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Effects and Influences of HIV Infection on Blood Counts and Inflammatory Markers in HIV Patients at General Hospital Nsukka in Enugu

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Abstract

Aims and objectives: The study's goal is to evaluate the haematopoietic and inflammatory indicators of people living with HIV/AIDS in Enugu North Senatorial Zone, Enugu State, Nigeria. Specifically, the effect of HAART on total blood counts in HIV patients and the influence of HIV infection on the inflammatory makers of HIV infected patients.

Materials and methods: The study employed a cross-sectional, prospective, hospital based clinical research on all consenting consecutive patients scheduled for ART treatment irrespective of age between the period of March 2020 to August 2020 at the General Hospital Nsukka that meet the eligibility criteria.

Subjects and sample size determination: The sample size of 137 was determining using Cochran formula for determining sample size, after which 137 subjects were purposively selected.

Statistical analysis: were expressed where appropriate as mean ± standard deviation. T-test was used in testing hypotheses at 5% level of significance.

Results: The differences in complete blood counts for WBC, RBC, MCV, HB, Platelet and neutrophil as indicated in the mean values of pre and post HAART was administered on HIV patients revealed that HAART improved patients WBC, RBC, MCV, HB, platelet and neutrophil respectively. The improvement in patients WBC, RBC and MCV was statistically significant ($P<0.05$). However, the difference in patients MCHC after the administration of HAART was not statistically significant different from patients MCHC before the administration of HAART ($P>0.05$). Hence, the administration of HAART on HIV patients did not improve MCHC of patients.

Conclusion: The improvement in the complete blood counts in HIV patients was an indication that HAART was effective in suppressing the activities of HIV in patients. Inflammation, as indicated by greater CRP is related to the immunosuppressant of the system whereas lower hsCRP is a good indicator to be used to monitor early effect of viral suppression of the patients affected by HIV

Keywords: Human immunodeficiency virus • Highly active antiretroviral therapy • Opportunistic Infection (OIs) Inflammation • Haematopoiesis

Abbreviations: HAART: Highly Active Antiretroviral Therapy; OIs: Opportunistic Infections; MCV: Mean Cell volume; HB: Haemoglobin; MCHC: Mean Cell Haemoglobin Concentration; PCV: Packed Cell Volume; CRP: C-Reactive Proteins; UNAIDS: Joint United Nations Programme on HIV/AIDS; NACA: National Agency for the Control of AIDS; HIV: Human Immunodeficiency Virus; PLWHA: People Living with HIV/AIDS; CD_4: Cluster of Differentiation 4; ART: Antiretroviral Therapy; WBC: Whole Blood Count; RBC: Red Blood Cell

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Introduction

Globally, 38.0 million individuals are infected with HIV. Adults account for 36.2 million HIV patients, while children account for 1.8 million (0-14 years). Around 1.9 million persons in Nigeria are infected with HIV, with a prevalence incidence of 1.4 percent among adults aged 15 to 49 [1]. Nigeria has the world's second-largest HIV epidemic, while adult prevalence is significantly lower (1.3 percent) than in other African nations such as South Africa (19 percent) and Zambia (11.5 percent) [2]. The Human Immunodeficiency Virus (HIV) is a persistent infection that posses several health risks throughout its lifespan. HIV has a significant impact on the bone marrow, taking over and diverting haematopoietic processes as well as triggering inflammatory signals. Anemia, changes in body chemistry, a reduction in blood production, and inflammation are all symptoms of HIV infection.

