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Effect of Pregnancy on Hematological Profile of Female Subjects from a Private Hospital in Benin City, Edo State, Nigeria

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ABSTRACT: Pregnancy is characterized by important variations in virtually every organ system to accommodate the growing and developing fetoplacental entity. Hence, the objective of this study is to assess the effect of pregnancy on hematological profile of female subjects attending a private hospital in Benin City, Edo State, Nigeria using eighty female volunteered individuals comprising sixty pregnant subjects and twenty nonpregnant subjects. The pregnant group was further categorized into three trimesters, each consisting of twenty participants. Results were presented as Mean ± SD and analyzed using GraphPad Prism 5 software (GraphPad Software Inc.), and $p < 0.05$ was considered statistically significant. Overall, the mean values of lymphocytes, red blood cells, hematocrit, hemoglobin, and platelets were decreased in the pregnant cohort when compared to the nonpregnant cohort, whereas an incremental rise in white blood cell, and granulocytes were observed in the pregnant cohort when compared to the nonpregnant cohort. A statistically significant difference ($p < 0.05$) in the mean hematocrit and hemoglobin values was observed when comparing the first-trimester participants with the control participants, although white blood cells, granulocytes, lymphocytes, red blood cells, and platelets were not different ($p > 0.05$). The average values for white blood cells, granulocytes, red blood cells, hematocrit, and hemoglobin between second-trimester individuals and those of nonpregnant individuals exhibited a significant variance ($p < 0.05$), while the average lymphocyte and platelet counts showed no significance ($p > 0.05$). the mean white blood cells, granulocytes, lymphocytes, red blood cells, hematocrit, hemoglobin, and platelet counts for the third-trimester subjects were significantly different ($p < 0.05$) when compared to the control subjects. The study outcome suggests that pregnancy affects hematological indices and may be a risk predictor for pregnancy-associated complications.

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Pregnancy is the period that covers conception and fetal development, and it usually lasts for about 40 weeks. There are three periods of pregnancy, also referred to as trimesters, each consisting of approximately 12 weeks (NICHD, 2021; Davis, 2021). During each trimester, there is a physiological modification of the maternal body to accommodate the developing fetus (Saleem *et al*., 2022). Pregnancy is considered an anabolic and catabolic phase requiring several metabolic adjustments to sustain the growth and developmental demands of the fetus while maintaining maternal homeostasis (King, 2000; Longo, 2018). Normal pregnancy may be characterized by both physiologic and pathologic changes (Mba *et al*., 2019). Consistent with these alterations are considerable weight gain, changes in hormonal secretions, a slight reduction in blood pressure, an increase in respiratory rate and tidal

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volume, and a reduction in functional residual capacity and peak expiratory flow rate (Saleem *et al*., 2022). Furthermore, these pregnancy-related changes may also be reflected in the hematological profile during the trimesters. The main hematological changes that occur include physiologic anemia, neutrophilia, mild thrombocytopenia, the elevation of procoagulant factors, and diminished fibrinolysis (Paidas *et al*., 2011).

Hematological assessment is an essential part of prenatal care that aids in evaluating the pregnant woman's state of health and may positively or negatively predict the pregnancy outcome (James *et al*., 2008; Allen, 2000; Klebanoff *et al*., 1991). It is important to note that the pregnancy outcome may be proportionate to the magnitude of the hematological change (Kaur *et al*., 2014). During the first trimester, the performance of a maternal assessment through the study of the patient's clinical record, along with other laboratory investigations, can assist in defining the risk for obstetric emergencies such as macrosomia, intrauterine growth restriction (IUGR), fetal abnormalities, miscarriage, stillbirth, pre-eclampsia (PE), gestational diabetes mellitus (GDM) and preterm delivery (Abell *et al*., 2015). The occurrence of hematological shifts during pregnancy is to accommodate the advancing fetal and placenta requirements, therefore, causing profound changes in the blood components. The raised plasma volume averages about 40 to 45% and is achieved by the activity of the female ovarian hormones, activating the juxtaglomerular renal cells to release renin and thereby triggering the renin-angiotensin system (RAS), with subsequent retention of salt in the kidney and body fluid expansion. This high plasma volume happens fast toward the late second trimester (Gebreweld *et al*., 2018). Dilutional anemia results from a heightened ratio of plasma volume to red blood cell (RBC) mass (Akinlaja. 2016). There is a widespread increase in plasma volume, red cell mass, and adaptive immunological differences initiated by leukocytosis, leading to a significant rise in white blood cell (WBC) count, with neutrophils increasing the most and stimulated by estrogen (Awajiomowa *et al*., 2022). Hemoglobin (HGB) concentration, hematocrit (HCT), and red blood cell counts remain unaffected until the early second trimester of pregnancy, followed by a drop (Kaur *et al*., 2014).

