BURDEN OF CYTOPAENIAS AMONG HIV POSITIVE PREGNANT WOMEN AT THE UNIVERSITY COLLEGE HOSPITAL, IBADAN

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ABSTRACT

Introduction: **Few studies have examined cytopaenia among HIV positive pregnant women.**

Objectives: To assess burden of cytopaenia among HIV positive pregnant women.

Methodology: **This cross-sectional study of women on HAART ≤6months, defined anemia as hematocrit <33%, leucopenia as total white blood cell count <3,000 cells/mm³ and thrombocytopenia as absolute platelet count <100,000 cells/mm³. Univariate and bivariate analyses were performed.**

Results: **Over 8 years, of 1,197 women, the mean age was 29.02(±5.4) years and mean gestational age 25.9(±8.1) weeks. Prevalence of anaemia was 76.8%, leucopaenia 6.9% and thrombocytopenia 4.7%. The mean haematocrit was 28.5%(±4.5); median white blood count 5,500/mm³; median platelet count 200,000/mm³ and median CD4 323 cells/mm³.**

Mean haematocrit was highest (29.7%±5.3) in women in the first trimester but lowest (28.4% ±4.6) in women in second trimester (p=0.04). Compared with earlier trimesters, women in the third trimester had higher median white blood count (5,600 cells/mm³), higher neutrophil (61.0% ±11.2) but lower lymphocytes (28.3%± 9.2) (p=0.18; 0.00, 0.00). Median absolute platelet count was highest (206,000 cells/mm³) in the first trimester but lowest (195,000 cells/mm³) in third trimester (0.04). Women with lower CD4 had higher prevalence of cytopaenias.

Conclusion: **Cytopaenias are not uncommon in this population especially with lower CD4.**

INTRODUCTION

The haematological profile of an individual is a simple, fast, cost-effective and reliable indicator of general health[1,2]. In the pregnant woman, the haematological profile has the potential to impact pregnancy and the outcome of that pregnancy[3]. Pregnancy is also associated with various changes in hematological indices such as decrease in red blood cell count and platelet count[1,4] and increase in white blood cell count[5]. Similarly, haematological problems may be experienced by the pregnant woman. Anaemia is the most common haematological disorder in pregnancy and has the potential for adverse pregnancy outcomes such as low birth weight, miscarriages and low immunity[6]. Anaemia in pregnancy results partly from a dilutional process secondary to a discrepancy between the rate of increase in plasma volume and that in red blood cell (RBC)

mass[1,4]. While the plasma volume increases by 25% - 80% between the sixth and twenty-fourth weeks of gestation, the increase in RBC mass is approximately 30% and occurs between the twelfth and thirty-sixth weeks of gestation[1]. Beside this physiological process, other possible causes of maternal anemia that the care provider must carefully evaluate for include nutritional deficiencies such as folate and iron deficiency, haemoglobinopathies[7,8] and parasitic infections such as malaria especially in highly endemic regions like Nigeria[8].

Similarly, pregnancy is associated with a drop in platelet count, with many studies reporting approximately 10% drop in platelet count by the end of pregnancy[9,10]. However, the majority of pregnant women still have

platelet count within the normal range with most cases being mild, and no adverse outcome for mother or baby[1]. In contrast to these reductions, various studies have reported that pregnancy is usually accompanied by leukocytosis mainly due to neutrophils[11,12]. Several changes have been reported in neutrophils during pregnancy. They include impairment of apoptosis due to increased inflammatory response, reduced chemotaxis and impaired respiratory burst [13,14]. These changes have been associated with a boost in non-specific (innate) immunity and are thought to be a compensation for the attenuation of specific immunity in pregnancy[15]. The impairment of specific immunity correlates with a reduction in lymphocyte count in pregnancy. Eosinophils and basophils also decline in number with increasing gestational age[5, 16].

