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Assessment of Some Systemic Inflammatory Markers and Haematological Parameters among Pregnant Women in Different Trimesters in Port Harcourt, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Authors NJ and EME designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors ESE and ODN managed the analyses of the study. Author LKG managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Pregnancy is a physiological condition that is associated some changes in haematological and immunological parameters. This study evaluated the levels of some systemic inflammatory and haematological parameters in pregnant women in Port Harcourt, Nigeria. A total of 275 pregnant women of age 20 to 70 years and 87 apparently healthy non-pregnant control subjects were involved in this study. Five millilitres (5ml) of blood were collected from the subjects into EDTA bottle for the evaluation of the parameters. ELISA technique was used in the determination of soluble transferrin receptor while Sysmex automation was used for the determination of the other parameters. The mean value of parameters for the study subjects were Hb(9.05± 1.22g/dl), sTfR(21.16± 9.11nmol/L), NLR (2.69 ± 0.91), PLR (8.78 ± 2.97), while for control subjects were Hb(12.19± 0.66g/dl), sTfR(18.21± 3.77nmol/L), NLR (2.86 ± 0.11), PLR (9.62 ± 2.79). The mean sTfR

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levels in pregnant women was significantly lower (p=0.001) than in control subjects. The pregnant women also had significantly lower values of Hb (p=0.0001), and PLT (p=0.017). According to trimesters, the levels of sTfR significantly increased with trimester (p=0.002), while that of PLR significantly increased in the second trimester (p=0.006). However, there were no significant differences in the levels of Hb (p=0.185) and NLR (p=0.70) among the trimesters. The results indicate that the pregnant women did not have levels of parameters that may indicate negative outcomes of pregnancy. It is recommended that systemic parameters be monitored among pregnant women in order to help in their medical management.

Keywords: Systemic inflammatory markers; pregnant women; Port Harcourt; trimesters; haematological parameters.

1. INTRODUCTION

Pregnancy represents a very important period for the existence and preservation of the human society. The protection and wellbeing of both mother and foetus during this period is therefore very fundamental. A number of physiological changes have been associated with pregnancy in humans. These changes are due to the effect of progesterone and oestrogen produced in the first to 12 weeks of pregnancy [1]. Plasma volume expands by 46 – 55%, while red cell volume expends by 18 – 25% [2]. These are due to the effect of progesterone and oestrogen on the kidney, which leads to the release of renin and consequently there is activation of the renin-angiotensin- aldosterone system (RAS) in humans. There is also increase in red cell mass up to 20% due to the effect of erythropoietin released from the kidney. This leads to haemodilution and an accompanying decrease in the level of haemoglobin. This phenomenon is known as physiological anaemia of pregnancy [1]. There have also been changes reported in packed cell volume (PCV) and red cell count [3]. Hormonal changes in pregnancy result from pregnancy-induced vasodilation and increase in vascular capacitance [4]. The changes that occur in the concentration of haemoglobin starts at about 16th week of gestation, and continues a downward trend to reach the nadir in second trimester because of plasma volume expansion [3].

Inflammation has been reported to be essential for human reproduction, being involved right from menstrual cycle to early pregnancy and then to labour. However, so many disease conditions have been associated with impaired inflammatory processes, including miscarriages [5]. Inflammation has been reported to play a key role in the timing of parturition in humans [6]. Pregnancy-related complications (PRCs), which include diabetes mellitus, gestational diabetes mellitus and pre-eclampsia, have been reported to be powerful contributory factors for morbidity and mortality in pregnancy; inflammation is very much involved in all these processes [7].

Changes in white blood cell count and platelets have also been reported. Some researchers have reported leukocytosis, which is due to physiological stress [8]. It may also result from increased inflammatory response during pregnancy, which can be attributed to selective immune tolerance, immuno-suppression [9]. There is preponderance of neutrophils on differential counts and this is probably due to impaired neutrophilic apoptosis during pregnancy. There is also monocytosis but there is decline in lymphocyte, eosinophil and also basophil [3].

Platelets and leukocytes are the main cellular elements that are known to be involved in the pathophysiology of inflammation. The total white blood cell count (WBC) is a relatively crude marker of inflammation. The ratio of neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR), are reportedly strong predictors of inflammation in the human system [10].

