African Journal of Laboratory Haematology and Transfusion Science

Volume 1, Issue 2&3: page 173-179 | 2022. ARTICLE ID: 2022-AJLHTS-0017
www.hbtssn.org/ajlhts ISSN (Print):2814-0591; (Online): 2814-0605

ORIGINAL ARTICLE

Selected Inflammatory and Thrombotic Indicators Among Persons Living With HIV Infection In Southern Nigeria

Abunimye Dennis A[1] *Akwiwu Euphoria C[1] Anyanwu Stanley O[2] Onukak Eme E[1] Akpotuzor Josephine O[1]

[1]Department of Haematology and Blood Transfusion Science, University of Calabar, Calabar.
[2]Department of Histopathology and Cytology, University of Calabar, Calabar.

Corresponding Author
Dr Euphoria C. Akwiwu
Department of Haematology and Blood Transfusion Science, University of Calabar, Calabar Nigeria

Email:
ecakwiwu@gmail.com

Received: May 01, 2022
Accepted: August 26, 2022
Published: September 30, 2022

Abstract

Introduction: Although viremia has been greatly addressed in the management of human immunodeficiency virus (HIV) infection by the advancement in antiretroviral therapy, not all HIV-associated morbidities have been resolved. Observations of increased cardiovascular risk in relation to antiretroviral therapy have been reported. Full blood count continues to be useful in disease management, and efforts are directed towards optimising its utility in medical practice. Derivatives of blood cell counts have in recent times proved to be informative with regards to the inflammatory-thrombotic cycle. The utility of these derived parameters in HIV within the study locality is worth exploring.

Methods: This single-site study was carried out at University of Calabar Teaching Hospital in Calabar, Cross River State of Nigeria. White blood cell and platelet counts were carried out by automation, while blood cell ratios were calculated. Statistical analysis of data was done using SPSS 22.0. A p-value of ≤ 0.05 was considered to infer a statistically significant difference.

Results: Significant reductions of white blood cell parameters were recorded in HIV, particularly among infected persons on antiretroviral therapy. Platelet count and plateletcrit were significantly lower, while mean platelet volume and platelet distribution width were higher in newly diagnosed persons compared to HIV-infected subjects on therapy and control subjects. Platelet-to-lymphocyte ratio was significantly higher among subjects on therapy compared to the rest of the groups.

Conclusion: Increase in platelet count following antiretroviral therapy could be posing a risk of platelet-driven morbidities as typified in the observed elevated thrombotic marker.

Key words: HIV, immunity, antiretroviral therapy, thrombosis

Introduction

The management of human immunodeficiency virus (HIV) infection has undergone tremendous reviews since the discovery of this medical condition. Quite early in the wake of identifying this disease entity, studies into its pathogenicity and pathophysiology brought to light the basic knowledge of its immune-related nature (1,2,3). At the forefront of the disease mechanism is the debilitating interference with host immunity. Hence the emergence of the CD4 cell count as a biomarker for prognosis and disease monitoring served as a major breakthrough in the management of HIV infection (4,5,6). Since then, other sensitive indicators of morbidity and overall survival such as viral load and anaemic indices have been integrated into the protocol for effective HIV management (7,8,9). Interestingly, with the advancement in HIV chemotherapy, not all HIV -associated morbidities have been addressed. It would appear that certain complications are being observed to be prevalent among infected persons on antiretroviral therapy (10,11,12,13). One such aspect of deep concern is that of HIV-associated cardiovascular involvement. Observations of increased cardiovascular risk in relation to antiretroviral therapy have been made by previous studies. More interesting is the identification of components of the full blood count, such as variations in blood cell size, as markers in this emerging field of concern(14).

The full blood count has continued to be useful in disease management, and efforts are directed towards optimising the utility in medical practice. This is particularly in recognition of increasing burden of healthcare cost. Thus, derivable parameters that are at no additional cost to patients are gaining advocacy especially if such parameters are observed to be significantly deranged in disease states. Derivatives of blood cell counts have in recent times proved to be informative with regards to the inflammatory-thrombotic cycle (15,16). The neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio, in particular, are suggestively better morbidity indicators compared to the individual parameters both in health and disease conditions (17,18). The utility of these derived parameters in HIV within the study locality is yet to be explored hence the present study.

Materials and methods

The present study was carried out among a total of 90 subjects at the University of Calabar Teaching Hospital at Calabar, Nigeria. Purposive sampling technique was used to enrol 30 participants each for the categories of newly diagnosed, subjects on HAART and control subjects. The subjects were between 25 and 45 years of age. Ethical approval was sought and duly obtained from the University of Calabar Teaching Hospital Health Research Ethics Committee, while informed consent was obtained from each participant.

Blood sample was appropriately obtained from each subject for white cell and platelet automated estimations using Mindray BC-5000

Haematology Analyzer (Mindray Medical International Limited, China). This equipment was controlled and calibrated according to manufacturer's instructions to ensure its fitness for use. Blood cell ratios were mathematically derived. Data generated were entered into Microsoft excel spreadsheet and analysed using Statistical Package for Social Sciences (SPSS) software version 22.0. Frequencies and one-way analysis of variance were used for analysis of data. The least significant difference (LSD) Post Hoc Test accompanied the ANOVA for interpretation of significant variance. Statistical significance was drawn at a $p \leq 0.05$.

