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# Assessment of the effect of anti-retroviral therapy on haematological parameters in HIV positive individuals in Zaria

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**A total of 230 patients receiving HAART for the first time and followed regularly were retained and their information gotten using a questionnaire. Of this number, 146 (63.5%) were on Stavudine + Lamivudine + Nevirapine (Regimen 1). 84(36.5%) while the remaining were on zidovudine + Lamivudine + Nevirapine (Regimen 5). The distribution was 75(32.6%) males and 155(67.4%) females. Blood was collected from each patient and analyzed (Baseline) using the Sysmex KX-21N for haematological parameters which include Haemoglobin (Hb), Packed cell volume (PCV), Total White Blood Cell count (WBC), Red blood Cell count (RBC), Platelet count, Neutrophil, Lymphocyte and Mixed count. All the values were repeated after 3 months treatment. The data were analysed using Graph pad InStat version 3. All patients had appreciable increase in CD4 levels, patients on regimen 1 had a significant increase in Hb, PCV and Lymphocyte count with P-value (<0.05). Patients on regimen 5 on the other hand had significant decrease in HB, PCV and Lymphocyte count with P-value (<0.05). In this study, haematological response is better in regimen 1 than regimen 5.**

**Key words:** HIV, highly active antiretroviral therapy (HAART), haematological parameters, anti-retroviral therapy, Zaria.

## INTRODUCTION

Antiretroviral drugs are medications for the treatment of infection by retroviruses, primarily HIV. When several of such drugs, typically three or four, are taken in combination, the approach is known as highly active

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**Table 1.** Age distribution of patients on HAART.

| Age (years) | No. of patients | Percentage |
|---|---|---|
| 0 – 10 | 7 | 3.0 |
| 11 -20 | 25 | 10.9 |
| 21 – 30 | 100 | 43.5 |
| 31 – 40 | 64 | 27.8 |
| 41 and above | 34 | 14.8 |
| **Total** | **230** | **100** |

antiretroviral therapy (HAART) (Dybul et al., 2002; Idowu et al., 2013). Standard antiretroviral therapy (ART) consists of the use of at least three antiretroviral (ARV) drugs to maximally suppress the HIV virus and stop the progression of HIV disease. Huge reductions have been seen in rates of death and suffering when use is made of a potent antiretroviral regimen (Obiomah et al., 2018; Akos et al., 2018). Hematological abnormalities are frequent among human immunodeficiency virus (HIV)-infected patients and may be directly attributed to the virus or may be caused by opportunistic infections, neoplasms or drugs that cause bone marrow suppression or hemolysis (Swati et al., 2016, Akos et al., 2018; Gebremedhin and Haye 2019), though that can be corrected, prevented and improved by treatment with HAART (Abdulqadir et al., 2018). In a work reported by Taha et al. (2002), levels of haemoglobin, haematocrit, granulocytes, and platelets were significantly lower among antiviral drug-treated groups compared with HIV negative controls ($P < 0.0001$). These changes were consistent with mild toxicity, and are more noticeable among HIV-infected infants (Ebonyi et al., 2017).

Cytopenia being a common complication of infection with HIV patients, in the course of the disease more than 70% of the patients develop anaemia frequently, requiring blood transfusion (Jacobson et al., 1990; Idowu et al., 2013). Neutropaenia, lymphocytopaenia and thrombocytopaenia are frequently seen indicating that more than one haematopoietic lineage may be impaired. Dysfunction of the bone marrow has been suggested as possible mechanism (Odunukwe et al., 2005; Sathiyavathi and Pugazhendy, 2014). Degree of cytopenia also reflects the severity of the disease. Some antiretroviral drugs have been documented to have cytopenic effect especially when used as monotherapy (Gebremedhin and Haye 2019). Adverse effects of lamivudine in combination with zidovidine cause neutropaenia, anaemia, thrombocytopaenia, and sometimes transient rise in liver enzymes and serum amylase (EMA, 2015). Adverse effects attributed to nevirapin has been reported as eosinophilia, granulopenia, jaundice and increased enzymes, while stavudine has also been reported to cause anaemia, neutropenia and thrombocytopenia (Kofu et al., 1992; Swati et al., 2016; Zerihun et al., 2019). The aim of this work therefore, is to find out the extent of the effect of HAART on haematological parameters in HIV positive patients in Zaria metropolis. This will also help to ascertain and recommend the particular drug combination that is suitable for HAART. And this can also help to ascertain if haematological response can be used as a tool for monitoring patients on treatment in areas where CD4 count is not available or cannot be done.

