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RESEARCH ARTICLE

HAEMATOLOGICAL INDICES IN PREGNANCY AND PUERPERIUM

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ABSTRACT

Background: Pregnancy is a time of considerable maternal adaptation during which the range of normal laboratory values for commonly requested clinical investigations is wider and even more arbitrary than in the non-pregnant state. Although, pregnancy specific values are becoming available due to increased awareness of the obstetrician for their need, the available reference values are mainly based on healthy Caucasians. There is a dearth of information on the reference values for haematological indices particularly in relation to the trimesters of pregnancy and in the puerperium.
Objectives: To determine the reference values for various haematological indices in trimesters of pregnancy and puerperium healthy pregnant and puerperal subjects compared to non-pregnant women
Methods: A cross-sectional prospective study involving 422 subjects carried out over a six-month period. Healthy pregnant, puerperal and non-pregnant subjects recruited for the study and grouped into six. Each subjects had her socio-demographic data and anthropometry documented and haematological indices determined by automated analysis using the Coulter counter method. The results were subjected to statistical analysis using 95% confidence intervals.
Results: The results from this study showed that the difference in the mean haematocrit values in pregnancy was statistically significant between the first and second trimesters (P=0.026) and also between the second and third trimesters (P=0.007). The mean RBC count also showed a significant difference between the first and second trimesters (P=0.032). Other red cell indices (MCV, MCH and MCHC) showed no statistically significant difference in between trimesters. The difference in the mean WBC count values was equally significant between the first and second trimester (P=0.023). A similar significant difference was observed in the mean platelet count between the first and third trimesters (P=0.002).
Conclusion: The lowest red cell parameters (haematocrit, haemoglobin concentration and RBC count) were recorded in the second trimester and there were varying statistically significant differences in the mean haematocrit, haemoglobin concentration, RBC, WBC and platelet values during the trimesters of pregnancy and the puerperium.

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INTRODUCTION

Pregnancy is a time of considerable maternal adaptation during which the range of normal laboratory values for commonly requested clinical investigations is wider and even more arbitrary than applied to non-pregnant state (Taylor and Lind, 1981). Successful outcome of pregnancy requires large number of physiologic adaptations (van Buul *et al*., 1995). These adaptations involve changes of metabolism in most organ systems resulting in alterations of both haematological and biochemical composition of blood. In order to be able to accurately interpret laboratory parameters of pregnant women, physicians caring for them have to be aware of these physiological changes that accompany pregnancy (Campbell and MacGillivary, 1972). Although there is a debate about the magnitude of change, there is general agreement that red cell mass is increased in second and third trimesters of pregnancy (Hytten and Dynesius, 1973; Lange and Leitch, 1971; Walters and Lim, 1975). The control of red blood cell production is probably multi-factorial but one important influence is the hormone erythropoietin. The production of erythropoietin is dependent on tissue oxygen level in the kidneys which in turn is governed by independent factors including atmospheric oxygen tension, pulmonary function, cardiac output, red cell mass and the oxygen affinity of haemoglobin (Taylor and Lind, 1979). During the first trimester of normal pregnancy, there are changes in cardiac output and oxygen affinity in haemoglobin which would tend to influence tissue oxygen levels in the kidney. Plasma erythropoietin level is thus increased in pregnancy but the magnitude of the bone marrow response to it, defined in terms of peripheral red blood cell count and mean

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cell volume will depend on the level of iron supply to the marrow (Hillman and Henderson, 1969; Jacobs and Finch, 1971). The haematological profile of an individual to a large extent reflects her general health status (Focusing on Anaemia, 2004) and many studies have identified the haematological profile of the pregnant woman as one of the factors affecting pregnancy and its outcome (Antenatal Care: routine care for the pregnant woman, 2002; Klebanoff *et al*., 1991; Allen, 2000; Meng *et al*., 1991; Reivez *et al*., 2007; Bothwell and Charlton, 1981). The most common parameter referred to amongst the haematological indices is an indicator of haemoglobin concentration and low haemoglobin (anaemia) is the most widely identified hemoglobin abnormality (Centre for Disease Control and Prevention, 1998). Maternal plasma volume increases by approximately 50% during first and second trimesters of pregnancy whereas the corresponding increase in red cell mass is only 20-30% giving rise to a state of physiological anaemia more profound in mid-pregnancy (Taylor and Lind, 1979; Pirani and Campbell, 1973; Letsky, 1987; Letsky, 1995).

Although pregnancy specific values are becoming available due to increased awareness of the obstetricians for their need (Taylor and Lind, 1979), the available reference values have been mainly those based on healthy Caucasians (Dacie and Lewis, 2001). Reference values for pregnant women have been proposed based on few studies in Nigeria and the tropics (Onwukeme and Uguru, 1990; Obisesan *et al*., 1998). Conflicting results have been documented regarding the statistical significance of variations in some of these haematological parameters at different trimesters. While some workers did not find any significant change between the second and third trimesters with respect to any of the haematological parameters studied amongst Nigerians (Obisesan *et al*., 1998; Famodu *et al*., 1992), Onwukeme and Uguru (1990) reported differences in total white cells and neutrophils counts in similar subjects. This difference was attributed to environmental factors, ethnic and tribal peculiarities (Dapper *et al*., 2006). The role of parity came into fore when Onwukeme in 1992 noted that variations in haemoglobin, heamatocrit, leucocytes and platelet counts in the puerperium were more marked in primipara than multipara (Onwukeme, 1992). Racial component to this variation of haematological values has been observed in various parts of the world. High proportion of low haemoglobin concentration was found in Black and Indian populations compared to Whites and Orientals living in the United Kingdom (Godsland *et al*., 1983). Analysis of data from two major nutritional surveys showed a mean haemoglobin level in Blacks 1g/dL less than Whites (Ghan *et al*., 1975; Abraham *et al*., 1974). This difference was independent of age, economic level and nutritional status (Koh *et al*., 1980; Dallman *et al*., 1978). Essien *et al*. (1973) also found lower platelet count in adult Nigerians than in Caucasian living in Nigeria. Flemin and Harrison found that total white cell and neutrophils counts were lower in Nigerians than the Caucasians (Flemin and Harrison, 1985). The available reference values based on healthy Caucasians may therefore, not be appropriate for our own population due to well recognized nutritional, environmental and genetic factors (Akingbola *et al*., 2003). Recent changes in nutritional status, dietary habits, environmental factors and economy of the country may influence the haematological indices of present day pregnant Nigerians.

