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■ Original Research Article

The Role of Salivary Progesterone in Predicting Women At-Risk of Preterm Delivery in Kano, Nigeria

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ABSTRACT

Background: Vaginal fetal fibronectin assay has been used as a gold standard biomarker for the prediction of preterm birth especially among symptomatic pregnant women with relatively good sensitivity and high specificity. However, recent evidence is emerging that salivary progesterone assay can be used to predict preterm birth. **Methodology**: A cohort study was used to assess the predictive values of salivary progesterone in women at-risk for preterm delivery at a tertiary hospital in Kano – Nigeria. Salivary samples were collected for progesterone level assay between 28-32weeks of gestation among 135 asymptomatic pregnant women. The study participants were followed up and the gestational age of delivery was determined, and receiver operator characteristic curve was plotted to determine the predictive cut off value for salivary progesterone. **Results**: The mean salivary progesterone was found to be 854.24 ± 192.25pg/ml and 1599.06 ± 226.09pg/ml for those who had preterm and term deliveries respectively. There was a statistically significant difference in the mean salivary progesterone between the two groups. At a cut off value of 1253.3pg/ml, salivary progesterone was found to have a Sensitivity of 100%, Specificity of 90.8%, Positive Predictive Value of 85.7 and Negative Predictive Value of 100%. **Conclusion**: This study found salivary progesterone quantitative assay to be useful in predicting preterm birth among women at-risk, with high diagnostic accuracy. Therefore, it can be used as screening tool for women at risk of preterm delivery.

Key words: Salivary; Progesterone; Assay; Preterm

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INTRODUCTION

Preterm birth is defined as the delivery of a baby before 37 completed weeks, after the age of viability.[1] Age of viability however differs among regions of the world, in developed nations like the United Kingdom and United States of America, 24 and 22 weeks respectively are used as their ages of viability, while in sub-Saharan Africa including Nigeria 28 weeks is used as the age of viability.[2,3]

Worldwide about 15 million babies are born preterm annually.[4] However, the incidence varies significantly across the globe. The countries with the greatest number of preterm births are; India, China, Pakistan, Indonesia, the United States of America and Nigeria,[4] mostly due to the increasing number of pregnancies from assisted reproductive technology and multiple gestation. The incidence of preterm delivery in southern Nigeria was quoted at around 16.9%,[5] with a rate of 12% in North central Nigeria[6] and a rate of 6.9% in North-western Nigeria.[7]

Previous studies have shown that effort in prolonging pregnancy among women with preterm labour has not yielded any significant result, moreover the efficacy and long term safety of the drugs used in the management of preterm labour especially tocolytics have not been proven, therefore many sonological, clinical and biological markers have been suggested for predicting preterm birth, some of the biomarkers proposed include corticotropin releasing hormone (CRH), human chorionic gonadotropin (HCG), cervicovaginal fetal fibronectin and serum progesterone and estriol.[8] The aim is to develop a biomarker that is rapid, and simple to perform with high sensitivity and specificity for the prediction of preterm delivery. Accurate prediction of preterm birth will help in the early commencement of preventive measures, especially among asymptomatic women, while for symptomatic women it will aid in-utero transfer to secondary and tertiary health facilities where neonatal services are readily available.

Transvaginal ultrasonography is the gold standard method for cervical length measurement in the second trimester and screening for spontaneous preterm delivery.[9,10,11] However, the cultural acceptability of transvaginal ultrasonography, the need for skilled sonologist and repeated sessions of transvaginal cervical length measurement, coupled with multiplicity of aetiology of preterm birth are some of its shortcomings.
Salivary progesterone has been shown to correlate well with serum concentration, and therefore reflect the unbound, unconjugated form which is the biologically active form.[12] Therefore salivary progesterone if found to be valuable in predicting preterm birth among women at-risk, it will go a long way in preventing preterm birth. Salivary progesterone has the advantage of easy sample collection, non-invasiveness, cost and requires simple technology that is readily available in our environment, and can be offered to both patients with or without symptoms of preterm birth.

This study aim to determine the predictive value of salivary progesterone quantitative assay for preterm delivery in women at-risk attending antenatal clinic in Aminu Kano Teaching Hospital, Kano – Nigeria.

MATERIALS AND METHODS

A prospective cohort study was conducted at the Obstetrics and Gynaecology Department of a tertiary hospital in Kano, Nigeria. The study population comprised pregnant women attending antenatal clinic. Pregnant women with singleton or multiple live fetuses between the gestational ages of 28-32 weeks with known risk of preterm delivery were included. Women with cerclage in-situ, those with chronic medical conditions, those with premature rupture of membranes (PROM)/cervical dilation >2cm and those with preterm labour were excluded. One hundred and thirty-five (135) clients that fulfilled the inclusion criteria were recruited for the study. The purpose and nature of the study was explained to the patients, and written consent was obtained.

