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Effect of HIV Infection and Antiretroviral Therapy on Some Red Cell Enzyme Activities and Coagulation Parameters

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Authors' contributions

This work was carried out in collaboration between all authors. Authors GIA and COO designed the study, wrote the protocol, managed the literature review and wrote the first draft of the manuscript. Author MOI managed the statistical analysis and computations. Author COO managed the analysis of the study, while authors ACO, SIO and JOO performed manuscript revision. The authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Aim: To assess G-6-PD, Pyruvate kinase enzyme activity and some coagulation parameters in HIV positive patients on antiretroviral treatment (ART) and those not on antiretroviral treatments with varying durations of infection and Antiretroviral treatments.
Study Design: Case-control study
Place and Duration of Study: Nnamdi Azikiwe University Teaching Hospital Nnewi, Nigeria from March to August 2013.
Methodology: We included 181 subjects; Sixty HIV patients on ART with infection and ART duration of <1 – 5, >5 – 8 and >8 – 17 years; Sixty HIV patients not on ART with an infection duration of <1 – 3, >3 – 6 and >6 – 11 years; and Sixty-one apparently healthy individuals control. Glucose-6-Phosphate Dehydrogenase (G-6-PD) activity, Pyruvate kinase (PK) activity, Activated Partial Thromboplastin time (APTT), Prothrombin time

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(PT), Platelet count (PLT)and Human Immunodeficiency virus (HIV) status were determined.
Results: G-6-PD, APTT and PT, for ART and non-ART were significantly higher (P< 0.05) compared with those of control. G-6-PD and PT were significantly higher in ART subjects when compared with non-ART (P<0.05). There was no significant difference in Pyruvate kinase activity and platelet count (P>0.05). G-6-PD activity was significantly higher in ART subjects with HIV duration of >8 – 17 years than<1 – 5 years and >5 – 8 years (P< 0.05), and also in non-ART subjects with HIV duration of>3 -6 years and>6 – 11 years compared with<1 – 3 years (P< 0.05). G-6-PD activity was significantly higher in ART duration of>8 – 17 years compared to ART durations of >5 – 8 years and <1 – 5 years (P< 0.05).
Conclusion: This study identified a significant increase in G-6-PD activity in HIV patients in proportion to the duration of infection and therapy while APTT and PT were significantly prolonged in HIV patients implying a derangement in the intrinsic and extrinsic coagulation pathways.

Keywords: Pyruvate kinase; G-6-PD; HIV/AIDS; prothrombin time; activated partial thromboplastin time.

1. INTRODUCTION

Human Immunodeficiency Virus (HIV) has emerged a global disaster ever since its discovery [1]. According to National Agency for Control of AIDS (NACA), Nigeria recorded an HIV prevalence of 3.4% in 2013 [2]. HIV/AIDS continues to spread globally and remains a worldwide pandemic affecting over 40 million people [3] [4]. It is now the leading cause of death in sub-Saharan Africa and the fourth leading cause of mortality worldwide and over 95% of these deaths occurred among young adults in the developing world [5]. Highly active antiretroviral therapy (HAART) has generally been taken as the gold standard in the management of HIV patients [6]. With its introduction in 1996, HAART appears to have effectively controlled viral replication in HIV/AIDS patients and has successfully improved their quality of life and prolonged their life-expectancy [7], with a near normal turnover of both CD4 and CD8 T-cell populations [8].

Anaemia is prevalent among HIV/AIDS patients, it is said to be present in 10%-20% of patients at initial presentation and in over 70% over the course of the disease [9]. It is certain that the presence of anaemia in people living with HIV worsens the prognosis since it is associated with progression to AIDS and shortened survival times for HIV infected patients [10]. The lifespan of a normal red blood cell is 120 days, after which they are destroyed within the Reticuloendothelial System [11]. However, in haemolytic anaemia which results from increased destruction of red cells, the lifespan of red cells are shortened and the red cells survive only a few days instead of a normal lifespan of 120 days, this is usually due to either hereditary or acquired causes. One of the major causes of haemolytic anaemia is defects within red cells from dysfunction of enzyme-controlled metabolism [11].