Therefore, it is desirable to investigate the reference values for our pregnant and puerperal population to assess the conformity of same with those established references in the literatures. Such a study is of importance since antenatal care and pregnancy outcome is in part predicated on monitoring of and response to these haematological indices. This study is therefore designed to present the range of variation in haematological values in apparently healthy pregnant women attending a large maternity hospital in Lagos, southwestern Nigeria.

Aim and objective

To determine the reference values for various haematological indices in pregnancy and puerperium compared to non-pregnant state and correlate the conformity of data obtained at 6 weeks post partum with that of non-pregnant women.

METHODOLOGY

The study was prospective, comparative study involving healthy pregnant and post-partum subjects in the Department of Obstetrics and Gynaecology, Lagos State University Teaching Hospital, Ikeja, Lagos in South-western part of Nigeria. About 15 new cases were booked every day of the week. The delivery rates were average of 340 births monthly and 4000 births per year. These were compared with age-matched non-pregnant subjects used as control. Approval for the study was obtained from the Ethics Committee of Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos, Nigeria. The subjects for the study were fully briefed on the research protocol in the language they understand.

Sample Size Determination

Sample size for single proportion

$$n = \frac{Z^2.p.(1-p)}{d^2}$$

n = sample size required for the study
Z = the standard normal deviate, usually 1.96 at 95% confidence level
p = prevalence rate (50% was used in this case)
d = precision rate (5%); degree of accuracy required Type of test
= two-sided test

$$n = (1.96)^2 \times 0.5 \times (1 - 0.5) \ (0.05)^2$$
$$= 383$$

A sample size of 383 was required for the study.

In order to accommodate possible attrition or unforeseen errors in completing the study questionnaire or blood sample processing, an additional 10% (39 subjects) of the calculated figure were recruited to bring the figure to 422 subjects.

Sampling technique

Stratified sampling (a probability sampling technique) was used to recruit subjects, following our inclusion and exclusion criteria. Six groups were observed in all; First trimester (up to 14 weeks gestation), second trimester (15– 27 weeks), third trimester (28weeks till term), early puerperium (2 – 4 days postpartum), late puerperium (6 weeks postpartum) and non-pregnant subjects (control). Convenience sampling method (a

non-probability sampling technique) was be used to recruit subjects within the different group as patients were recruited consecutively until the desired sample size was attained. Seventy-one subjects were recruited in the second and third trimester groups while 70 subjects were recruited each for first trimester, early puerperium, late puerperium and non-pregnant subjects making up the total 422 subjects as determined by the sample size calculated. Inclusion criteria for pregnant subjects were healthy women with no adverse medical/obstetrics history and for post-natal subjects were vaginal delivery with estimated blood loss less than 500ml while non-pregnant subjects were healthy women within the reproductive age group. Exclusion criteria include denial of consent, febrile illness in the last four weeks, features or laboratory diagnosis of haemoglobinopathy or bleeding disorder, chronic medical ailment, bleeding in pregnancy (threatened abortion or ante-partum haemorrhage), hypertensive disease in pregnancy including pre-eclampsia and eclampsia and diabetes mellitus. Others were blood transfusion, multipara with last childbirth or miscarriage less than two years, multiple pregnancy, grandmultipara, patients who were delivered by caesarian section and acute renal, liver or systemic diseases acquired during pregnancy. All pregnant women were routinely placed on iron supplementation (ferrous sulphate 200mg thrice daily) and folic acid 5mg daily from the second trimester. Malaria chemoprophylaxis with sulphadoxine-pyrimethamine combination was given after quickening and four to six weeks later according to our institutional policy.

Clinical management

3ml of venous blood is drawn from the antecubital vein by means of venepunture into the vacutainer tubes containing di-potassium ethylene di-amine tetra-acetic acid (K_2-EDTA). Being a cross-sectional study, blood samples were collected from different subjects at 8-14 weeks in first trimester, 22-28 weeks in second trimester and 34-40 weeks in third trimester. Early post partum samples were taken 2-4 days post delivery in lying-in ward. Late postpartum samples were obtained in the postnatal clinic six weeks after delivery. Healthy non-pregnant subjects were recruited among first attendees at the family planning clinic that met the inclusion and exclusion criteria. Samples were collected between 1100 and 1300 hours and refridgerated after proper labeling for identification. They were analyzed within 2-4 hours of collection. Sample analysis was done at the Research laboratory of the Department using BC-3000 Haematology Analyzer Model 2003-2005 (Shenzhen Mindray Bio-medical Electronic Company Limited. China). Indices of measurement included the haemoglobin concentration (Hb), heamatocrit (Hcrt), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), white blood cell count (WBC) with differentials neutrophil and lymphocyte count, red blood cell count (RBC) and platelet count (Platelet), all of which were determined by auto-analysis. Results were recorded in the laboratory form.

