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Iron-Related Parameters of HIV-Infected Patients Attending University of Calabar Teaching Hospital, Nigeria

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Abstract : *This study was carried out at University of Calabar Teaching Hospital Calabar, Nigeria. It assessed iron-related parameters 69 human immunodeficiency virus (HIV)-infected patients aged 9-65 years and 55 age-matched HIV sero-negative apparently healthy individuals. Immunochromatographic method was employed for HIV screening. The CD_4 cell count and full blood count were carried out by automation (Cyflow SL3 and Sysmex respectively). Serum iron (SI) and total iron binding capacity (TIBC) were determined colorimetrically with test kits from TECO Diagnostics, USA, while percentage transferrin saturation with iron was derived by calculation. Serum ferritin (SF) and soluble transferrin receptor (sTfR) were analyzed using enzyme linked immunosorbent assay technique. The mean values of red blood cells (RBC), Haemoglobin (Hb), Haematocrit (Hct), TIBC and CD_4 count of the HIV sero-positive patients were significantly lower ($P<0.05$) while mean cell volume (MCV), platelet (PLT), lymphocyte (LYM), %TS and SF were significantly higher ($P<0.05$) than the values for the control subjects. The mean red blood cell count and serum ferritin values of HIV-positives who were not on anti-retroviral therapy (ART) was significantly higher ($P<0.05$) than those of HIV positives on ART. There was gradual reduction in serum iron and percentage transferrin saturation with iron ($P<0.05$) as the years of ART increased.*

Keywords: *Human immunodeficiency virus, iron, serum ferritin*

I. Introduction

Haematologic abnormalities have been reported to be among the most common complications of human immunodeficiency virus (HIV) infection. These abnormalities involve all lineages of blood cells [1]. Beyond this observation, the assessment of iron-related parameters has become imperative considering the role of iron in effective erythropoiesis. Already, an observation of anaemic tendency among infected subjects has been made. This complication reportedly worsens with disease progression [2][3], giving room to the hypothetical suggestion that HIV infection may be associated with ineffective erythropoiesis.

Presently, CD_4 count is the most commonly used marker to determine HIV progression despite attempts at providing substitutes [4]. The utility of CD_4 count include assessment of immune responses and stages of HIV disease as well as risk of mother to child transmission. More basically though, it often determines the therapeutic approach in the management of HIV infection [5][6]. However, with the finding of progressive anaemia as a morbidity indicator in HIV/AIDS, efforts at providing suitable routine biomarkers that will clarify the nature of anaemia in HIV infection have become necessary particularly for countries struggling with inadequate funding of health intervention programmes.

II. Methods

This research work was carried out in University of Calabar Teaching Hospital Calabar, Nigeria. All participants were within the age of 9 and 65 years comprising 69 male and female patients serologically diagnosed for HIV infection at the center and 55 apparently healthy individuals who were non-reactive to HIV serologic kits. The HIV patients consisted of 29 infected subjects yet to be placed on ART, while the remaining 40 were already on ART with treatment duration ranging up to 12 years. Ethical approval for the research was obtained from the University of Calabar Teaching Hospital Medical Ethical Committee, while informed consent was given by each participant. Eight milliliters of venous blood was collected aseptically from each subject out of which 4mls was dispensed into a plain tube for serum harvesting and the remaining 4mls dispensed into dipotassium ethylene diamine tetra-acetic acid (EDTA K_2) bottle for CD4 T-cell count and haematologic parameters. The haematologic parameters were haematocrit (Hct), haemoglobin concentration (Hb), mean cell volume (MCV), mean cell haemoglobin (MCH), mean cell haemoglobin concentration (MCHC), red blood cell (RBC) count, white blood cell (WBC) count, lymphocyte (LYM) count, neutrophil (NEUT) count, mixed cell (MxD and platelet (PLT) counts.

Immunochromatographic method was employed for HIV screening using Determine HIV 1/2 (Alere Medical Company Ltd, Matsudoshi, Japan, Lot No: 42532k100) and Chembio HIV 1/2 (Stat-Pak Assay. L ot

No: 1106151A). The CD_4T-cell count was conducted using Partec cyflow cytometer, while full blood count was carried out using Sysmex KX-21N from Sysmex Corporation, Japan. Serum iron (SI) and total iron binding capacity (TIBC) were determined colorimetrically with test kits from TECO diagnostics, USA. Percentage transferrin saturation with iron was derived by dividing the serum iron concentration by the TIBC value and multiplying by 100 (expressing as percentage). Serum ferritin (SF) and soluble transferrin receptor (sTfR) were analyzed using enzyme linked immunosorbent assay test kits from Human, Germany and Biovendor research and Diagnostic, USA respectively. SPSS 19.0 was used for the statistical analyses of data. Pearson's correlation coefficient (r) was used to express relationship between two variables. A two tailed P-value of <0.05 was considered indicative of a statistically significant difference.

