CERVICOVAGINAL FLUID BETA HUMAN CHORIONICGONADOTROPIN ASSAY AS AN EARLY PREDICTOR OF SPONTANEOUS PRETERM DELIVERY AMONG ANTENATAL PATIENTS

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ABSTRACT
Background: *The aim of this study was to assess the usefulness of the beta subunit of beta hCG in cervicovaginal secretions as a biochemical predictor of spontaneous preterm delivery among pregnant women with and without preterm delivery risk.*

Methodology: *This was an eight-month prospective case control study of pregnant women with or without risk factors for preterm delivery. The study was carried out at Ifako- Ijaiye General Hospital Lagos/ Lagos State University Teaching Hospital, Ikeja Lagos Nigeria. One hundred and fifty pregnant women which consisted of 50 cases with preterm delivery risk and 100 controls without preterm delivery risk were recruited as participants. A structured interviewer administered questionnaire which had been pretested, was used to collect data. Two cervicovaginal fluid samples at 26 weeks and 32 weeks were collected from each of the participants and it was quantitatively assayed using ELISA for presence of beta hCG. The participants were followed up till delivery.*

Results: *Fifteen participants out of the 50 cases delivered their babies preterm, while only 2 participants out of the 100 controls had preterm delivery. The 15 cases who delivered preterm had significant increase in their mean beta HCG value from 7.44±1.74 at 26 weeks to 32.6±1.32 at 32 weeks with p value<0.001. There was however no statistical difference in the mean beta HCG at 26 weeks and at 32 weeks for the control group.*

Conclusion*: The concentration of beta HCG in the cervicovaginal fluid is a useful early predictor of preterm delivery especially among patients with risk factors.*

Keywords*: Preterm delivery, risk factors, cervicovaginal fluid, quantitative assay, Nigeria*

INTRODUCTION

Preterm birth, according to the World Health Organization (WHO) is defined as child- birth occurring at less than 37 completed weeks or 259 days of gestation.[1] Preterm birth has been further sub categorized into; extremely preterm (less than 28 weeks of gestation), very preterm (28 to 31 weeks of gestation) and moderate to late preterm (32 to 36 weeks of gestation). The lower the gestational age in

weeks the higher the incidence of neonatal morbidity and mortality.

Preterm babies account for 5-25% of all deliveries and up to 75% of perinatal mortality[2]. Every year, an estimated 15 million babies are born preterm, (that is more than 1 in 10 babies), and more than 60% of these births occur in Africa and South Asia[1.] The average incidence is 9.7% in USA, 11% overall in North America and 5.4% in Europe. In Africa, incidence rate varies from 20.3% in Malawi, 15.2% in Zimbabwe to 12% in Nigeria.[2,3]

Preterm birth remains a significant perinatal challenge, major determinant of neonatal morbidity and mortality with long term adverse health consequences.[2] It is one of the greatest unsolved obstetric problems worldwide[4] and one of the most important issues in reproductive health.[5] Worldwide, preterm deaths constitute 28% of the 4 million annual new born deaths with 99% of these deaths occurring in developing countries.[2] In Nigeria, preterm babies account for 40-60% of all perinatal death.[7] The survival of these preterm infants is a function of both their biological maturity and technological advancement.[7] Many survivors face lifetime of disability, including learning disabilities, visual and hearing problem and delayed developmental milestone.

Infants born preterm compared to term infants could experience difficulty with feeding, blood glucose control, jaundice, temperature instability, apnoea, respiratory distress and sepsis either singly or in combination.[2]

Most preterm births happen spontaneously[1,8]. Preterm birth that are the result of conditions that directly threaten the health of the mother or foetus are categorized as indicated preterm births[9] and these could result to early induction of labour or caesarean birth, whether for medical or non-medical reasons. It has been estimated that spontaneous preterm delivery accounts for about 55% of preterm delivery.[4]

The onset of preterm labour is thought to be brought on by multiple mechanisms or pathways that may have been initiated weeks to months before the actual presence of clinical symptoms.[10,11]

According to the model studied by Lockwood *et al*, four pathogenic processes namely activation of maternal or fetal hypothalamic pituitary adrenal axis, decidual chorioamniotic systemic inflammation, decidual haemorrhage and pathological distension of the uterus precipitates premature delivery.[12]