Neutrophil lymphocyte ratio refers to the ratio of absolute neutrophil count to the absolute lymphocyte count, and is seen as a marker of the immune response of the body to offending agents. It is can also serve as a rapid and simple parameter of systemic inflammation and stress. Platelet lymphocyte ratio refers to the ratio of platelet count to lymphocyte count. It is another parameter that reportedly increases during thrombosis and inflammation [11]. These parameters are potent markers of inflammation that underlies the basic pathologies of various human diseases [12]. Again, these parameters can easily be obtained from the routine full blood count (FBC) results from the laboratory, thus their use do not come with additional costs to the

patients or the health facility. There have been growing interests in NLR and PLR because of their immense values in the prediction and prognosis of various medical conditions [12].

This study is aimed at assessing of these parameters as a means to help predict poor inflammatory processes in pregnant women.

2. METHODOLOGY

Two hundred and seventy five (275) pregnant women in different trimesters were involved in this study. They were within the ages of 20 to 45 years. Eighty-eight (88) apparently healthy non-pregnant women were also involved as control subjects. All subjects consented to participate in the study.

The subjects with sickle cell anaemia, HIV infection, hookworm infestation or severe malaria were excluded from this study.

Blood sample was collected from each subject using standard techniques. Five milliliters (5ml) of the sample was put in ethylene diethyltetraacetic acid (EDTA) bottles and used for the assay of the haematological parameters using haematology autoanalyser while soluble transferrin receptor was determined using ELISA technique.

The data generated from this study were analysed using SPSS version 23. The analytic tool was ANOVA. P-values less than 0.05 were considered statistically significant.

3. RESULTS

The table describes the comparison of parameters in sTfR, Hb, WBC, LYM, PLT, Neutrophil-Lymphocyte ratio and Ratio- Platelet-Lymphocyte ratio between the pregnant women and the control subjects.

The table describes the comparison of parameters in sTfR, Hb, WBC, LYM, PLT, Neutrophil-Lymphocyte ratio and Ratio- Platelet-Lymphocyte ratio between the pregnant women in different trimesters.

4. DISCUSSION

This study evaluated the levels of some haematological parameters among pregnant women in different trimesters. The haemoglobin level of the pregnant women was significantly lower than control subjects. In pregnancy there is an increase in plasma volume due to increase in production of oestrogen and progesterone, and progesterone increases the synthesis of aldosterone and consequently increase sodium and water retention [13]. Corresponding to the rise in plasma volume there is an increased level of adrenomedullin, a vasodilator. This increase in plasma volume exceeds the rise in red cell volume, leading to a fall in maternal haemoglobin [14].

Soluble transferrin receptor was significantly higher in the pregnant women compared to the control subjects. This finding may be as a result of increased iron demand during pregnancy. This agrees with the work of another researcher [15], which reported that soluble transferrin is not affected by pregnancy unless there is presence of iron deficiency which occurs in pregnancy. Another researcher [16], had also reported that in individuals with iron deficiency anaemia that is an increased level of sTfR compared to control subjects.

The pregnant women also had significantly higher WBC count and neutrophil, but lower Lymphocyte and Platelet counts compared to the control subjects. Increase in WBC during pregnancy results from physiological stress associated with pregnancy, and may be due to increase in neutrophils [17]. The increase in neutrophil may be due to haemostatic response to apoptosis of neutrophil which is altered in pregnancy [18]. The decrease in lymphocyte count is probably due to the pregnancy and related hormonal changes which would have a negative impact on the blood count of the total lymphocytes [19]. The platelet count for the pregnant women was significantly lower than that of control subjects. This may be attributed to the haemodilution that occurs in pregnancy [20]. Platelet count in the pregnant women was significantly lower compared to control subjects. In all, majority of the changes in platelet count during pregnancy are due to gestational thrombocytopenia. Other contributory factors include hypertension, immune processes, rare constitutional thrombocytopenias, infections, as well as malignancies [20].

According to trimesters, there was a progressive decline in the haemoglobin level from the first to the third trimester. There were significant changes in WBC, and Platelets counts but not in lymphocyte, neutrophil counts across the trimesters. WBC significantly increased from the first to the third trimester. There was also an

Table 1. Parameters between the pregnant women and control subjects

	sTfR (nmol/l)	Hb (g/dl)	WBC (x10^9/L)	LYM (%)	NEUT (%)	PLT (x10^9/L)	NL Ratio	PL Ratio
Pregnant women (n=275)	22.16± 9.11	9.05 ± 1.22	7.48 ± 1.75	25.20 ± 6.75	65.73 ± 7.48	215.30 ± 47.72	2.69 ± 0.91	8.78 ± 2.97
Control (n=88)	18.21 ± 3.77	12.19 ± 0.65	7.19 ± 1.60	26.02 ± 6.92	63.16 ± 7.27	224.67 ±37.17	2.86 ± 0.11	9.62 ± 2.79
p-value	<0.001	<0.001	0.014	0.03	0.031	0.047	0.15	0.017

