P53 PROTEIN LEVEL AND EVIDENCE OF ONGOING COAGULATION AMONG HIV-INFECTED PERSONS ACCESSING TREATMENT AT UNIVERSITY OF CALABAR TEACHING HOSPITAL NIGERIA

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Research note

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Abstract

Objective The human immunodeficiency virus (HIV) infection has been associated with hemostatic disturbance. In Nigeria, particularly Calabar, not much is known about the nature of these derangement among infected subjects. This study was carried out with a view to assessing tumour suppressing activity and ongoing coagulation among HIV-infected subjects. The data presented is a side product of investigation on morbidity indicators among persons living with HIV infection in Calabar, Nigeria. **Result** The CD4 cell count and P53 protein level reduced while D-dimer level increased in HIV infection. Platelet count also reduced while platelet distribution width increased with the condition. While CD4 cell count improved with Highly Active Antiretroviral Therapy administration, D-dimer level, mean platelet volume and platelet distribution width reduced. This study observed reduced tumour suppression and increased coagulation activities alongside immunosuppression in HIV infection. **Keywords:** Coagulation, HIV infection, immunosuppression.

Introduction

Early intervention in the management of HIV infection is a challenge in resource-poor settings often due to late presentation to hospitals and inadequate screening of the populace [1,2,3]. Among the infected persons in our local population, widespread derangement in biomarkers and morbidity indicators that mirror poor health status prevail [4,5]. Coagulation disturbances and cancer have been identified as factors for increased mortality among people living with HIV infection. Impaired immunity and the development of these other morbidities are thought to reflect an unending cycle that eventually progresses HIV infection to AIDS [6, 7, 8, 9,10]. In Nigeria, particularly Calabar, not much is known about the nature of the hemostatic disturbance seen in HIV infection. There is also paucity of information on levels of cancer biomarkers among infected subjects. This study was carried out with a view to assessing tumour suppressing activity and ongoing coagulation among HIV-infected subjects.

The data presented is part of a research on morbidity indicators among persons living with HIV infection attending clinics at University of Calabar Teaching Hospital, Calabar Nigeria.

Methods

Ninety persons living with HIV infection who were attending clinics at University of Calabar Teaching Hospital were enrolled with ninety age and sex-matched HIV sero-negative individuals who served as control subjects. The enrollment of persons living with HIV infection took into consideration certain sub-groups on the basis of commencement of highly active antiretroviral therapy (HAART). Thirty persons were newly diagnosed and were yet to embark on HAART. The remaining 60 were already undergoing treatment. Blood specimen was collected from each participant for analyses of CD4 cell and full blood counts by automation, serum was used for the assays of P53 protein and D-dimer levels using enzyme-linked immunosorbent assay test kits. Data analysis was done using SPSS version 22.0. Student t-test was used to compare means between test and control subjects. One-way analysis of variance was used

to compare means across the HAART-naïve and two other groups on different HAART protocols. Pearson's correlation was used to analyze relationships. Statistical significance was drawn at a $p \leq 0.05$.

Results

Persons living with HIV infection who participated in this study were adults from eighteen years and above. The age group with the highest number of participants was 36-45years which featured 34.4% (31 out of 90) of all the persons. This was followed by age group 26-35years which had 31.1% (28 out of 90) of the subjects. The least number of participants, 7.8% (7 out of 90) came from the group above 55years of age. More females 63.3% (57 out of 90) than males 36.7% (33 out of 90) were observed accessing medical care at the study center. In addition, more than half of these persons were married 60% (54 out of 90) at the time of the study. A third of the persons living with HIV infection were enrolled from those newly diagnosed. The remaining 60 were already undergoing treatment. Two HAART protocols were observed among subjects who were being treated; Tenofovir+Lamivudine+Efavirenz (TLE) and Lamivudine+Zidovudine+Nevirapine (LZN). Subjects on TLE were 48.3% (29 out of 60), while those on LZN were 51.7% (31 out of 60) (Table 1 in the Supplementary Files).

The CD4 cell count and P53 protein level were found to be reduced while D-dimer level increased in HIV infection. The platelet parameters considered in this study were platelet count, mean platelet volume (MPV) and platelet distribution width (PDW). Platelet count was observed to be reduced while platelet distribution width (PDW) increased with the condition (Table 2 in the Supplementary Files).

