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Original Research Article

Preterm deliveries and progesterone levels in pregnant women attending antenatal care in a health care facility in Sokoto state, Nigeria: a preliminary study

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ABSTRACT

Background: Progesterone related complication during pregnancy is currently being viewed as one of the underlying causes of miscarriages and preterm deliveries. Progesterone assay is often neglected during routine screening in antenatal clinics (ANC) in primary health care centres in Nigeria. This study was designed to monitor 40 volunteer expecting mothers between the ages 18-35 years with a history of child birth and to evaluate serum progesterone levels accordingly for pregnancy in second and third trimesters.

Methods: Volunteers were categorized according to their age and stage of pregnancy. Progesterone was estimated in serum collected from each volunteer using ELISA kits (Cayman chemicals, USA).

Results: The results showed that age disparity among subjects did not play a role in the observed progesterone levels in both trimesters. Second trimester progesterone levels (37.73 ± 0.32 ng/ml) were closest to lower limits of reference ranges for second trimester pregnancy (25.60-89.40 ng/ml). However, third trimester average serum progesterone levels of 36.31 ± 0.26 ng/ml fell below minimum values of 42.50 ng/ml expected in normal pregnancy. Three preterm deliveries were recorded among the monitored subjects while an incidence rate of 1:32 births was observed for all deliveries received at the facility within the five months period all monitored subjects gave birth.

Conclusions: The preponderance of low gestational progesterone constitutes a risk factor to delivery at term. It is recommended that local ANC programme include progesterone monitoring and therapy as an intervention strategy against preterm births.

Keywords: Antenatal, Malnutrition, Preterm delivery, Primary healthcare, Progesterone

INTRODUCTION

Preterm birth is defined by the world health organization as babies born alive before completion of 37 weeks of pregnancy and further classified as extremely preterm (22-27 weeks), very preterm (28-31 weeks) and moderately preterm (32-36 weeks) Delnord et al.¹ Preterm delivery is a leading cause of child morbidity globally. An estimated 15 million babies (or 1 in 10 babies) are born too early every year. A regional and

global estimate for preterm births ranks Nigeria third (after China and India) with 773,600 preterm births.² Cases of preterm births may be under reported with the recent spate of population redistribution and rural - urban migration in many developing countries. The Nigerian health system at all levels promotes the advocacy for antenatal care for pregnant women. However, risk factors associated with preterm deliveries are often neglected and many health centres lack necessary life-saving facilities for preventing preterm morbidity.

Causes of preterm delivery are diverse and complex. However, reports have indicated the use of progesterone as a therapeutic agent has potential benefits for women at risk of preterm birth.³ Progesterone, a steroid hormone is important in the maintenance of pregnancy. After follicle rupture and release of ovum during menstrual cycle, the corpus luteum takes the function of progesterone secretion.

If fertilization occurs, the corpus luteum will continue to grow and secrete progesterone for most part of the first trimester. Subsequently, the placenta assumes the role of progesterone biosynthesis and secretion.⁴ Progesterone also acts as an immune-steroid by blocking T-cell lymphopoiesis hence promoting maternal immunotolerance of fetal semi-allograft.^{5,6} Studies have shown that the expression ratio of progesterone receptors PR-A/PR-B play a role in the functional withdrawal of progesterone at onset of labour.⁷ Thus changes in progesterone levels could be associated with cases of miscarriages and preterm births. Assay for serum progesterone levels unfortunately, is often neglected in routine antenatal care (ANC) in most primary health care centres in Nigeria.

Hence records on levels of progesterone and other pregnancy maintaining hormones (e.g. 17 β -estradiol) among local women during normal pregnancy are either scarce or non-existent. In Sokoto State, North Western Nigeria, child birth rate is high but data on birth classification as preterm are usually not prioritized.

This study was therefore designed as a preliminary study to evaluate second and third trimester progesterone levels and monitor preterm births in pregnant women attending ANC in women and Children Welfare Centre (WCWC) a government facility in Sokoto metropolis.

METHODS

Criteria for selection of subjects

This study was conducted between March - December, 2018 following ethical approval from the Sokoto State Ministry of health.

Selection of participating subjects was purposive which was based on pregnant mothers attending ANC and were care givers for their children weaned at less than 2 years who are in-patients receiving therapeutic diet in the health centre facility.

This was to allow for close monitoring of the selected pregnant subjects. A total of 40 volunteer pregnant women (age range 18-35 years) were selected and were made up of 20 subjects each in second and third trimesters respectively.

The subjects were grouped further according to their age, with a class interval of 10 for each trimester.

Blood sample collection

Blood (3 ml) was collected in plain containers from the upper arm of each volunteer by venipuncture while in a sitting position. The samples were spun at 3000 rpm for 10 minutes at 25°C and serum obtained was transferred into well labeled microfuge tubes for serum progesterone assay.

Serum progesterone assay

Progesterone ELISA kits were obtained from Cayman (Cayman chemicals, USA). Procedures provided by manufacturer were followed to prepare buffers, progesterone standards and develop samples using the titre plate provided.

The 96 titre well plate containing prepared samples was then placed on an orbital shaker and allowed to incubate for 1 hour after which the wells were rinsed using prepared wash buffer.

Ellman's reagent (200 μ L) and 50 μ L progesterone tracers were added to the wells and allowed to develop optimally for 90 minutes on the shaker. Absorbance of developed plate was read at 420 nm using a microplate reader (Rayto-RT2100C). A standard curve was prepared for estimation of progesterone in samples collected.

Statistical analysis

Results obtained were presented as mean values of triplicate determinations of serum progesterone levels. Student t-test was used to compare mean serum progesterone values between age groups for each trimester at 95% level of significance ($p < 0.05$).