The physiological stress of pregnancy causes the WBC to increase early and is maintained throughout the pregnancy period (Kaur *et al*., 2014). In differential count, whereas the neutrophils are the primary raised leukocytes, most likely due to inadequate neutrophil apoptosis and while having an augmented oxidative metabolism, eosinophils and basophils have no significant change (Chandra *et al*., 2012). In addition, Mba *et al*. in 2019 reported a reduction in lymphocyte (LYMPH) counts in the first and second trimesters with a somewhat third-trimester rise. Monocytosis usually arises in the first trimester but reduces as the pregnancy advances (Chandra *et al*., 2012). Physiological leukocytosis appears from raised inflammatory responses stimulated by the fetal selective immune tolerance, immunomodulation, and immunosuppression (Osonuga *et al*., 2011). There is a steady decrease in platelet (PLT) counts during pregnancy, especially in the third trimester (Chandra *et al*., 2012), with increased aggregation towards the last few weeks of pregnancy (Kaur *et al*., 2014). Gestational thrombocytopenia, although typically benign and asymptomatic (Akinlaja. 2016), is caused by multiple factors.

In Nigeria, previous researchers have evaluated the hematological differences that occur during gestation among women in Port Harcourt (South-South) (Awajiomowa *et al*., 2022), Bauchi (North-East) (Kadas *et al*., 2020), Benue (North-Central) (Michael *et al*., 2017), Sokoto (North-West) (Musa *et al*., 2016), Abia (South-East) (Ifeanyi *et al*., 2014), and Lagos (South-West) (Akinbami *et al*., 2013). This study is significant because the quality and quantity of hematological parameters can affect pregnancy outcomes and is a risk predictor for pregnancy-associated complications. Therefore, due to limited studies on the outcome of pregnancy on hematological indices in Benin City, this study is designed to evaluate the effect of pregnancy on the hematological profile of female subjects attending a private hospital in Benin City, Edo State, Nigeria.

MATERIALS AND METHODS

The research participants for this study were randomly selected from St. Philomena Catholic Hospital in Benin City. Overall, eighty female individuals volunteered and took part in the investigation, comprising sixty expectant mothers (as test subjects) and twenty nonpregnant individuals (as control). The test group was further categorized into three trimesters, each consisting of twenty participants. Before their involvement, informed consent was acquired from the subjects who were within the age bracket of 21-35 years. The clinical and demographic information about each participant was gathered from their medical records and a pre-tested semi-structured survey, respectively.

Sample Collection and Analysis: Blood samples for the analysis were obtained using EDTA bottles and centrifugated at 3500 rev/min for 15 minutes to collect

the plasma. The collection of blood samples and hematological analysis were done in the morning of each day and within 2 hours using a hematology analyzer.

Ethics: Ethical approval for the study was obtained from St. Philomena Catholic Hospital Ethics and Collaboration Committee. Moreover, the subjects granted informed consent following the requisite protocols.

Statistical Analysis: All data were presented as Mean ± SD using GraphPad Prism 5 software (GraphPad Software Inc.). One-way ANOVA (analysis of variance) and Dunnett's multiple comparisons test, with a single pooled variance were used where necessary, and a P-value of 0.05 ($p \leq 0.05$) was considered statistically significant.

RESULTS AND DISCUSSION

Subjects' demographics: Values were expressed using frequency, percentage, and range. Table 1 illustrates the breakdown of participants' ages in years. Among individuals aged between 31 and 35 years, pregnant women accounted for 21.25% of the study cohort. The largest proportion of participants fell within the 26-30 age bracket, with 45% being pregnant and 7.5% nonpregnant.