The Human Immunodeficiency Virus (HIV) infection is not uncommon in pregnancy in sub-Saharan Africa[16]. HIV is associated with hematological abnormalities, the most common manifestation being reduction in and impaired function of all blood cell lines; red blood cells (anemia), white blood cells (leucopenia or neutropenia) and platelets (thrombocytopenia) collectively called cytopenias.[16] Cytopaenias increase in frequency as HIV progresses and are often fatal without intervention.[17-19] Anemia is the most common cytopaenia and its presence has been associated with faster disease progression and an independent predictor of survival.[17-21] The use of highly active antiretroviral therapy is associated with significant improvement in patient survival and improvement in anaemia especially severe anaemia[18, 22, 23].

Studies about the prevalence and factors associated with cytopaenia in patients living with HIV/AIDS has largely been done among the general adult HIV population[17, 18, 21, 25-28]. However, the magnitude of this problem has not been adequately described among HIV positive pregnant women.[7, 29]

Objectives: This study was designed to describe the burden of and associated factors for cytopaenias (anaemia, leucopaenia and thrombocytopaenia) at different trimesters of pregnancy among HIV positive pregnant women presenting for care at the University College Hospital who were either HAART naïve or on HAART for 6 months or less.

METHODOLOGY
This was a cross-sectional retrospective review of the records of women who registered for care at the Prevention of Mother-to-Child transmission (PMTCT) unit of the University College Hospital (UCH), Ibadan. The hospital offers PMTCT services supported by the Government of Nigeria and the AIDS Prevention Initiative in Nigeria (APIN) program. HIV positive pregnant women access these services having being referred from the UCH antenatal clinic, and other clinics in the environs. PMTCT services provided include administration of anti-retroviral therapy for PMTCT, infant feeding counseling and family planning counseling.

At presentation, vital signs of patients are evaluated and ill patients triaged accordingly. In line with the National testing algorithm, patients presenting newly with positive results are bled again and the HIV tests repeated. Patients confirmed HIV positive are then bled for selected hematological, immunological and chemistry parameters. Post-test and follow-up counselling is started immediately by trained counsellors. Clinics are conducted every day except on Fridays. At subsequent clinics visits, patient will listen to general health talks and then separated to specific groups such as the PMTCT clinic where more targeted information will be made available by PMTCT counsellors. Pregnant women are then attended to by physicians trained in administration of antiretrovirals and PMTCT care. All pregnant women are eligible for antiretroviral therapy as part of prophylaxis for PMTCT. During the period under study, 1821 enrolled in the PMTCT program.

Variables recorded at the first clinic visit include socio-demographic characteristics and possible risk factors for HIV acquisition. In addition, baseline laboratory testing is conducted on all patients enrolling into the program and includes measurement of CD4+ T lymphocyte (CD4) count by flow cytometry and plasma HIV RNA (viral load) by Roche Ampiclor RNA PCR. Complete blood count and differential is performed using Sysmex KX-21N, an automated 3-part differential haematology analyzer (Sysmex Corporation obe, Japan)[30]. The program maintains an electronic database of the records of all patients enrolled. The data used for this study was sampled from the data base.

Anemia was defined as hematocrit less than 33%[31]. Severity of anaemia was graded as mild (28-32%), moderate (20-27%) and severe (< 20%)[32]. Other cytopaenias were defined as follows: leucopenia if total white blood cell count was less than 3,000 cells/mm³.[16] Thrombocytopenia was defined as absolute platelet count less than 100,000 cells/mm³.[33,34] Severity of thrombocytopenia was graded as mild (50, 000 – 99, 999 cells/mm³), moderate (20, 000- 49, 999 cells/ mm³) and severe (< 20, 000 cells /m mm³).[33,34]

Statistical analysis

Continuous variables were summarized using means (standard deviation) or medians as found appropriate and categorical variables were summarized using frequencies and percentages. Differences between continuous variables were tested with student's T-test, ANOVA or Mann-Whitney test as appropriate while categorical variables were compared using the chi square test. The independent factors investigated included demographic variables (e.g. age, marital status, highest level of education attained) and clinical/laboratory characteristics (e.g. CD4 cell count, viral load etc). The association between these factors and presence of the cytopaenias were evaluated.