The most rational way of reducing the impact of preterm deliveries on neonatal mortality is by reducing their incidence. This would be guided by proper understanding of the risk factors associated with these deliveries[7]. Some of the risk factors that could lead to preterm delivery include history of previous spontaneous preterm birth, low socioeconomic status, bacterial vaginosis, asymptomatic bacteriuria, urinary tract infection, maternal anemia history of second trimester miscarriages, multiple pregnancies, uterine malformations, maternal medical conditions such as pre-

eclampsia, diabetes, heart disease, among many others.[7,13,14,15]

The identification of risk factors for predicting preterm birth is advantageous because it allows for the initiation of risk specific treatment for at risk women and these may provide insights into a better understanding of the mechanisms leading to preterm birth[16,-20] However, methods for identifying women at risk of preterm birth by the reliance of demographic, behavioral, and biological risk factors have low sensitivities.[16]

Many biomarkers have been studied and have been used as predictors of preterm delivery. Some of which include interleukin 6[21-25], C reactive protein[26-29],fibronectin[30,31] and human chorionic gonadotropin which is the major biomarker identified to be studied.

Human chorionic gonadotropin (hCG)is a glycoprotein which can be used as an effective marker to predict preterm delivery. Beta hCG is produced by the placenta during pregnancy. Therefore, it is found in high concentrations in maternal plasma and amniotic fluid.[32] The appearance of beta hCG in both the maternal serum and amniotic fluid is probably the result of direct beta hCG diffusion from the placenta.[33] From the time of conception, concentrations of maternal serum and amniotic fluid beta hCG rise to a peak between 8 and12 weeks of gestation and then decline to plateau at approximately 18 to 20 weeks[32,33,] and remains at a stable state. The amount of beta hCG in the cervico-vaginal secretions mirrors the levels in the maternal serum and the amniotic fluid. However, the further elevation of beta hCG levels in the cervico-vaginal secretions may be due to the inflammatory process that can precede the onset of labour.[32,34] It may be related to the elevation of beta hCG levels in the cervical secretions before active labour. Disruption of the chorion and the decidua as occurs when onset of labour was imminent has been postulated as the mechanism for testing beta hCG presence in the cervico-vaginal secretions.[35]

Some researchers have discovered in previous studies that cervico-vaginal fluid beta hCG in patients with preterm labour may be used as a predictive test.[32,33] However, some of the results of these studies were inconclusive, which may be because they assessed normal pregnant women without known risk factors[36-42] for preterm delivery. Very few of these studies were done in Africa particularly Nigeria.

It is also known that the presence of bacterial vaginosis during pregnancy has been consistently associated with a two-fold increase in risk of spontaneous preterm birth.[36] Previous studies reviewed did not make mention of it and no screening test was done on the subjects to confirm or eliminate its presence. In this study however, all subjects were made to first undergo screening for the presence of bacterial vaginosis using the Amstel Criteria in order to eliminate confounders. All other identified gaps from previous studies have been incorporated in this study with the aim of improving on the existing knowledge.

Preterm birth as earlier mentioned is a major cause of perinatal mortality with nearly half

of the cases having long term neurologic morbidity.[1,37] Hence the need for timely prediction of preterm delivery cannot be over emphasized.[8,34] The prediction of spontaneous preterm birth is important because it would allow for the identification of women at risk, in whom specific interventions could be instituted in order to prevent preterm delivery and its attendant consequences.

This study was therefore aimed at assessing the usefulness of the beta subunit of hCG in cervico-vaginal secretions as an early biochemical predictor of spontaneous preterm delivery among pregnant women with and without risk factors for preterm delivery. The main focus of this study is to determine the prevalence of preterm delivery, to compare the beta hCG levels among the participants and to determine whether there is an association between beta hCG values and preterm delivery among the cases.

METHODOLOGY

Sampling Technique

The Inclusion criteria include: Gestational age from 20 weeks at the time of enrollment, singleton gestation, preterm contraction with cervical dilatation of 3cm and below, intact amniotic membrane, absence of other maternal or fetal complication such as hypertension, diabetes or congenital anomaly in the fetus.

The Exclusion criteria include: Confirmed rupture of membrane, cervical cerclage, amniocentesis, presence of blood in vagina, anomalies in fetus necessitating early delivery, cervical dilatation of 4cm and above, prior tocolysis, medical condition like hypertension, diabetes, sickle cell or chronic renal disease.