Key: sTfR – Soluble transferrin receptor, Hb- Haemoglobin, WBC- white blood cell, LYM-Lymphocyte, NEUT- Neutrophil, PLT- Platelet, PL Ratio- Neutrophil-Lymphocyte ratio, PL Ratio- Platelet-Lymphocyte ratio

Table 2. Comparison of parameters trimester

	sTfR (nmol/l)	Hb (g/dl)	WBC (x10^9/L)	LYM (%)	NEUT (%)	PLT (x10^9/L)	NL Ratio	PL Ratio
1st Trimester (n=91)	21.34± 12.86^a	9.20± 0.95	7.11± 1.59^a	26.43±7.36	64.00±8.51^a	222.11±38.18	2.65± 0.91	8.22±2.67^a
2nd Trimester (n=94)	21.76± 6.06^a	9.02± 1.28	7.70± 1.80^b	26.02±6.61	64.84±7.08^a	224.22±48.49	2.73±0.94	9.24±3.08^b
3rd Trimester (n=90)	28.71± 6.76^b	8.70± 1.61	7.75± 1.81^b	26.61±5.29	67.78±5.24^b	224.09±61.96	2.60±0.68	7.68±2.67^c
p-value	0.002	0.185	0.032	0.858	0.021	0.091	0.70	0.006
F-value	8.213	34.32	3.56	43.65	54.90	6.98	0.35	5.17

Key: Values with different superscripts are significantly different (p<0.005); Key: sTfR – Soluble transferrin receptor, Hb- Haemoglobin, WBC- white blood cell, LYM-Lymphocyte, NEUT- Neutrophil, PLT- Platelet, PL Ratio- Neutrophil-Lymphocyte ratio, PL Ratio- Platelet-Lymphocyte ratio

increase in neutrophil count from the first to the third trimester. Lymphocyte count was highest in the third trimester while Platelet count was highest in the second trimester. These observed differences in these parameters are probably due to immune response in pregnancy [21]. The change in platelet count can be attributed to haemodilution that occurs in pregnancy [21].

There was a significant increase in serum transferrin receptor level with the highest level occurring in the third trimester. This finding agrees with another study [22] who had reported that there is a gradual increase in STfR as the age of pregnancy increases. STfR is an indicator if iron status in pregnancy [22]. STfR has been reported to increase in iron deficiency anaemia [23] and the level is a reflection of the functional iron status of the subjects [24] and also erythropoietic activity [25]. sTfR generally increases during pregnancy [26], and the increase reflects the body's attempt at increasing the intracellular iron concentration [27]. It is also an indication of the body's ability to deal with infections [28].

There was no significant difference in the NLR (neutrophil-lymphocyte ratio) between the pregnant women and the control subjects (p=0.15). Similarly, the NLR did not differ significantly among the pregnant women according to trimesters (p=0.70). NLR has been reported to be a predictive factor in preeclampsia [29], Gestational diabetes mellitus [30] and other conditions such as type 2 diabetes mellitus, thyroiditis, heart failure [31]. Our results could be because our study was performed on pregnant subjects who do not have obvious complications. This finding agrees with another work [32], who had earlier reported a similar finding. The inflammatory mediators that are secreted by neutrophils can cause the degeneration of the vascular cell walls [33]. On the other hand, the mediators produced by lymphocytes are reported to have anti-atherosclerotic potential and so helps in the regulation of inflammation [31].

The platelet-to-lymphocyte ratio was significantly lower in the pregnant women compared to the control subjects (p=0.017). Raised PLR (platelet-to-lymphocyte ratio) has been associated with inflammation, thrombotic events and malignancies [34]. This finding may suggest that pregnant women are not predisposed to the events associated with raised level of inflammation in pregnancy, such as preeclampsia, and preterm birth [35].

The pregnant women in the second trimester had significantly higher platelet-to-lymphocyte ratio compared to the pregnant women in the other trimesters (p=0.006). This is probably because PLR reportedly rises with anaemia, and is known to occur more in the second trimester [36]. This finding agrees with the earlier study [37].

5. CONCLUSION

This study evaluated the levels of systemic inflammatory parameters among pregnant women in Port Harcourt. The sTfR levels were significantly raised in the pregnant women; it increases with trimesters. The PLR was significantly reduced in the pregnant women compared to control subjects. However, among the pregnant women, those in the second trimester having the highest values. There were no significant differences in the NLR values. Results from this study, the pregnant women did not have levels of parameters that may indicate negative outcome resulting from pregnancy.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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