Ethical Considerations

The antiretroviral treatment program was approved by the University of Ibadan/University College Hospital Ibadan Joint Institutional Review Board. Informed consent forms were signed by all patients during enrollment procedures. The electronic medical record systems for the patient data are implemented on a password-protected computer systems for the purpose of privacy and confidentiality of data. Patients' folders containing case report forms are kept in safe cabinets with locks in the medical records section and access is restricted to authorised persons only.

RESULTS

The clinic records covering a 8-year period (January 1st 2006 and 31st December 2013) of one thousand, eight hundred and twenty-one (1, 821) women enrolled in the APIN-PMTCT clinic for care were reviewed. Six hundred and twenty-four (624) women had missing data and were excluded from further analysis. The data of one thousand, one hundred and ninety-seven (1, 197) women are presented here. The mean age of the women was 29.02 (± 5.4) years. The mean gestational age at presentation was 25.9 (± 8.1) weeks. Slightly over half (53.3%) presented in the third trimester of pregnancy. About two-thirds (65.1%) of the women were between 25 and 34 years (Table 1). More than half (63.5%) had had more than 6 years of formal education. Majority (77.5%) were either engaged in one form of buying and selling or in low skilled occupation such as farming. Almost all the patients (92.1%) were married. The burden of cytopaenias is as shown in Figure 1. While over three quarters (76.8%) were anaemic, leucopaenia was observed in 6.9% of the patients and less than five percent (4.7%) had thrombocytopaenia.

Table 2 shows the distribution of haematological variables by trimester. Overall, the mean haematocrit value for the women was 28.5% (± 4.5), the median

Table 1: Distribution of selected maternal socio-demographic characteristics by trimester

Variable	Trimesters				
	All (1197)	1st (110)	2nd (449)	3rd (638)	p value
Age					
<20 years	31 (2.6%)	2 (7.1%)	7 (23.8%)	22 (69.1%)	0.748
20-24 years	205 (17.1%)	20 (9.6%)	75 (36.8%)	110 (53.6%)	
25-29 years	415 (34.7%)	36 (8.8%)	163 (39.2%)	216 (52.0%)	
30-34 years	364 (30.4%)	34 (9.3%)	140 (38.4%)	190 (52.3%)	
35-39 years	145 (12.1%)	15 (10.5%)	54 (37.2%)	76 (52.3%)	
≥ 40 years	37 (3.1%)	3 (8.0%)	10 (28.0%)	24 (64.0%)	
Formal Education					
Nil	95 (7.9%)	11 (11.2%)	33 (35.2%)	51 (53.6%)	0.501
6 years or less	342 (28.6%)	28 (8.4%)	129 (37.6%)	185 (54.0%)	
7-12 years	504 (42.1%)	42 (8.3%)	186 (37.0%)	276 (54.7%)	
more than 12 years	256 (21.4%)	26 (10.1%)	101 (39.4%)	129 (50.5%)	
Occupation					
Unemployed/trainee/student	93 (7.8%)	10 (10.6%)	38 (40.7%)	45 (48.7%)	0.629
Low skilled/farming	273 (22.8%)	25 (9.2%)	97 (35.5%)	151 (55.3%)	
Trading (Buying and selling)	655 (54.7%)	59 (9.0%)	259 (39.5%)	337 (51.5%)	
Government worker (junior)	63 (5.3%)	4 (6.9%)	22 (34.3%)	37 (58.8%)	
Government worker (senior)	29 (2.4%)	4 (13.2%)	12 (42.1%)	13 (44.7%)	
Housewife	84 (7.0%)	9 (11.0%)	29 (34.0%)	46 (55.0%)	
Marital Status					
Married	1102 (92.1%)	97 (8.8%)	409 (37.1%)	596 (54.1%)	0.04
Not married	95 (7.9%)	13 (14.0%)	38 (39.5%)	44 (46.5%)	

