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Significance of β- human chorionic gonadotropin in pre eclampsia and normotensive mothers

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Abstract
Objective: Preeclampsia is most commoniy encountered problem in pregnancy. The aim of the present study was to assess the levels of beta HCG in preeclampsia and normal women without hypertension.
Method: This was a prospective case control study undertaken on 25 preeclamptic patients and 25 healthy antenatal women in OB-GYN Department of Rajah Muthiah Medical College, Annamalai University between the periods of 2016-2018.
Result: The mean maternal serum β-human chorionic gonadotropin levels in preeclampsia were 44463.26±30595.25miu/ml that is significantly greater than normotensives (7346.200±4479.0855 of p value< 0.001). The number of complications in the preeclampsia group are increased than the normal antenatal women group.
Conclusion: Mean βhcg levels tend to be significantly more in preeclampsia than healthy pregnant mothers. The higher β hcg levels associated with more neonatal and maternal complications.

Keywords: Gonadotropin, Preeclampsia, normotensive, eclampsia, hCG

Introduction

Pregnancy associated hypertensive disorder is known to affect neonatal and maternal outcomes [1, 2] Nearly 8% of pregnancies in India are affected and it is considered to be the most common cause of IUGR, perinatal morbidity and mortality [3, 4, 5]. There are multitudes of hypothesis postulated to understand the mechanism of pregnancy induced hypertension which all points towards early placental abnormalities. Human placenta synthesis protein, steroids, and glycoprotein hormones throughout the pregnancy and it is been proclaimed as a disorder of trophoblastic cells [6, 7, 8]. Despite major researches, still it is not clearly understood and explained. Human chorionic gonadotrophin is one among the several biomarkers that has been studied in implicating the causal association of preeclampsia. It is well known that multiple gestation and molar pregnancies have more incidence of pregnancy associated hypertension and pre-eclampsia than normal single ton pregnancies because of higher serum levels of β-human chorionic gonadotrophin (hCG) [9]. An link between pre-eclampsia and elevated third trimester β-HCG levels was also reported [10].

The human chorionic gonadotropin (hCG), synthesized from syncytiotrophoblastic cells of placenta, is a glycoprotein made up of two non covalently linked subunits, α and β. It peaks in the maternal serum by 8-10 wks of GA and then slowly decreases to reach a plateau at 18-20 weeks of gestation. The free β-subunit is produced from 3 sources namely, direct trophoblast cell secretion, splitting of hCG into free α- and free β-subunits, and by macrophage or neutrophil enzymes breaking the hCG molecules. The circulating level of free β-hCG level maternal serum corresponds to only about 0.3-4% of the total hCG.

Histological examination of placenta in preeclamptic cases reveal focal cellular necrosis in the syncytiotrophoblast and increased mitosis so there will be increased proliferation of cells in the cytotrophoblast. In addition, the proliferating trophoblastic cells in severe preeclampsia is changed rapidly into syncytiotrophoblastic cells within 72 hours. The normal placenta during pregnancy contains dominance of cytotrophoblastic cells in early weeks of gestation and the syncytiotrophoblastic cells in late trimester. Vascular damage in placenta causes reduced oxygen supply which leads to more hCG secretion by hyperplastic cytotrophoblastic cells.

The current study is conducted.

1. To study the serum β HCG levels in antenatal mother with preeclampsia and eclampsia complicating pregnancy (Group A) and healthy antenatal mother without any complications (Group B).

2. To find out the association between preeclampsia and selected risk factors.
3. To find out the association between preeclampsia and selected outcomes

Materials and methods

Study Design: prospective case control study.

Study Area: IP ward of OBS and Gynaec Department of Rajah Muthiah medical college and hospital, Annamalai University, Chidambaram, Tamilnadu.

Study Population: Antenatal mothers of 18-35 years os age between 34-38 weeks of gestation with preeclampsia and the patients without hypertension.

Exclusion Criteria: Pregnant females with chronic hypertension, GDM, Multifetal gestation, anemia, previous H/O pre-eclampsia, family H/O hypertension, presence of other medical disorders(kidney diseases, thyroid disorders, tuberculosis.

Cases included 25 antenatal women between 34-38 weeks with preeclampsia complicating pregnancy consenting for study. Controls included were antenatal women between 34-38 weeks gestation with normal range of BP consenting for study.

Data was collected using a semi-structured interview schedule which included the variables of the study. The height and weight of the people were measured and BMI was calculated using the formula.