Alterations in the haematological characteristics of the bone marrow are one of the changes that occur in the body as a result of HIV. One of the most prevalent problems among persons living with HIV/AIDS (PLWHA) is haematological alterations [3]. The combined effect of HIV virus infection, medications used during AIDS therapy, inflammatory mediators generated during infection and the actions of potential Opportunistic Infections (OIs) targets the bone marrow, the source of blood production. HIV infection has direct and indirect effects on haematopoietic progenitor cells, impacting bone marrow homeostasis and cell proliferation and differentiation during haematopoiesis. Changed cellularity with a decrease in all haematological lineages, dysplastic alterations in the erythroid and granulocytic series, megaloblastic abnormalities in the erythroid series and reticulum endothelial iron block are the primary effects. In the environment of persistent immunological activation, HIV infection is also characterized by a continuing loss of CD_4+ T-lymphocytes and an imbalance in cc, which leads to a progressive loss of immune effectiveness [4].

Antiretroviral therapy, which suppresses HIV's activity, is still the most widely used medical treatment. According to Kibaru, et al., the use of zidovudine, lamivudine, and stavudine was related with considerable improvement in hemoglobin concentration, and the prevalence of anemia decreased from 65.5 percent to 46 percent after 12 months of Highly Active Antiretroviral Therapy (HAART) [5]. Huang, et al. found substantial increases in mean Hb from 13.9 to 14.1 g/dl following 3 months of HAART therapy in another research. Huang, et al. found that after using HAART, Mean Cell Volume (MCV) increased from 55 to 98.9 fl to 105.5 fl and 106 fl after 3,6,9, and 12 months, respectively [6,7].

Despite HIV therapy and all efforts by global health organizations, many individuals living with the illness remain at risk, with no access to testing, care, or medication, and no cure. Steps must be made to prevent life threatening adverse effects including HAART related haematotoxicity, according to studies [8]. The WHO has designated efavirenz, tenofovir with lamivudine, or emtricitabine plus nevirapine as the preferred firstline antiretroviral drugs in resource constrained developing countries, based on availability, safety, and efficacy, despite the lack of data on HAART usage in these regions [9]. When efavirenz isn't an option, the Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI) of choice are still nevirapine. Individuals on efavirenz based HAART who were given tenofovir-emtricitabine had better rates of HIV replication suppression than patients who were given zidovudine-lamivudine.

Patients haematopoietic and inflammatory biomarkers are commonly used to assess the efficacy of antiretroviral treatment. The characteristics that monitor the normal, pathogenic, and drug induction in the bone marrow activities and impact the formation of normal cells are known as haematopoietic and inflammatory biomarkers. Following the onset of infection, the system receives a signal that may partially or completely misdirect the function. When this occurs, all that is required is to measure the indices and examine the fluctuations. There is currently a scarcity of data on the levels of haematopoietic and inflammatory markers in Nigeria. The study's goal is to evaluate the haematopoietic and inflammatory indicators of people living with HIV/AIDS in Enugu North Senatorial Zone, Enugu State. Specifically, the assessed the effect of HAART on total blood counts in HIV patients and the influence of HIV infection on the inflammatory makers of HIV infected patients.

Materials and Methods

Study design

The study employed a cross-sectional, prospective hospital based clinical research on all consenting consecutive patients scheduled for ART treatment of age 15-60 years between the period of March 2020 to August 2020 at the general hospital Nsukka that met the eligibility criteria.

Area of the study

The study was conducted at general hospital Nsukka. This hospital is one of the seven general hospitals in Enugu state and also a comprehensive site for the testing and management of ART patients. Nsukka is a local government area in Enugu State, South eastern Nigeria.

Subjects and sample size determination

The sample size of one hundred and thirty seven (137) was determining using Cochran formula for determining sample size, after which subjects were purposively selected.

Ethical clearance/informed consent

An ethical approval was obtained from the health and research and Ethical committee of the ministry of health Enugu state. Blood sample was collected from the subjects with informed consents.

Questionnaire

A structured questionnaire was filled by the subjects/participants in order to obtain demographic data, clinical history and treatment regimen whether on first or second line.

Inclusion and exclusion criteria

Subjects included were those of 15 to 60 years diagnosed as HIV seropositve and put on ART drugs. Exclusion subjects' categories were subjects above 60 years and pregnant women with HIV seropositive were not included.