RESULTS

Progesterone levels of subjects in their second and third trimesters are presented in Tables 1 and 2. The results suggest age disparity did not impact significantly ($p > 0.05$) on progesterone levels in both trimesters. Values obtained for second trimester progesterone levels (36.69 \pm 0.57 to 37.73 \pm 0.32 ng/ml) were closest to the lower limit when compared with reference range for progesterone in normal pregnancy in Nigerian women while progesterone levels observed for third trimester subjects fell below levels expected in normal pregnancy.⁸

Presented in Figure 1 is a summary of monthly preterm deliveries in Women and Children Welfare Centre Sokoto between August and December, 2018.

The primary health care facility recorded a total of 714 live births within the period all the selected subjects were expected to deliver and 23 of these deliveries were preterm which represents an average of 1:32 preterm births for the months under review (Figure 1).

Table 1: Second trimester serum progesterone levels of subjects attending antenatal clinic, WCWC, Sokoto.

Age (years)	N	Progesterone levels (ng/ml) ^a	*Progesterone reference range in normal pregnancy ⁸ (ng/ml)
18-27	10	37.73±0.32	25.60 - 89.40
28-37	10	36.69±0.57	

N = number of subjects; a = p>0.05.

Table 2: Third trimester serum progesterone levels of subjects attending antenatal clinic, WCWC, Sokoto.

Age (years)	N	Progesterone levels (ng/ml) ^a	* progesterone reference range in normal pregnancy ⁸ (ng/ml)
18-27	10	36.70±0.42	42.5-89 ng/mL
28-37	10	36.31±0.26	

N = number of subjects; a = p>0.05.

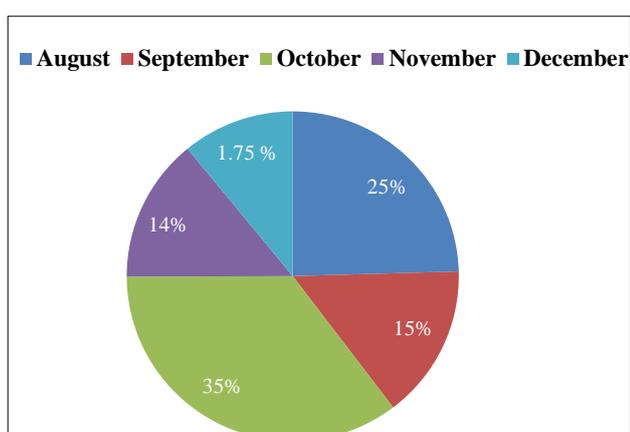


Figure 1: Monthly record of percentage preterm delivery within expected delivery dates of selected pregnant subjects attending ANC at women and children welfare centre Sokoto.

DISCUSSION

High level of progesterone does not prevent parturition at term but a physiological withdrawal of the hormone predisposes to induction of preterm delivery.⁹ Changes in progesterone (and β -estradiol) levels occur as pregnancy approaches term thus an early onset of depleted progesterone levels and/or down regulation of its receptors predisposes to preterm birth.^{10,11} The observed low serum progesterone in 2nd and 3rd trimester pregnancy (Tables 1 and 2) signifies the need for interventions to prevent early onset of uterine contraction.^{9,12} A study conducted by Kant et al, observed that 84.2% of women with less than 24 ng/ml serum progesterone levels had their pregnancies terminated; the majority of whom were subjects between 35-39 years.¹³ Similarly, there are reports that relate advanced maternal age with complications in pregnancy and other adverse outcomes associated with child birth.¹⁴⁻¹⁶ Out of the total live births in WCWC, Sokoto within the period under study, three preterm deliveries were recorded in October for 2 subjects in their mid-thirties while the single case recorded for a 25 years old subject was moderately

preterm and was referred to another hospital for intensive care. High prevalence of preterm deliveries is similarly observed in other regions of the country. Butali et al in their study reported 16.80% incidence of preterm births in Nigeria.¹⁷ Oluwafemi and Abiodun reported incidence of preterm delivery in the Mother and Child Hospital, Akure South Western Nigeria as 15.4% while analyses of hospital based data for University of Nigeria Teaching Hospital (UNTH) Enugu, South East Nigeria showed a preterm prevalence of 16.9% in 2014.^{18,19} It is not clear whether age was a determining factor in the prevalence reported for these studies however, the general acceptance and utilization of hospital based maternity services in these regions may have contributed to the high cases observed on record. Equally challenging is the effectiveness of adopted routine ANC to prevent perinatal mortalities in many hospitals in the country.

Pregnancy complications among young mothers may be rare or isolated, however, recurrence and high incidence of such complications within a community may be a signal for a common underlying cause. Importantly, early marriage is a common socio-cultural practice especially in Northern Nigeria where maternal and child malnutrition is significant. It has been shown that the reproductive health indicators in the north western region of Nigeria follow a similar pattern for malnutrition with a prevalence of 40%. Regional reports indicate about 70-80% of pregnant women do not have access to skilled perinatal care and 30-40% of this figure failed to attend ANC.²⁰ Factors like malaria and other infectious diseases that are endemic in this region equally predispose to pregnancy associated complications a situation that could be worsened by low progesterone levels which is rarely assessed during pregnancy.

CONCLUSION

Serum progesterone levels of selected pregnant women attending Women and Children Welfare Centre Sokoto was determined to be generally low and falls below the normal levels expected for third trimester pregnancy. Provisions for inclusion of progesterone monitoring in

routine ANC is recommended for primary health care centres as an intervention for the rising incidence of preterm deliveries.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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