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HAEMOTOLOGICAL RESPONSES OF HIV/AIDS PATIENTS DURING THE FIRST NINE MONTHS OF ANTIRETROVIRAL THERAPY IN TREATMENT CENTRES IN NORTH CENTRAL, NIGERIA.

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ABSTRACT

The long use of Highly Active Antiretroviral Therapy (HAART) for the management of Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS) has been found to improve the health status of HIV/AIDS patients. This research work was carried out to assess the haematological profile of HIV patients on antiretroviral therapy with short term monitoring. Of the 2,322 HIV infected patients that were monitored for nine months from June, 2013 to February, 2014 in some selected ART clinics in North Central Nigeria for changes in haematological profiles. The profiles for white blood cell (WBC) counts and packed cell volume (PCV) were analyzed at three month intervals for nine months using automated hematological analyzer (Sysmex KX-21N, Japan). There was increased in mean WBC counts from $3.90 \times 10^9 \pm 0.0251$ to $5.43 \times 10^9 \pm 0.0208$ cells/L and mean PCV from 36.12 ± 0.0695 to $36.52 \pm 0.0594\%$ after nine months. The changes in profiles were statistically significant ($p \leq 0.05$). The present study shows that the use of HAART can improve haematological profiles, hence protect against anaemia and diseases that can progress to mortality and morbidity. Therefore, enlightenments on the side effects, potential toxicities and other challenges caused by ARV drugs usage should be encouraged and considered to achieve the desired goal in treatment decisions.

Keywords: HAART, Hematological, HIV/AIDS, Morbidity, Mortality, PCV, WBC counts

INTRODUCTION

Acquired Immune Deficiency Syndrome (AIDS) is immunological condition caused by the lentivirus subfamily of retroviruses (HIV), which results in depilation of cell mediated immune responses. HIV/AIDS is also called the slow killer and a global

pandemic. The major problem with HIV/AIDS threat is that most individuals who are infected do not know about it and many are frightened to go for HIV screening in order to ascertain their status, thereby affecting other individuals. In 2012, about 35.3 million

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individuals have been infected with HIV globally and new cases of infections being about 2.3 million that year, although, this was lower than 3.1 million new cases in 2001 and about 16.8 million are women and 3.4 million are less than 15 years old. The region largely affected with the virus is Africa (UNAIDS, 2013). As at 2010, about 68% (22.9 million) of these HIV cases and 66% (1.2 million) of these deaths cases occurred in this region, although, findings show that an estimated 5% of the adult population are infected (UNAIDS, 2011) and this was believed to be the causes of the most 10% deaths in children. Transmission of mother-to-child as at 2013 in Botswana and South Africa has decreased below 5% with improvement in many other Africa nations due to better ways of accessing antiretroviral therapy (UNAIDS, 2013).

Prevalence of HIV in Nigeria was estimated to be 1.8% in 1991 to 4.5% in 1996, 5.8% in 2001, 5.0% in 2003 and 4.4% as at 2005. Although, the national prevalence seemed to stabilize between 2005 and 2010 as shown by reported findings of 4.4% (2005), 4.6% (2008), and 4.1% (2010). These prevalence ranges from 1.0% in Kebbi State to 12.7% in Benue State. Of the overall national prevalence of 4.1% obtained in 2010, it is estimated that 3.1million people in Nigeria are living with HIV/AIDS in 2010 and about 1.5 million required HAART (FMoH, 2011). In the year 2014, national prevalence was further reduced to 3.0%. Nevertheless, a prevalence of 3.2% HIV prevalence implied that over

3.4 million Nigerians are now living with the virus and about 2.5 million requiring HAART (FMoH, 2015).

Addition of several antiretroviral drugs (ARVDs) is known as HAART that aids in slowing the rate at which HIV replicates to make copies of itself in the body of infected patients. The addition of ARVDs is the recent standard of care for treating patient with HIV/AIDS, which is better than using only one drug or medicine (mono-therapy) in treating HIV infected patients (Apollo *et al.*, 2014). It was reported that approximately, seven million people who live with AIDS are now accessing HAART and there is more number of patients getting the treatment, which has leads to reduction in AIDS related morbidity and mortality (Piyawa *et al.*, 2014).

Hematopoietic challenges (blood cell production) occur in peoples living with HIV. This change affects all three cell lines (white blood cells, red blood cells and platelets) that come from stem cells in the marrow (Addis *et al.*, 2014). Therefore, HIV-infected children and adults may suffer from neutropenia (lowered levels of white blood cells called neutrophils), thrombocytopenia (lowered levels of platelets), anemia (lowered levels of red cells) or any combination of these three. The causes and mechanism underlying these abnormalities are dynamic and varies, but are not fully understood (Daka *et al.*, 2013). It was also reported that white blood cells and red blood cells profiles are affected by age, sex, diet, malnutrition, co-

infection and the consumption of toxic drugs (Addis *et al.*, 2014).