Data processing and statistical analysis

Data were analyzed using SPSS version 16.0 (Statistical Package for Social Sciences, Inc., Chicago, Illinois); a statistical computer software. Descriptive statistics (minimum, maximum, mean, and standard deviation) were determined for all haematological indices and other appropriate variables. Proportions and percentages were calculated for categorical variables. One-way analysis of variance (ANOVA), a parametric inferential statistical procedure was used to compare the means of haematological indices in the different groups of patients (Non pregnant, 1st trimester, 2nd trimester, 3rd trimester, early puerperium, and late puerperium). Bonferroni Post Hoc Multiple Comparison was used to compare difference within variables during pregnancy and puerperium with reference to non-pregnant subjects. P-values less than 0.05 were considered to be statistically significant at 95% confidence level.

RESULTS

During the study period, a total of 422 subjects who had complete blood count examination and satisfactorily filled the data collection form were included in the analysis. The age of the subjects studied ranges from 17 to 41 years while the mean values and the standard deviations and ranges for age, weight, height and body mass index of all subjects were as shown in Table I. There was statistically significant difference in only the weight across all groups (P=0.032) in Table I. The subjects in the third trimester group had the highest mean weight (75.34+13.80kg) while the non-pregnant subjects had the least mean weight (62.70+11.60kg). Age, height and body mass index did not show significant difference across the six groups (Table I). One hundred and twenty-three subjects were para 0, 153 subjects were para 1, and 84 subjects were para 2. The remaining 72 subjects were para 3 and 4. Ninety-six percent of the subjects were married, 74.4% had tertiary education while 20% had secondary education. 70.4% of the respondents were from the Yoruba tribe, 16.4% were Igbo and 9.8% were from the Minority group. Only 3.6% respondents were Hausas. 76.8% of the subjects were Christians and 23.2% were Muslims.

HAEMATOCRIT (Packed Cell Volume)

The haematocrit decreased gradually from 31.98 + 2.31% in first trimester to 30.24 + 3.68% in the second trimesters but increased to (32.18 + 3.19%) in third trimester (Table II). It dropped further in early puerperium to (31.49 + 3.71%) but gradually rose to (36.10 + 3.25%) obtained in the late puerperium (Table III). The corresponding value for non-pregnant subjects was 33.84 + 3.39% (Figure I). A total of 233(55.2%) subjects had anaemia (51% mild and 4% moderate) using the haematocrit of 33% as benchmark. The breakdown of anaemic subjects in different groups revealed 55% of those in first trimester, 61% among second trimester and 52% in third trimester subjects. The remaining were 53% of those in early puerperium, 24% of those in late puerperium and 42% of the non-pregnant subjects. None of the subject had severe anaemia. Comparison of the mean haematocrit values for all groups using analysis of variance (ANOVA) was statistically significant with P= 0.001.

Haemoglobin concentration

The mean haemoglobin concentration decreased gradually from 10.22 + 0.88g/dl in first trimester to 9.63 + 1.25g/dl the second trimesters but subsequently increased to 10.18 + 1.14g/dl in third trimester (Table II). It declined in early puerperium marginally to 10.13 + 1.28g/dl and thereafter increased progressively to 11.37 + 1.27g/dl in the late puerperium (Figure II). The mean haemoglobin concentration was 10.50 + 1.50 g/dl in non-pregnant subjects. Following the

analysis of haemoglobin concentration, 66 (15.6%) subjects had moderate anaemia and 222(52.6%) had mild anaemia using the WHO criteria. Comparison of the mean haemoglobin concentration values for all groups (ANOVA) was statistically significant with P= 0.001.

Mean Corpuscular Volume (MCV)

The mean corpuscular volume changed little in the subjects studied. The MCV in the first trimester (81.13 + 4.84fl) increased to 83.67 + 5.54fl and 84.41 + 7.10fl in second and third trimesters respectively (Table II). After delivery, the MCV dropped to (82.86 + 7.12fl) in early puerperium and (82.68 + 5.94fl) in late puerperium which was close to the non-pregnant value of 82.41 + 5.57fl (Figure III). With the P value of 0.222, the mean values of the MCV in all groups showed no statistically significant difference.

Mean Corpuscular Haemoglobin (MCH)

The mean corpuscular haemoglobin increased slightly from 26.26 + 2.00pg in the first trimester to 26.55 + 2.70 pg and 26.60 + 2.91pg in second trimester and third trimesters respectively (Table II). After delivery, it gradually declines to 26.30 + 3.13pg in early puerperium and 26.06 + 2.53pg in late puerperium which was higher than 25.52 + 2.78pg in non-pregnant subjects. (Figure IV). Comparing the trend in the mean corpuscular haemoglobin in all groups, it was not significant at the P value of 0.189.

Mean Corpuscular Haemoglobin Concentration (MCHC)

The MCHC decreased from 32.01 + 1.54g/dl in the first trimester to 31.73 + 1.72g/dl and 31.59 + 1.45g/dl in the second and third trimesters respectively (Table II). The MCHC thereafter increased slightly to 31.85 + 1.83g/dl in early puerperium but dropped again to 31.57 + 1.68g/dl in late puerperium which was higher than 31.07 + 2.04g/dl in non-pregnant subjects (Figure V). Comparing the trend of the means of corpuscular haemoglobin concentration in all groups, it was statistically significant with the P value of = 0.033.