## MATERIALS AND METHODS

### Data source

Written informed consent was obtained from patients in the hospital before issuing the questionnaire. Data were collected through using the structured and pre-tested questionnaire.

### Methods

Questionnaire containing detailed information about the patient was issued and only individuals who adhere strictly to their therapy residing within Zaria metropolis were used for this study. The baseline sample was collected for analysis and the patient continued therapy for another 3 months when another sample was collected for analysis. A total of 230 patients were enrolled in this work and 49 healthy individuals not on HAART were used as control. All pregnant women patients on admission and those residing outside Zaria metropolis were excluded from this work. For the purpose of this work an automated haematology counter was used, (Sysmex KX-21N) and baseline haematological indices such as Haemoglobin, white blood cell (WBC) count and WBC differential count were obtained. 4 millilitres (4mls) of blood was collected from the antecubital fossa of each individual enrolled in the program using EDTA anticoagulant vacutainer. Reagent such as: Cellpack WBC/Hb lyse reagent: Stromatolyser-WH were used and standard operating procedure was observed according to manufacturer's instruction.

### Statistical analysis

The data statistical analysis was performed using the information entered into SPSS version 20.0 software. While $P < 0.05$ was considered statistically significant.

## RESULTS

In the study, a total of 230 adults on HAART consented to participate in this study giving a response rate of 100% as shown in Table 1. Out of the 230 that participated, the

**Table 2.** Sex Distribution of Patients in Relation to Age

| Age (years) | Sex | | Total (%) |
|---|---|---|---|
| | Male | Female | |
| 0 – 10 | 2(28.6%) | 5(71.4%) | 7(100) |
| 11 -20 | 11(44%) | 14(56%) | 25(100) |
| 21 – 30 | 15(15%) | 85(85%) | 100(100) |
| 31 – 40 | 26(40.6%) | 38(59.4%) | 64(100) |
| 41 and above | 21(61.8%) | 13(38.2%) | 34(100) |
| **Total** | **75** | **155** | **230** |

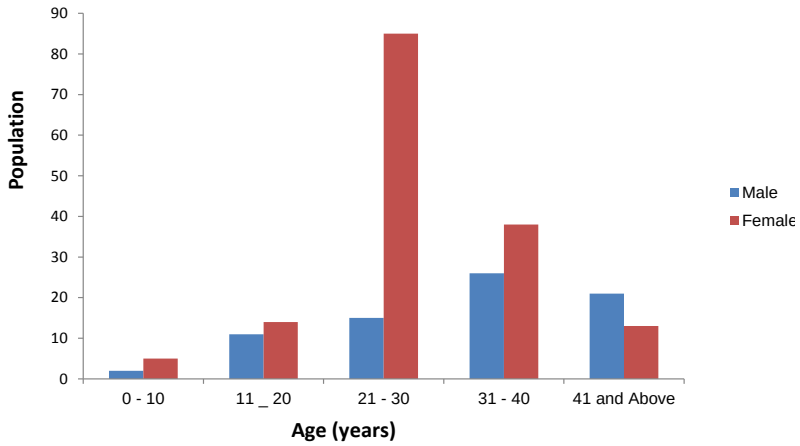


**Figure 1.** Showing sex distribution of patients in relation to age.

**Table 3.** Distribution of patients in relation to drug regimen.

| Regimen | Drug combination | No of patients (%) |
|---|---|---|
| 1 | Stavudine+Lamivudine+Nevirapine | 146 (63.5%) |
| 5 | Zidovudine+Lamivudine+Nevirapine | 84 (36.5%) |
| **Total** | | **230 (100%)** |