Results

This research on selected inflammatory and thrombotic indicators among persons living with HIV infection in Southern Nigeria was carried out at the University of Calabar Teaching Hospital, Calabar. A total of 90 male and female subjects were enrolled in the study. In terms of HIV status of the participants, those on HAART were made up of 33.3%, those that were newly diagnosed were 33.3%, while sero-negative control subjects were also 33.3%.

The total white blood cell count (WBC) and absolute monocyte count varied significantly across the groups. Absolute neutrophil and lymphocyte counts were observed to be significantly lower in HIV subjects on HAART compared to newly diagnosed and control subjects (Table 1).

Among the platelet parameters, platelet count and plateletcrit were significantly lower among the newly diagnosed group compared to the other groups, while mean platelet volume and platelet distribution width were observed to be higher in newly diagnosed compared to HIV subjects on HAART and control subjects (Table 2). In addition, platelet-to-lymphocyte ratio was significantly higher among subjects on HAART compared to the rest of the groups as shown on Table 3.

Discussion

This study observed lower total and differential white blood cell counts in HIV, particularly among infected persons on antiretroviral therapy. Cytopenia in relation to HIV infection has been among the major haematological derangements observed in its management. This is thought to be driven by the mechanism of haemato-suppression, thus suggesting the possibility of reversal where viral load is sufficiently reduced (19,20,21,22,23). To this end, effective administration of antiretroviral therapy is expected to ameliorate HIV-associated cytopenia in addition to arresting viral replication and immune deficiency. However, there appears to be conflicting reports regarding values of peripheral white blood cell lineages following antiretroviral therapy. Decline in total white blood cell count together with the granulocyte and lymphocyte sub-populations following administration of antiretroviral therapy have also been reported by previous studies (24,25).

The present study also recorded lower platelet count and plateletcrit alongside higher mean platelet volume and platelet distribution width in the newly diagnosed HIV subjects. The risk of thrombocytopenia has been linked to the HIV pathophysiology. Possible mechanisms for its occurrence include increasing viremia, immune response to viral invasion, disease progression and adverse effect from certain antiretroviral agents (26). There are reports of HIV-associated thrombocytopenia with a predominance of the mild form across the African region. Findings of these studies reveal a pattern of improved platelet count following antiretroviral therapy (27,28, 29). In addition, lower platelet count and higher platelet distribution width have been reported in Calabar, Nigeria (30). The study observed that although the finding of lower platelet count could arise from insufficient production as well as increased consumption,

the finding of higher platelet distribution width value suggested the later. Platelet distribution width represents the variability in platelet size and is thought to be an important marker of platelet activation (31).

In the light of the foregoing, increase in platelet count following antiretroviral therapy without a check in platelet activation may be inimical to the management of HIV infection in the long run. Interestingly, as advancement in antiretroviral therapy continues to receive endorsement, there are also reports of associated cardiovascular disease risk (32,33,34). Several studies have linked both the infection and antiretroviral therapy with increased risk of platelet-driven cardiovascular events, particularly myocardial infarction (35, 36, 10, 12). Thus, the finding of raised platelet-to-lymphocyte ratio among subjects on antiretroviral therapy in the present study quite significant and informative as it reveals the utility of this parameter in determining the risk of cardiovascular complication. In conclusion, improvement of platelet count by antiretroviral therapy could be posing a risk of platelet-driven morbidities as typified in the observed elevated thrombotic marker.

Conflict of Interest: Authors declare no conflict of interest.

Table 1.White cell parameters of study participants

Parameters	Subjects on HAART (n = 30)	Subjects newly diagnosed (n = 30)	Control subjects (n = 30)	P-value
WBC (x 10^9/l)	2.36±0.76*	3.81±1.46*	4.73±1.47	0.001
Neutrophil (x10^9/l)	1.09±0.79*	1.73±1.21	2.21±1.02	0.001
Lymphocyte (x10^9/l)	1.54±0.56*	2.08±0.77	2.00±0.67	0.005
Eosinophil (x 10^9/l)	0.71±0.05	0.12±0.15	0.11±0.08	0.166
Monocyte (x10^9/l)	0.24±0.13*	0.30±0.20*	0.40±0.32	0.022

Key: **HAART** = Highly active antiretroviral therapy, **WBC** = White blood cell.
*Significantly different from other groups

Table 2.Platelet parameters of study participants

Parameters	Subjects on HAART (n = 30)	Subjects newly diagnosed (n = 30)	Control subjects (n = 30)	P-value
PLT (x 10^9/l)	194.70±57.26	176.87±63.38*	218.67±50.71	0.022
MPV (fl)	9.57±1.23	10.35±1.45*	9.55±1.12	0.027
PDW (%)	15.64±0.51	16.11±0.57*	15.70±0.94	0.023
PCT (%)	2.01±0.60	1.62±0.63*	1.98±0.55	0.024

Key: **HAART** = Highly active antiretroviral therapy, **PLT** = Platelet count, **MPV** = Mean platelet volume, **PDW** = Platelet distribution width, **PCT** = Plateletcrit.
*Significantly different from other groups

Table 3.Blood cell ratios of study participants

Parameters	Subjects on HAART (n = 30)	Subjects newly diagnosed (n = 30)	Control subjects (n = 30)	P-value
NLR	0.85±1.04	0.88±0.63	1.17±0.79	0.212
PLR	149.30±85.50*	98.78±57.86	117.91±41.65	0.011

Key: **HAART** = Highly active antiretroviral therapy, **NLR** = neutrophil-to-lymphocyte ratio, **PLR** = platelet-to-lymphocyte ratio Neutrophil.
*Significantly different from other groups

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