Red Blood Cell count (RBC)

The red blood cell count decreased from 3.88 + 0.28 × 10^6/µl in the first trimester to 3.64 + 0.49 × 10^6/µl in second trimesters and increased marginally thereafter to 3.84 + 0.51 × 10^6/µl and 3.86 + 0.53 × 10^6/µl in third trimester (Table II) and early puerperium respectively. Subsequently, it rose markedly to 4.39 + 0.49 × 10^6/µl in late puerperium which was higher than 4.12 + 0.43 × 10^6/µl of non-pregnant subjects (Figure VI). Comparing the trend of the mean value of red blood cell count in all groups, it was statistically significant at P value of 0.001.

White Blood Cell count (WBC)

The mean white blood cell count increased gradually form 6.97 + 1.89 × 10^3/µl in first trimester to 8.19 + 1.93 × 10^3/µl in second trimester. It then dropped to 7.26 + 1.86 × 10^3/µl in the third trimester (Table II). It thereafter rose markedly to 10.25 + 3.92 × 10^3/µl in early puerperium and then declined sharply to 5.53 + 1.42 × 10^3/µl in late puerperium which was the lowest value of all the subgroups (Figure VII). The value for non pregnant subject was 5.82 + 1.62 × 10^3/µl. Comparing the trend of mean white blood cell count in all groups, it was statistically significant with the P value of = 0.001.

Neutrophil count

The mean neutrophil count increased from 63.38+7.74% in first trimester to 69.14 + 6.09% in the second trimester but dropped slightly to 66.72 + 8.25% in third trimester (Table II). It rose slightly again to 69.71 + 9.10% in early puerperium but declined markedly to 51.03 + 8.19% in late puerperium close to the non-pregnant value of 63.38 + 7.74% (Figure VIII). Comparing the trend of the means of neutrophils in the different groups, the P value of 0.001 showed statistically significant difference.

Lymphocyte count

The mean lymphocyte count decreased from 26.51 + 5.77% in the first trimester to 22.76 + 6.09% in second trimester. It subsequently increased slightly to 23.91 + 5.91% in third trimester (Table II). However, it declined to 21.87 + 7.04% in early puerperium and rose markedly thereafter to 37.74 + 8.08% in late puerperium compared to 39.46 + 7.55% in non-pregnant subjects. (Figure IX). The trend of the mean value of lymphocytes in all groups showed statistically significant difference at the P value of 0.001.

Platelet count

The mean platelet count decreased gradually during pregnancy from 239.69 + 62.48 × 10^3/µl in the first trimester to 214.38 + 54.01 × 10^3/µl and 202.18 + 55.19 × 10^3/µl in second and third trimesters respectively (Table II). It rose slightly to 203.66 + 46.76 × 10^3/µl in early puerperium and markedly to 245.71 + 58.97 × 10^3/µl in late puerperium which was close to 250.76 + 69.47 × 10^3/µl obtained in non-pregnant subjects (Figure X). Six (1.4%) subjects had platelet count between 94 -100×10^3/µl and 33(7.8%) had platelet count between 101-149× 10^3/µl. Comparing the trend of the means of platelet count in all groups, the P value of 0.001 showed statistically significant difference.

Comparison of variables across the trimesters of pregnancy and puerperium

The mean values for each variable in pregnancy were compared between the trimesters (Table IV). The difference in the mean haematocrit was found to be statistically significant between first and second trimester (P=0.026) and second and third trimesters (P=0.007). There was no statistically significant difference in the mean haemoglobin concentration in between trimesters among the subjects. There was statistically significant difference between RBC count in first and second trimester only. Other red cell indices MCV, MCH, MCHC showed no statistically significant difference in between trimesters. Comparison of the mean values of WBC between first and second trimester showed statistically significant difference which is similar to that obtained for mean platelet value between the first and third trimesters. Table V showed comparison of the mean values among variables in early puerperium, late puerperium and non-pregnant subjects. The difference in the mean haematocrit values between i) early and late puerperium (P<0.001), ii) early puerperium and non-pregnant subjects (P<0.001) and iii) late puerperium and non-pregnant subjects (P<0.001) were found to be statistically significant.

Table I. Age, Weight, Height and Body Mass Index Values in pregnancy and puerperium

	First Trimester	Second Trimester	Third Trimester	Early Puerperium	Late Puerperium	Non Pregnant	P-value
Age (years)	31.04 + 3.85	30.07 +4.18	30.08 +3.85	29.99 +4.08	30.27 +4.64	29.99 +5.68	P=0.655 NS
Weight (Kg)	69.12 +14.20	69.06 +12.60	75.34 +13.80	73.51 +10.10	72.68 +13.94	62.70 +11.60	P=0.032 S*
Height (m)	1.57 +1.07	1.58 +1.10	1.58 +1.40	1.57 +1.35	1.58 +1.16	1.59 +1.22	P=0.867 NS
B.M.I (Kg/m^2)	28.04 +4.45	27.66 +5.80	30.20 +4.28	29.82 +6.65	29.09 +5.56	24.80 +3.86	P=0.089 NS

Table Legend: NS=not significant, S*= Statistically significant, B.M.I – body mass index
Values are given as mean + standard deviation

