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Role of Serum Alphafeto Protein & Beta Human Chorionic Gonadotropin in Patients with Pre-Eclampsia

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Abstract: ***Background:*** ***Preeclampsia remains a major cause of prenatal morbidity and mortality worldwide. Cause of preeclampsia is still ill defined and there is no appropriate test for predicting occurrence of the disorder. This study aimed to assess association between preeclampsia and serum levels of β-human chorionic gonadotropin (β-hCG) and alphafeto-protein (AFP).*** ***Method:*** ***The study had cross-sectional design and carried out on 500 pregnant women admitted to R.N.T. Medical college, Udaipur. Subjects were divided into 3 groups normotensive pregnancies, mild preeclampsia and severe pre-eclampcia. The level of β-hCG and AFP were measured using Enzyme-linked lmmunosorbent Assay (ELISA) method and results were analyzed statistically using SPSS version 17. Results:- Out of 500 pregnant women 250 were controlled and 250 were preeclamptic women. Out of 250 preeclampsia women 200 were mild preeclampsia and 50 were severe pre-eclampsia. Maternal serum of β-hCG and AFP were markedly raised in pre-eclampsia in comparision to controlled and paralled with the severity of preeclampsia. Conclusion: A significant positive correlation between second trimester serum markers and developed of pre-eclampsia was observed . β-hCG and AFP may be good indicator for severe pre-eclampsia but it is not suitable for early diagnosis of the disease. Performing more studies in this field is recommended to confirm this hypothesis.***

Keywords: Alphafeto-protein, β-human chorionic gonadotropin, pre-eclampcia

1. Introduction

Pre-eclampsia is a multisystem disorder of unknown etiology with hypertension, proteinuria and/or edema which predisposes to potentially lethal complications such as eclampsia, abruption-placenta, acute renal failure, cerebral hemorrhage and circulatory collapse. Approximately 7 to 10% of all pregnancies are complicated by hypertensive disease, 70% of which is gestational hypertension pre-eclampsia related and 30% are due to chronic hypertension (Sibai, 2010). Pre-eclampsia is defined as a systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg on 2 occasions at least 4 hrs a part after 20 weeks gestation in women with a previously normal blood pressure or ≥ 160 mm Hg systolic or ≥ 110 mm Hg diastolic, confirmed with in a short interval (minutes) to facilitate timely anti-hypertensive therapy and proteinuria ≥ 300 mg / 24 hrs or a protein / creatinine ratio ≥ 0.3 mg/dl or a dipstick reading of ≥ 1+. In the absence of proteinuria, pre-eclampsia is diagnosed as new onset hypertension with the new onset of any the following : thrombocytopenia, renal insufficiency, or cerebral or visual systoms. (ACOG, 2013) AFP is a glycoprotein produced by the fetal liver and gastrointestinal tract. Its level is raised due to functional alteration of trophoblastic cells, leading to increased leakege, as trophoblastic dysfunction is the primary problem in pre-eclampsia (Dayal M, 2011). It has been suggested that maternal serum alpho-fetoprotein (MSAFP) screening, apart from identifying fetuses with open neural tube defects and chromosomal abnormalities, could also identify pregnancies at high risk of adverse outcomes (Seppala M, 1973). The human chorionic gonadotropin (hCG) is a glycoprotein composed of two non-covalently linked subunits, α and β, and is produced by syncytiotrophoblast cells of the placenta. Maternal serum hCG peaks at 8-10 wk of gestation and then declines to reach a plateau at 18-20 wk of gestation. The free β-subunit can derive from three sources, namely, direct trophoblast cell production, dissociation of hCG into free α and free β subunits, and by macrophage or neutrophil enzymes nicking the hCG molecule (Cole LA et al 1993). The free β-hCG circulating in maternal serum corresponds to only about 0.3 – 4% of the total hCG (Spencer K 1991). The normal placenta differentiates during pregnancy with the cytotrophoblast dominant in early gestation and the syncytiotrophoblast dominant in late pregnancy. Placental vascular damage leading to decreased oxygen supply might result in increased hCG production by hyperplasic cytotrophoblastic cells (Majumdar S et al 2005). The aim of this present study was to find out the role of AFP and β – hCG in pathogenesis of pre-eclampsia and its association with severity of pre-eclampsia.