Table 1: Distribution of age among participants in the study

Age group (yrs.)	Nonpregnant control group (% Frequency)	Pregnant group (% Frequency)	Total (%)
21 - 25	14 (17.5 %)	7 (8.75 %)	21 (26.25 %)
26 - 30	6 (7.5 %)	36 (45 %)	42 (52.5 %)
31 - 35	0 (0 %)	17 (21.25 %)	17 (21.25 %)
% total	20 (25 %)	60 (75 %)	80 (100 %)

Values were expressed using Mean ± SD.

Comparing the hematological indices of the study participants: From Table 2, the mean HCT and HGB counts were statistically different ($p < 0.05$) when comparing the first-trimester participants with those of the nonpregnant control group, although WBC, GRAN, LYMPH, RBC, and PLT were insignificant ($p > 0.05$).

The mean values for WBC, GRAN, RBC, HCT, and HGB in Table 3 were significantly different ($p < 0.05$) when comparing the second-trimester subjects to the nonpregnant control. Conversely, no significant variations ($p > 0.05$) in LYMP and PLT existed. When comparing the third-trimester subjects to the nonpregnant group (Table 4), there were statistically significant differences ($p < 0.05$) in all the hematological indices evaluated. Generally, the mean levels of LYMPH, RBC, HCT, HGB, and PLT were observed to be decreased in the pregnant cohort when compared to the control, whereas mean WBC and GRAN levels were higher in the pregnant group when compared to the control group.

This research was conducted to establish the mean values specific to each trimester for hematological indices in pregnant females in comparison to nonpregnant individuals serving as the control subjects. Normal pregnancy has been shown to cause alterations in both maternal physiology and anatomy with corresponding changes in the blood (Musa *et al*., 2016). One of the straightforward and dependable ways of assessing the overall healthiness of pregnant women is to evaluate the hematological indices. During pregnancy, it becomes vital to comprehend these physiological changes and to interpret any need for therapeutic interventions (Awajiomowa *et al*., 2022).

Table 2: Comparing the first-trimester subjects' hematological indices with those of the nonpregnant control group.

Parameters	Control	1st trimester	ANOVA, p-value
WBC (x 10^9/L)	5.65 ± 2.12	5.87 ± 0.97	> 0.05
GRAN (x 10^9/L)	49.40 ± 11.15	55.06 ± 8.19	> 0.05
LYMPH (x 10^9/L)	33.30 ± 7.22	31.75 ± 6.67	> 0.05
RBC (x 10^{12}/L)	4.54 ± 0.90	3.92 ± 0.83	> 0.05
HCT (%)	38.70 ± 4.24	34.40 ± 2.16*	< 0.05
HGB (g/dL)	13.47 ± 1.63	11.02 ± 0.73*	< 0.05
PLT (x 10^9/L)	232.4 ± 31.61	229.7 ± 41.49	> 0.05

**Represents statistical significance*

Table 3: Comparing the second-trimester subjects' hematological indices with those of the nonpregnant control group.

Parameters	Control	2nd Semester	ANOVA, p-value
WBC (x 10^9/L)	5.65 ± 2.12	6.61 ± 0.33*	< 0.05
GRAN (x 10^9/L)	49.40 ± 11.15	58.08 ± 8.17*	< 0.05
LYMPH (x 10^9/L)	33.30 ± 7.22	28.27 ± 6.90	> 0.05
RBC (x 10^{12}/L)	4.54 ± 0.90	3.49 ± 1.12*	< 0.05
HCT (%)	38.70 ± 4.24	29.70 ± 1.53*	< 0.05
HGB (g/dL)	13.47 ± 1.63	10.24 ± 0.54*	< 0.05
PLT (x 10^9/L)	232.4 ± 31.61	221.6 ± 26.58	> 0.05

**Represents statistical significance*

Table 4: Comparing the third-trimester subjects' hematological indices with those of the nonpregnant control group.

