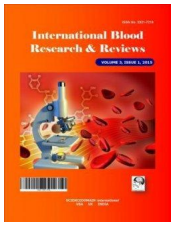

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Progesterone and 17β-Estradiol Levels during Normal Pregnancy and the Puerperium among Women Attending a Tertiary Health Facility Clinic in Jos, Plateau State, Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Author BOO designed the study, wrote the protocol and wrote the first draft of the manuscript. Author BOO managed the literature searches, performed the Biochemical assays. Authors MIE and LFOO managed analyses of the study and author LAO managed the statistical analyses. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Progesterone and Estrogen are the chief pregnancy hormones. Their levels increase during pregnancy to aid successful maintenance of pregnancy, which depends on maternal tolerance of the fetal semi allograft.
Aim: To determine levels of progesterone and 17β-estradiol, at different trimesters during normal pregnancy and the puerperium, which may be used as baseline data for Nigerian women.
Study Design: Cross-sectional study.
Place and Duration of Study: The study was carried out in the antenatal clinic of Bingham University Teaching Hospital Jos, from April, 2011 to August, 2012.

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Methodology: A total of three hundred and thirty (330) apparently healthy women between the ages of 18 and 42 years (mean age, 27.88±4.9 years) were studied. The study included two hundred and ten (210) women selected at different trimesters of pregnancy, seventy (70) women at six weeks post partum and fifty (50) non pregnant women as controls. Blood pressure measurements were done using the Auscultatory technique with mercury Sphygmomanometer. Hypertensive subjects were excluded. Serum progesterone and 17β-estradiol concentrations were measured by Electrochemiluminescence immunoassay (ECLIA) on Elecsys 2010, Auto analyzer.
Results: Out of the 330 women included from the onset, 260 completed the procedures. The relationship between Age group and Parity versus Serum levels of progesterone and 17β-estradiol were found not to be significant ($P > 0.05$). However, the hormonal levels increased significantly ($P = .000$) from the first trimester (49.158±7.97 ng/ml to 142.21±73.194 ng/ml) to the third trimester (3121.24±2076.6 to 11648.58±8325 pg/ml) respectively. These values declined sharply during the 6 weeks post partum period to (0.344±0.213 ng/ml and 39.44±16.23 pg/ml) for both progesterone and 17β-estradiol. The post partum women and the control showed no significant difference ($P = .281$).
Conclusion: The levels of progesterone and 17β-estradiol increased progressively throughout pregnancy and declined sharply to levels lower than the non-pregnant state during the puerperium. The levels recorded in this study are significantly higher than earlier reports among the African - Americans and the Caucasians. Thus the data generated in this study may be used as baseline values for management of pregnant women in Nigeria.

Keywords: Normal pregnancy; puerperium; progesterone; 17β-Estradiol; changes.

1. INTRODUCTION

Successful maintenance of pregnancy depends on maternal tolerance of the fetal semi allograft [1]. Progesterone in conjunction with other hormones such as cortisol and prolactin has strong immunomodulatory effects leading to immunotolerance during pregnancy [2]. Progesterone also induce protective immune environment in the decidua during early pregnancy which includes production of the immunomodulatory progesterone-induced blocking factor (pibf) protein by decidual cells [3]. The highly active progesterone ester 17α-hydroxyprogestrone has been administered to risk groups with previous recurrent abortions or previous premature births and to patients with premature contractions and short cervices [4,5].

On the other hand, example in animal models shows that direct estrogen injection into the uterine arteries produces striking increase in blood flow, and 17β-estradiol is the most potent estrogen in this role [6]. Also, estrogen regulated mechanisms may also allow the fetus to govern production and secretion of progesterone during the third trimester. In primates, estrogen regulates the biosynthesis of placental progesterone by regulating the availability of ldl-cholesterol for conversion to pregnenolone and its downstream steroid products [6].

Progesterone and estrogen are the chief pregnancy hormones. Amount of estrogen produced by a woman during one pregnancy is more than what she can have throughout her entire life when not pregnant. Her progesterone levels also are extraordinarily high [7].

Lof et al. [8] reported the levels of these hormones among the Swedish women. Bronneberg also reported an increase in hormone levels during egg laying cycles in ostriches [9]. In Nigeria, levels of progesterone and 17β- estradiol have been reported during menstrual cycle and at parturition [10,11]. However, record of these hormones level among the Nigerian women during normal pregnancy is either scarce or non existence, hence the aim of this study to generate such data and determine the changes during pregnancy and puerperium. Data generated from this study will serve as baseline data which would aid in policy formulation and implementation with respect to pregnancy and puerperium as well as proper assessment and monitoring of pregnant women who may be at risk to premature labour and/or premature child birth.