Table 2: Distribution of hematological variables by trimester

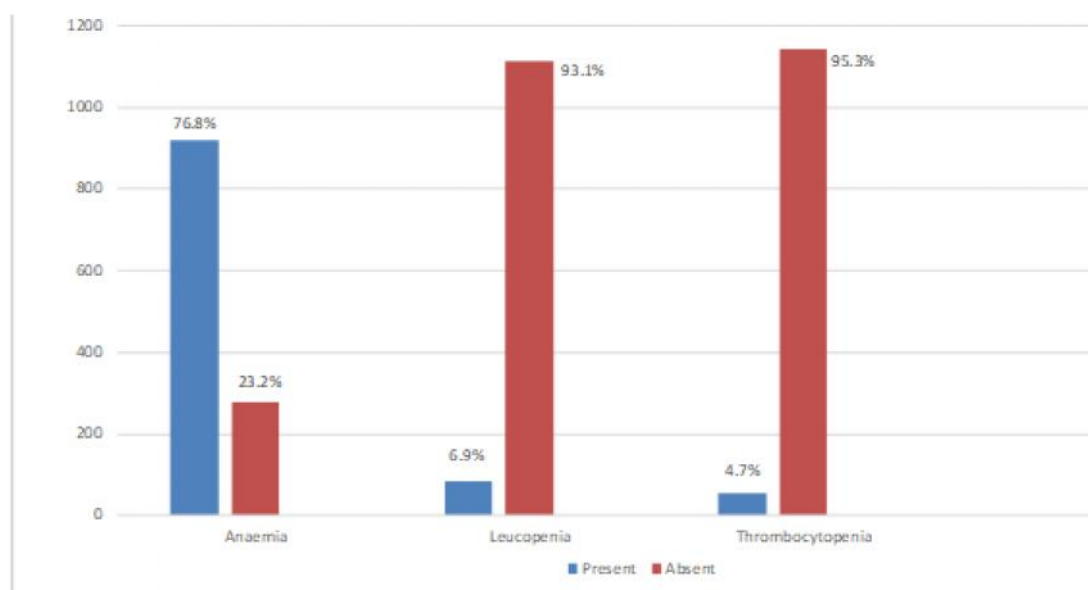| Variable	Trimesters				
	All (1197)	1st (110)	2nd (449)	3rd (638)	p value
Haematocrit	28.5	29.7	28.4	28.5	0.04
	(± 4.5)	(± 5.3)	(± 4.6)	(± 4.3)	
Degree of anaemia					
Nil anaemia	283 (23.7%)	43 (39.3%)	105 (23.5%)	135 (21.5%)	0.00
Mild anaemia	657 (54.9%)	50 (44.9%)	236 (52.6%)	371 (57.9%)	
Moderate anaemia	205 (17.1%)	10 (9.0 %)	87 (19.4%)	108 (16.8%)	
Severe anaemia	52 (4.3%)	7 (6.7%)	21 (4.6%)	24 (3.8%)	
WBC (cells/mm³)	5,500	5, 400	5,400	5,600	0.18
	(4.0-19,800)	(1,200-9, 600)	(4.0-17, 020)	(4.0-13, 000)	
Neutrophil (%)	60.5	55.2	60.9	61.0	0.00
	(±11.8)	(±14.9)	(±10.2)	(±11.2)	
Lymphocyte (%)	28.8	32. 8	28.9	28.3	0.00
	(±9.7)	(±11.2)	(±9.6)	(±9.2)	
Platelet	200.0	206.5	203.0	195.5	0.04
(X1000 cells/mm³)	(13.5- 888.0)	(24.0-674.0)	(22.0-832.0)	(18.8-686.0)	
Degree of Thrombocytopenia					
Normal values	1141 (95.3%)	104 (95.6%)	434 (96.7%)	603 (94.3%)	0.22
Mild	42 (3.5%)	3 (2.2%)	13 (2.8%)	26 (4.4%)	
Moderate	12 (1.0%)	3 (2.2 %)	2 (0.5%)	7 (1.1%)	
Severe	2 (0.2%)	0 (0.0%)	0 (0.0%)	2 (0.2 %)	
CD4 count	323	294	323	333	0.02
	(0-3102)	(0-1289)	(1-1431)	(0-1730)	
Log viral load	4.1	4.2	4.1	4.0	0.05
	(±1.1)	(±1.2)	(±1.1)	(±1.1)	

