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Profiling Haematological Changes in HIV Patients Attending Fevers Clinic at the Central Regional Hospital in Cape Coast, Ghana: A Case-Control Study

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ABSTRACT

HIV is associated with a wide variety of haematological changes resulting from marrow defects, immune cytopenias as well as opportunistic infections. The study was conducted to evaluate haematological changes in HIV patients attending Fevers Clinic at the Central Regional Hospital, Cape Coast, Ghana. A case-control study design was used to recruit 150 HIV seropositive patients on antiretroviral treatment (ART) and 50 HIV seronegative control patients. Blood was sampled from both infected and controls for Full Blood Count (FBC) analysis using Cell Dyn 1800 Automated Analyzer, Erythrocyte Sedimentation Rate (ESR) using the Westergren method and CD4 count using the Becton Dickinson (BD) FASCount analyzer. HIV+ patients have FBC parameters ranging from a high of 80% to a low of about 25% whilst control patients have normal FBC parameters ranging from a least of 80% and above. All control patients had normal ESR values whilst 91(65.8%) of HIV+ patients have abnormally high ESR values. Paired mean double-tailed comparison showed that Haemoglobin level (Hb), Red Blood Cell count (RBC), Haematocrit (HCT), Mean Cell Volume (MCV), Mean Cell Haemoglobin (MCH), White Blood Cell (WBC), Mean Corpuscular Haemoglobin Concentration (MCHC), Neutrophil and CD4 count were significantly reduced while ESR values of HIV+ subjects were significantly higher than those of control subjects ($P<0.05$). Platelet and Leukocytes were however higher in control patients than HIV+ patients but insignificant ($P>0.05$). This work provide further evidence on the profound changes in haematological profile of HIV+ patients which factor must be considered in their treatment to ensure total well-being.

Keywords: ESR, CD4, Hb, RBC, WBC.

INTRODUCTION

In 2009, the number of people living with HIV in sub-Saharan Africa reached 22.5 million (20.9 million–24.2 million), 68% of the global total whilst the number of people living with HIV in Ghana were estimated at 260 000, and 140 000 respectively.[1] HIV infection is associated with

a wide variety of haematological changes as a result of marrow defects and immune cytopenias directly resulting from HIV infection, opportunistic infections or lymphoma and the side-effects of drugs used to treat HIV itself or complicating infection or lymphoma.[2] The result of marrow defect associated singular targeting of individual haematological parameters usually leads to severe changes in the profile of these infected people. Example is medication-induced anaemia, particularly from zidovudine (ZDV).[3] A study by Dangana[4] discovered that ESR results of HIV/AIDS subjects were increased significantly when compared to values of control subjects as a result of decreased erythrocyte count that resulting in anaemia. Additionally, HIV destruction of CD4+ T cells which regulate cellular and humoral immunity by interacting with other T lymphocytes, B lymphocytes, macrophages, and natural killer cells does results in a decrease in WBC counts with its associated increased infections in these patients.

HIV infection is accompanied by marked haematological changes that complicate health and treatment of patients. Hence it is important to determine the exact and extent of haematological changes in HIV patients which will lead to a holistic treatment and improve quality of life of these patients.

MATERIALS AND METHODS

Study Area and Design

The study was conducted at the Central Regional Hospital, Cape Coast in the Central Region of Ghana, the main referral hospital in the Municipality and region as well as an HIV designated centre. The study was designed as a case-control comparative study over a six months period with a bi-weekly purposive sampling of HIV infected patients visiting the clinic routinely for medical review and blood donors donating blood to the hospital.

Ethical Considerations

The study was approved by the Central Regional Hospital and the Department of Laboratory Technology, University of Cape Coast and informed consent was obtained from all study participants. All procedures followed were in accordance with the ethical standards of the Ghanaian Ministry of Health as well as the Helsinki Declaration of 1975.[5]

Patients Selection Criteria

The study targeted medically diagnosed HIV positive patients on HAART between the ages of 18-65yrs who are schedule to visit the hospital at regular intervals (every three months) for routine medical review. Control patients were blood donors who qualified for donation and donated blood. One hundred and forty nine (149) confirmed HIV patients and fifty (50) healthy HIV-negative control subjects were enrolled in the study

Patients Exclusion Criteria

Patients at the extremes of age, pregnant women, those on chemotherapy were excluded since they may naturally have very weakened immune system. Additionally, patients not responding to HAART treatment from previous visits were also excluded.

Laboratory Investigations

Study participants were enrolled after agreeing and signing an informed consent form. Venous blood was sampled from participants into EDTA tubes. CD4+ lymphocytes count was determined using the Becton Dickinson (BD) FASCount system (Becton, Dickinson and Company, Califonia, USA) whilst haemoglobin, haematocrit, red cell indices, platelet count,

total white cell count and differential were determined by automated blood analyzer (CELL-DYN 1800, Abbott Laboratories Diagnostics Division, USA). ESR was determined manually using the Westergren pipette method. [6]

Normal CD4+ count of >500 cells/µL and normal haematological parameter values are according to the Ghana Health Service Guidelines; Ministry of Health, Ghana.

