta Parul[2], Varma Manju[1], Ghosh UK[1], Bhargava Anudita[3]

[1]Professor, [2]Resident, [3]Associate Professor,
Moti Lal Nehru Medical College, Allahabad

Abstract :

Objective s: To evaluate the variations and potential clinical use of second trimester serum markers as predictor of preeclampsia. *Methods :* In a prospective study β HCG, α feto protein and inhibin A levels were estimated in 50 antenatal women in the second trimester (12-24 weeks) by ELISA technique. Results were noted in terms of development of preeclampsia, mean serum levels of all three markers, mode of delivery and fetal outcome. *Resuflts :* Out of 50 women, 10 developed preeclampsia (20%). A significant rise of mean serum β HCG level (16130.2 MIU/ml, >2.5 MoM,p <0.001), mean serum AFP level (161.7 ng/ml, >2.5 MoM, P<0.001) and mean inhibin-A level (1248.49 pg/ml, >2.0 MoM, P<0.001) was present in those who developed preeclampsia. Out of 10 preeclamptic women one had IUD, four fetuses were growth retarded, two babies were born before term and six were low birth weight babies, whereas out of 40 normotensive women only five had IUGR, three preterm delivery and 32 delivered at term without and complication. *Conclusions :* A significant positive correlation between second trimester serum markers and development of preeclampsia was observed (p<0.001). Thus with the second trimester serum marker study, prediction of preeclampsia is possible at incipient stage and its adverse pregnancy outcome can be minimized.

Keywords: β HCG, alfa feto protein, inhibin A, predictor of preeclampsia, preterm, IUGR

Introduction

Preeclampsia is a multisystem disorder of unknown etiology with hypertension, proteinuria and/or edema which predisposes to potentially lethal complications such as eclampsia, abruptio placentae, acute renal failure, cerebral hemorrhage and circulatory collapse. Much of the neonatal mortality is due to premature delivery and intrauterine hypoxia leading to IUGR, therefore early diagnosis and intensive management of preeclampsia is of utmost necessity. If incipient preeclampsia can be diagnosed, intensive obstetric care can be utilized more effectively in patients who are at greater risk and this may improve maternal and fetal prospects. Alfa feto protein is secreted from fetal gastrointestinal tract and its level is raised due to functional alteration of trophoblastic cells, leading to increased leakage, as trophoblastic dysfunction is the primary problem in preeclampsia.

β HCG & inhibin A are selected from trophoblastic cells and in preeclampsia there is reactive hyperplasia of cells thus leading to raised levels. The present study analyzes the variations and potential clinical use of second trimester serum markers as predictor of preeclampsia.

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Correspondence :

Dayal Meena
Professor
347/1, Tagore Town, Allahabad.
Tel.: (0532) 2465606, Cell : 9415235606

Material and Methods

The study was conducted on fifty antenatal women of gestational age between 12 and 24 weeks, in the Department of Obstetrics and Gynaecology, M.L.N Medical College, Allahabad.

Detailed history was taken and thorough clinical examination was done. Patients with preexisting hypertension, twins in present pregnancy, heart disease, renal disease and diabetes were excluded from the study, as all these conditions can affect serum marker levels by its own. Apart from routine hematological investigations, estimation of maternal serum markers was done by ELISA technique. Blood samples were collected with all aseptic precautions. Serum was separated by centrifugation. All reagents were brought to room temperature. 25 µ L of serum samples were put into microplate well. 100 µ L of enzyme reagent (β HCG/ AFP/Inhibin A) were added to all wells, incubated and contents were discarded. Then 300 µ L of wash buffer was added and decanted. 100 µ L of working substrate solution was added and incubated. Then 50 µ L of stop solution was added and absorbance in each well was read by ELISA reader.

Results

Out of the 50 antenatal women, 10 developed preeclampsia while 40 remained normotensive. Maximum

Table 1.

Systolic/Diastolic BP and β HCG, AFP, Inhibin A level in preeclamptic group

S.No.	Systolic BP mm Hg	Diastolic BP mm Hg	β HCG (MIU/ml)	AFP (ng/ml)	Inhibin A (pg/ml)
1	160	120	38,400	315	2759
2	150	100	18,500	266.4	1751.2
3	150	96	16,510	202	1504.6
4	150	94	14,816	208	1618
5	150	90	14,410	79.2	962.4
6	140	94	12,640	82.4	412.2
7	140	90	6,960	7.8	462
8	150	104	20,106	280	1850
9	140	100	13,110	168	813
10	130	90	5850	8.2	362.5

Table 2.