TABLE II. Haematological values in the three trimesters of pregnancy

	First Trimester N=70	Second Trimester n=71	Third trimester n=71	Sig. Difference
Haematocrit (%)	31.98+3.39 (25.50-38.6)	30.24+3.68 (24.9-35.4)	32.18+3.19 (26.4-39.2)	Yes p=0.001
Haemoglobin Concentration (g/dL)	10.22+0.88 (8.00-12.90)	9.63+1.25 (7.80-11.60)	10.18+1.14 (8.80-12.90)	Yes p=0.001
RBC count ($x10^6/\mu l$)	3.88+0.28 (3.16-4.63)	3.64+0.49 (2.28-6.14)	3.84+0.51 (2.79-5.38)	Yes p=0.001
Mean Corpuscular Volume (MCV)(fl)	82.13+4.84 (67.30-93.50)	83.67+5.54 (68.30-96.10)	84.41+7.12 (68.10-105.20)	No p=0.222
Mean Corpuscular Haemoglobin (MCH) (pg)	26.26+2.00 (21.10-31.90)	26.55+2.70 (20.50-31.60)	26.60+2.91 (19.70-32.90)	No p=0.189
Mean Corpuscular Haemoglobin Concentration (MCHC) (g/dL)	32.01+1.54 (29.00-36.00)	31.73+1.72 (29.00-35.30)	31.59+1.45 (28.90-35.00)	Yes p=0.033
WBC count ($\times 10^3/\mu l$)	6.97+1.89 (3.60-11.10)	8.19+1.93 (4.70-15.40)	7.26+1.86 (3.10-12.40)	Yes p=0.001
Neutrophils (%)	63.38+7.74 (39.30- 80.20)	69.14+6.09 (54.90-82.50)	66.72+8.25 (48.50-84.50)	Yes p=0.001
Lymphocytes (%)	26.52+5.77 (11.50-39.40)	22.76+6.09 (8.70-39.90)	23.91+5.91 (11.30-37.90)	Yes p=0.001
Platelet count ($\times 10^3/\mu l$)	239.69+62.48 (112 - 439)	214.38+54.01 (102 – 353)	202.18+55.19 (117 – 404)	Yes p=0.001

All values = mean + standard deviation, range in parenthesis.Sig.= significant

TABLE III. Haematological values in puerperium and non-pregnant subjects

	Early puerperium n=70	Late puerperium n=70	Non pregnant n=70	Sig. Difference
Haematorit (%)	31.49+3.71 (25.70-37.90)	36.10+3.25 (28.90-48.10)	33.84+3.39 (26.40-39.20)	Yes p=0.001
Haemoglobin Concentration (g/dL)	10.13+1.28 (8.30-12.90)	11.37+1.27 (9.70-14.10)	10.50+1.50 (8.50-15.10)	Yes p=0.001
RBC count ($x10^6/\mu l$)	3.86+0.53 (2.75-4.90)	4.39+0.49 (3.33-5.74)	4.12+0.43 (3.10-5.49)	Yes p=0.001
Mean Corpuscular Volume (MCV)(fl)	82.86+7.12 (67.70-96.50)	82.68+5.94 (67.70-94.20)	82.41+5.57 (64.20-94.10)	No p=0.222
Mean Corpuscular Haemoglobin (MCH)pg	26.26+2.00 (20.00-30.40)	26.55+2.70 (21.00-31.30)	26.60 + 2.91 (18.70-30.20)	No p=0.189
Mean Corpuscular Haemoglobin Concentration (MCHC) (g/dL)	32.01 +1.54 (27.10-35.50)	31.73 +1.72 (28.60-35.60)	31.59 + 1.45 (27.90-34.80)	Yes p=0.033
WBC count ($\times 10^3/\mu l$)	10.25+3.92 (4.20-23.30)	5.53+1.42 (3.20-9.40)	5.82+1.62 (3.60-13.70)	Yes p=0.001
Neutrophils (%)	69.71+9.10 (46.90- 89.50)	51.03+8.19 (31.20-69.00)	48.04+8.32 (30.90-70.70)	Yes p=0.001
Lymphocytes (%)	21.87+7.04 (7.30-37.80)	37.74+8.08 (22.30-59.40)	39.46+7.55 (22.16-58.00)	Yes p=0.001
Platelet count ($\times 10^3/\mu l$)	203.66 +46.76 (100 - 317)	245.71 +58.97 (117 – 404)	250.76 +69.47 (92 – 458)	Yes p=0.001

n= number of subjectsSig.= significant
All values are mean + standard deviation, range in parenthesis.

Table IV. Haematological values over the three trimesters of pregnancy in the study population

Parameters	Trimester 1	Trimester 2	Trimester 3	p-value		
				1st & 2nd	1st & 3rd	2nd & 3rd
RBC (x10^6/µl)	3.88 ± 0.28	3.64 ± 0.49	3.84 ± 0.51	0.032*	1.000	0.167
Hb (g/dl)	10.22 ± 0.88	9.63 ± 1.25	10.18 ± 1.14	0.067	1.000	0.116
PCV (%)	31.98 ± 2.31	30.24 ± 3.68	32.18 ± 3.19	0.026*	1.000	0.007*
MCH (pg)	26.26 ± 2.00	26.55 ± 2.70	26.60 ± 2.91	1.000	1.000	1.000
MCHC (g/dl)	32.01 ± 1.54	31.73 ± 1.72	31.59 ± 1.45	1.000	1.000	1.000
MCV (fl)	82.13 ± 4.84	83.67 ± 5.54	84.41 ± 7.10	1.000	0.393	1.000
WBC (× 10^3/µl)	6.97 ± 1.62	8.19 ± 1.89	7.26 ± 1.86	0.023*	1.000	0.222
Platelets (× 10^3/µl)	239.69 ± 62.48	214.38 ± 54.01	202.18 ± 55.19	0.152	0.002*	1.000

