Original Article

PROGNOSTIC ACCURACY OF β HCG LEVEL IN PREDICTING PREGNANCY OUTCOMES AMONG PRE-ECLAMPTIC PATIENTS AT THE FEDERAL MEDICAL CENTRE, YENAGOA.

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Abstract

Background: Serum beta human chorionic gonadotropin (β hCG) is one of the placental peptides that have been associated with the severity of preeclampsia.

Objective: To evaluate the accuracy of quantitative serum beta hCG as prognostic indicator of pregnancy outcome among preeclamptic patients at the Federal Medical Centre, Yenagoa.

Materials and Methods: This is a hospital based prospective case control study where one hundred patients with preeclampsia (who satisfied the inclusion criteria) were recruited consecutively as they were admitted into the antenatal or labour ward. One hundred non preeclamptic patients were also recruited as control. Foetomaternal data were recorded into a protocol. Adverse perinatal outcomes such as IUGR, IUFD and Birth Asphyxia were also recorded into the protocol. Levels of maternal quantitative serum beta human chorionic gonadotropin as well as complications of the disease such as Eclampsia, HELLP syndrome and acute renal failure were also recorded into the protocol.

Data entry and statistical analysis was done using statistical package for social science (SPSS for windows version 22.0 SPSS Inc; Chicago, USA). Student t-test was used to determine association between quantitative variables. Level of significance was set at $P < 0.05$.

Results: The mean age in the study group was 28 ± 6.7 years while in the control group it was 31 ± 6.5 years. The difference in age was not statistically significant (p = 0.53). The mean serum quantitative serum β hCG were significantly higher amongst participants with preeclampsia than in those without preeclampsia (405.6 ± 995µmol/L vs 232.7 ± 26.3 µmol/L, p = 0.00) and (26776.6 ± 19590.5 miu/ml vs 7973.6 ± 4193.7 miu/ml, p < 0.00) respectively. β hCG was statistically associated with the occurrence of Eclampsia (p = 0.01), Severe Hypertension (p = 0.01), IUGR (P = 0.01) and Birth Asphyxia (P = 0.05). The prognostic accuracy of serum β hCG in predicting pregnancy outcomes were: HELLP syndrome (0.25, 0.33, 0.44) Eclampsia (0.13, 0.39, 0.50), Acute Renal Failure (0.33), IUGR (0.39), IUFD (0.27) and Birth Asphyxia (0.38).

Conclusion: The mean quantitative serum β hCG was higher amongst participants with preeclampsia than in those without preeclampsia. Serum β hCG level was found to be a useful prognostic indicator for foetomaternal outcome in women with preeclampsia. While its use is relevant in our locality, further studies of other serum markers is recommended.

Keywords: Pre-eclampsia, B hCG, Prognostic marker, Pregnancy outcome, Yenagoa.

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INTRODUCTION

Preeclampsia has remained a significant socio-economic, cultural and public health burden in the developing countries, though lesser threat in the developed countries.[1] It stands as one of the leading causes of maternal and perinatal morbidity and mortality in the developing world.[1] Approximately 37,000 women die annually because of preeclampsia and its related complications. Perinatal mortality rate of 5.84 per 1,000 births has been attributed to severe preeclampsia/eclampsia, hence its significant contribution to perinatal mortality in our environment.[2]

Preeclampsia is a pregnancy specific disease characterized by hypertension and proteinuria arising de novo after the 20th week of gestation in a previously normotensive and non proteinuric woman.[3] The prevalence of preeclampsia varies significantly worldwide due to its wide variation in epidemiological studies. Estimates of prevalence of preeclampsia by World Health Organisation shows that it is seven times higher in developing countries than in developed countries.[4]

Serum beta human chorionic gonadotropin (β hCG) is one of the placental peptides that have been associated with the severity of preeclampsia. This is alluded to the fact that preeclampsia is characterized by disturbed trophoblastic physiology hence early placental dysfunction could be reflected by altered hCG concentration.[5] The relationship between increasing β hCG levels and severity of preeclampsia was first noted by Smith et al in 1936.[6] Since then numerous studies have suggested that elevated maternal serum β hCG level may be associated with severe preeclampsia.