Consenting pregnant women who had risk factors for preterm delivery and those without risk factors who were presenting for routine antenatal care at estimated gestational age from 20 weeks to Ifako-Ijaiye General Hospital haven met the inclusion criteria were recruited into the study as cases and controls respectively. They were all matched for age, gestational age and parity, and were consecutively enrolled until the required sample size was attained.

Data Collection

Gestational ages of the participants were estimated on the basis of the first day of menstruation (LMP); which was corroborated with a first trimester sonograph. In cases where the estimation difference between LMP and ultrasonography were more than ten days, the reported age on the basis of ultrasonography were taken as the gestational age. A structured interviewer administered questionnaire was administered on the subjects. It consisted of 21 items, with both open and closed ended questions, few items requiring multiple responses. The questionnaire was pretested, and the feedback of the pretest was corrected before re-administration. Some of the information obtained included the socio demographic data, previous obstetric history, assessment for risk factors for preterm delivery, complications in index pregnancy, assay for the quantity of beta hCG

in cervico-vaginal secretions and the outcome of pregnancy.

Sample Collection

Two separate cervico-vaginal fluid samples were taken at 26 weeks gestational age and at 32 weeks gestational age from the subjects (patients with risk factors for preterm delivery) and the control (without risk factors), to determine the level of increase or decrease in the beta hCG values. They all avoided douching and did not have sexual intercourse 24 hours prior to sample collection. The first sample was collected at 26 weeks gestation. During this process, the participants were in dorsal position, haven been counselled, and consent obtained. In the presence of good light source, a single speculum examination was done using an appropriate size sterile Cuscos speculum. Firstly, the vagina walls were assessed for the presence or absence of a thin, homogenous grey coloured vaginal discharge. Then, a cotton tipped swab was used to collect specimen from the lateral vaginal walls. The swab was then touched on a litmus paper and it was observed for colour change. The same swab was mixed with about 0.2mls of normal saline in a test tube. A drop of the solution was placed on a glass slide and a drop of 10% potassium hydroxide was added. It was immediately evaluated for the presence of fishy odour. Another drop of the solution was also placed on a glass slide, covered with a cover slip and was examined at 400 X magnification with a light microscope for the presence of clue cells. Bacterial vaginosis was clinically diagnosed if three out of the four criteria were met. A second cotton tipped swab was placed again, first into the endo cervical canal and then into the posterior fornix of the vagina, each for 30s, and cervico vaginal fluid samples were obtained. The swab was then placed in a tube containing 1ml of saline solution and the tube was shaken for one minute before the swab was disposed. The tube was labelled with identity/serial number allocated to each patient in the questionnaire. At 32 weeks gestation, cervico vaginal samples were also collected from the subjects and controls and were assayed for beta hCG. All samples were kept frozen up to the time of assay.

Laboratory Analysis

A quantitative analysis using beta hCG Enzyme Immunoassay Biotek ELX800TM Reader model (2004) and

ELX50TM Washer model (2005) manufactured by Biotek Instruments Winooski, Vermont, USA was used. This is a solid-phase enzyme-linked immune sorbent assay (ELISA). The assay procedure began with thawing of the sample, then centrifugation of the solution was done at 1000 X g for 10 minutes to remove the particulate matter. The remaining solution was quantitatively tested for the presence of beta hCG.

Data Processing and Analysis

Data collected was entered into the computer for analysis. The data obtained which were already presented in tables were processed and analyzed using Statistical Package for Social Science (SPSS) for windows version 19 USA, 2012. Percentages, means, median, interquartile range and standard deviation of numerical variables were calculated. Test of

normality was performed to determine whether the outcome variable followed normal distribution. Student 't' test and Mann Whitney U test was used to compare numerical variables, while Paired 't' test was used to compare means of numerical variables taken at two different occasion.

Mann Whitney U test was used to compare medians of numerical variables that were not normally distributed. Chi squared test and fisher's exact test was used to compare categorical variables.

Receiver Operator Characteristics (ROC) Curve Analysis was used to find the best cut off level of beta hCG in the cervico-vaginal secretions to predict preterm delivery. Logistic regression was done to determine predictors of preterm delivery. Confidence interval of 95% was used for all statistical tests. Significance was set at 0.05.