Blood specimen collection

By venipuncture, 10 ml of blood was collected 5 mls dispensed into plain vacutanier tubes to obtain serum whereas 5 mls was dispensed into tubes containing Ethylene-Diamine-Tetra Acetic Acid (EDTA) labeled with the subject's identification number, age, sex. The blood sample in the plain containers was spun for 5 minutes at 3000 rpm. The serum was separated from the red cells using a dry clean Pasteur pipette into a dry clean plain specimen container. The serum was then stored at -20°C.

Methodology for specific objectives

C-reactive protein assay: Principle CRP and hsCRP testing on the COBAS C311 is an immunoturbidimetric assay for the *in vitro* quantitative determination of CRP in human serum and plasma on Roche/Hitachi Cobas System. Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The aggregates are determined turbidimetrically.

Complete blood count: The complete blood count was made up of haemoglobin, haematocrit, total whole blood count, granulocyte, lymphocyte differential, absolute lymphocyte, absolute granulocyte, red blood cell count, mean cell volume, mean cell haemoglobin, mean cell haemoglobin concentration, platelet count, platelet distribution width, plateletcrit were analyzed using Sysmex auto-analyzer K x 21N. Procedure was followed according to the user's manual.

CD_4 count was done using PARTEC Cyflow machine according to manufacturer's instructions.

Statistical analysis: The results obtained in this study were analyzed statistically. These were expressed where appropriate as mean ± standard deviation. T-test was used in testing hypotheses at 5% level of significance.

Results and Discussion

Effect of HAART on the complete blood counts of HIV patients

The results of the blood counts in HIV patients at different CD_4 ranges are presented in Table 1. The results in Table 2 show the mean and standard error of (WBC), Mean Cell Haemaglobin Concentration (MCHC), Red Blood Cell Count (RBC) and Mean Cell Volume (MCV) of HIV patients before (pre) and after (post) HAART was administered on them. From the table, it can be seen that the grand mean for the Complete Blood Count (CBC) result for the pre administration of HAART and post administration of HAART were 5.34 ± 0.11 and 5.95 ± 0.003 for WBC, 4.57 ± 0.05 and 4.89 ± 0.002 for RBC, 84.91 ± 0.71 and 86.19 ± 0.002 for MCV and 29.14 ± 0.16 and 29.72 ± 0.003 for MCHC, 11.27 ± 0.15 and 8.33 ± 0.15 for HB, 263.66 ± 6.53 and 251.03 ± 6.51 for Platelet count and 45.69 ± 0.87 and 42.17 ± 0.86 for neutrophil differential. The difference in complete blood counts for WBC, RBC, MCV, HB, platelet and neutrophil as indicated in the mean values of pre and post that is before and after HAART was administered on HIV patients revealed that HAART improved patients WBC, RBC, MCV, HB, Platelet and Neutrophil respectively. The improvement in patients WBC, RBC and MCV was statistically significant ($P<0.05$). However, the difference in patients MCHC after the administration of HAART was not statistically significant different from patients' MCHC before the administration of HAART ($P>0.05$). Hence, the administration of HAART on HIV patients did not improve MCHC of patients. This finding is similar with findings of Bani, et al. who in their study reported that Lymphocyte (%), Haemoglobin, MCV, MCHC were all significantly higher at post HAART administration. Although, there were divergent reports with respect to post administration performance of HAART,. The study of Bani, et al. recorded significant decreases in total platelets count, WBC, neutrophil (%) at post HAART administration.