2. METHODOLOGY

A total of three hundred and thirty (330) apparently healthy normotensive women between the ages of 18 and 42 years (27.88±4.9 years) were studied. Educational exposure of the pregnant women varied from nine [0-9 years (primary)], thirteen [0-13 years (secondary)] to

above seventeen [>17 years (tertiary)]. We included primigravida (para-0), para-1, 2, 3, 4 and multigravida (>5). The study included two hundred and ten (210) women randomly selected at different trimesters of pregnancy, seventy women at six weeks post partum and fifty (50) non pregnant women of child bearing age as controls. The study was carried out in the antenatal clinic of Bingham University Teaching Hospital, Jos. The study procedure was well explained to each participant and written informed consent was obtained from each of them. Samples were collected from each woman during the mid-trimester period between 8.00 a.m and 9.00 a.m. First trimester (8-10 weeks), second trimester (20 weeks) third trimester (32 weeks) and 6 weeks postpartum visit. Control samples were collected during the midlutenic phase for progesterone and ovulatory peak for estradiol.

2.1 Hormonal Assay

Serum progesterone and 17β-estradiol were measured using fully automated hormonal assay equipment, Roche Elecsys 2010 (Roche diagnostics Gmbh, Mannheim, Germany).

2.2 Test Procedure

Sample information was programmed into the equipment according to manufacturer's instruction. For 17β-estradiol, 35 µl of serum was uploaded into the equipment, while for progesterone 30 µl was uploaded for the assay. At the completion of the test, the results were printed out directly from an inbuilt printer.

2.3 Exclusion Criteria

Questionnaire was applied on each woman for Biodata and Medical history to exclude pregnant women with medical history of Kidney disease, diabetes, hypertension and other chronic illnesses.

2.4 Blood Sample Collection

Plain vaccutainer tube was used to collect blood samples for hormonal assay. Tourniquet was applied to upper forearm of the subject after assuming a comfortable sitting position. The site chosen for vene-puncture was wiped with 70% alcohol for sterilization. Five milliliters (5 ml) of blood was then collected into the vaccutainer tube with minimal stasis. The tube was properly labeled with the subject's name, sample number and date of collection. The blood was allowed to clot at room temperature, and serum separated and harvested into clean dry well labeled sample bottles following centrifugation at 3000 rpm for 5 minutes. The samples were kept at -700C in aliquots until they were analyzed.

2.5 Data Management and Analysis

Results were presented in mean ± standard deviation (sd). All data obtained in the study were analyzed using anova (analysis of variance) followed by a fisher's least significant difference post- hoc test to determine pair wise difference among group means(spss.16). The level of significance was set at $p < .05$.

3. RESULTS

Tables 1 to 4 show the correlation analysis between Age and Parity versus progesterone and 17β-estradiol levels. The subjects age and parity were found not to be significantly associated with their progesterone and 17β-estradiol levels at P value < .05.

Table 1. Showing relationship between age and progesterone (ng/ml) level at different trimesters during normal pregnancy and the puerperium

Trimester	Correlation coefficient (r)	P value
First trimester	-0.176	0.254
Second trimester	0.058	0.718
Third trimester	0.146	0.432
6 weeks (post partum)	-0.284	0.129

Significant at P < .05

Table 2. Showing relationship between age and 17β-Estradiol (pg/ml) level at different trimesters during normal pregnancy and the puerperium

Trimester	Correlation coefficient (r)	P value
First trimester	-0.377	0.012
Second trimester	-0.207	0.189
Third trimester	-0.213	0.249
6 weeks (post partum)	-0.081	0.671

Significant at P <0 .05

Table 3. Showing relationship between parity and progesterone (ng/ml) level at different trimesters during normal pregnancy and the puerperium

Trimester	Correlation coefficient (r)	P value
First trimester	-0.032	0.834
Second trimester	-0.034	0.828
Third trimester	-0.024	0.898
6 weeks (post partum)	-0.195	0.303

Significant at P <0 .05

Table 4. Showing Relationship between parity and 17β Estradiol (pg/m) level at different trimesters during normal pregnancy and the puerperium

Trimester	Correlation coefficient (r)	P value
First trimester	-0.158	0.307
Second trimester	-0.272	0.081
Third trimester	0.038	0.840
6 weeks (post partum)	-0.280	0.134

Significant at P <0 .05

Serum levels of Progesterone increased in value progressively during pregnancy (49.2±7.97, 94.03±32.77, 142.21±73.19 n/ml) for 1st, 2nd and 3rd trimesters respectively (p<0.001), and the levels was significantly higher than the non-pregnant control (11.17±4.77 ng/ml) (P < .001). Also, the increases within the trimesters were significant (p<0.001). The hormonal levels declined drastically during the six weeks postpartum period to 0.344±0.213 ng/ml (Fig. 1).