RESULTS

A total of 150 parturient who met the inclusion criteria and consented to the study were recruited. This was made up of 50 parturient who had risk factor for preterm delivery classified as the subjects/cases and 100 parturient without risk factor classified as controls. All the parturient in the control group tested negative for bacterial vaginosis. Only 3 out of 50 parturient in the study group (cases) tested positive for bacterial vaginosis.

The age range of the studied population was from 25 to 35 years, the mean age of the subjects was 31.7±4.48 and 31.8±4.50 for control. There was no statistically significant difference in age, level of education, religion, marital status and occupation between the two groups. p-value >0.001.

Table 1: Socio demographic characteristics of the case and the control group.

Variable	Case n = 50 (%)	Control n = 100 (%)	x2	p
Age group (years)				
Less than 25	2 (4.0)	4 (4.0)	1.70	
0.636				
25 - 29	12 (24.0)	30 (30.0)		
30 - 34	25 (50.0)	39 (39.0)		
⩾ 35	11 (22.0)	27 (27.0)		
Mean±SD	31.7±4.48	31.8±4.50		
Education level				
Secondary	3 (6.0)	14 (14.0)	2.123	
0.145				
Tertiary	47 (94.0)	86 (86.0)		
Religion				
Christianity	41 (82.0)	92 (92.0)	3.32	
0.069				
Islam	9 (18.0)	8 (8.0)		
Marital status				
Single	2 (4.0)	0 (0.0)	4.054	
0.110*				
Married	48 (96.0)	100 (100.0)		
Occupation				
Professional	25 (50.0)	46 (46.0)	Not valid	
Artisan	6 (12.0)	10 (10.0)		
Business	12 (24.0)	33 (33.0)		
Civil servant	2 (4.0)	8 (8.0)		
Unemployed	5 (10.0)	3 (3.0)		

NB: *= Fishers' exact test

All the parturient recruited have had previous parous experiences. Most of them were para1, (58% of the subjects and 48% of the control) while others were para 2, (32% of subjects and 40% of the control). Others were para 3 and above, (10% of the subjects and 12% of the control). There was no statistically significant difference between the gestational age at enrolment between the two groups, p-value >0.001.

Table 2: Obstetric history of the case and the control group

Variable	Case n = 50 (%)	Control n = 100 (%)	x2	p
Parity				
1	29 (58.0)	48 (48.0)		
2	16 (32.0)	40 (40.0)		
⩾ 3	5 (10.0)	12 (12.0)		
Gestation age at enrolment				
20 – 22	10 (20.0)	22 (22.0)	1.256	
0.534				
23 – 25	21 (42.0)	49 (49.0)		
⩾26	19 (38.0)	29 (29.0)		
Gravidity				
2	20 (40.0)	29 (29.0)		
3	16 (32.0)	37 (37.0)		
⩾ 4	14 (28.0)	34 (34.0)		

Out of the 50 cases, only 15(30%) delivered preterm, while 35 (70%) delivered at term. However, among the 100 controls group only 2(2%) delivered preterm while the rest 98(98%) delivered at term. There was a statistically significant difference in the outcome of pregnancy between the cases and the control group with p-value<0.001.

Table 3: Outcome of pregnancy in case and control group

_Delivery p	Case n = 50 (%)	Control n = 100 (%)	x2
Preterm	15 (30.0)	2 (2.0)	15.947
<0.001			
Term	35 (70.0)	98 (98.0)	

The prevalence of preterm delivery was 30% among the cases and 2% among the control group.

Most of the cases 38(76%) delivered via spontaneous vaginal delivery while the remaining 12(24%) delivered via caesarean section. Sixty- seven (67%) out of the women in the control group delivered via spontaneous vaginal delivery while 33(33%) delivered via caesarean section. There was no statistically significant difference between the modes of delivery in both groups (p-value > 0.001).

Table 4: Mode of delivery among the cases and controls

Delivery	Case n = 50 (%)	Control n = 100 (%)	x2	p
SVD	38 (76.0)	67 (67.0)	1.286	
0.257				
CS	12 (24.0)	33 (33.0)		

The mean birth weight of the babies delivered by the cases was 3.3±0.55 kg, and 3.5±0.36 among the controls. There was a statistically significant difference in the mean birth weights between the cases and control group with p-value <0.05.