Fig. 1: Prevalence of various cytopaenias among HIV positive pregnant women

Table 3: Comparing characteristics of women with cytopaenias and women without cytopaenias

Variable		Anaemia		Thrombocytopenia		Leucopenia	
		Nil 278 (23.2%)	Present 919 (76.8%)	Nil 1141 (95.3%)	Present 56 (4.7%)	Nil 1114 (93.1%)	Present 83 (6.9%)
Mean age		28.8 (± 4.8)	28.9 (± 5.3	28.8 (± 5.2)	29.7 (± 5.1)	28.8 (± 5.2)	29.7 (± 5.5)
p value		0.96		0.23		0.12	
Mean gestational age (weeks)		25.1 (± 8.9)	26.7 (± 7.6)	26.2 (± 7.9)	28.4 (± 8.2)	26.3(± 7.8)	26.2 (± 7.8)
p value		0.01		0.52		0.92	
Age group							
< 20 years	(31)	6 (20.0%)	25 (80.0%)	30 (96.8%)	1 (3.2%)	31 (100.0%)	0 (0.0%)
20-34 years	(984)	236 (24.0%)	748 (76.0%)	938 (95.3%)	46 (4.7%)	917 (93.2%)	67 (6.8%)
≥ 35 years	(182)	36 (19.7 %)	146 (80.3%)	173 (95.1%)	9 (4.9%)	166 (91.3%)	16 (8.8%)
p value		0.41		0.93		0.29	
Education							
Nil	(95)	18 (19.0%)	77 (81.0%)	86 (90.5%)	9 (9.5%)	86 (90.5%)	9 (10.0%)
Primary	(342)	65 (19.0%)	277 (81.0%)	324 (94.7%)	18 (5.3%)	313 (91.5%)	29 (8.7%)
Secondary	(504)	117 (23.2%)	387 (76.8%)	489 (97.0%)	15 (3.0%)	472 (93.7%)	32 (6.5%)
Tertiary	(256)	78 (30.5%)	178 (69.5%)	242 (94.5%)	14 (5.5%)	243 (94.9%)	13 (5.3%)
p value		0.02		0.02		0.15	
Marital status							
Married	(1102)	260 (23.6%)	842 (76.4%)	1052 (95.5%)	50 (4.5%)	1028 (93.3%)	74 (6.7%)
Not married	(95)	21 (22.1%)	74 (77.9%)	89 (93.7%)	6 (6.3%)	86 (90.5%)	9 (9.5%)
p value		0.26		0.82		0.57	
CD 4 (cells/mm³)							
≤200	(306)	32 (10.2%)	274 (89.8%)	285 (93.4%)	21 (16.6%)	256 (83.5%)	50 (16.5%)
201-350	(320)	58 (18.0%)	262 (82.0%)	298 (93.7%)	22 (6.3%%)	304 (95.0%)	16 (5.0%)
351-500	(243)	62 (25.4%)	181 (74.6%)	237 (97.5%)	6 (2.5%)	236 (97.1%)	7 (2.9%)
>500	(328)	126 (38.4%)	202 (61.6%)	321 (97.8%)	7 (2.2%)	318 (96.9%)	10 (3.1%)
p value		0.00		0.01		0.00	
Viral load (copies/mm³)							
<200	(186)	69 (37.0%)	117 (63.0%)	176 (94.6%)	10 (5.4%)	177 (94.7%)	9 (5.3%)
200-1000	(54)	16 (29.8%)	38 (70.2%)	53 (98.2%)	1 (1.8%)	52 (95.6%	2 (4.4%)
>1000	(957)	193 (20.2%)	764 (79.8%)	12 (95.3%)	45 (4.7%)	885 (92.4%)	72 (7.6%)
p value		0.00		0.74		0.45	