In the same vein, Serum levels of 17β-Estradiol increased in value progressively throughout pregnancy (3121.24±20 76.6, 8678.05±4388, 11648.58±8.33 pg/ml) for 1st, 2nd and 3rd trimesters respectively (p<0.001), and their level were significantly higher than the non- pregnant control of (236.41±137.44 pg/ml) (P < .001). The increase within the trimesters were also significant (p<0.001). The hormonal levels declined drastically during the six weeks postpartum period to 39.44±16.23 pg/ml as shown in Fig. 2.

We attempted to evaluate the influence of educational status of the pregnant women. From our observation, the less educated pregnant women (i.e.≤ 12 years) had the highest concentration of the hormones. Their Progesterone levels were higher than the highly educated (Tertiary i.e.>16 years) and the intermediate (secondary 13-15 years) by 43% and 33% respectively. However, the highly educated women's progesterone levels were higher than the intermediate by 6%, these differences may not be significant considering the sample size. We observed that for 17β-Estradiol, its concentration was higher in both the less educated and intermediate than the highly educated women (Table 5).

Progesterone levels during normal pregnancy and the puerperium (ng/ml)

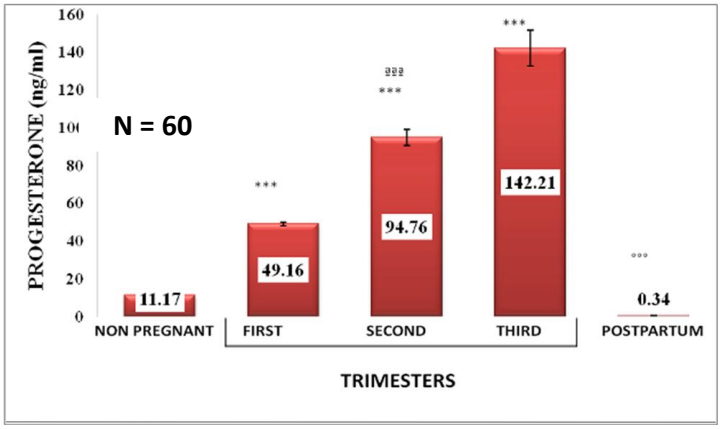

Fig. 1. Bar chart showing serum progesterone level of non-pregnant, pregnant and 6 wks postpartum women

****p<0.001 vs control; [aaa]p<0.001 vs 1st and 3rd trimesters; °°°p<0.001 vs 1st, 2nd and 3rd trimesters*

17β- Estradiol levels during normal pregnancy and the puerperium (pg/ml)

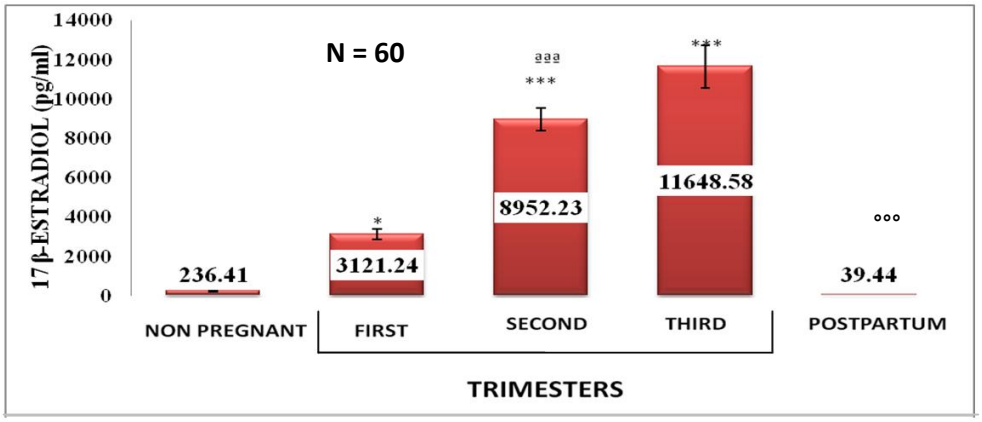

Fig. 2. Bar chart showing serum 17 β-Estradiol level of non-pregnant, pregnant and 6 wks postpartum women

****p<0.001 vs control; * p<0.05 vs control; [aaa]p<0.001 vs 1st and 3rd trimesters; °°°p<0.001 vs 1st, 2nd and 3rd trimesters*

Table 5. Showing the comparison of educational status with hormonal levels during first and second trimesters

Hormones	Primary (0- 9 years)	Secondary (0-13 years)	Tertiary (>17 years)
Progesterone (ng/ml)	96.66±27.9	67.06±25.43	71.95±37.18
17β-Estradiol (pg/ml)	7786±2075	5692.14±4170.14	5674.39±4682.6