Preeclampsia is a common problem worldwide and Federal Medical Centre, Yenagoa is no exception. Maternal serum beta human chorionic gonadotropin has been reported to be useful in the prognostication of the disease and may reflect the severity of the condition.[7,8]

The objective of the study is to evaluate the accuracy of quantitative serum beta hCG as prognostic indicator of pregnancy outcome among preeclamptic patients, to compare quantitative serum beta human chorionic gonadotropin levels among preeclamptic and non-preeclamptic patients and to determine the prognostic accuracy of quantitative serum beta human chorionic gonadotropin level in predicting pregnancy outcomes among preeclamptic patients at the Federal Medical Centre, Yenagoa, Bayelsa State, Nigeria.

The ability to detect the mild form of preeclampsia would allow closer surveillance and early intervention to improve outcome.[9] The resultant effect of this study on the subject matter will give room for a well-coordinated planning and interventions that may at least bring about the expected reduction in perinatal and maternal morbidity and mortality in our locality.[1]

MATERIALS AND METHODS

The study was conducted in the Obstetrics and Gynaecology Department of the Federal Medical Centre, Yenagoa, Bayelsa State, Nigeria. The hospital is a tertiary health institution that provides all levels of health care services to patients especially in Bayelsa, Rivers and Delta states. It was a prospective case control study between March 1st 2018 to August 1st 2018. The first group of the study population comprised 100 consecutive Preeclamptic patients admitted for management into the antenatal ward and labour ward of Federal Medical Centre, Yenagoa over the period of the study. The second group (control) of the study population comprised 100 consecutive non-preeclamptic patients admitted for management into the antenatal ward and labour ward. The values of their serum quantitative serum beta hCG were evaluated on admission. Patients were followed up to delivery and their pregnancy outcome evaluated. The study was carried out within 5 months.

Inclusion criteria included all preeclamptic admitted into the antenatal ward and labour ward of Federal Medical Centre, Yenagoa, who consented to be part of the study within the study period.
Controls – (Normal healthy pregnant women) whose serum uric acid level and quantitative serum beta human chorionic gonadotropin were assessed within the same period. Exclusion criteria included patients with chronic hypertension, chronic hypertension with superimposed preeclampsia, pregnancy induced hypertension, renal disease, diabetes mellitus, heart failure and ischaemic heart disease were excluded from the study. Women who refused to give consent were also excluded from the study.

The sample size for the study was calculated using the formula:
$n=z^2pq/d^2$ [10]
n= minimum sample size
z= standard normal deviation set at 95% confidence limit=1.96
p= prevalence of preeclampsia in previous study
q=1-p (complementary probability)
d= margin of error = 5%=0.05
Prevalence of preeclampsia that was used in this study based on a previous study done in Bayelsa state was 5.6%[1]

Therefore;
Therefore, 100 patients who met the inclusion criteria were recruited for this study.
In our centre, about 400 patients register for antenatal care per month and about 5%-10% when followed up to the third trimester are estimated to develop preeclampsia. This study was carried out within 5 months.

Patients were recruited consecutively as they were admitted into the antenatal ward and labour ward with preeclampsia. Thorough history and examination were used in selecting patients based on the inclusion and exclusion criteria. The blood pressure was measured with the use of manual sphygmomanometer while the patient was in supine position on a couch with a left side tilt. An appropriate size cuff that covers at least 2/3rd of the upper arm was used. The systolic blood pressure was taken at the first point the sound was heard while the diastolic blood pressure was taken as Korotkoff V.