Haematological measurement can also be useful for clinical monitoring of HIV positive patients where viral load testing and CD4+ cells count estimations are not readily available (Chen *et al.*, 2007). Effective HAART consistently results in sustained reduction of HIV ribonucleic acid (RNA) replication and therefore, gradual increased in white blood cell counts. Owiredu *et al.* (2011), reported that the use of HAART was effective in decreasing the prevalence of anaemia cases by improving upon haemoglobin and haematocrit values and this positive impact leads to increased survival in people living with HIV/AIDS. Chukwurah *et al.*, (2007), also reported that HAART regimens and nutrition supplements have been found to increase platelet counts at values greater than packed cell volume (PCV) and erythrocyte sedimentation rate in HIV positive patients on treatments.

Complications regarding haematological changes have been reported to be the most common causes of morbidity and mortality in HIV patients and are generally marked with cytopenia such as anaemia, neutropenia, lymphopenia and thrombocytopenia (Apollo *et al.*, 2014). The occurrence and severity of the cytopenia generally correlate to the stage of the infection with anemia being the most commonly encountered complications; and is considered a significant predictor of progression to AIDS or death (Opie, 2012).

Since the introduction of HAART, there were reported improvements in haemoglobin and haematocrit values resulting in decreased morbidity and mortality of HIV patients (Odunukwe *et al.*, 2002). Omoreghie *et al.*, (2008) also in their findings, reported that there was no increase in the haematocrit values of HIV patients treated with HAART when compared with those that are not on HAART. It was against this background of such confusing reports that we decided to look at the efficacy, find out about the confusing reports and to have a second thought about highly active antiretroviral therapy (HAART) in this HAART period. Therefore, this research work was carried out to assess the responses of HAART regimens on haematocrit (PCV) and WBC counts; and to establish the need for continuous monitoring of these parameters in the management of HIV infected patients.

MATERIALS AND METHODS

Study Area

The study area for this research work was North Central, Nigeria. North Central Nigeria consists of six states and Federal Capital Territory (FCT) Abuja (National Population Commission and ICF Macro, 2009). The states selected for the study are Kogi, Nasarawa, Niger States and FCT based on systematic random sampling technique. This method of selection guarantees that all states are equally likely to be drawn or selected.

Ethical Approval

Approval for the study was sorted and obtained from Health Research and Ethics Committees (HREC) of

these selected hospitals in North Central Nigeria. This includes Federal Medical Centres Keffi, in Nasarawa State, Lokoja, in Kogi State and General Hospitals Asokoro, in Federal Capital Territory Abuja and Suleja, in Niger State.

Study Design

This research work was a non-randomized prospective study designed to determine the hematological profile of HIV/AIDS infected adults who were on HAART in North Central Nigeria. The objectives and benefits of the research work were explained in details to the participating individuals. Data were collected after informed consent obtained and strict confidentiality of their responses was kept during and after the study period. The hematological profiles of the respondents were assessed and reviewed after every three (3) months for nine (9) months. The patients were taken into the study when found eligible for ART as per the national guidelines on ART and fulfillment of the eligibility criteria. The patients must also be above 18 years of age, HAART naive and not critically ill. Those exempted from the study were patients below 18 years, any person who is on ART and critically ill individuals.

Study population.

A total of two thousand three hundred and twenty - two (2,322) of HIV positive cases and ART naive patients of both female and male adult of various ages presenting at the various selected ART hospitals were recruited and followed-up/monitored for the short term treatment period of nine (9) months.

Sample Collection and Preparation

A volume of 5ml of venous blood was collected from each patient into well labeled Ethylene Diethyle Tetra Acetic Acid (K_2 EDTA) tubes for haematological analysis according to the standard protocol.

Haematological Assay

Haematological parameters white blood cell (WBC) count and packed cell volume (PCV) were analysed using automated haematology analyzer (Sysmex KX-21N, Japan), according to manufacturer's instructions.

Data Analysis

The data was analysed using SPSS (17.0 Version Inc., Chicago, USA) and expressed at 95% confidence interval (CI) and the p-value were considered significant at $p \leq 0.05$. The mean and standard error of mean (\pm SEM) of the WBC counts and PCV values were calculated. The comparison between mean were done using one-way analysis of variance (ANOVA) and the results are presented using figures.