Table legend text: Mean (± S.D)±
RBC – Red blood cell, Hb – Haemoglobin, PCV – Packed cell volume, MCH – Mean corpuscular haemoglobin, MCHC – Mean corpuscular haemoglobin concentration, MCV – Mean corpuscular volume, WBC – White blood cell * indicates the level of significance p < 0.05. Values are represented as Mean± S.D

Table V. Haematological values over the puerperium and non pregnant women in the study population

Parameters	EPP	LPP	NP	p-value		
				EPP & LPP	EPP& NP	LPP & NP
RBC (x10^6/µl)	3.86 ± 0.53	4.39 ± 0.49	4.12 ± 0.43	0.000*	0.013*	0.011*
Hb (g/dl)	10.13 ± 1.28	11.37 ± 1.27	10.50 ± 1.50	0.000*	1.000	0.001*
PCV (%)	31.49 ± 3.71	36.10 ± 3.25	33.84 ± 3.39	0.000*	0.000*	0.001*
MCH (pg)	26.30 ± 3.13	26.06 ± 2.53	25.52 ± 2.78	1.000	1.000	1.000
MCHC (g/dl)	34.35 ± 1.05	34.42 ± 1.30	34.33 ± 1.43	1.000	0.111	1.000
MCV (fl)	85.89 ± 7.28	87.49 ± 7.02	86.70 ± 6.85	1.000	1.000	1.000
WBC (× 10^3/µl)	10.25 ± 3.92	5.53 ± 1.42	5.82 ± 1.62	0.000*	0.000*	1.000
Platelets (× 10^3/µl)	203.55 ± 46.76	245.32 ± 58.97	250.76 ± 69.47	1.000	0.000*	1.000

Table legend text:
RBC – Red blood cell, Hb – Haemoglobin, PCV – Packed cell volume, MCH – Mean corpuscular haemoglobin, MCHC – Mean corpuscular haemoglobin concentration, MCV – Mean corpuscular volume, WBC – White blood cell EPP – early puerperium, LPP – late puerperium, NP – non pregnant women
* indicates the level of significance p < 0.05. Values are represented as Mean ± S.D

However, the difference between the mean values of early puerperium and late puerperium and late puerperium and non-pregnant subjects were found to be statistically significant in haemoglobin concentration and RBC count values (P<0.05). No significant difference was observed in MCV, MCH, MCHC when mean values were compared between early and late puerperium, puerperal and non-pregnant groups. The mean values of WBC count also revealed statistically significant difference between early puerperium and late puerperium (P<0.001). However, only pairing of early puerperium and non-pregnant subjects showed statistically significant difference in the mean platelet count.

DISCUSSION

It is well known that pregnancy imposes substantial burden on maternal haemopoietic system because of the need for erythropoiesis in the face of expanding blood volume. Therefore studies providing reference haematological and other parameters in apparently healthy individuals in various physiological states will certainly continue to be relevant (Magwendeza *et al*., 2000; Flagar-Meztric *et al*., 2000). Although, the phenomenon of changes in normal laboratory values induced by pregnancy is well recognized, very few laboratory provide reference range for pregnant women (Abbassi-Ghanavati *et al*., 2009). This study discussed the findings of a cross-sectional study of complete blood count utilizing automated techniques in normal pregnant and puerperal subjects attending a large tertiary maternity unit in Lagos. The highest mean weight in the subjects in third trimester of pregnancy is consistent with the established physiological weight changes in pregnancy since most weight gain occurred in the last two trimesters (Du Bois and Du Bois, 1916). However, despite this significant difference in weight, significant difference in the body mass index was not observed in all study groups. This was in agreement with the observation that the contribution of body mass index to variation in haematological indices was negligible (Godsland *et al*., 1983). This study did not demonstrate significant association between parity and the various study groups. While parity is known to influence haematological indices in pregnancy (Aimakhu and Olayemi, 2003) and puerperium (Onwukeme, 1992), the role of parity in determination of haematological profile was not examined in this study. More so, grandmultiparous women and those with short inter-pregnancy interval which could lead to depleted iron store with consequent iron deficiency anaemia have been excluded from this study.

Red Blood Cell (RBC) count and indices

This study showed clearly that there is significant fall in haematocrit, haemoglobin concentration and RBC count in pregnancy especially in the first and second trimester followed by a small rise in the third trimester. The trend in these indices is comparable to reports in other studies (Taylor and Lind, 1979; Flemin and Harrison, 1985; James *et al*., 2008). While some workers noted consistent decrease in the haematocrit throughout pregnancy (Akingbola *et al*., 2003), other did not find any significant change (Onwukeme and Uguru, 1990; Obisesan *et al*., 1998; Dapper *et al*., 2006). The mean values of haematocrit in this study are higher than those reported by Dapper *et al*. (2006) but similar to that obtained by Akingbola