A patient was said to be hypertensive when her blood pressure was persistently equal to or greater than 140/90 mmHg measured at least 6 hours apart. Urine collection was done in the antenatal ward and labour ward. Patients were trained and instructed adequately on how to collect clean catch midstream urine. This involved initial cleaning of the vulva with copious amount of clean water. The labia were parted and the first part of the urine was voided and the next stream of urine (about 5 millilitres) was collected into a clean, dry urine bottle with patient's name and number written on it. Trained nurses were recruited to supervise the process. The urine specimen was taken to the laboratory for protein estimation using dipstick.

Permission was obtained from the Head of Department, Chemical Pathology of the Federal Medical Centre, Yenagoa, one staff was trained on the objective and protocol of the study. Protein estimation was based on the colour changes of the dipstick compared to the corresponding colour chart on the reagent container. The diagnosis of proteinuria was made when two midstream samples of urine collected at least four hours apart showed one or more plus of albumin using dipstick and in suspicious cases, urine microscopy, culture and sensitivity was done to exclude urinary tract infection. For the diagnosis and classification of preeclampsia, Davey and McGillivray's classification adopted by the International Society for the Study of Hypertension in pregnancy (ISSH) was used.

Patients that met the criteria for preeclampsia were recruited into the study. Once the diagnosis was confirmed, a blood specimen was collected from the patient under aseptic conditions. Urine specimen and blood specimen were also collected from normal non preeclamptic (healthy pregnant women) as controls.

The laboratory work was done in the Department of Chemical Pathology of the Federal Medical Centre, Yenagoa. Permission was obtained from the Head of department. Three staff were trained on the objective and protocol of the study. All patients who met the inclusion criteria were properly counselled and consent obtained from them. Five millilitres of blood were collected from their cubital vein using a sterile needle and a syringe into a plane specimen bottle. Serum was separated by centrifugation for ten minutes at 3,500 rpm. The supernatant was transferred by Pasteur pipette into a test tube for immediate analysis or stored at 2-8 ℃ until time of analysis usually within 24 hours.

Socio-demographic data and clinical characteristics such as age, tribe, marital and booking status was obtained and recorded in the protocol. In addition, the gestational age at delivery, birth weight, 5-minute Apgar scores and admission to special care baby unit was noted. Adverse perinatal outcomes like Intrauterine growth restriction (IUGR), Birth Asphyxia and Intrauterine foetal death (IUFD) were also noted. Mothers admitted into intensive care unit were followed up and their outcomes recorded. Maternal adverse outcomes such as Eclampsia, Acute renal failure and HELLP syndrome were also noted. The blood samples were sent to the laboratory for analysis.

DATA ANALYSIS

Data entry and statistical analysis was done using statistical package for social science (SPSS for windows version 22.0. SPSS Inc; Chicago, USA). Percentages, means and standard deviations were calculated. Chi-square was used to determine association between qualitative variables. Student t-test was used to determine association between quantitative variables. Level of significance was set at

P < 0.05. Tables were used to illustrate patterns of variables. Sensitivity, specificity, predictive values and accuracy were calculated for the serum markers in relation to foetal and maternal outcomes of women who had preeclampsia.

RESULTS

One hundred preeclamptic women (study group) and one hundred non preeclamptic women (control group) were recruited for this study. The predominant age group in both the study group and the control group was 25 - 34 years age group with 52 (52.0%) and 56 (56.0%) respectively. It was followed closely by the age group 16 – 24 years with 34 (34.0%) in the study group and in the control group, age group 35 – 44 with 30 (30.0%). The mean age in the study group was 28 ± 6.7 years, while in the control it was 31 ± 6.5 years. The difference in age between the groups was not statistically significant (p = 0.53).

Primipaternity was a known risk factor for preeclampsia and the difference between groups was statistically significant (p = 0.00) as 69% (69/100) the cases were pregnant for their partners for the first time as against 45% (45/100) for the control group.