age group 21-30 recorded the highest number of participants 100 (43.5%), followed by age group 31-40 with 64 (27.8%) participants, with the least being age group 0-10 with 7 (3.0%). The mean age of the participant was 25.5 years. Seventy five (32.6%) participants were male, while one hundred and fifty five (67.4%) were females. In the male age group, ages 31-40 has the highest number of participants 26 (40.6%), with the least ages 0-10 with 2 (28.6%). The female participants ages 21-30, 85 (85%) has the highest number of patient participation, with the least age 0-10 5(71.4%) as compare with the male participants as shown in Table 2. The sex distribution as indicated by the participant in relation to age is shown in Figure 1. With the age 21-30 having the highest number of female participants, while age 31-40 recorded the highest male participant, with age 0-10 having the least number of both female and male participants. The two hundred and thirty HAART patient that participated in this study, 146 (63.5%) were on Stavudine+Lamivudine+Nevirapine (Regimen 1), while the remaining participants 84 (36.5%) were on Zidovudine+Lamivudine+Nevirapine (Regimen 5) as shown in Table 3. The baseline comparison of the haematological parameters of patients on regimen 1 after 3 months showed a marked increase in Hb, Packed cell volume (PCV) and lymphocytes counts with P-value (<0.05) as shown in Table 4 and Figure 2, while that of regimen 5 is as shown in Table 5 and Figure 3. Comparing the haematological parameters in relation to their response after 3 months, indicated that participants on regimen 1 showed a better response to treatment than participant in regimen 5 as shown in Table 6, with their

**Table 4.** Comparison between Baseline Values and 3 Months Values in Regimen 1.

| Parameter | Baseline | | 3 Months | |
|---|---|---|---|---|
| | Mean | SD | Mean | SD |
| RBC x $10^6$/uL | 4.5 | 1.23 | 4.6 | 1.11 |
| Haemoglobin (g/dL) | 10.9 | 1.42 | 12.0 | 1.18 |
| PCV (%) | 33.8 | 4.10 | 36.6 | 3.59 |
| Platelet x$10^3$/uL | 238.6 | 117.34 | 226.5 | 52.07 |
| WBC x$10^3$/uL | 5.4 | 1.04 | 4.9 | 0.94 |
| Lymphocyte (%) | 39.1 | 14.97 | 42.4 | 12.48 |
| Neutrophils (%) | 47.8 | 1.14 | 45.5 | 1.07 |

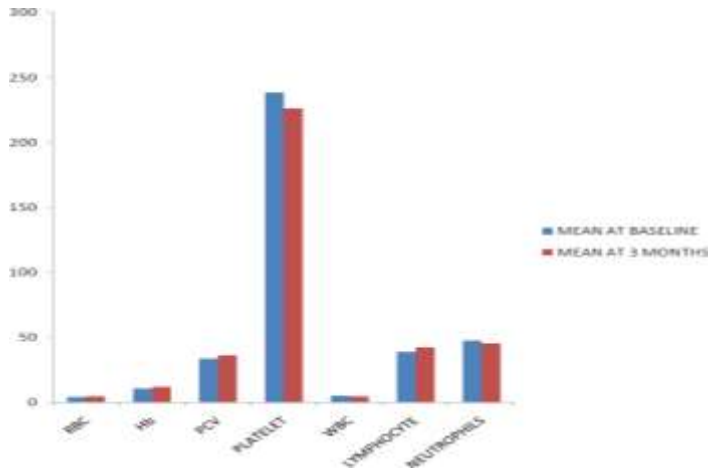


**Figure 2.** Showing mean values between baseline and 3 months in regimen 1.

**Table 5.** Comparison between baseline values and 3 months values in regimen 5.

| Parameter | Baseline | | 3 Months | |
|---|---|---|---|---|
| | Mean | SD | Mean | SD |
| RBC × $10^6$/µl | 4.7 | 1.39 | 4.5 | 1.06 |
| Haemoglobin (g/dL) | 12.2 | 1.27 | 11.6 | 1.25 |
| PCV (%) | 37.5 | 4.00 | 34.6 | 3.82 |
| Platelet ×$10^3$/µl | 237.6 | 77.27 | 231.6 | 56.77 |
| WBC ×$10^3$/µl | 4.6 | 1.14 | 4.6 | 0.95 |
| Lymphocyte (%) | 43.3 | 13.9 | 35.0 | 8.2 |
| Neutrophils (%) | 45.6 | 14.8 | 52.9 | 10.1 |

P-value (<0.05) showing a significant decrease in HB, PCV and lymphocytes counts in Tables 7 and 8 respectively.