et al. (2003). The increased haematocrit in the third trimester has been attributed to plateau of plasma volume expansion from the 30th week of gestation compared to sustained erythropoiesis throughout pregnancy (Pirani and Campbell, 1973; Letsky, 1995). The mean values for haemoglobin concentration in the three pregnant groups in this study were lower than the 11.0 g/dL recommended by the WHO. Similar observation has been made in other studies in pregnant Nigerian women (Onwukeme *et al*., 1990; Obisesan *et al*., 1998; Dapper *et al*., 2006; Akingbola *et al*., 2003). By WHO criteria (World Health Organization, 1972), 68.2% of this study population presented with anaemia (52.6% mild and 15.6% moderate anaemia). Similar reports of anaemia in pregnancy have been documented in several Nigerian studies 51.4% (Aimakhu and Olayemi, 2003), 50-60% (Iloabachie and Meniru, 1990) and 36-56% (Reviews April, 1998). However, using a lower haemoglobin concentration of 10g/dL as proposed by Harrison (2001) and Ogunbode (Ogunbode, 1995), only 15.6% of the subjects would be qualified as being anaemic. The cause of anemia has been ascribed to increased physiological demand of pregnancy and plasma volume expansion in excess of increased red cell mass. The effects are more marked in developing countries like Nigeria probably due to lack of balanced dietary intake, hookworm infestation, malaria and frequent pregnancies with short intervals (Anorlu *et al*., 2006). Complications of anaemia include increased risk of miscarriage, still birth, premature delivery, intra-uterine growth restriction and low birth weight. The relationship between anaemia and adverse pregnancy outcome, despite much research, is still unclear. The evidence that maternal anaemia can reduce a pregnant woman's ability to withstand blood loss or that it increased the risk of spontaneous abortion, preterm delivery, low birth weight and maternal mortality (Sloan *et al*., 2002; Rosso, 1990; Llewellyn-Jones, 1965) is inconclusive (World Health Organization, 1999; Rush, 2000). However, anaemia once discovered must be properly evaluated to identify the cause and prompt treatment instituted. In practice, for more than 3 decades, many hospitals use a lower level of haemoglobin concentration of 10g/dL or less as indicating anaemia. This level has been justified on the basis of the work of Lawson in 1967 which showed that serious harm to the fetus did not occur until haemoglobin value was below 10g/dL or packed cell volume below 30% (Aimakhu and Olayemi, 2003). Studies on the relationship between maternal haemoglobin concentration at term and the birth weight did not report any adverse feto-maternal (Aimakhu and Olayemi, 2003) or perinatal outcome (Akinola *et al*., 2008).

It is also noteworthy that hypervolaemia of pregnancy that played a significant role in occurrence of anaemia in pregnancy is not without benefit. While it safeguards the mother against adverse effect of blood loss associated with parturition, it is also important for fetal growth and well-being. This facilitates adequate blood flow in the feto-placenta unit and enhances transfer of oxygen and nutrients to the fetus. On the other hand, high haematocrit that may represent failure of plasma volume expansion can also lead to low birth weight even after controlling for hypertension and pre-eclampsia (Steer *et al*., 1995). The mechanism by which this effect is mediated is unknown but may be related to increased blood viscosity with consequent disturbance in flow. In this study, the MCV rose progressively but insignificantly during pregnancy to the peak in third trimester and gradually decline during the puerperium close to the non-pregnant level at 6 weeks postpartum. This finding is similar to reports by other authors (Dapper *et al*., 2006; Koh *et al*., 1980; Akingbola *et al*., 2003). This rise in MCV is more pronounced in iron supplemented pregnant women (Letsky, 1991) as in this study population. Since the haemoglobin concentration which provides a quantitative measure of the severity of anaemia lacks sensitivity and specificity (Van de Broek *et al*., 1998), the MCV may be a better index of anaemia in pregnancy than haemoglobin concentration and haematocrit because both are reduced by increase in plasma volume (Taylor and Lind, 1979). Considering the fact that Lower haematological values has been reported for Africans than Caucasians (Ezeilo, 1981; Ukaejiofo *et al*., 1979), it may be deduced that the apparently lower values of haematocrit and haemoglobin concentration in the context of normal MCV and MCHC reflects the true range of normal values of these indices in Nigerian population rather than being considered anaemic. Similar findings have been reported by other Nigerian authors (Onwukeme and Uguru, 1990; Obisesan *et al*., 1998; Akingbola *et al*., 2003). For practical use, haemoglobin concentration (Hb) of 10g/dL or haematocrit of 30% in the context of normal MCV may be considered as a general discriminatory value for anaemia in pregnant women in this environment. This has been suggested by previous workers (Harrison, 2001; Ogunbode, 1995; Kuhner and Schmidt, 2000). Therefore incidence of anaemia in the six groups at haemoglobin concentration of 10g/dL or less becomes 17.6% overall. The breakdown among different groups was 4%, 20% and 10 % among the first, second and third trimester groups respectively. While 17%, 3% and 11% represents anaemia in early puerperium, late puerperium and non-pregnant groups respectively.

It was also noted in this study that the MCH increased slightly but not significantly during pregnancy reaching the peak in third trimester. Thereafter, it declined during puerperium to 26.06pg at 6 weeks post-partum which was close to the non-pregnant value of 25.52pg. This finding was consistent with similar reports (Taylor and Lind, 1979; Akingbola *et al*., 2003). Other workers also observed progressive decrease in the MCH during pregnancy (Dapper *et al*., 2006; James *et al*., 2008). The MCHC decline slightly but significantly during pregnancy, then increased marginally in early puerperium and thereafter reduce to 31.57g/dL in the late puerperium compared to 31.07g/dL obtained for non-pregnant subjects. This was consistent with the findings of Taylor and Lind (Taylor and Lind, 1979). The haemoglobin concentration, haematocrit and RBC count dropped slightly in early puerperium and increased thereafter towards normal level at the end of puerperium. This finding is comparable to that of other authors (Taylor and Lind, 1979; Onwukeme, 1992; Flemin and Harrison, 1985; James *et al*., 2008). While some authors reported similar mean values of haemoglobin and haematocrit for late puerperium and non-pregnant subjects (Onwukeme, 1992; James *et al*., 2008), the mean values of these indices in this study at late puerperium were higher than that for non-pregnant subjects.