CD_4 cells/µl of blood	WBC x 10^9/L		MCHC(g/dL)		RBC x 10^6/L		MCVfl	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
0-100	4.6 ± 0.00	4.84 ± 0.00	29.00 ± 0.00	29.91 ± 000	3.46 ± 0.00	3.99 ± 0.00	93.7 ± 0.00	94.02 ± 0.00
101-200	6 ± 1.32	6.92 ± 0.01	29.66 ± 0.6	30.04 ± 0.0006	4.14 ±0.35	4.9 ± 0.004	86.86 ± 6.2	87.32 ± 0.004
201-300	4.36 ± 0.28	5.03 ± 0.008	28.89 ± 0.44	29.43 ± 0.003	4.75 ± 0.17	5.03 ± 0.002	84.54 ± 1.98	84.99 ± 0.002
301-400	5.09 ± 0.36	5.76 ± 0.002	29.45 ± 0.56	29.89 ± 0.008	4.62±0.15	5.01 ± 0.003	87.1 ± 2.57	87.99 ± 0.002
401-500	5.54 ± 0.27	5.99 ± 0.0008	29.39 ± 0.34	30 ± 0.002	4.66 ± 0.14	5.03 ± 0.001	85.91 ± 1.59	86.02 ± 0.002
501-600	5.25 ± 0.28	6.03 ± 0.002	29.41±0.38	29.9 ± 0.002	4.58 ± 0.13	0.002 ± 0.002	84.47 ± 1.97	84.99 ± 0.002
601-700	5.98 ± 0.42	6.22 ± 0.002	28.57 ± 0.72	29.64 ± 0.003	4.65 ± 0.13	5.05 ± 0.003	86.11 ± 2.9	86.9 ± 0.003
701-800	5.23 ± 0.36	5.99 ± 0.003	29.4 ± 0.35	30.03 ± 0.002	4.77 ± 0.17	5.04 ± 0.003	82.25 ± 2.05	82.92 ± 2
801-900	5.88 ± 0.54	6.62 ± 0.003	28.18 ± 0.75	28.99 ± 0.003	4.61 ± 0.16	5.03 ± 0.003	79.13 ± 3.29	79.91 ± 0.002

901-1000	4.84 ± 0.36	5.04 ± 0.006	29.6 ± 0.47	30.05 ± 0.005	4.42 ± 0.29	4.91 ± 0.004	89.48 ± 5.15	90.11 ± 0.003
>1000	6.7 ± 0.37	7.06 ± 0.001	28.84 ± 0.47	29.05 ± 0.002	4.35 ± 0.15	4.9 ± 0.002	82.93 ± 1.41	83.02 ± 0.002
Grand mean	5.34 ± 0.11	5.95 ± 0.003	29.14 ± 0.16	29.72 ± 0.003	4.57 ± 0.05	4.89 ± 0.002	84.91 ± 0.71	86.19 ± 0.002
t-test 0.05	**0.00		0.5 ±	**0.00	**0.002			

Where; CD_4=Test=Seropositive patients, WBC=White Blood Cells, MCH=Mean Cell Haemoglobin, MCHC=Mean Cell Haemoglobin Concentration, RBC=Red Blood Cell, MCV=Mean Cell Volume, P Value=Probability Value, **=Significant at 0.05 level

Table 1. Effect of HAART on complete blood counts in HIV patients.