white blood cell count of the women was 5, 500 cells/mm³ and the median total platelet count was 200, 000/mm³ (13, 500 to 888, 000). The median CD4 count at presentation was 323 cells/mm³ (range 0-3102) and mean log viral load was 4.1 (± 1.1). The mean haematocrit was observed to be highest in women who presented in the first trimester of pregnancy but lowest in women who presented for care in the second trimester of pregnancy. These differences were statistically different (p= 0.04). Most of the women with anaemia had mild anaemia (54.9%). Women who presented for care in the third trimester of pregnancy had higher median white blood cell count than women who presented at earlier trimesters of pregnancy. Similarly, these women also had higher percentage of neutrophil but lower percentage of lymphocytes. These differences were statistically significant (p=0.001 and 0.001 respectively). Finally, the absolute platelet count was observed to be highest in women who presented in the first trimester of pregnancy but lowest in women who presented for care in the third trimester of pregnancy. The proportion of women with platelet count in the thrombocytopaenic range, was highest in the women who presented in the third trimester of pregnancy although these differences were not statistically significant (p=0.22).

Table 3 compares women with cytopaenia and women without cytopaenia. The women with anaemia were more advanced in their pregnancies and had fewer years of education. These differences were statistically significant (p=0.01 and 0.02 respectively). Similarly, women with thrombocytopaenia had fewer years of education (p=0.02). Age and marital status

had no impact on the prevalence of cytopaenias. Women with lower CD4 count had higher prevalence of all cytopaenias. Apart from anaemia, increasing viral load did not appear to have any impact on prevalence of leucopaenia and thrombocytopaenia.

DISCUSSION

The aim of this study was to describe the burden of and associated factors for cytopaenias at different stages of pregnancy. We were also able to evaluate the effect of the immunologic and virologic status of the women on these cytopaenias among HIV positive pregnant women. HIV has profound effect on haemopoiesis thus blood cell counts are useful in the evaluation, management and monitoring of HIV positive pregnant women. The most prevalent cytopaenia observed among our patients was anaemia which occurred in about three quarters (76.8%) of the women followed by leucopenia (6.9%). Higher proportion of anaemia and thrombocytopenia were observed in women who presented at later trimesters of pregnancy. Similarly, higher values of white blood cell count was observed in women who presented at later gestational age of pregnancy, in contrast to non-pregnant HIV positive women in whom neutropaenia is prominent occurring in 10-15% of patients [25].

The mean haematocrit in our group of women was 28.5% which is similar to a value of 29.3% among HIV positive pregnant women in Abidjan reported by Rosa Ramon[7]. However, this is lower than the values of 30.2% reported by Akinbami *et al,* 31.3% by Akingbola *et al* and 34.9 % by Purohit among the general obstetric population. These studies were done in Lagos (Nigeria), Ibadan (Nigeria) and the West Indies respectively.[1,31,32] We noted that women in the first trimester of pregnancy had the highest levels of haematocrit compared to women either in the second or third trimesters. This is similar to the pattern observed in pregnant HIV negative women by Akinbami *et al,* Akingbola *et al* and Purohit *et al* .[1,31,32] Physiological anaemia may account for this pattern. During the second trimester of pregnancy, additional progesterone and estrogen are secreted by the placenta causing a release of renin from the kidneys. Stimulation of the Renin-aldosterone angiotensin system will cause sodium retention and increased plasma volume and consequently a fall in maternal haematocrit.[33] In late pregnancy, however, plasma volume increases at a slower rate and this accounts for the slight rise in haematocrit that is usually observed in the third trimester [2]. A different pattern of rise then fall towards the end of pregnancy was observed by Osonuga *et al* and Obeagu *et al* [34, 35]. Smaller sample size by the latter two study groups may account for this discrepancy.