Mean ± SD

4. DISCUSSION

Serum levels of progesterone and 17β-estradiol increased in the pregnant women. The increase was progressive from the first trimester, reaching its peak at the third trimester of pregnancy. Although, we observed considerable variability in the level of increase among the pregnant women, the differences observed between the primigravida and the multigravida were not significant (p> 0.05). The correlation analysis also showed that age of the pregnant women had no influence on the levels of both Progesterone and Estradiol increase during pregnancy. The values obtained in this study were comparable to those reported earlier [8], among Swedish women where increases of 600%, 750% in the 25th and 33rd weeks of gestation were obtained. Also there were records of increase in hormonal levels during egg laying cycles in Ostriches [9]. The concentration of Progesterone and Estradiol among the Nigerian women as revealed by this study is higher than those of African-Americans recorded by Potischman and co workers in Boston MA Hospital [10]. This study however, confirmed a higher concentration of the pregnancy hormones among Africans than the Hispanics and the Caucasians as earlier reported, which actually may give credit to some earlier researcher's observations on why Africans have lower risk of cancers (Table 6).

Ethnicity is one factor that has been attributed to the differences but the actual factor which is responsible for these variations are yet to be fully established and call for further research in that area. Our study is also in consonance with their evaluation on educational status' influence on the hormonal levels. In this study, the highly educated had lower concentrations of Progesterone and 17 β-Estradiol than the less educated, the low sample size in this group is a major limitation to testing the significance of the difference.

Other records exist on the levels of progesterone and 17β-estradiol during normal menstrual cycles of Nigerian women [11], at parturition in maternal and fetal blood [12], but to our knowledge the levels of these hormones have not been recorded during uncomplicated

Table 6. Concentrations of progesterone and estradiol among Nigerians and other ethnic groups

Hormones	Nigerians (n = 120	Hispanics (n = 109)	African-Americans (n=56)	Caucasians (n=255)
Estradiol (pg/ml)	5900 (±3232)	1757(1,602 -1927)	1793(1588-2023)	1597(1507-1691)
Progesterone (ng/ml)	71.6 (±20.4)	40.2(37.1-43.50)	46.1(41.5-51.1)	41.8(39.8-44.0)

Mean ± SD

pregnancy and the puerperium. This study has provided a data defining the actual levels of these hormones among Nigerians. What is responsible for the increased concentrations of these hormones is the presence of "feto/placental unit" during pregnancy [13]. Progesterone is produced by the corpus luteum of the ovary up to the first 7-10 weeks of the pregnancy but from implantation of the embryo onwards, the placenta takes over the production [14]. Batra, proposed that the major function of progesterone in pregnancy is to lower estradiol concentration in the myometrium, leading to a higher progesterone/estradiol (P/E2) ratio which in turn is required for the maintenance of pregnancy [15]. The regulation or rather the lowering of estradiol concentration in the myometrium by progesterone is probably achieved by an inhibitory action of progesterone on estrogen receptor synthesis [13]. Progestrone accompanies and modulates estrogen actions [15]. Plasma progesterone and estrogens are cleared rapidly immediately after parturition within three to four days to non pregnant level [16]. Actual lactation occurs after birth due to the more rapid clearance of progesterone in contrast to prolactin, which allowed prolonged prolactin elevation without progesterone inhibition. The levels observed in the 6 weeks postpartum period in this study were slightly lower than the non-pregnant control level, supporting the earlier of progesterone and estrogens is for pregnancy and by the presence of the unique endocrine system "the maternal-fetal-placental unit" [13]. The observation of wide deviations from the mean in the levels of increase which varied largely from woman to woman may be what is responsible for the wide differences in the reaction of different women to pregnancy, such as nausea and vomiting. While some may have nausea and vomiting throughout the pregnancy, others experience only nausea or salivating, while some do not have any discomfort. The mechanisms of these actions/experiences may be subject of another research. It is known from records that under the influence of estrogen, the decrease in gastric secretion of Hydrochloric acid and pepsin leads to decreased fat absorption and increased digestive upsets and nausea commonly experienced by pregnant women [17].

5. CONCLUSION

The levels of progesterone and 17β-estradiol increases progressively throughout pregnancy and declined sharply to levels lower than the non-pregnant state during the puerperium. Age, Parity and educational status seem not to have influence on the increase. High levels of pregnancy hormones may contribute to low level of risk to cancers among Nigerians. The data generated in this study may be used as baseline values for management of pregnant women in Nigeria.

CONSENT

The authors declare that written informed consent was obtained from each patient before being recruited for the study.

ETHICAL CLEARANCE

The study was approved by the Ethical Committee of Bingham University Teaching Hospital, Jos, and was performed in accordance with the guidelines of the Declaration of Helsinki of 1964.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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