Table 5: Mean Birth weight of the babies born by the cases and the control group.

Delivery	n	Mean Birth weight	t	p
Case	50	3.3±0.55	3.014	0.003
Control	100	3.5±0.36		

There was an increase in the mean BHCG value from 26 weeks to 32 weeks gestation among the cases, and this was statistically significant with a p-value of <0.001. However, there was no statistically significant difference in the mean BHCG value at 26 weeks and at 32 weeks among the control group.

Table 6: Mean BHCG levels in cases and controls at 26 and 32 weeks

Variable		Mean	Paired t	p
Case	BHCG at 26 weeks	4.15±6.0	4.278	<0.001
	BHCG at 32 weeks	11.55±14.55		
Controls	BHCG at 26 weeks	3.44±3.29	0.081	0.935
	BHCG at 32 weeks	3.41±2.95		

The 15 cases who delivered preterm babies had significant increase in their mean beta HCG value from 7.44±1.74 at 26 weeks to 32.6±1.32 at 32 weeks with p value<0.001. There was however no statistically significant difference in the mean beta HCG at 26 weeks and at 32 weeks for the remaining 35 cases that delivered their babies at term.

The increase in the BHCG value from 26 weeks to 32 weeks among the 15 parturient (cases) who delivered preterm showed a possible association between increase in BHCG values and the occurrence of preterm delivery. This was statistically significant with p-value of <0.001.

Table 7: Mean BHCG levels for the cases (who delivered preterm and term babies) at 26 and 32 weeks.

Variable	Mean	Paired t	p
Preterm (15 cases)			
At 26 weeks	7.44±1.74	14.286	<0.001
At 32 weeks	32.6±1.32		
Term (35 cases)			
At 26 weeks	2.74±0.86	0.280	0.781
At 32 weeks	2.96±0.80		

There was no statistically significant difference in the levels of BHCG at 26 weeks and at 32 weeks among the control groups who delivered preterm and term babies.

Table 8: Mean BHCG levels in controls (who delivered preterm and term babies) at 26 and 32 weeks.

Variable	Mean	Paired t	p
Preterm			
At 26 weeks	6.16±1.20	0.096	0.927
At 32 weeks	6.06±0.85		
Term			
At 26 weeks	3.26±0.34	0.063	0.950
At 32 weeks	3.24±0.30		

The beta HCG values in the study population (the cases) at 26 weeks and at 32weeks was not normally distributed (Figure 1 &2).

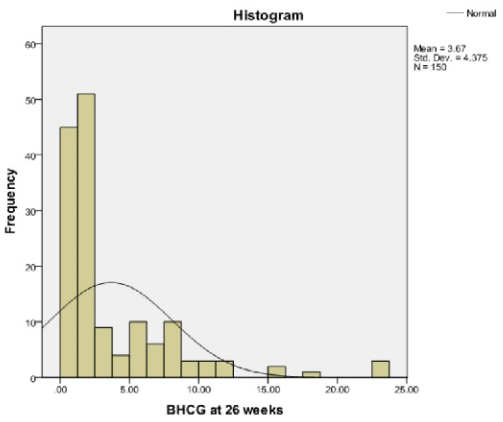

Figure 1: The beta HCG values in the study population (the cases) at 26 weeks

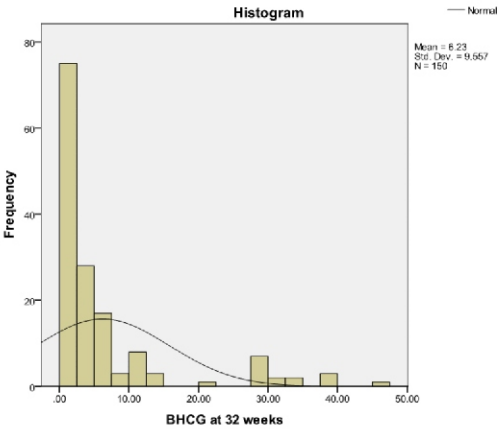

Figure 2: The beta HCG values in the study population (the cases) at 32weeks

The median BHCG value at 26 weeks for the cases and the controls were 1.4miu/ml and 1.8miu/ml respectively. At 32 weeks, the value increased to 1.95miu/ml and 2.63miu/ml for the cases and the control group. However, there were no significant differences in the median BHCG value between the cases and the controls at 26 weeks and at 32 weeks.