RESULTS

Of the 2,322 HIV infected patients that were monitored in this study, 1418 (61.1%) were female while 904 (38.9%) were male patients. The mean age of the study group was 38.0 (18 – 58) years.

The mean PCV monitored for the nine - months period on the two thousand three hundred and twenty-two (2,322) HIV infected patients monitored is shown in Fig 1. The mean PCV value at baseline was $36.12 \pm 0.0695\%$ after three months, the mean PCV value increased to $36.74 \pm 0.2902\%$, at the end of the 6th

month; it dropped to $36.27 \pm 0.0566\%$ and further increased to $36.52 \pm 0.0594\%$ at the end of 9th month. The fluctuations observed for the mean PCV value at 6th month were statistically significant ($p = 0.001$).

The mean baseline WBC count was $3.90 \times 10^9 \pm 0.0251$ cells/L, at the end of the 3rd month, it

was $4.22 \times 10^9 \pm 0.0158$ cells/L, at the end of the 6th month; it increases to $4.73 \times 10^9 \pm 0.0181$ cells/L and further increased to $5.43 \times 10^9 \pm 0.0208$ cells/L at the end of 9th month (Fig 2). The changes in the WBC count was statistically significant ($p = 0.02$).

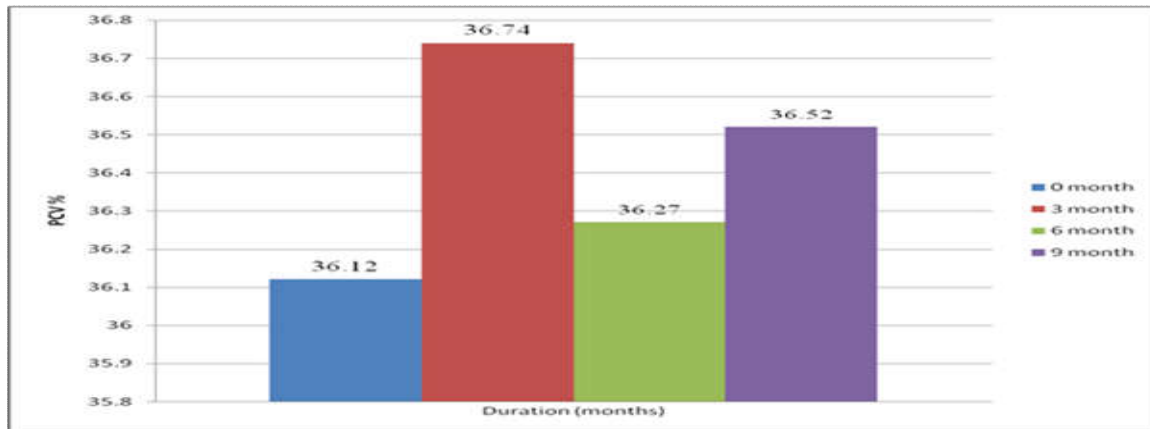


Figure 1: Mean packed cell volume (PCV) value of HIV infected patients monitored for nine Months in North Central Hospitals, Nigeria.

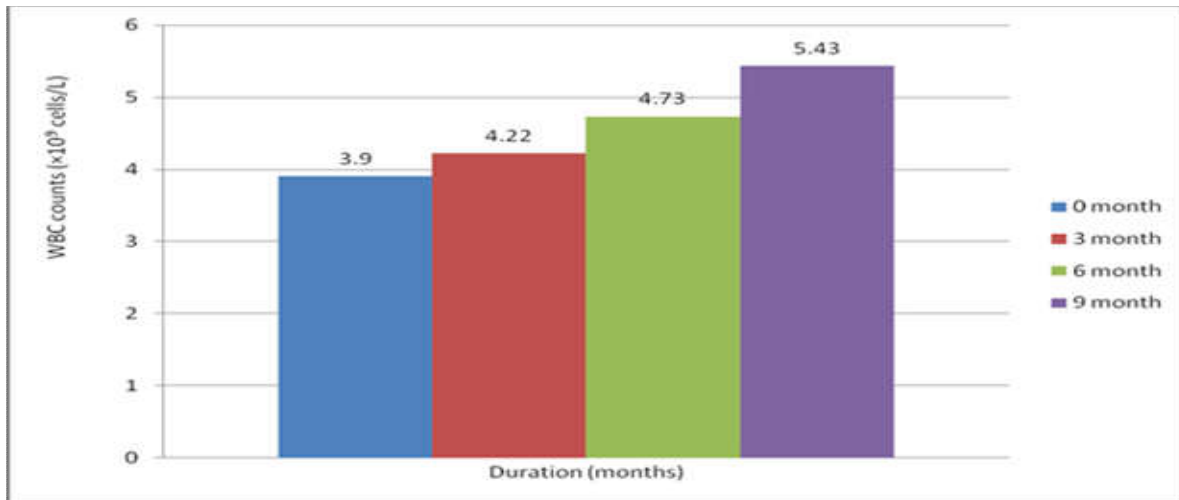


Figure 2: Mean White Blood Cell (WBC) counts of HIV infected patients monitored for nine months in North Central Hospitals, Nigeria.