Most 98 (98.0%) and 100 (100.0%) of the patients in the study group and control group respectively were in their 3rd trimester of pregnancy (7 – 9 months). Majority 42 (42.0%) of the urinalysis with dipstick (protein) result in the study group was +2. It was closely followed by 34 (34.0%) of patients with +3 results. Only 24 (24.0%) had a +1 results. Only 3 (3%) of the patients in the control group had proteinuria. Thirty-five (35.0%) of patients of the study group had a positive family history of pregnancy induced hypertension (PIH). Sixty-five (65.0%) did not have any family history of PIH. While in the control group, 7% had a positive family history of PIH. Amongst those that have positive family history of PIH in the study group, 15 (42.9%) said their sisters and they themselves has had PIH in the past, while 5 (14.3%) said their mothers have had PIH previously. In the study group and control group, 28 (28.0%) and 48 (48.0%) respectively has had a previous pregnancy. Amongst those that have had a previous pregnancy in the study group, 24 (85.7%) carried their pregnancy to term, while, 3 (10.7%) had miscarriages, and 1 (3.6%) had ectopic pregnancy. Amongst those that have had a previous pregnancy in the control group, 35 (72.9%) carried their pregnancy to term, while 11 (22.9%) had miscarriages, and 2 (4.2%) had ectopic pregnancy.

Table 1: Laboratory data of study group (preeclamptic) and control (normal).

Variable	Study group		Control	
	Mean + SD	Range	Mean + SD	Range
β-hCG mUI/ml	26776.6 ±19590.5	(2827 - 131510)	7973.6 ± 4193.7	(113 - 14778)

Table 1 shows a mean β-hCG of 26776.6, standard deviation of 19590.5 and a range of 2827 – 131510 in the study group (pre-eclamptic) and a mean β-hCG of 7973.6, standard deviation of 4193.7 with a range of 113 – 14778 in the control group.

Table 2: Differences in Laboratory data of study group (pre-eclamptic) and control.

Variable	Study group	Control		
	Mean + SD	Mean + SD	t test	p value
β-hCG (mIU/ml)	26776.6 ± 19590.5	7973.6 ± 4193.7	12.4	0.001

Table 2 shows statistical significance of the β-hCG level (p = 0.001) of the study group (pre-eclamptic compared to the control group.

Table 3: Relationship between biochemical risk factors and maternal/foetal complications in preeclamptic participants

RISK	COMPLICATIONS						
HIGH SERUM B-HCG LEVEL n=62	HELLP n (%)	ECLAMPSIA n (%)	ARF n (%)	IUGR n (%)	IUFD n (%)	BIRTH ASPHYXIA n (%)	SEVERE HTN n(%)
PRESENT	3 (4.8)	11 (17.7)	4 (6.45)	9 (14.5)	2 (3.22)	15 (24.4)	32 (51.6)
ABSENT	59 (95.2)	51 (82.3)	58 (93.55)	53 (85.5)	60 (96.8)	47(75.6)	30(48.4)
P VALUE	P=0.11	P=0.01*	P=0.19	P=0.01*	P=0.44	P=0.005*	P=0.001*

Table 3 shows that amongst those with elevated serum β hCG levels; 4.83 % (3/62) had HELLP syndrome. This association was not statistically significant (p = 0.11); 17.7% (11/62) suffered eclampsia. This association was statistically significant (p = 0.01); 6.45% (4/62) suffered acute renal failure. This association was not statistically significant (p = 0.19); 51.61% (32/62) had severe hypertension. This association was statistically significant (p = 0.01); 14.5% (9/62) had babies who suffered IUGR. This association was statistically significant (p = 0.01); 3.22% (2/62) suffered IUFD. This association was not statistically significant (p = 0.44); 24.4% (15/62) had babies who suffered birth asphyxia. This association was statistically significant (p = 0.005).