III. Results

The mean values of haematologic and iron-related parameters measured in this study are presented in Table 1. The mean values of RBC, Hb, Hct, TIBC and CD_4 count of the HIV sero-positive patients were significantly lower (P<0.05) while MCV, lymphocytes, PLT, %TS, SF and were significantly higher (P<0.05) compared to control subjects.

The mean red blood cell count and serum ferritin value of HIV-positives who were not on ART was significantly higher (P<0.05) than those of HIV positives on ART (Table 2). Table 3 shows the results of HIV positive subjects on ART based on their duration of treatment. There was no statistically significant difference in all the parameters measured (P>0.05) except for serum iron and percentage transferrin saturation with iron. There was gradual reduction in serum iron and percentage transferrin saturation with iron (P<0.05) as the years of ART treatment increased.

IV. Figures And Tables

Table 1Haematologic, iron related parameters and CD_4 count of HIV negative and HIV positive subjects

Parameters	HIV Negative(55)	HIV Positive(69)	p-value
WBC (x 10^9/1)	5.26±0.14*	5.28±0.53	P>0.05
RBC (x 10^{12}/1)	4.78±0.07	3.96±0.08	P=0.01
Hb (g/dl)	14.29± 0.22	11.62±0.23	P=0.01
Hct (%)	42.17±0.65	36.82±0.64	P=0.01
MCV (fl)	87.97 ± 0.89	93.83±1.80	P=0.01
MCH (Pg)	28.34±0.36	31.11±3.17	P>0.05
MCHC (g/dl)	33.60±0.28	39.13±5.58	P>0.05
PLT (x10^9/l)	217.71±6.24	245.09±10.32	P=0.03
CD4 (cells/ml)	817.92±30.77	306.66±24.42	P=0.001
SI(µg/dl)	101.74±3.45	109.34±4.91	P>0.05
TIBC (µg/dl)	294.78±7.03	227.77±6.72	P=0.01
%TS	34.62±1.23	49.00±2.11	P=0.01
SF (ng/ml)	89.33±7.34	269.38± 38.09	P=0.001
sTfR (µg/ml)	1.55±0.16	1.75±0.23	P>0.05
LYM (x 10^9/l)	2.26±0.10	2.50±0.30	P=0.04
MxD (x10^9/l)	0.60±0.03	0.50±0.10	P>0.05
NEUT (x10^9/l)	2.40±0.10	2.50±0.20	P>0.05

*Values are given as mean ± standard error of mean

Table 2Haematologic, iron related parameters and CD_4 count of HIV positives on ART and HIV positives not on ART

Parameters	HIV positives on ART (40)	HIV positives not on ART(29)	p-value
WBC (X10^9/l)	4.65±0.26*	6.14±1.19	P>0.05
RBC (X10^{12}/l)	3.82±0.09	4.17±0.13	P=0.03
Hb (gldl)	11.59±0.29	11.67±0.39	P>0.05
Hct (%)	36.98±0.70	36.62±1.20	P>0.05
MCV (fl)	95.37±2.88	91.71±1.60	P>0.05
MCH (pg)	30.86±0.86	36.21±7.48	P>0.05
MCHC (gldl)	38.09±6.80	40.55±9.52	P>0.05
PLT (X10^{91}l)	239.18±13.03	253.24±16.91	P>0.05
CD_4 (ce11s/ml)	281.20±25.70	341.79±25.85	P>0.05
SI (µg/dl)	115.13±6.24	101.14±7.76	P>0.05
TIBC (µg/dl)	235.58±8.66	217.00±10.48	P>0.05
TS (%)	50.10±2.69	47.48±3.40	P>0.05
SF (ng/ml)	106.64±22.14	493.84±65.86	P=0.001
sTfR (ng/ml)	1.85±0.30	1.60±0.38	P>0.05
LYM (X10^9/l)	2.47±0.40	2.54±0.70	P>0.05
MxD (X10^9/l)	0.45±0.10	0.65±0.10	P>0.05
NEUT (X10^9/l)	2.09±0.10	2.97±0.50	P>0.05

*Values are given as X mean ± standard error of mean.