The prevalence of anaemia in this group of HIV positive pregnant women was 76.8%. This is higher than 3% reported from a study in Korea[25], 11.9% in a multi-country study[36], 18.9% from a study in rural Uganda[37] and 37.7% in a Brazilian study.[21] Factors associated with anaemia in our study include fewer years of formal education, higher gestational age and advancing degree of immune suppression. While females may particularly be more likely to have anaemia (as a result of additional demands during pregnancy and menstrual loss)[36-38] increasing immune suppression (measured by CD4 cell count) has also been reported as a risk factor for anaemia.[25,39] The etiology of anemia in HIV-infection is multifactorial. The anemia is often the normocytic normochromic anemia of chronic inflammation due to reduced erythropoietin production and will resolve rapidly with the use of anti-retrovirals.[40] Other causes include infiltrative conditions of the bone marrow (e.g. neoplasms or infection including HIV itself)[41], hemolytic causes (e.g. red blood cell autoantibodies)[42] and nutritional deficiencies[43]. In the context of HIV infection, anaemia has often been implicated as an independent marker of HIV disease progression and mortality.[19, 44] Indeed, women with severe anaemia at baseline may have a 13 times greater risk of death during the first year of ART.[13] Indeed, given the background high maternal mortality ratio in populations where HIV is often prevalent, such as Nigeria,[45] it is even more pertinent that care providers identify and vigorously manage HIV positive pregnant women who are also anaemic in order to prevent maternal mortalities.

The median WBC count observed in this group of HIV positive pregnant women was 5,500 cells/mm³, which is lower than the values reported by Akinbami *et al*, Akingbola *et al* and Obeagu *et al* for HIV negative pregnant women in Nigeria.[1,31,35] The value is however similar to that reported by Ramon *et al* among HIV positive pregnant women[7] but higher than a report from Uganda among the adult HIV positive population[16]. The white blood cell count was observed to be higher in women with more advanced pregnancies like the pattern observed by several workers.[1,12,31,32,34,35] The increase in WBC observed in pregnancy has been attributed to an increase in neutrophils and maybe the result of redistribution of the WBCs between the marginal and circulating pools.[12]

The mean neutrophil percentage was observed to be 60.5%. Compared to the general obstetric population, our observed value is similar to the value of 62.6% reported from Abia[35], higher than 52.9% from Ogun state[34] both in Nigeria but lower than 70.0% reported

by Purohit in the West Indies.[32] Among the HIV positive population however, Ramon reported a similar value of 61.4% for pregnant women[7] while Dikshit reported a higher value of 70.6% among the adults[45]. Similarly, higher percentage of neutrophils was observed in women who presented later in pregnancy. This is because pregnancy imposes an inflammatory response in the woman resulting in significant increment in total white blood cell (WBC) and neutrophil counts in all trimesters of gestation. In addition, increase in the circulating level of granulocyte monocyte colony stimulating factor, a growth hormone for leucocyte has been reported.[46] On the other hand, with leucopenia, neutropenia is the most clinically relevant subtype because it is a good indicator of the risk of infection. The presence of neutropenia in HIV infection exacerbates the susceptibility to infections such as bacteraemia, meningitis but particularly to invasive fungal infections.[47] Conflicting patterns have however been reported by some other workers.[32,34,35]