Table 4: Prognostic Accuracy Scoring of serum B-HCG

Pregnancy outcome/ Serum marker	Sensitivity	Specificity	PPV	NPV	Accuracy
Severe HTN	80	70	91.42	46.47	0.78
HELLP	100	30.92	9.09	100	0.33
ECLAMPSIA	84.61	32.18	28.21	93.33	0.39
ACUTE RENAL FAILURE	80	30.52	5.71	96.67	0.33
IUGR	90.91	32.58	14.29	96.67	0.39
IUFD	28.57	26.88	7.41	83.33	0.27
BIRTH ASPHYXIA	76.19	29.33	23.19	81.48	0.38

Table 4 shows the prognostic accuracy of serum β-hCG for pregnancy outcome. It's more accurate for severe HTN (0.78), Eclampsia (0.39), IUGR (0.39) and birth asphyxia (0.38).

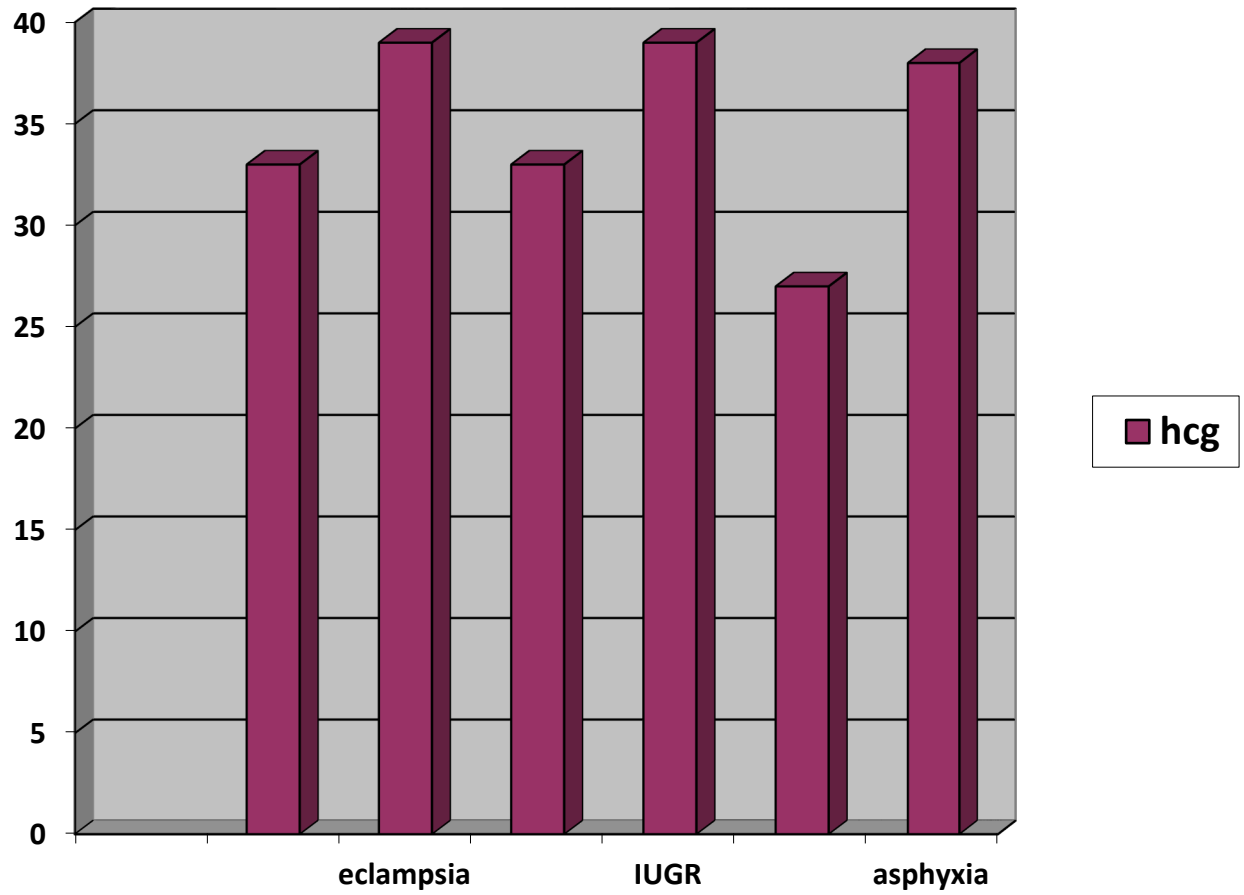

Figure 1: Bar chart showing the accuracy of serum B hCG in predicting adverse pregnancy outcome. The accuracy is highest for eclampsia, IUGR and Asphyxia.

DISCUSSION

In this study, the mean age of cases and controls were 28 ± 6.7 and 31± 6.5 respectively. The mean age of cases is higher than 27± 4.9 and 27.2± 5.6 years reported in Calabar by Kooffrey et al[11] in 2014 and Ogun Sotunsa et al[12] in 2016 respectively. The results from this study are consistent with the usual risk factors for preeclampsia including primipaternity and family history of preeclampsia.[13, 14] Primipaternity was more common in the study group (70%) than in the control group (45%) with the difference being statistically significant (p = 0.00). This is in keeping with theories surrounding the origins of preeclampsia identifying pregnancy by a new spouse or partner as a risk factor for the condition.[13, 14]

More women in the study group (35%) as compared to the control group (7%) had a family history of hypertensive disease in pregnancy. Genetic factors have been implicated in the development of preeclampsia. Daughters of women with preeclampsia are about four times more likely to develop the disease than daughter in-laws and it has been established that it is familial.[13, 15]

The mean quantitative serum β hCG level amongst the subjects (26776.6 ± 19590.5) was statistically significantly higher (p < 0.001) than the mean quantitative serum β hCG level amongst the control (7973.6 ± 4193.7). The higher serum β hCG levels noted in the study population is in keeping with findings from other studies.[8,16,17] No client with multiple gestation or molar gestation was recruited to be a part of this study and as such it is unlikely that these would have affected the outcome of the study.