The poor correlation between the mean values of all RBCs indices in late puerperium compared to non-pregnant values suggests that complete return of these indices to normal may be complex. Taylor and Lind (1979) in their longitudinal study did not achieve the non-pregnant values in their subject until 6 months after delivery. This may be due to the fact that haematological indices do not undergo simple reversal to non-pregnant values at the end of puerperium because of probable shift in fluid and cellular compartments which is poorly understood.

White Blood Cells

The white cell count in this study rose markedly from first to second trimester and then reduced slightly in the third trimester. It rose again in early puerperium to the peak level and thereafter decreased significantly during puerperium to reach the non-pregnant value at 6 weeks postpartum. This trend is similar to that reported by Tameika *et al*. (2008) but differs from those reports that noted progressive leucocytosis throughout pregnancy (Obisesan *et al*., 1998; Akingbola *et al*., 2003; Sejeny *et al*., 1975). However, few workers have also reported a decrease (Dapper *et al*., 2006). This leucocytosis might be attributable to normal acute inflammatory response to placenta delivery and episiotomy site in early puerperium. Since an increased white cell count is universal in early puerperium, it may not be justifiable to interpret leucocytosis alone at this time as being indicative of infection (Taylor and Lind, 1981) without considering other clinical features of sepsis. The trend in the neutrophil count in this study followed that of white blood cell supporting the fact that changes in white cell count in pregnancy predominantly reflects changes in neutrophils (Kuhner and Schmidt, 2000). Many studies have also reported gradual decrease in WBC and neutrophil count from early to late puerperium when non-pregnant values were achieved (Onwukeme, 1992; Flemin and Harrison, 1985). The lymphocyte count in this study decreased from first to second trimester then rose slightly in third trimester to decline again in early puerperium. Thereafter, it increased significantly during puerperium to a mean value close to the non-pregnant level at 6 weeks post-partum. This finding was inconsistent with others that reported gradual decrease in lymphocyte count during pregnancy (Flemin and Harrison, 1985; Akingbola *et al*., 2003). The increased in lymphocyte count during the puerperium observed in this study was also observed by others workers (Onwukeme, 1992; Flemin and Harrison, 1985). The lymphocytosis in the puerperium has been attributed to presence of soluble factors (possibly $alpha_2$-globulin and acute phase reactants). Of importance also is the physiological response to trauma at delivery rather than any reflection of immuno-regulatory events (Pitkin and Witte, 1979; Lurie *et al*., 2008).

The platelet

This study showed that the platelet count decreased progressively during pregnancy to term. This was the common trend in most reports (Sejeny *et al*., 1975; Cabaniss and Cabaniss, 1987; Shaper *et al*., 1968). While some workers have reported increased platelet count during pregnancy (Obisesan *et al*., 1998), it may follow an undulating pattern by increasing in second and declining in the third trimester (Akingbola *et al*., 2003). The reason behind this fall in platelet count during pregnancy is not definite. While some workers opined that it may be due to the dilutional effect of relative increase in plasma volume assuming platelet production is fairly constant during pregnancy (Pekonen *et al*., 1986), others have attributed it to benign gestational thrombocytopaenia (Sejeny *et al*., 1975). After delivery, the platelet count rose again from early puerperium markedly to non-pregnant level by 6 weeks postpartum (Taylor and Lind, 1979). The rise in the platelet count after delivery can be considered as a compensatory increase in platelets production after a period of platelet consumption during separation and delivery of the placenta (van Buul *et al*., 1995). This also helps in maintaining haemostasis after delivery to prevent post-partum haemorrhage.

In this study, 98.6% of all subjects have platelet counts over 100,000 $x10^3/\mu l$ while only 1.4% had thrombocytopaenia. This 1.4% value of platelet count less than 100,000 is lower than the 3.6% reported by Akingbola *et al*. (Flemin and Harrison, 1985). Though, the incidence is low in this study, thrombocytopaenia occurring during pregnancy deserves evaluation. The cause can usually be determined by thorough history, physical examination and directed laboratory studies. It is important to consider normal reference ranges specific to pregnancy when interpreting some laboratory results that may be altered by normal changes of pregnancy. Unless these normal gestational related alterations are taken into account when evaluating laboratory values in pregnant and puerperal women, physiologic adaptations of pregnancy can be misinterpreted as pathologic or alternatively, pathological findings may not be recognized (Abbassi-Ghanavati *et al*., 2009). This study describes the changes in haematological indices in pregnancy and puerperium and suggests accurate reference range of values for haematological parameters in apparently normal and healthy pregnant and puerperal patients. Important observation lies in the fact that while lower haematological values were reported for pregnant and non-pregnant women, values of haemoglobin concentration 10g/dL or lower and haematocrit of less than 30% may be considered as anaemia in presence of normal MCV or MCHC. This study has a few limitations. Firstly, it was a cross-sectional study. A longitudinal study may be more desirable because observed changes and trends during pregnancy and puerperium may be more accurate. It could have also excluded unobserved individual differences in the study population. Secondly, the sample studied is hospital-based and findings obtained may not be applicable to the general population. Despite these limitations, this study probably provides accurate values of the range of haematological indices expected of apparently healthy pregnant and postpartum women attending Ayinke House Maternity Hospital in Lagos.

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