2. Material and Methods

The present study was conducted at the Department of obstetrics and gynecology, R.N.T. Medical College, Udaipur, after taking approval from ethical committe from 2011 to March 2013. The prospective randomized study was conduction on 500 pregnant women of gestational age between 12-24 weeks with singleton pregnancy. Patients with chronic hypertension, twin pregnancy, molar pregnancy, chromosomally abnormal fetus, diabetes, chronic renal diseases, autoimmune disorders, cardiovascular diseases were excluded from the study. A part from routine hematological investigations, estimation of AFP and β-hCG levels in maternal serum were done by ELISA technique. Blood samples were collected with all aseptic precautions. Pre-eclampsia was considered as defined by American college of Obstetrics and Gynecologists (ACOG, 2013) the systolic blood pressure ≥ 140 mm Hg or ≥ 90 mm Hg diastolic on two occasions at least 4 hrs apart after 20 weeks gestation in women with a preciously normal blood pressure. Severe pre-eclampsia is defined by the systolic blood pressure ≥ 160 mm Hg or diastolic ≥ 110 mm Hg on 2 occasions 4 hours or more apart while the patient is bed rest. Statistical analyses were performed with SPSS software. The

difference of pregnancy out comes among the control, mild pre-eclampsia, and severe pre-eclampsia groups were carried out with ANOVA, student's t–test. P value < 0.05 was considered statistically significant.

3. Result

Table 1: Distribution of various groups of subjects according to severity:

Sr. No.	Group studies	Number of subjects (N)
1.	Healthy pregnant women (controls)	250
2.	Pre-eclamptic primigravidas (Mild)	200
3	Pre-eclamptic primigravidas (Severe)	50
Total		500

Table 2: Demographic characteristics of normal pregnancy and pre -eclampsia cases

Sr. No.	*Parameters*	*Normal Pregnancy (N = 250)*	*Mild Pre – eclampsia (N = 200)*	*Severe Pre-eclampsia (N = 50)*	*P-Value*
1.	Means gestational age (weeks)	20.20 ± 2.25	22.42 ± 3.25	21.30 ± 2.90	> 0.05
2.	Mean maternal age (years)	20.58 ± 2.30	23.2 ± 3.10	21.80 ± 2.90	> 0.050
3.	Mean systolic blood pressure (mm Hg)	114.25± 7.42	156.24± 7.90	183.86 ± 8.24	< 0.001
4.	Mean diastolic blood pressure (mm Hg)	76.61 ± 8.67	99.51 ± 4.87	113.06 ± 5.11	< 0.001

Table 3: Laboratory data of normal pregnancy, mild and severe pre-eclampsia :

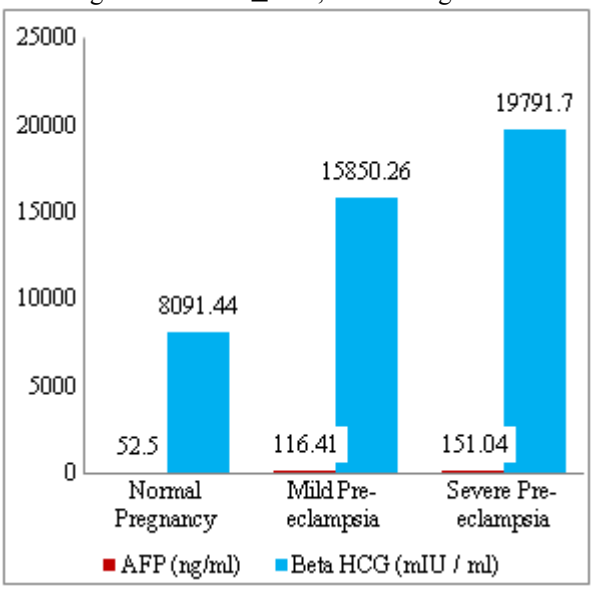
Sr. No.	Parameters	Normal Pregnancy (N = 250)	Mild Pre- eclampsia (N = 200)	Severe Pre-eclampsia (N = 50)	P- Value
1.	Urea (mg/dl)	15.50 ± 2.59	24.52 ± 3.99	35.46 ± 4.94	< 0.001
2.	Creatinine (mg/dl)	0.74 ± 0.14	0.83 ± 0.07	1.46 ± 0.27	< 0.001
3.	Uric acid (mg/dl)	4.85 ± 1.31	5.83 ± 1.00	7.60 ± 0.77	< 0.001

Graph 1: Laboratory data of normal pregnancy, mild and severe pre-eclampsia :

Table 4: Comparison of β- hCG and AFP levels in normal pregnancy, mild and serve Preeclampsia.