Data Analysis

Data analysis was performed using SPSS 16.0 software. Descriptive analysis was done whilst One-way ANOVA and Pearson's Correlation undertaken. ($P \leq 0.05$) is significant and ($P \geq 0.05$) is not significant.

RESULTS

The study sampled 149 HIV positive (HIV+) and 50 HIV negative (HIV-) control patients. From the HIV+ sampled population, 32 (21.5%) were males and 117(75.5%) females whilst 46(92.0%) of HIV- patients were males and 4(8.0%) were females. A large number of HIV+ patients 51(34.2%) were aged 31-40 years, 33(22.1%) aged 21-30 years and the least 3(2.0) aged 61-70 years. Majority of the sampled HIV- patients 24(48.0%) were aged 21-30 years followed by 31-40 years 17(34.0%) (Table I). Table II shows the mean and standard distribution of measured parameters of HIV+ and HIV- patients. Several of the measured parameters (Hb, RBC, HCT, MCV, MCH, MCHC, N, ESR and CD4) showed significant differences in the measured haematological parameters between HIV+ and HIV- patients. HIV+ patients had low levels of RBC 131(73.2%) and HCT 119(79.9%), high L 92(61.7%), N 54(36.2%), MCV 37(24.8%) and MCH 37(21.8%). Majority of HIV- patients had normal parameters except high L 38(76.0%) (Table III). All the 50(100%) of the sample HIV- patients have normal ESR (<20mmfall/hr) and CD4 count (>500cells/µl). Most HIV+ patients 91(65.8%) have high ESR (<20mmfall/hr) and 91(61.1%) low CD4 counts (<500cells/µl) respectively.

Table I: Age Distribution of HIV+ and HIV- Sampled Patients

Age (Years)	HIV+	HIV-
0 -10	10(6.7)	0(0)
11-20	8(5.4)	2(4.0)
21-30	33(22.1)	24(48.0)
31- 40	51(34.2)	17(34.0)
41- 50	28(18.8)	5(10.0)
51- 60	16(10.7)	2(4.0)
61- 70	3(2.0)	0(0.0)

Table II: Mean of Measured Parameters of HIV+ and HIV-Patients and the Associated *P*-Values

Parameters (Normal Ranges)	HIV+	HIV-	*P*-Value
HB (11-18)g/dl	10.20±2.05	14.74±1.13	<0.001
RBC (4.2-6.30)M/µL	3.71±0.73	5.40±0.43	<0.001
HCT (37-51)%	32.19±6.30	46.05±3.02	<0.001
MCV (80-97)fl	87.70±13.90	84.57±8.24	<0.001
MCH (26-32)pg	27.40±5.02	27.36±1.80	<0.001
MCHC (31-36)g/dl	31.43±1.01	32.00±0.84	0.011
WBC (4.1-10.9)K/µL	6.07±7.28	6.53±1.25	<0.001
N (37-92)%	54.42±13.29	56.76±4.80	0.005
L (10-58.5)%	45.64±13.29	43.24±4.80	0.085
PLT (140-440)K/µL	238.71±87.85	207.56±119.50	0.111
ESR (0-20)mmfall/hr	55.79±46.67	3.68±2.90	<0.001
CD4 (Normal >500cells/µL; HIV+ <500cells/µL)	504.15±383.09	1234.98±406.01	<0.001

Table III: Frequency Distribution of Measured Parameters of HIV+ and HIV- Patients

	HIV+			HIV-		
Parameters	**Normal (%)**	**High (%)**	**Low (%)**	**Normal (%)**	**High (%)**	**Low (%)**
HB	90 (60.4)	0(0.0)	59(39.6)	50(100)	0(0.0)	0(0.0)
RBC	40(26.8)	0(0.0)	109(73.2)	48(96.0)	2(4.0)	0(0.0)
HCT	30(20.1)	0(0.0)	119(79.9)	48(96.0)	2(4.0)	0(0.0)
MCV	66(44.3)	37(24.8)	46(30.9	42(84.0)	1(2.0)	7(14.0)
MCH	61(40.9)	37(18.1)	51(40.9)	40(80.0)	0(0.0)	10(20.0)
MCHC	109(73.2)	0(0.0)	40(26.8)	45(90)	0(0.0)	5(10.0)
WBC	109(73.2)	0(0.0)	40(26.8)	50(100)	0(0.0)	0(0.0)
N	83(55.7)	54(36.2)	12(8.1)	50(100)	0(0.0)	0(0.0)
L	51(34.2)	92(61.7)	6(4.0)	12(24.0)	38(76.0)	0(0.0)
PLT	134(89.9)	2(1.3)	13(8.7)	40(80.0)	1(2.0)	9(18.0)

DISCUSSION

Haematological abnormalities are among the most common complications of HIV which involves all lineages of blood cells.[7] Results from the study showed that HIV infection affect haematological indices of patients regardless of age, sex and HAART. Majority of the HIV+ patients were females 117(78.5%) whilst majority of the randomly selected HIV- patients were males 46(92%).