## DISCUSSION

Haematological abnormalities is often associated as a value (<0.05) showing a significant decrease in HB, PCV and lymphocytes counts in Tables 7 and 8 respectively. health challenge with HIV infected individuals, the assessment of such is vital to the general response of the infected individual to anti-retroviral therapy. Anti-retroviral drugs (ARD) are known to be toxic to liver and bone marrow, in several studies the relationship of HIV viruses and anti-retroviral drug effect on haematological parameters has been reported (Kwame et al., 2018; Zerihun et al., 2019). The study observed an overall effect of HAART in relation to haematological parameters in patients attending (HAART) Clinic in Zaria. The

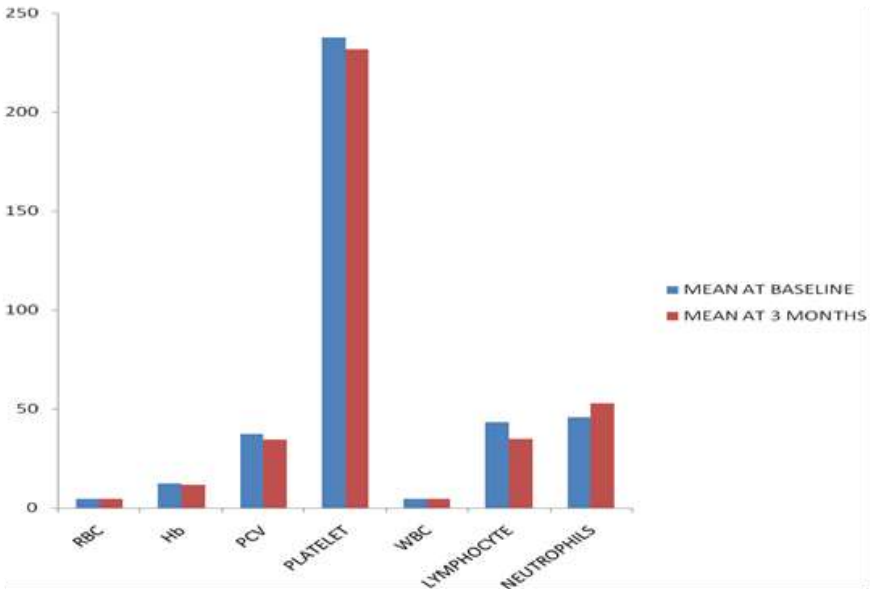


**Figure 3.** Showing mean values between baseline and 3 months in regimen 5.

**Table 6.** Mean haematological parameters in relation to mean controls.

| Parameter | Control | | Regime 1 | | Regimen 5 | |
|---|---|---|---|---|---|---|
| | Baseline | 3 months | Baseline | 3months | Baseline | 3months |
| RBC | 5.1 | 5.2 | 4.5 | 4.6 | 4.7 | 4.5 |
| HB | 13.3 | 13.5 | 10.9 | 12.0 | 12.2 | 11.6 |
| PCV | 39.9 | 40.4 | 33.8 | 36.6 | 32.5 | 34.6 |
| Platelet | 316.2 | 329.4 | 238.6 | 226.5 | 237.6 | 231.6 |
| WBC | 5.88 | 6.08 | 5.4 | 4.9 | 4.6 | 4.6 |
| Lymphocyte | 38.0 | 37.0 | 39.1 | 42.4 | 43.3 | 35.0 |
| Neutrophils | 57.3 | 58.3 | 47.8 | 45.5 | 45.6 | 52.9 |