DISCUSSION

The treatment of HIV/AIDS patients using antiretroviral therapy (ART) drug are usually followed with many other adverse issues, for example: peripheral neuropathy, pancreatitis, myopathy, lactic acidosis, nephrotoxicity, hepatic steatosis and bone marrow suppression. Adverse effects of these drugs includes bone marrow suppression (anemia and neutropenia), fever, vomiting and nausea, malaise, myalgia, insomnia and diarrhea (Oshikoya *et al.*, 2012).

The result from this study shows a remarkable increased in the PCV after initiation of ART at 3 months from $36.12 \pm 0.0695\%$ to 36.74 ± 0.2902 . This observation was in agreement with other studies, in which PCV in ART naive is significantly higher compared to HAART experienced patients (Owiredu *et al.*, 2011; Denué *et al.*, 2013). Although, it was also observed in this research work that there was a slight decline in PCV value during the monitoring period at the end of the 6th month to $36.27 \pm 0.0566\%$ from the baseline of $36.12 \pm 0.0695\%$, this fluctuation observed in the mean PCV value was statistically significant ($p = 0.001$) and this may be due to other infections, adverse effects or malnutrition that results in the development of anaemia. This observation was similar to those made by Oshikoya *et al.*, (2012) in their study, in which they found out that haematological disorders are among the commonest related problem associated with the HIV infected persons and adverse problems of ARV drugs are caused by non-adherence to medications.

Despite a significant increase in the PCV at 9th month (36.52 ± 0.0594), close to 17% of the HIV patients had lower PCV implying the need for frequent screening of PCV and subsequent finding of its cause, although, in this study based on our results we were unable to ascertain the specific reasons why these infected individuals had lower PCV despite treatment with HAART. After 9th month of therapy using HAART, increase in WBC count was a predictor of anemia suggesting good recovery and probably low viral load estimations in those patient with anemia before 6th month of HAART. Results on viral load estimation and CD4⁺ count would have been useful for proper monitoring and arguments but they were not routinely done during this follow-up.

The knowledge of the use and side effects of these drugs is very important in the management and treatment of HIV infected persons due to increase in antiretroviral therapy usage (Pryce *et al.*, 2008; Oshikoya *et al.*, 2012). Although, adverse drug reactions (ADRs) such as anaemia have multiple etiologies and therefore, patients with haematologic complications should be monitored for other pathophysiologic processes that might result in or contribute to anaemia, thrombocytopenia or neutropenia. It was also reported by Opie, 2012 that haemoglobinopathies or glucose-6-phosphate dehydrogenase enzyme deficiency may have contributed to haematologic adverse effects.

The increased in the WBC count monitored for nine (9) months was statistically significant ($p = 0.02$) in this

research work and this may have aid in the functional betterments of these two important components of innate antimicrobial immunity, such as monocytes and neutrophils. This may have also contribute to the increased cell-mediated immune responses against other infections in HIV/AIDS patients treated with various HAART regimens as observed in this study. This was similar to observations made by Derbe *et al.*, 2013 on responses against other infections in HIV/AIDS treated individuals with various HAART. It was also similar to report by Amegor *et al.*, (2009), that ART brought statistically significant increase in WBC from 4070 ± 250 cells/ μl at baseline to 4760 ± 170 cells/ μl after antiretroviral drugs usage in a study that was done in Markurdi, Benue state, Nigeria.

CONCLUSION

These findings in this research work suggest that HAART may induce changes in clinically important haematological parameters (packed cell volume (PCV) and white blood cells (WBC)) leading to the correction of some abnormalities such as anemia during the follow-up. Therefore, enlightenments on the potential toxicities, side effects of ARV drugs and regular follow-up of these patients by assessing their haematological profiles should be encouraged and considered to achieve the desired goal in treatment decisions. Hence, it is very vital to investigate, find out the real causes and appropriate treatment of these abnormalities (e.g anemia) in order to reduce death rates in HIV/AIDS patients.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

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