HIV+ patients had significantly (P<0.001) low mean and frequency of Hb (10.20±2.05); 59(39.6%), RBC (3.71±0.73); 109(73.2%) and HCT (32.19±6.30); 119(79.9) compared with HIV- patients with Hb (14.74±1.13); 50(100%), RBC (5.40±0.43); 50(100%) and HCT (46.05±3.02); 48(96%). This confirms research by Dangana[4] who also had a significant drop in Hb levels (P<0.05) and Friel & Scadden[8] who observed that the yearly incidence of developing anaemia increases with disease progression affecting 3% of all patients with asymptomatic HIV infection. The low RBC parameters could be as a result of decreased red blood cells production or ineffective erythropoiesis. Anaemia has been shown to be a statistically significant predictor of progression to [AIDS] and is independently associated with increased risk of death in patients with HIV.[9] The significant decrease in MCV and MCH (P<0.001) compared to HIV- patient indicates that HIV+ patients experiences microcytic hypochromic anaemia conditions.

Total leucocyte (WBC) counts of HIV+ patients were found to be significantly (P<0.001) lower (6.07±7.28) as compared with HIV- control patients (6.53±1.25). This observation is similar in to works.[4] Leucocytopenia is known to increase the incidence of opportunistic infections in HIV patients. Majority of HIV+ patients had normal Neutrophil values 83(55.7%) resulting in a mean of 54.42±13.29 which is within the normal (37-92) %. However, 12(8.1%), were neutropenia confirming study by Attili[10] who observed 22.7% neutropenia in HIV+ patients. Leiderman[11] related the decrease in neutrophil count to soluble inhibitory substances produced by HIV infected cells noted to suppress neutrophils production in vitro whilst Wickramashinge[12] related the decrease to decreased colony growth of the progenitor cells which leads to decreased production of both granulocytes and monocytes by the infected cells known to suppress neutrophil production. Neutropenia makes HIV/AIDS patients susceptible to bacterial infections like tuberculosis. Both HIV+ patients and HIV- control patients had high Lymphocyte count 92(61.7%) and 38(76%) respectively resulting in no significant difference between the two groups (P=0.085).

Mean platelet count of HIV+ patients (238.71±87.85) was insignificantly (*P*=0.111) higher than HIV- patients (207.56±119.50) since majority of HIV+ patients had normal platelet count 134(89.9%) confirming previous works.[10,13] However, thrombocytopenia is known to complicate HIV infection has observed.[7] According to Sullivan[14] thrombocytopenia may be as a result of increased platelets destruction or decreased platelet production in subjects not on antiretroviral treatment (ART). This may tend to affect the normal haemostasis such that the individual become predisposed to bleeding tendency. In this study all test subjects were on ART and this may be responsible for the normal platelet count observed.

The CD4 count of HIV+ subjects showed significant (P<0.001) decrease with a mean of (504.15±383.09) as compared to control subjects (1234.98±406.01) resulting in 91(61.1%) with CD4 counts <500 cells/µL made up with 16(17.5%) having CD4 counts <200 cells/µL. CD4 Count is the most commonly used marker to determine HIV progression. It helps to obtain information on immune responses and staging of HIV disease, risk of mother to child transmission, and use of and response to antiretroviral treatment.[6] According to WHO[15] guidelines, preventive therapy should be started when an HIV+ person who has no symptoms registers a CD4 count under 200 cells per cubic millimeter of blood.

The mean Erythrocyte sedimentation rate (ESR) of HIV+ patients was significantly (*P*>0.001) higher (55.79±46.67) compared with HIV- control patients (3.68±2.90) due to decreased erythrocyte count (anaemia) and haematocrit such that 91(65.8%) had high ESR values agreeing with the work.[4,16] In a study ESR determination in HIV infected patients was found to be a predictor of the development of AIDS and that ESR is important when coupled with a CD4 count of <500cells/µL and an elevated b2-microglobulin in predicting the progressing to AIDS.[17]

CONCLUSION

HIV infected patients are affected by several haematological changes affecting both RBC and WBC indices resulting in anaemia, leucocytopenia and high ESR leading to reduction in energy, predisposition to infections and inflammation even in patients under HAART. Thus holistic treatment of HIV+ patients should include supplements to monitor and improve these indices.

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