Table 9: Median BHCG at 26 and 32 weeks in cases and controls

Variablen		Median BHCG (IQR)	U	p
At 26 weeks				
Case	50	1.4 (IQR 0.845, 5.550)	2196.00	0.225
Control	100	1.8 (IQR 1.00, 5.900)		
At 32 weeks				
Case	50	1.950 (IQR 0.80, 28.425)	2456.0	0.861
Control	100	2.63 (IQR 1.0, 5.0)		

The Receiver Operator Characteristic (ROC) curve was used to determine the cut- off point of BHCG at 32 weeks for both the cases and the control group. The cut -off point of BHCG for predicting preterm delivery was 24miu/ml and this had a sensitivity of 100%, specificity of 97.1% positive predictive value of 93.8% and negative predictive value of 100%.

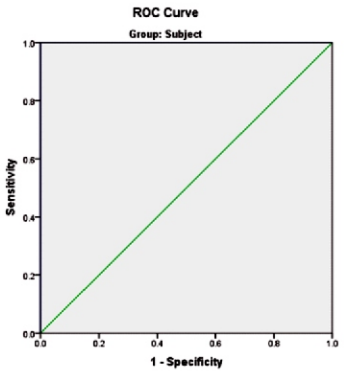

Figure 3: ROC curve of BHCG at 32 weeks of gestation discriminating preterm delivery among cases

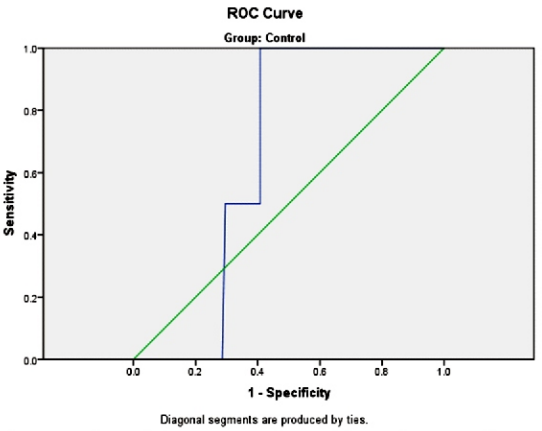

Figure 4: ROC curve of BHCG at 32 weeks of gestation discriminatiog preterm delivery among controls

Table 10: Area under the ROC curve, optimal cut-off points of BHCG in cases and control

βHCG at 32 weeks	AUC (95%CI)	P	Cut off value (miu/ml)	Sensitivity	Specificity	PPV	NPV	Kappa
Case	1.000 (1.00 - 1.00)	<0.001	24.0	100.0%	97.1%	93.8%	100%	0.731
Control	0.651 (0.529, 0.772)	0.529	2.87	100.0%	59.2%	4.7%	100%	0.040

DISCUSSION

In this study, a total of 15 women out of the 50 cases had preterm delivery, while the remaining 35 delivered their babies at term. Only 2 parturient from the 100 controls delivered preterm babies. The remaining control group delivered their babies after 37 completed weeks.

From this study, the prevalence of preterm delivery was 30% for those with risk factors for preterm delivery (the subjects) and 2%

for those without risk factor (the controls). This rate was higher than would be expected from a community-based study. The reason for this high prevalence rate may be because the study center is a tertiary center which attends to have high- risk patients and manage referrals of complicated cases such as preterm labor from primary and secondary centers across the state. This may have caused a reduction in the denominator and have thus exaggerated the preterm delivery rate in this center.

Prevalence rate of 30% was higher than 6.2% and 12% documented from earlier studies done in Nigeria by Ibharesebhor *et al*[43] and Mokuolu *et al*[7], respectively. Ibharesebhor *et al* conducted a 6 years retrospective study of admissions into neonatal unit of Benin teaching hospital. However, the preterm delivery rate got may not be the true estimate of the center.[7] This is because late preterm deliveries without any apparent health challenge were not admitted and this could have led to under-reporting of the absolute figure, which could have affected the overall prevalence rate reported.[7]

In the study conducted by Mokuolu et al [7,] gestational age was calculated using the LMP and it was not corroborated with first trimester ultrasound scan. A preterm baby may have been erroneously labeled as a term IUGR. Also, all the women unsure of their LMP were eliminated from the study. All these factors could have reduced the overall preterm prevalence rate recorded in that center.