BMI= wt in kgs/ht (mt^2).

2ml of blood was collected and sent to laboratory to quantify beta HCG by Chemo luminescent Micro practical Immunoassay (CIMA) and it will be compared in two groups. The study people were then followed till the outcome of their pregnancy and variables like birth weight, APGAR score were recorded.

All the data collected were entered into Microsoft excel spreadsheet and analysed using SSPS version 20. Both descriptive and inferential statistics were applied. In case of quantitative variables independent t test was applied. In case of qualitative variables Chi square test was applied. For correlation between β-human chorionic gonadotropin and BP, spearman's correlation was applied.

Results

Table 1: Comparison of demographic table between the two group variables

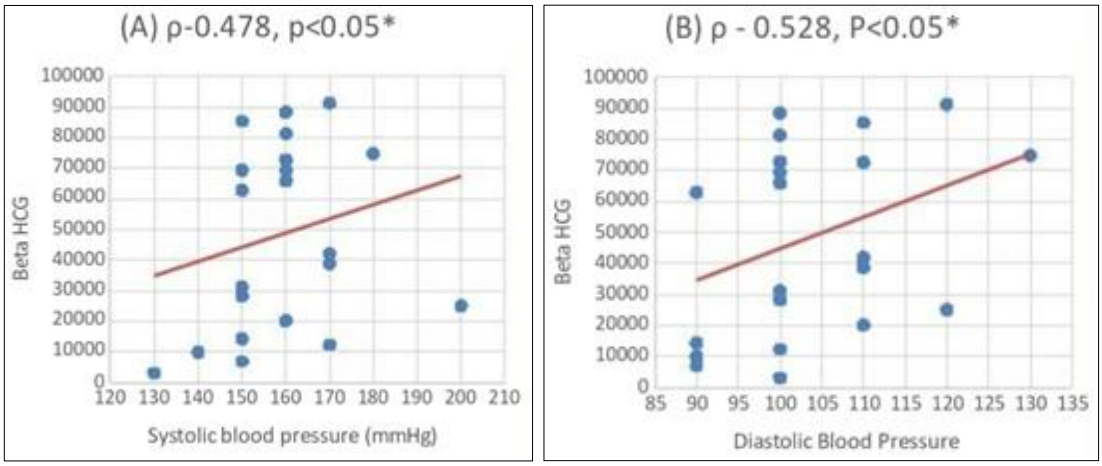
Variables	Group	N	Mean	Std. Deviation	t value	p value
AGE	A	25	25.12	4.295	1.457	0.152
	B	25	23.68	2.445		
BMI	A	25	25.3204	2.21557	0.414	0.680
	B	25	25.0936	1.60626		
GA(days)	A	25	255.1200	10.69782	2.703	0.009
	B	25	265.4000	15.72419		

25 preeclamptic mother were recruited as cases and 25 pregnant mothers without preeclampsia were taken as controls. No significant difference with respect to age between the two groups, with mean age in group A and B being 25.12 and 23.68 years, respectively (p=0.152). In terms of BMI both groups were similar with mean BMI in case and control groups being 25.32 and 25.09 respectively (p=0.414). Gestational age of the preeclamptic cases were lesser than the controls and the difference was significant statistically. (Table 1).

Table 2: Comparison of beta hcg and blood pressure among the cases

	Group	N	Mean	Std. Deviation	t value	p value
SBP	A	25	157.60	14.224	16.448	<0.001
	B	25	108.00	5.000		
DBP	A	25	102.40	10.520	13.479	<0.001
	B	25	69.20	6.403		
BETA HCG	A	25	44463.260	30595.2524	6.002	<0.001
	B	25	7346.200	4479.0855		

The mean maternal serum β-human chorionic gonadotropin levels in preeclampsia were 44463.26±30595.25 miu/ml that is significantly greater than the pregnant women without preeclampsia (7346.200±4479.0855 of p value < 0.001). The minimum value of beta HCG level in preeclamptic patients was 3087MIU/ml and the maximum value 91374MIU/ml. Also the lowest value of beta HCG in controls was 2345MIU/ml and upper limit values was 22784MIU/ml.



*Spearman correlation was applied.

Fig 1: Correlation among the cases.
A. Systolic blood pressure and beta-HCG
B. Diastolic blood pressure ABD beta-HCG.