Parameters	Control	3rd trimester	ANOVA, p-value
WBC (x 10^9/L)	5.65 ± 2.12	7.02 ± 0.33*	< 0.05
GRAN (x 10^9/L)	49.40 ± 11.15	59.48 ± 9.33*	< 0.05
LYMPH (x 10^9/L)	33.30 ± 7.22	28.06 ± 5.79*	< 0.05
RBC (x 10^{12}/L)	4.54 ± 0.90	3.55 ± 0.59*	< 0.05
HCT (%)	38.70 ± 4.24	30.10 ± 1.45*	< 0.05
HGB (g/dL)	13.47 ± 1.63	9.86 ± 0.22*	< 0.05
PLT (x 10^9/L)	232.4 ± 31.61	201.44 ± 9.50*	< 0.05

**Represents statistical significance*

The study results revealed that the mean WBC counts gradually increased from first to third trimesters and this rise in WBC counts was higher when compared to that of the nonpregnant control subjects, with second and third trimesters significant differences ($p < 0.05$). It concurs with studies reported by Awajiomowa *et al*. (2022) and Michael *et al*. (2017), but the WBC count was significantly higher in all the trimesters of pregnancy when compared to the nonpregnant control. In other similar studies, there were increasing WBC counts from the first to the third trimester, however, no comparison was shown between the pregnant women and the nonpregnant women (Gebreweld *et al*., 2018; Akinbami *et al*., 2013; Akingbola *et al*., 2006). In contrast with our study, Musa *et al*. (2016) and James *et al*. (2008) observed a rise in WBC count from the first trimester to the second trimester, which dipped during the third trimester though not below the level for the first trimester.

In the current investigation, the mean granulocyte (GRAN) counts among individuals across all pregnancy groups steadily increased from first to third trimesters and were higher in comparison to the control group. Nevertheless, the second and third trimesters of the mean granulocyte counts were significantly higher ($p < 0.05$) when compared to the control group. In agreement with the above, Musa *et al*. (2016) reported a gradual increase in granulocyte count from the first trimester to the third trimester but did not compare their results with that of the nonpregnant women. This current finding is in contrast with those of Ichipi-Ifukor *et al*. (2013) and Wahed *et al*. (2008) who documented a significantly higher granulocyte count in nonpregnant women when compared with pregnant women. Due to its role in the defense mechanism of the body, leukocytosis - a common finding during normal pregnancy, has been documented in several studies to be induced by increasing response to inflammation resulting from fetal selective immune tolerance, immunosuppression, and immunomodulation (Mba *et al*., 2019; Musa et al., 2016; Kaur *et al*., 2014). Even without infection, factors such as anxiety, pain, nausea, and vomiting have been reported to elicit leukocytosis (Akingbola *et al*., 2006). Moreso, during pregnancy, leukocytosis is considered to be induced by the physiologic stress of pregnancy (Chandra *et al*., 2012).

In this present study, the mean lymphocyte counts for the pregnant women decreased from first to third trimesters and were slightly lower than those of the nonpregnant women. However, a statistically significant difference ($p < 0.05$) was observed between the third-trimester and the nonpregnant subjects. This is in line with the study reported by Mba *et al*. (2019) and Gebreweld *et al*. (2018), although in their studies, there was no significant difference in the lymphocyte count between the pregnant women and the nonpregnant women. While in this present study, there was no significant difference in the lymphocyte counts between the first and second trimesters of pregnancy and the control, there was no significant difference in the lymphocyte counts between the first trimester of pregnancy and the nonpregnant subjects in a similar study (Eledo *et al*., 2015). However, our study is contrary to that reported by Okpokam *et al*. (2015) and Ichip-Ifukor *et al*. (2013), where the mean lymphocyte counts were significantly raised in pregnant women compared to nonpregnant women. It has been asserted that during the first few weeks of pregnancy, increasing total lymphocyte count will remain elevated throughout the second and third trimesters of pregnancy, and this may be due to fetal immunity build-up by the body (Ichip-Ifukor *et al*., 2013; Luppi, 2003).