Mean value of β HCG, AFP, inhibin A

Serum markers	Preeclamptic cases (N=10)	Normotensives (N=40)	P Value
β HCG (MIU/ml)	16130.2 (>2.5 MoM)	4621.8 (0.95 MoM)	>0.001
AFP (ng/ml)	161.70 (>2.5 MoM)	24.6 (91.2 MoM)	<0.001
Inhibin A (pg/ml)	1348.49 (>2.0 MoM)	461.4 (1.15 MoM)	<0.001

Table 3.
Mode of delivery

Mode of delivery	Preeclamptic group		Normotensives group	
	No.	%	No.	%
Normal vaginal Delivery	4	40	28	70
Forceps Delivery	2	20	2	5
Cesarean section	4	40	10	25

Table 4.
Fetal outcome

Fetal outcome	Preeclamptic		Normotensives	
	No.	%	No.	%
IUD	1	10	0	0
IUGR	4	40	5	12.5
Preterm	2	20	3	7.5
Term	3	30	32	80

Table 5.
Observations in different series

Author	Year	Mean maternal serum marker (MoM)		
		β HCG (MoM)	AFP (MoM)	Inhibin A (MoM)
Gravett et al[1]	1992	>5.0	>2.5	-
Gonen et al[2]	1992	>3.0	>2.5	-
Cuckle[3]	1998	-	-	2.01
Yaron et al[4]	1999	>2.0	>2.5	>2.0
Aquilina et al[5]	2000	-	-	>2.0
Duric et al[6]	2003	>2.0	>2.02	>2.0
Present study	2005	<2.5	>2.5	>2.0

number of women - six (60%) patients with preeclampsia and 25 (62.5%) normotensives were young; in the age group of 20 to 25 years, six (60%) hypertensive and 28 (70%) normotensives were primigravidae. Out of the 10 preeclamptic women, seven had significant proteinuria whereas none of the normotensive women presented with significant proteinuria (>2 +). All preeclamptics had edema whereas only 10% normotensives had edema.

Mean systolic BP was 150±7.07 mmHg and mean diastolic BP was 100.4±3.1 mmHg in hypertensives whereas it was 114 and 80.4 in normotensives (Table 1). This difference was statistically significant (P<0.05). β HCG level was more than 10,000 MIU/ml with mean of 16130.2 MIU/ml (>2.5 MoM) in preeclamptics whereas none of the normotensive women had such a high level. All had β HCG <5000 MIU/ml with mean of 4621.8 MIU/ml (0.95 MoM) (p<0.001). Mean AFP value in normotensives was 24.6 ng/ml (1.2 MoM) whereas in hypertensives it was >100 ng/ml with mean of 161.7 ng/ml (>2.5 MoM) (P value <0.001). Mean Inhibin A level was 461.4 pg/ml in normotensives while it was high (p<0.001) i.e 1248.4 pg/ml in preeclamptic women (Table 2).

Operative delivery was required in 60% of the preeclamptics while 70% of the normotensives had normal vaginal delivery (Table 3). Maximum number of babies (60%) born to preeclamptic mothers had low birth weight (<2500 g) whereas 75% babies born to normotensives had birth weight >2500 g. Out of the 10 preeclamptic women one had IUD, four babies were growth retarded, and two babies were born before term whereas out of 40 normotensive women only five had IUGR, three had preterm delivery and 32 delivered at term without any complications (Table 4)

Discussion

Preeclampsia is a syndrome which develops towards the end of pregnancy. Its pathogenesis is still not clearly defined hence there is no specific diagnostic tests for its prediction. Difference between systolic and diastolic BP in normotensive women and hypertensive women was statistically significant ($p<0.05$). In the present study, eight out of 10 hypertensive patients had b HCG >2.5 MoM ($p<0.001$), six had AFP level > 2.5 MoM ($p<0.001$), five had inhibin A >2.0 MoM ($p<0.001$). Fetal outcome in preeclamptic patients was one IUD, four (40%)IUGR babies, two (20%) preterm and three (30%) term babies as compared to normotensive group in which 32 (80%) were term babies. Similar results were obtained by Gravett et al[1], Gonen et al[2], Cuckle[3] (Table 5). Gonen et al[2] observed that 52% of the babies born to preeclamptic group were of low birth weight whereas 20% normotensives had <2500gm babies. Yaron et al[4] (1999) found that b HCG >2.5 MoM, AFP >2.5 MoM was significantly ($p>0.001$) associated with PIH, preeclampsia, IUGR, preterm delivery and IUD. In accordance with the present study Aquilina et al[5] (2000) also observed that women with inhibin A concentration >2.0 MoM were likely to acquire preeclampsia ($p<0.001$) and low birth weight babies. Thus there was a positive correlation between β HCG, AFP and inhibin A levels and occurrence of preeclampsia. Nearly similar were the observations of Duric et al[6].

In proportion of pregnancies which subsequently developed preeclampsia, maternal serum β HCG, AFP and inhibin A were raised months before the diagnosis. Preeclampsia is a major cause of fetal and maternal morbidity, perinatal mortality and the main cause of maternal mortality. It usually presents clinically towards the end of pregnancy, after the disease process is well established. The new markers provide an opportunity to study the early natural history of disease and possibly to conduct treatment trails.

The present study confirmed the value of second trimester maternal serum AFP, β HCG and inhibin A levels as predictors of pregnancy outcome. Moreover, we evaluated all the three serum markers individually and in combination therefore, allowing the comparison of their specific values as predictors of outcome. Given the significant increase in the risk of adverse pregnancy outcomes associated with abnormal serum marker levels, the clinician should be alerted and steps taken to diagnose some of these complications (eg. preeclampsia, intrauterine growth restriction) as early as possible, because this may prevent some of the associated morbidity and mortality. In the presence of abnormal markers we suggest close monitoring of maternal blood pressure and ultrasonographic follow up of fetal growth patterns, including Doppler velocimetry studies of placental perfusion.

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