The prevalence rate of 30% was also higher than 15.2% and 20.3% got from a Zimbabwean and a Malawi study[2,3]. The reason for these disparities may be because of geographical variations, early identification of at -risk groups and timely institution of preventive measures in each of the respective areas.

Prevalence rate of 2% for those without risk of preterm delivery was actually lower than all the previous values got from different studies done across the globe. This may possibly be because of the strict recruitment criteria used for this study which may have led to over screening during their selection as controls.

In this study, the mean cervico-vaginal fluid beta HCG values recorded among cases who delivered preterm was significantly higher than those who delivered at term (32.6±1.32 vs 2.96±0.80).

This was similar to the findings documented by Minoo *et al.*[5] They studied 60 patients with symptoms of preterm labor at estimated gestational ages between 24 to 36 weeks. They found that the mean beta HCG value for those who delivered preterm was significantly higher than those who delivered at term (34±7.47 vs 10.02±7.66). Sak *et al*[33] also studied 55 patients with risk factor for preterm delivery at gestational ages between 25 to 36 weeks. It was also discovered that the preterm delivery group had significantly higher cervico-vaginal fluid beta HCG values when compared with the normal controls (94.7±37.7 vs 35.5±14.8).

However, Massome *et al*[44]reported contrary

results to findings from previous studies. Their study failed to demonstrate a significant correlation between elevated levels of cervicovaginal HCG and the occurrence of preterm delivery. The reason may be because a single cervicovaginal fluid sample was collected and assayed for beta HCG compared with numerous samples assayed from previous studies. This may justify why the result gotten may not adequately represent the true value of beta HCG as numerous samples may show increasing trend. Likewise, the method of laboratory analysis used for the assay may have affected the ultimate result.

Among the control group, the 2 parturient who delivered preterm babies did not have any significant increase in the values of their beta HCG both at 26 weeks and at 32 weeks. The reason why they delivered preterm was quite unknown. It could have been due to some unidentified factors among the women which precipitated preterm delivery in them.

From this study, the cut off value of cervicovaginal beta hCG as stated in the ROC curve for the prediction of preterm delivery at 32 week gestation for the cases was 24miu/ml with a sensitivity of 100%, specificity of 97.1%, positive predictive value of 93.8% and negative predictive value of 100%. This cut off was lower than the value of 50 miu/ml documented by Bernestein *et al*[45], 77.8 miu/ml documented by Garshabi *et al*[46] and Sak *et al.*[33] It was however similar to 22.5miu/ml documented by Minoo et al [5] and 27.1miu/ml documented by Guvenal *et al.*[32] The sensitivities got in this study (100%) was higher than all the sensitivities reported in previous studies 87.5%,by Guvenal *et al*[32],87% by Garshabi *et al*[46],97% by Minoo *et al*[5], 50% by Bernestein *et al*[45] and 76% by Sak *et al.*[33]

The differences identified in the cut off values and the sensitivities in this study compared with previous studies done may have been due to natural hormonal differences among the different races and the varied geographical regions. It may also be due to differences in sample sizes, inclusion and exclusion criteria, and the methodology used.

However, despite the differences in the cut off values of beta HCG, the sensitivity, specificity, positive and negative predictive value, it has been shown from previous studies that cervicovaginal fluid beta HCG has a value in predicting preterm delivery. Similar result as earlier documented was also discovered in this study. It can therefore be inferred from the findings got from this study that elevated beta HCG can be used as an independent predictor of preterm delivery especially among patients with risk factors for preterm delivery.

Hence, this study indicates that cervicovaginal fluid beta HCG of >24miu/ml if discovered between gestational ages of 26 weeks and 32 weeks can identify approximately 100% of women who will deliver preterm.

Conclusion

In this study, there was a significant association between the value of quantitative beta HCG in cervicovaginal fluid and preterm delivery. Increasing concentrations of

quantitative beta HCG in cervicovaginal fluid may be a useful, reliable and early biochemical marker to predict preterm delivery. It is cheap, easy and free of complications.

Recommendation

The result from this study may form the basis for the conduct of a bigger study which result may then be used as a basis for closer follow up and institution of intervention for at risk groups. This would necessarily reduce the incidence of preterm delivery and its attendant complications.

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