Measurement of Variables

An interviewer administered questionnaire was used to obtain information such as age, parity, gestational age (from LMP/first trimester scan), weight, height, BMI, educational status, previous obstetrics history and socioeconomic status. Salivary samples were collected for progesterone level assay between 28-32weeks of gestation from the study participants. Free progesterone level in saliva was measured using the Salivary Free Progesterone ELISA Kit (PRG32-K01). The study participants were followed up and the gestational age of delivery was determined.

Data Analysis

The results were collated and analysed using SPSS version 27 software (IBM Corporation, Armonk, NY). The participants were grouped into two based on the delivery gestational age. Those that delivered at 37 weeks and above were categorized as term while those that delivered before 37 weeks were Preterm. The mean salivary progesterone for term and preterm delivery was determined and presented in tables. Qualitative variables were presented using frequencies and percentages where appropriate and presented in tabular forms and figures. Student t-test was used to determine difference in mean salivary progesterone between the two groups. *P* value <

0.05 was considered statistically significant. The sensitivity, specificity, positive predictive value, and negative predictive value were determined using the predictive validity test. Receiver operating curve (ROC) graph was plotted to determine the cut off value for salivary progesterone with the highest predictive value.

RESULTS

The mean age of participants was 34.8±6.06 and 34.36±5.91 years among patients who delivered preterm and term respectively. Majority of the patients were multiparous in both groups. Majority were Hausa/Fulani by tribe in both groups, and mainly of low socioeconomic status.

Table 1: Socio-demographic characteristics

Characteristics	Preterm Frequency(percentage)	Term Frequency(percentage)	P-value
Age			
Mean ± SD	34.79 ± 6.06	34.36 ± 5.91	0.69
< 20	0(0)	2(2.3)	
20 -24	5(10.4)	7(8.0)	
25-29	4(8.3)	10(11.5)	
30-34	7(14.6)	7(8.0)	
35-39	23(47.9)	50(57.5)	
≥40	9(18.8)	11(12.6)	
Total	48(100)	87(100)	
Parity			0.52
0	2(4.2)	5(5.7)	
1-4	32(66.7)	64(73.6)	
≥5	14(29.2)	18(20.7)	
Total	48(100)	87(100)	
Ethnicity			0.68
Hausa/Fulani	41(85.4)	77 (88.5)	
Igbo	1(4.2)	1 (1.1)	
Yoruba	2(4.2)	1 (1.1)	
Others	4(8.3)	8 (9.2)	
Total	48 (100)	87 (100)	
Socioeconomic Status			0.24
High	19(39.6)	25(28.7)	
Medium	10(20.8)	29(33.3)	
Low	19(39.6)	33(37.9)	
Total	48(100)	87(100)	
Anthropometric & Obstetrics Characteristics.	**Preterm (mean ± SD)**	**Term (mean ±SD)**	**P-Value**
Weight	70.33 ±12.281	72.21 ±12.081	0.39
Height	159.198±5.251	158.149 ±4.87	0.25
BMI	27.67±3.92	28.8±4.02	0.11
Booking G.A	24.27 ±3.09	23.37 ±2.79	0.09

The mean weight was 70.33±12.3, and 72.21±12.08kg in preterm and term respectively. The mean height was 159.20±5.25 and 158.15±4.87cm in preterm and term parturient respectively. The body mass index (BMI) were 27.67±3.92 and 28.8±4.02 respectively, while their mean gestational age at booking were 24.27±3.92 and 23.37±2.79weeks respectively.

Table 2: Predictive Value of Salivary Progesterone Assay

Salivary progesterone (pg/ml)	Preterm	Term	Total
≤1253.85	48	8	56
>1253.85	0	79	79
Total	48	87	135
Sensitivity 100%	Specificity 90.8%	PPV 85.7%	NPV 100%

Table 3: Mean Salivary Progesterone Level in Preterm and Term Delivery

	Preterm (Mean ±SD)	Term (Mean ±SD)	P-Value
Salivary Progesterone (pg/ml)	854.242±192.25	1599.062±226.091	<0.05