**Table 7.** P-values for regimen 1.

| Parameter | P-value | Remark |
|---|---|---|
| RBC × $10^6$/µl | 0.2527 | Not Significant |
| Haemoglobin (g/dL) | 0.0001 | Significant |
| PCV (%) | 0.0001 | Significant |
| Platelet ×$10^3$/ µl | 0.2566 | Not Significant |
| WBC ×$10^3$/ µl | 0.0001 | Significant |
| Lymphocyte (%) | 0.0421 | Significant |
| Neutrophils (%) | 0.1277 | Not Significant |

percentage difference of about 57.5% was seen in the first group placed on drugs in regimen 1 which includes Stavudine + Lamivudine + Nevirapine, compare with those in group two placed on regimen 5 which contains Zidovudine + Lamivudine + Nevirapine. Patients on regimen 1(non-zidovudine containing HAART) had an appreciable significant increase in haemoglobin (Hb) and packed cell volume (PCV) value both having P-values of 0.0001 as shown in Tables 4, 6 and 7. This is in line with the works of Odunukwe et al. (2005); Ebonyi et al. (2017)

**Table 8.** P-values for regimen 5.

| Parameter | P-value | Remark |
|---|---|---|
| RBC × $10^6$/ µl | 0.4471 | Not Significant |
| Haemoglobin (g/dL) | 0.0021 | Significant |
| PCV (%) | 0.0001 | Significant |
| Platelet ×$10^3$/ µl | 0.5710 | Not Significant |
| WBC ×$10^3$/ µl | 0.9883 | Not Significant |
| Lymphocyte (%) | 0.0001 | Significant |
| Neutrophils (%) | 0.0003 | Significant |

who noted an increase in haemoglobin and PCV in 50 patients placed on regimen 1. It also agrees with the works of Osaro et al., (2009). Abdulqadir et al. (2018) and Gumel et al., 2019) who noted a significant increase in haemoglobin from baseline values. There was also a statistically significant decrease in WBC with P-value 0.0001.This agrees with Umar et al. (2007) who established a decrease in leucocyte count upon administration of regimen 1. However this is in contrast with the work of Ejele et al. (2004) who noted that there was no significant change in leucocyte level. Lymphocyte also had a statistically significant increase with P-value of 0.0421 which also agrees with the work of Odunukwe et al. (2005), Osaro et al. (2009), Enawgaw et al. (2014) and Ako et al. (2018) on statistically significant increase in lymphocyte count. Other parameters such as Red Blood Cell, Neutrophil and Platelets were not statistically significant. On regimen 5 (zidovudine containing HAART), statistically significant decrease were noted in haemoglobin, PCV, lymphocyte count and a significant increase in neutrophil count as shown in Tables 5, 6 and 8. This is in line with the work reported by Aurpibul et al. (2008) on decrease in haemoglobin level following the substitution of stavudine with zidovudine. It also agrees with the work of Nacoulma et al. (2007) and Gebremedhin and Haye (2019). On anaemia in patients on zidovudine containing HAART but is in contrast with this work on the increase in neutrophil count. It is also in line with the work of Taha et al. (2002), who reported a significant decrease in haemoglobin and lymphocyte value, and that of Balakrishnan et al. (2010) and Ifeanyichukwu and Bright (2016) who reported anaemia due to zidovudine-induced pure red cell aplasia. However, other parameters such as Red Blood Cell, Platelet and White Blood Cell were not statistically significant. This is in contrast with the report of Aurpibul et al. (2008) and Sheela et al. (2016) on a significant decrease in White Blood Cell count on substitution of stavudine with zidovudine.

## Conclusion

As a result of this work, it is concluded that regimen 1 (stavudine + lamivudine + nevirapin) combination results in improved haematological values of HIV patients especially values like Haemoglobin and PCV. While regimen 5 (zidovudine containing HAART) could be responsible for most cases of anaemia and leucopenia in HIV patients.

## RECOMMENDATIONS

(i) Since the haematological effects could be noticed within the three months of study, it therefore indicates that haematological response could be used for patients monitoring in settings where CD4 count cannot be done.
(ii) Haematological parameters should be made mandatory for patients on HAART as a way of checking other complications that may arise due to drug administration.
(iii) Also regimen 1(stavudine + lamivudine + nevirapin) should be used in preference to regimen 5 (zidovudine containing HAART) as this will reduce the adverse effects on haematological parameters.

## CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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