CD_4 cells/µl of blood	HB g/dl		Platelet x 10^6/L		Neutrophil count %	
	Pre	Post	Pre	Post	Pre	Post
0-100	9.40 ± 0.00	6.32 ± 0.00	249.00 ± 0.00	233.93 ± 0.00	32.20 ± 0.00	29.70 ± 0.00
101-200	10.54 ± 0.99	8.24 ± 0.99	258.60 ± 20.18	243.53 ± 20.18	37.44 ± 4.82	34.94 ± 4.82
201-300	11.34 ± 0.42	8.26 ± 0.42	231.43 ± 17.42	224.83 ± 17.25	46.22 ± 2.78	42.73 ± 2.78
301-400	11.58 ± 0.51	9.70 ± 0.51	255.75 ± 24.11	240.68 ± 24.11	42.96 ± 3.76	39.39 ± 3.76
401-500	11.63 ± 0.34	8.55 ± 0.34	271.16 ± 16.88	256.04 ± 16.88	46.09 ± 2.07	42.52 ± 2.07
501-600	11.55 ± 0.45	8.47 ± 0.44	274.05 ± 15.92	258.98 ± 15.92	42.40 ± 2.31	38.83 ± 2.31
601-700	11.89 ± 0.62	8.81 ± 0.62	251.90 ± 24.53	236.83 ± 24.53	44.45 ± 3.29	40.88 ± 3.29
701-800	11.31 ± 0.39	8.23 ± 0.38	241.33 ± 17.91	226.26 ± 17.91	47.41 ± 3.00	43.84 ± 3.00
801-900	10.42± 0.36	7.34 ± 0.36	247.30 ± 28.91	232.23 ± 28.91	43.31 ± 3.02	39.74 ± 3.03
901-1000	11.97 ± 0.42	8.89 ± 0.42	320.25 ± 28.47	305.18 ± 28.47	51.63 ± 4.90	48.06 ± 4.90
>1000	10.88 ± 0.33	7.79 ± 0.33	282.03 ± 15.99	273.96 ± 15.74	49.79 ± 1.52	46.22 ± 1.52
Grand Mean	11.27 ± 0.15	8.33 ± 0.15	263.66 ± 6.53	251.03 ± 6.51	45.69 ± 0.87	42.17 ± 0.86
t-test 0.05	**0.00		**0.00	**0.00		

HB=Haemoglobin, PLT= Platelet, Neutrophil count, P Value=Probability value, **=Significant at 0.05 level

Table 2. Effect of HAART on complete blood counts in HIV patients.

Effect of HIV infection on the inflammatory makers of HIV infected patients

The results of HIV infection on the inflammatory makers of HIV infected patients at different C-Reactive Protein (CRP) and high sensitivity CRP (hsCRP) ranges are presented in Table 2. The results in Table 2 show the mean and standard error of CRP and high sensitivity CRP hsCRP of HIV patients. From the Table, it can be seen that the grand mean for the initial (before) CRP and hsCRP (after) of HIV patients were 7.06 ± 0.04 mg/dl and 0.77 ± 0.002 mg/dl respectively, while the grand mean for the final CRP and hsCRP (after) of HIV patients were 7.55 ± 0.02 mg/dl and 0.71 ± 0.004 mg/dl. The difference in the CRP and hsCRP values of HIV patients between times was significant. The differences were statistically significant for CRP and hsCRP (P<0.05) (Table 3).

CRP Ranges	Mean CRPmg/dl		hsCRP Ranges	Mean hsCRPmg/dl	
	Before	After	Before	After	
3.0-4.0	3.19 ± 0.01	3.89 ± 0.005	0.3-0.4	0.39 ± 0.0009	0.36 ± 0.001
5.0-6.0	5.36 ± 0.07	5.90 ± 0.02	0.5-0.6	0.58 ± 0.002	0.52 ± 0.006
7.0-8.0	7.24 ± 0.05	7.94 ± 0.02	0.7-0.8	0.79 ± 0.002	0.72 ± 0.004
9.0-10.0	9.28 ± 0.03	9.94 ± 0.02	0.9-1.0	0.99 ± 0.002	0.92 ± 0.008
>10.0	10.23 ± 0.03	10.08 ± 0.01	>1.0	1.08 ± 0.0006	1.01 ± 0.001

Grand mean	7.06 ± 0.04	7.55 ± 0.02	Grand mean	0.77 ± 0.002	0.71 ± 0.004
t-test 0.05	0		0		

Table 3. Effect of HIV infection on the inflammatory makers of HIV infected patients.

Conclusion

The improvement in the complete blood counts in HIV patients was an indication that HAART was effective in suppressing the activities of HIV in patients. Inflammation, as indicated by greater CRP is related to the immunosuppressant of the system whereas lower hsCRP is a good indicator to be used to monitor early effect of viral suppression of the patients affected by HIV.

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