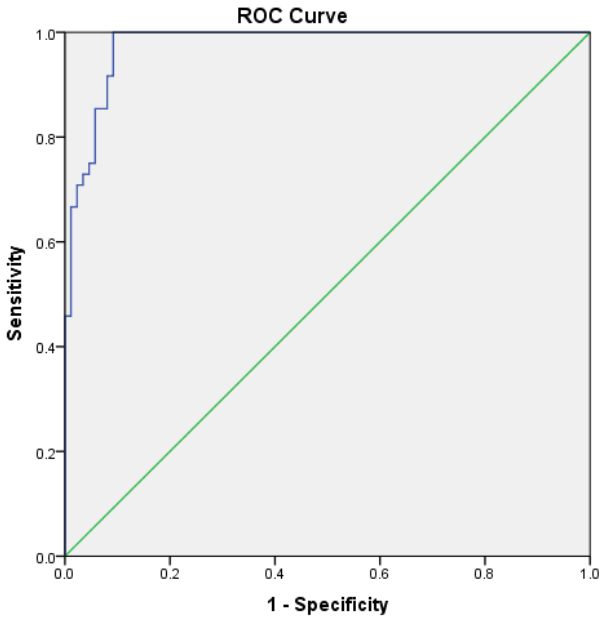

Figure 1: Receiver operator curve (ROC) for salivary progesterone test

Figure 1

Area	Std. Error[a]	P-Value	95% Confidence Interval	
			Lower Bound	Upper Bound
.976	.010	.000	.956	.997

The mean salivary progesterone was found to be 854.24 ± 192.25 and 1599.06 ± 226.09 for those who had preterm and term deliveries respectively. There was a statistically significant difference in the mean salivary progesterone between the two groups. This is shown in Table 2.

A receiver operator characteristic curve was plotted (Figure 1). At a cut off value of 1253.85pg/ml, salivary progesterone was found to have a Sensitivity of 100%, Specificity of 90.8%, Positive Predictive Value of 85.7 and Negative Predictive Value of 100% . This is shown in Table 3.

DISCUSSION

This study found that salivary progesterone assay had a high predictive value, with high sensitivity, specificity, negative predictive value, positive predictive value and accuracy at a cut-off point of 1253.85pg/ml. At this value, salivary progesterone had sensitivity of 100%, specificity of 90.8%, positive predictive value of 85.7%, negative predictive value of 100%, and accuracy of 94%. This is similar to the findings of a study conducted in university hospital Egypt, where the sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 85%, 90%, 98.5%, 85.7%, and 92.1% respectively, using a cut-off point of ≤933.6pg/ml of salivary progesterone.[13] The difference in cut-off point of salivary progesterone used in their study may be due to difference in gestational age of recruitment between 26 to 34weeks gestation, and their study was a case control study in which their cases are women with signs of labour, and healthy pregnant women as control.[13] Another study in Egypt to assess the role of salivary oetriol and progesterone among women at risk found a similar sensitivity, specificity, positive and negative predictive values of 100%, 97.8%, 97.8% and 100% respectively, at salivary progesterone cut-off point of 1.6ng/ml.[14]

Another study conducted in a teaching hospital, Iraq to compare the predictive values between cervical length measurement and salivary progesterone at cut-off point of 234.3pg/ml found a sensitivity, specificity, positive and negative predictive values and accuracy of 96.7, 90.0, 90.6 and 96..4% respectively.[15] The difference may be attributed to smaller sample size of 30, methodology being a case-control study, including symptomatic women, and setting a lower progesterone cut-off value.

In another study conducted in Delhi, India, where salivary progesterone was assayed in asymptomatic pregnant women between 24 to 28weeks of gestation, it was noticed that salivary progesterone level declines from first to second visit among women that delivered before 34weeks of gestation, with salivary progesterone cut-off point set at 2575pg/ml, below which more than 80% of participants delivered before 34weeks of gestation, with sensitivity, specificity, positive predictive and negative predictive values of 83, 86, 60 and 95% respectively.[16] The difference in the above study may be attributed to gestational age of recruitment between 24 to 28weeks, and the use of higher salivary cut-off point of 2575pg/ml, thereby having lower predictive values.

Another study in Madras, India, where salivary progesterone assay was compared with trans-vaginal cervical length measurement to predict preterm birth at 24 to 28weeks of gestation and repeated at 29 to 32weeks of gestation, reported salivary progesterone sensitivity and specificity of 100% and 94.2% at cut-off point of 3903pg/ml and sensitivity and specificity of 100% and 100% at cut-off point of 2975pg/ml respectively.[17] The difference may be attributed to gestational age of recruitment, and smaller sample size of 90.

The mean salivary progesterone was 854.242±192.25 and 1599.062±226.091pg/ml among study participants who had preterm and term delivery respectively. This is similar to the findings in a case-control study in Cairo Egypt, where cervical length measurement and salivary progesterone was compared among cases and controls at similar gestational age of recruitment between 26 to 34weeks, they found a higher predictive value for salivary progesterone than cervical length measurement with mean salivary progesterone of 728.9±222.3 and 1099.9±189.4pg/ml among cases and controls respectively.[18]

CONCLUSION

This study found salivary progesterone quantitative assay to be useful in predicting preterm birth among women at-risk, with high diagnostic accuracy. Therefore, it can be used as screening tool for women at risk of preterm delivery.

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