In our current study, the mean RBC count for subjects in all trimesters of pregnancy was lower than that of the nonpregnant control subjects. Moreover, a first to second-trimester drop, followed by a rise in the third trimester, with mean values somewhat lower than in the first trimester were observed. When compared to the control group, the RBC counts for the second and third trimesters were significantly decreased ($p < 0.05$). This is consistent with the study by Musa *et al*. (2016), though there was no comparison between nonpregnant and pregnant women. In a similar study, the mean RBC counts were noted to have decreased from the first to third trimesters, and this decline was significantly lower when compared to the nonpregnant subjects (Mba *et al*., 2019). The slight reduction in the mean values of RBC and HGB has been attributed to

the expanded need for iron and oxygen with advancing pregnancy, as more iron and oxygen are needed to meet the requirements of the growing fetus (Akinbami *et al*., 2013; Amah-Tariah *et al*., 2011). In a contrary study, Awajiomowa *et al*. (2022) reported a steady rise in the mean values of RBC from the first to the third trimesters of pregnancy, with no significant difference compared with the nonpregnant control. However, the slight incremental rise in the mean RBC and HGB with advancing gestational age could be due to the influence of estrogen and progesterone that are stimulated by the placenta and induce the release of renin from the kidneys which in turn improves erythropoiesis (Akinbami *et al*., 2013; Akingbola *et al*., 2006).

A first to second-trimester decline in the mean hematocrit levels with a third-trimester increase but not above the first-trimester levels were reported in this current study. Nonetheless, in comparison to the control group, significantly decreased ($p < 0.05$) mean hematocrit levels were seen in the pregnant group. This is in agreement with the studies reported by Mba *et al*. (2019), Gebreweld *et al*. (2018), and Musa *et al*. (2016). In contrast, Awajiomowa *et al*. (2022) documented an incremental rise in mean hematocrit values from the first to third trimesters of pregnancy, and this was not statistically significant when compared to the nonpregnant women. The mean hemoglobin concentration for the pregnant group progressively decreased from first to third trimesters, and the mean values during pregnancy were significantly ($p < 0.05$) lower when compared to the control group. This study confirms the research reported by Okpokam *et al*. (2015), Ichipi-Ifukor *et al*. (2013), Akinbami *et al. (2013),* and Saadiya *et al*. (1990), demonstrating that anemia is more typical in the third trimester of gestation. However, it contradicts the study undertaken by Awajiomowa *et al*. (2022), who reported a steady rise in the mean HGB values from the first trimester to the third trimester, and this minute increase was not significant when compared with the nonpregnant control. As gestation advances, the iron requirement increases, and it's critical for fetal development. In this study, the progressive decline in HCT and HGB noticed during the pregnancy periods may be ascribed to physiological hemodilution stimulated by a comparative shift in the balance of blood plasma volume to RBCs and/or increased rate of infection such as malaria, hormonal alterations, and circumstances that facilitate fluid retention and iron deficiency (Akinlaja, 2016; Ichipi-Ifukor *et al*., 2013; Akinbami *et al*., 2013).

Similarly, the mean platelet counts for the pregnant participants decreased from first to third trimesters. When comparing the third-trimester group to the nonpregnant control group, a significant difference ($p < 0.05$) was found. Correspondingly, the research undertaken by Mba *et al*. (2019) indicated a steady decline in platelet count from the first to the third trimesters but no significant difference was discovered between the control and the pregnant women in all the trimesters. Contrary to this study, a gradual rise in the mean platelet values from the first to the third trimesters was observed in the study reported by Awajiomowa *et al*. (2022), however, this increase was not significant when compared with the nonpregnant control. In another contrasting study, the platelet count fell from the first to the second trimesters and subsequently rose in the third trimester above the value recorded for the first trimester (Musa *et al*., 2016). About 75% of thrombocytopenia in pregnancy is considered to be benign and asymptomatic for both maternal and fetal health and therefore, does not necessitate medical intervention. The remaining 35% of thrombocytopenia in pregnancy may be associated with illness that may result in bleeding difficulties at delivery, requiring obstetric emergencies (Michael *et al*., 2017). In normal pregnancy, hemodilution may result due to increased blood plasma volume. While there is a reduction in PLT count by almost 10%, a remarkable decline arises in the third trimester (Akinbami *et al*., 2013). In addition, the progressive decrease in mean platelet counts as pregnancy advanced may be due to raised blood volume, elevated platelet activation, and shortened life span in the uteroplacental circulation (Kaur *et al*., 2014; Chandra *et al*., 2012).

Conclusion: In conclusion, from this study, we observed that hematological parameters were affected in the different trimesters of pregnancy and as pregnancy advanced. Consequently, proper monitoring and interpretation of hematological indices should be encouraged to avoid pregnancy hematological complications occasioned by anemia, leukocytosis, and thrombocytopenia.

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