The association between serum β hCG levels and eclampsia (p =0.00) as well as HELLP (p = 0.04) were found to be statistically significant. However, the association with acute renal failure did not achieve statistical significance (p = 0.05). Serum β hCG levels had a statistically significant association with IUGR (p =0.00) and birth asphyxia (p = 0.00). There was no association between serum β HCG and IUFD (p =

0.05). Estimation of serum β hCG has been used as a marker to determine normal and abnormal pregnancy outcomes and has been found to be associated with severe pre-eclampsia.[8,16,18] The severity of preeclampsia may be determined by clinical features or abnormal laboratory parameters.[14] The adverse pregnancy outcomes in this study are considered as features of severe preeclampsia.

CONCLUSION

The mean quantitative serum β hCG was higher amongst participants with preeclampsia than in those without preeclampsia. Serum β hCG level was found to be a useful prognostic indicator for foetomaternal outcome in women with preeclampsia. While its use is relevant in our locality, further studies of other serum markers is recommended.

LIMITATION

This was a hospital-based study. The results may not reflect the findings in other tertiary institutions in Nigeria or the West African sub-region.

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CONFLIT OF INTEREST

The authors declare that there are no conflicts of interest.

AUTHORS' CONTRIBUTIONS

Author 1 designed the study, performed the statistical analysis, wrote the protocol, managed literature searches and wrote the first draft of the manuscript. Authors 2, 3 and 4 reviewed and managed the analyses of the study. Author 5 carried out the laboratory investigations. Authors 6 and 7 participated in literature searches. All authors read and approved the final manuscript.

CONSENT

Written informed consent was obtained from every patient that participated in the research.

ETHICAL APPROVAL

The research work was examined and approved by the hospital research and ethics committee.

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