When correlated between Beta HCG, systolic and diastolic BP among the preeclampsia group, the beta HCG levels was seen to raise with increase in systolic or diastolic BP and is found to be statistically significant.

Table 3: Comparison of type of delivery and neonatal complications between the two groups.

Parameters	Group A	Group B	P Value
Type of delivery			
a. Vaginal	5 (20)	12 (48)	0.029
b. LSCS	20(80)	13(52)	
Birth Weight In KGS	2.2804±0.55	2.7800±0.41	0.001
Apgar Score			
At 1 min	4.80±1.780	6.20±0.764	0.001
At 5 min	6.40±1.826	7.40±0.764	0.015
	N%	N%	
IUGR	85.7%	14.3%	0.002

The percentage of LSCS were higher in Preecclamptic women(80%) and vaginal deliveries were more in normal pregnant women (48%) which is statistically significant of p value 0.029. This indicates that there were more operative deliveries in preeclamptic women (Table 3).

The mean birth weight (2.2804±0.55 Kgs) was lower than normal antenatal women (2.7800±0.41kgs). The mean APGAR score were significantly reduced at 1 min and 5minutes in this study. The percentage of IUGR was also more in preeclamptic groups (85.7%) than normal antenatal women (Table 5).

Discussion

In gestational hypertension the rise of blood pressure is due to constriction of blood vessels and angiogenesis was impaired which leads to hypoxia and hyperplasia of trophoblastic cells which causes increased production of placental hormone ultimately leading to more level of circulating β-HCG. As pre-eclampsia is a disorder of trophoblastic cells, elevated β-HCG is thought to cause early placental damage or dysfunction. Zygmunt *et al* (2002) stated that HCG may play an important regulatory role in angiogenesis and vasculogenesis of placenta. In the current study mean age for preeclampsia was 25.12±4.295 years and for normotensive patients it was 23.68±2.44 years which was statistically not significant, similar to sumithra yadav *et al*. In our study there was no significant difference in BMI between the both groups and the same was also reported in the K. Yousefnejad *et al*. [11] study.

Also in K.Yousefnejad *et al* study, there was no difference between two groups in gestational age, but in this study that there is statistically significant difference in preeclamptic and normal antenatal women of mean gestational age in days are 255.12±10.69 and 265.400±15.72 respectively. This could be one of the reason why pre eclampsia is referred earlier to a tertiary care center and hence can belong to a lesser gestational age than controls.

Study by Dayal Meena, Gupta Paru [12] showed high levels of β human chorionic gonadotropin in preeclamptic cases 16,130.2 (2.5 MoM) than normal pregnant group with β HCG level 4,621.8 (0.95MoM) with p-value <.001. In our study, the mean maternal serum beta HCG levels in preeclampsia were 44463.26±30595.25 miu/ml that is significantly greater than the normal antenatal mothers (7346.200±4479.0855 of p value< 0.001). Casart *et al*. [13] showed beta HCG level in 30 pre-eclampsia cases in their 3rd trimester and 30 antenatal women with normal BP, which showed greater level of β HCG values in preeclampsia. Similar to this study, findings in our study revealed that beta HCG level in preecampsia was more than the controls and this difference is statistically significant. (p<0.001).

Data from lambert's *et al* reviewed that beta HCG in preeclamptic cases are more than healthy antenatal women and this difference was more in severe and moderate preeclampsia. In the lambert's study, there was no significant difference between mild preeclampsia and controls. In the present study, the pre eclampsia could not be categorized into mild, moderate and severe. Heikkida *et al*. [14] also showed that an elevated maternal serum beta HCG concentration is a marker of early onset and severe disease with significant maternal and neonatal morbidity. Similar to this study, in our study 1min and 5 min

Apgar reduced and percentage of IUGR are more, when beta HCG values raised in preeclamptic cases. Also maternal adverse effects such as eclampsia, abruption are also high when beta HCG levels increased in preeclamptic patients.

The purpose of the present study was to find out the beta HCG levels between the preeclampsia and eclampsia group and normal pregnant women without hypertension and later followed up to find the outcomes. Sub-group analysis was not feasible due to smaller sample size.

Conclusion

Mean beta HCG levels tend to be significantly higher in preeclampsia than normal antenatal mother. Similarly adverse outcomes were more among antenatal women suffering from preeclampsia than the normal antenatal women. Beta HCG levels could act as a predictor for both preeclampsia and its complications. More research should be done focussing on the above hypothesis and a robust cohort study design would aid in producing more valid result.

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