Table 3Haematologic, iron related parameters and CD_4 count of HIV positives ART classified based on duration of treatment

Parameters	0-3yrs(15)	3-6yrs(15)	6-9yrs(7)	9-12yrs(3)	P-value
WBC (x 10^{12}/l)	4.29±0.43*	4.87±0.48	4.54±0.37	5.53±1.16	p>0.05
RBC (x 10^{12}/l)	3.90±0.14	3.82±0.17	3.67±0.17	3.77±0.11	p>0.05
Hb (g/dl)	12.03±0.42	11.35±0.61	11.40±0.48	10.98±0.23	p>0.05
Hct (%)	38.19±1.09	36.52±1.42	36.21±0.96	35.00±0.67	p>0.05
MCV (fl)	91.88±6.25	97.21±3.91	99.99±4.97	92.93±3.94	p>0.05
MCH (pg)	31.24±1.31	30.43±1.71	31.70±2.17	29.13±1.09	p>0.05
MCHC (g/dl)	31.45±0.48	49.17±18.14	31.49±0.78	31.33±0.28	p>0.05
PLT (x10^9/l)	234.20±18.18	262.87±22.96	217.57±34.40	196.00±54.01	p>0.05
SI(µg/dl)	128.27±8.14[a]	117.67±10.85[b]	103.71±15.13[c]	63.33±11.87[d]	P=0.05
TIBC (µg/dl)	220.33±9.93	253.80±16.36	236.71±26.13	218.00±18.23	p>0.05
%TS	58.87±3.51[a]	46.67±4.08[b]	47.14±7.60[c]	30.33±7.06[d]	P=0.03
SF (ng/ml)	133.65±49.97	95.32±26.41	77.83±36.45	95.37±55.75	p>0.05
sTfR (µg/ml)	1.01±0.16	1.97±0.59	3.00±0.83	2.83±2.36	p>0.05
CD4 (cells/ml)	223.46±35.10	274.93±42.48	366.29±54.61	402.67±142.68	p>0.05
LYM (x 10^9/l)	2.16±0.23	2.95±0.96	2.28±0.22	2.06±0.64	p>0.05
MxD (x10^9/l)	0.29±0.11	0.67±0.16	0.22±0.14	0.66±0.16	p>0.05
NEUT (x10^9/l)	1.85±0.19	2.21±0.19	2.04±0.19	2.81±0.67	p>0.05

*****Values are given as mean ± standard error of mean
a, b, c, & d = significant variations at P<0.05

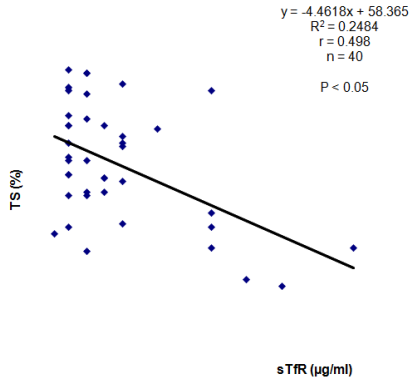

Figure 1: Correlation between sTfR and TS of those on ART

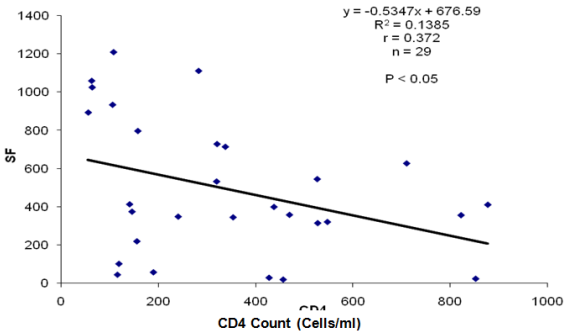

Figure 2 : Correlation between CD4 Count and SF of those not on ART

V. Discussion And Conclusion

General observation of data indicated that HIV-positive patients had significantly (P<0.05) lower RBC, Hb, Hct, TIBC and CD4 count compared with control subjects. The MCV, PLT, %TS, SF and LYM values were significantly (P<0.05) higher in these patients when compared to control subjects. This finding has confirmed anaemic trend among infected persons as observed in previous studies [2][3], and the most commonly used marker to determine HIV progression; CD_4 count, was again significantly (P<0.05) lower than that of control subjects. Total iron binding capacity was interestingly reduced despite the obvious need for more iron to be incorporated. This is consistent with anaemia of chronic infections/diseases where iron is sequestered as a protective host response.

The mean concentration of serum ferritin of HIV positive patients was three times higher with a decrease in TIBC level when compared with control subjects. These findings with reference to previous studies

may be attributed to the inhibitory role that ferritin reportedly plays in T-cell proliferation and functions [7]. Ferritin level increased with disease progression, suggesting its involvement in the cell-mediated immunodeficiency observed in AIDs [8].

There was gradual resolution of both SI and %TS levels, while sTfR: SF ratio also progressively returned to normal from an initial high value as duration of treatment increased. On the other hand, the CD4 count noticeably built up within this period. Apparently the sTfR: SF ratio may serve as a good indicator of response to therapy as has been suggested by other researchers [9][10]. The significant ($P<0.05$) variations in TIBC, %TS and SF observed in HIV infected subjects may be indications of derangement in iron metabolism resulting from iron sequestration in phagocytic cells induced by release of cytokines. It is therefore plausible to suggest that iron supplementation in response to anaemia should be avoided in HIV infection except where iron status confirms depletion of iron stores. Other nutritional interventions such as antioxidant supplementation could be explored as adjuvant to antiretroviral therapy.

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