Sr. No.	Parameters	Normal Pregnancy (N = 250)	Mild Pre - eclampsia (N = 200)	Severe Preeclampsia (N = 50)	P-Value
1.	AFP (ng / ml)	52.50 ± 15.52	116.41 ± 7.92	151.04 ± 7.2	< 0.001
2.	β-hCG (mIU/ ml)	8091.44 ±1493.68	15850.26 ± 17839.53	19791.70 ± 987.02	< 0.001

Values are given as mean ± SD ,P < 0.05 significant



Graph 2: Comparison of β-hCG and AFP levels in normal pregnancy, mild and serve Preeclampsia.

Distribution of various group of subjects according to severity are shown in table 1. (i) mild pre-eclampsia cases of those who showed ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic one 2 occasions at least 4 hrs apart after 20 wks gestation in women with a previously normal blood pressure. (ii) Severe pre-eclampsia cases of those who showed ≥ 160 mm Hg systolic or ≥ 110 mm Hg diastolic, on 2 occasions 4 hours or more apart while the patient is an bed rest. (ACOG, 2013) Out if 250 pre-eclampsia and 200 were mild pre-eclampsia and 50 were severe pre-eclampsia. The clinical results of mild and severe pre-eclampsia patients were compared (Table 2 & Table 3). Demographic data of women with preeclampsia and healthy normotensive controls are shown in Table 2. No significant difference were observed in terms of gestational age & maternal age when compared normotensive controls and pre-eclampsia groups. Systolic and diastolic blood pressure were significantly increased in mild and severe (P < 0.001) pre-eclampsia women, when compared with normotensive controls. The levels of urea, creatinine and uric acid were found to be significantly increased in severe preeclampsia women (Table – 3). AFP & β-hCG levels were significantly higher in mild & severe (P < 0.001) pre-eclamptic women, when compared with normotensive controls. (Table – 4).

4. Discussion

In pre-eclampsia the rise of blood pressure is due to vasoconstriction and impaired angiogenesis leading to hypoxia and hyperplasia of trophoblastic cells which causes hypersecretion of placental hormone ultimately leading to high level of circulating β– hCG. In this study, we found that serum β– hCG levels were significantly elevated in severe preclampsia, compared with the centrols. This finding indicates that an abnormal secretory function exists in patients with severe preeclampsia. In preeclampsia, placental pathologic examination reveals focal cellular necrosis in the syncytiotrophoblast and increased mitotic activity with cellular proliferation in the cytotrophoblast (Jones CJP 1980). In addition, the proliferating cytotrophoblast in severe pre–eclampsia is rapidly transformed into syncytio-

trophoblast with in 72 hours (Hoshina, 1982). The normal placenta differentiates during pregnancy with the cytotrophoblast dominate in late pregnancy (Enders AC 1965). It is well known that the cytotrophoblast is an undifferentiated stem cell and the syncytotrophoblast is a differentiated trophoblast transformed from the cytotrophoblast (Kliman HJ, 1987). In 1934, Smith et al talked about increasing hCG levels in severe preeclampsia for the first time. Luckas M (1998), Benn PA (1996) & Ashour AM (1997) indicate that an unexplained elevation of serum hCG significantly correlated with the occurrence of preeclampsia. By contract pouta et al and Aguilina et al demonstrated no relation between levels of serum hCG and severity of pre – eclampsia .Stamilio et al also found no association between severe preeclampsia and elevated second trimester hCG levels. Alpha – feto protein (AFP) is produced in the fetal liver and yalksac, and secreted into the fetal circulation and amniotic fluid, passed into the maternal circulation via the placenta and its concentration is 100 fold increase in the first trimester of pregnancy compared with non pregnant women. In our study, unexplained high levels of MSAFP have been associated with pre – eclampsia. Our findings are consistent with the study by Tikkanen et al (2007), Waller et al (1996) and Willaims et al (1992) about the correlation of pre – eclampsia and MSAFP, while Khoo's study (1978) showed, in preeclampsia women; significantly lower mean AFP values were obtained. Raly et al also found the AFP values in the severe pre – eclampsia group differed significantly from all other groups. Brazerol et al (1999) reported that the explanation for the association between elevated maternal serum alphafeto protein and adverse pregnancy outcome is not clear, but is probably a marker of placental dysfunction, including partial placental abruption, feto maternal bleeding and abnormal implantation.

5. Conclusion

Pre-eclampsia remains a major cause of perinatal morbidity worldwide. Exact etiology is still not defined. It usually presents clinically toward 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 elevated levels of AFP and β-hCG_are associated with pre-eclampsia in second trimester.

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