The mean lymphocyte percentage observed was 28.8% with lower values in women with more advanced pregnancies. This value is lower than that reported for HIV negative pregnant women by Osonuga et al [34] and Obeagu et al [35] but higher than 22.8% reported by Purohit.[32] It is however lower than the value of 32.8% reported by Ramon et al among HIV positive pregnant women.[7] HIV infection in these women may not completely explain the fall in lymphocyte count towards the end of pregnancy. A report of similar dynamics in the lymphocyte count throughout pregnancy was reported in HIV negative pregnant women in the same hospital, contrary to the finding of Osonuga et al and Obeagu et al who noted a rise then fall.[31,34,35] These contradictory findings in the dynamics of lymphocyte count throughout pregnancy has been explained in relation to the mechanism which prevent rejection of the fetal allograft.[15]

The median platelet count in all the women was observed to be 200, 000 cells/ml with lower values in women with more advanced pregnancies. This value is lower than values reported by Akinbami et al in Lagos, Akingbola in Ibadan and Purohit in West Indies.[1, 31, 32] It is however higher than the value of 198,000 cells/ml reported by Obeagu et al in Abia.[35] All of these authors worked with the general obstetric population. Similarly, slightly higher figures were reported by several workers who evaluated HIV positive individuals. These include Ramon et al [7] (225, 000 cells/mm³ among pregnant women) and Dikshit, de Santis and Kyeyune (reported 249,500 cells/mm³, 227, 000 cells/mm³ and 244,000 cells/mm³ respectively among the HIV positive adult population).[17,21,45] After anemia, thrombocytopenia is

the second most common hematologic abnormality that occurs during pregnancy. Similar to our observations on the platelet count dynamics in this study, Akinbami et al and Akingbola et al in their studies also reported a fall in platelets count in later trimesters of pregnancy.[1, 31] This drop in platelet count has been attributed to a dilutional effect and accelerated destruction of platelets passing over the scarred trophoblastic surface of the placenta.[48] Other possible causes of thrombocytopenia in pregnancy include hypertensive disorders of pregnancy (15-20%), an immune related process (3-4%) or occasionally rare constitutional thrombocytopenia (1-2%).[49]

Cytopenias, in particular anaemia, in HIV infected individuals have been shown to predict disease progression and mortality.[19,21,22,50] The causative role of HIV in vivo in altering the bone marrow micro-environment to inhibit haematopoiesis and directly resulting in cytopenia is uncertain[51, 52]. However, cytopenia occur more frequently with advanced HIV or as viral replication persists and patients may present with multiple cytopenias.[20,53] The highest rates of cytopaenia have been noted to occur in patients with advanced HIV (CD4 count <200).[21,38,45] The association of low CD4 cell count with cytopaenia may be due to the dysregulatory effect of HIV on the function of early haematopoietic progenitor cells through the viral accessory protein Negative factor (N. F.)[20].

The main limitation of this analysis is that it is a cross sectional retrospective review of records which makes determination of temporal relationship between cytopaenia, and associated factors difficult. Furthermore, we did not evaluate for other causes of cytopaenias e.g. malaria, hemoglobinopathies, nutritional deficiencies e.t.c., prevalent in this population. These causes are not part of the protocol of care in the clinic where this review was conducted.

In conclusion, this study provides an opportunity to describe the burden and associated factors for cytopaenias in HIV positive pregnant women. Cytopaenias are not uncommon in this group of pregnant women. Anaemia was more common than leucopaenia or thrombocytopaenia in this group of women and requires attention given its prognostic role in HIV disease mortality and the background history of high maternal mortality in the population studied. Cytopaenias were more prevalent with lower CD4. HAART has been shown to satisfactorily correct this as its administration is associated with increase in CD4 cell count and a reversal of the dysregulatory effect of HIV on the function of early haematopoietic progenitor cells which is responsible for the cytopaenia.

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