Subjects on highly active antiretroviral therapy (HAART) were either taking Tenofovir+Lamivudine+Efavirenz (TLE) or Lamivudine+Zidovudine+Nevirapine (LZN). Both drug combinations impacted similarly on the measured parameters. While CD4 cell count improved with HAART administration, D-dimer level, mean platelet volume (MPV) and PDW reduced (Table 3 in the Supplementary Files).

Discussion

Although HIV infection affects all ages, the current study enrolled persons from eighteen years of age and above mainly for the ease of obtaining consent. The age group with the highest number of participants was 36-45years which featured 34.4% persons. This was followed closely by age group 26-35years which had 31.1% subjects. Altogether, the age group between 26-45 years constituted 65.5%. This frequency pattern for age, combined with that for gender (63.3% female participation) as well as that for marital status (60% of married persons) reveals a significant pattern. It implies that among adults living with HIV infection, women of child-bearing age constitute the highest group receiving medical attention for HIV infection. This trend has implications for the control of HIV infection in this locality as the risk of mother to child transmission could be better managed within conventional health facilities.

This study observed alongside a lower value of CD4 cell count, reduced serum p53 protein level. In the progression of HIV infection to AIDS, both decline in immunity and the development of cancer are considered important morbidity and mortality factors [6,8,9,10,11]. In resource-poor settings, cancer screening among HIV-infected persons is yet to commence despite the need to monitor this aspect of health for infected persons [12]. The p53 gene and its protein play a significant role in the immunosuppression of cancer and is also known to mediate against the replication of the human immunodeficiency virus, thus serving as a host-restriction factor. It is therefore thought that the silencing of the p53 pathway promotes both viral replication and disease progression in HIV infection [13,14]. The two HAART protocols in use at the health facility were observed to improve the CD4 cell count but showed no significant variation for the serum p53 protein. There may be need to go beyond this stage of treatment if tumour immunosuppression is to be addressed. This could impact on disease progression from HIV infection to AIDS in Africa.

In addition to the reduced serum p53 protein, the studied population showed evidence of activated coagulation as observed in the lower platelet count but higher PDW and D-Dimer values. Although the finding of lower platelet count could arise from insufficient production as well as increased consumption, the observation of higher PDW value suggests the latter. The PDW represents the variability in platelet size and is thought to be an important marker of platelet activation [7, 15,16,17,18,19] More importantly, D-dimer is the degradation product of fibrinogen and fibrin during fibrinolysis. Although there are various fibrin-degradation products that result from plasmin-mediated breakdown, D-dimers is considered a specific marker for fibrinolysis in that only fragments originating from fibrin polymers that had undergone factor XIII mediated cross-linking retain an intact covalent bond between two adjacent D domains; hence the term D-dimers. It therefore reflects ongoing activation of the hemostatic system and more specifically represent breakdown products of cross-linked fibrin clot formation [20,21,22]. The D-dimer, MPV and PDW varied across the HAART groups in relation to the HAART-Naïve group. The drugs impacted positively on the coagulation parameters studied, thus suggesting a better hemostatic state among persons living with HIV infection who are on HAART compared to those yet to commence HAART.

Limitations

The study could not adopt a follow up approach in assessing the impact of therapy on the measured parameters.

List Of Abbreviations

AIDS	Acquired immunodeficiency syndrome
ANOVA	Analysis of variance
CD4	Cluster of differentiation
HAART	Highly active antiretroviral therapy

HIV	Human immunodeficiency virus
LZN	Lamivudine+Zidovudine+Nevirapine
MPV	Mean platelet volume
PDW	Platelet distribution width (PDW)
TLE	Tenofovir+Lamivudine+Efavirenz

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from University of Calabar Teaching Hospital Health Research Ethics Committee (UCTH/HREC/33/553), while written informed consent was obtained from each participant.

Consent for publication

Not applicable

Availability of data and materials

The authors do not wish to share their data because some aspects of the research are yet to be completed.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

E.C.A., A.O.O. and J.O.A. conceptualized and designed the research. E.C.A. wrote the original draft of the paper. E.C.A. and A.O. O. were responsible for sample collection/ analyses and data analyses. J.O.A. reviewed and edited the paper. All authors have read and approved the manuscript for submission.

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Tables

Due to technical limitations, tables are only available as a download in the supplemental files section.

Supplementary Files

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- [Table1.jpg](#)
- [Table3.jpg](#)
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