Glucose-6-Phosphate Dehydrogenase (G-6-PD) deficiency and Pyruvate Kinase (PK) deficiency are the most common erythrocyte enzymopathies which usually results in haemolysis of red cells [12]. According to previous study [11], in practice, these two enzymopathies must be first excluded when haemolysis due to enzyme deficiency is suspected. G-6-PD is a major enzyme of the Pentose Phosphate Pathway where it catalyses

the oxidation of Glucose-6-Phosphate (G6P) with the simultaneous reduction of nicotine adenine dinucleotide phosphate (NADP) to reduced NADP (NADPH). A defect in G-6-PD enzyme activity and the resultant insufficient NADPH supply to the glutathione-antioxidant system results in haemolysis in response to oxidative drugs, infections and conditions of stress. Interestingly, HIV thrives in a highly oxidized environment and oxidative stress has been reported to be involved in HIV infection [13]. Pyruvate Kinase deficiency (PKD) is the most common erythrocyte enzymopathy involving the Embden-Meyerhof pathway of anaerobic glycolysis [14]. Pyruvate kinase catalyses the conversion of Phospho-enolpyruvate to pyruvate in the erythrocyte, that results in the production of adenosine triphosphate (ATP). Deficiency of Pyruvate kinase manifests clinically as a haemolytic anaemia, but the clinical severity varies from a mildly compensated anaemia to severe life-threatening manifestations that can require long term transfusion therapy and splenectomy in early childhood [12,15]. The enzyme activity rate in most patients who are deficient is 5 – 15% of the normal activity.

Coagulation abnormalities in HIV may be caused by inherited factor deficiencies, acquired factor deficiencies, or acquired inhibitors. Results from studies showed that HIV infection affect haematological indices of patients regardless of age, sex and Highly Active Antiretroviral Therapy (HAART). According to an earlier study [16], thrombocytopenia which is known to complicate HIV infection 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. This study, therefore, aimed at assessing G-6-PD, Pyruvate kinase enzyme activity and some coagulation parameters in HIV seropositive patients on antiretroviral treatment (ART) and those not on antiretroviral treatments with varying durations of infection and Antiretroviral treatments in comparison to the seronegative subjects (control).

2. METHODS

2.1 Study Site

This study was carried out at Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi, Anambra State, a tertiary health institution serving patients of high, middle and lower socio-economic status. It houses a major HIV/AIDS Centre (IHVN Clinic) serving patients from all parts of the state and beyond, with a registered HIV Sero-positive patient population of over 6000.

2.2 Subject Recruitment

One hundred and eighty one (181) subjects aged between 18-60 years were recruited by simple random sampling and categorized into three groups comprising; Sixty adult HIV Sero-positive subjects on antiretroviral therapy (ART) - Lamivudine, Zidovudine, Nevirapine (30 males and 30 females), Sixty adult HIV Sero-positive subjects not on antiretroviral therapy (25 males and 35 females) and Sixty-one adult Sero-negative control subjects (31 males and 30 females) respectively.

2.3 Sample Collection

Eight millilitres (8mls) of blood sample was collected aseptically from the veins by venepuncture and aliqoted as follows; Two millilitres (2mls) into a plastic bottle containing 0.22mls (220µl) of 3.2% Sodium citrate to give a final blood: citrate ratio of 9:1. The sample was mixed properly by reverse uniform inversion and centrifuged within one hour at 3000rpm for 10 minutes at room temperature. The clear plasma was separated into a clean dry plastic container and used for Prothrombin time (PT) and Activated Partial Thromboplastin time (APTT) determination. Three millilitres (3mls) was drawn into bottles containing di-potassium salt of Ethylenediamine tetra-acetic acid (K_2-EDTA) at a concentration of 1.5mg/ml of blood and used for Glucose-6-Phosphate Dehydrogenase enzyme activity assay while three millilitres (3mls) was drawn into plain sample bottles. Serum was obtained after clotting by spinning at 3000rpm for 10 minutes and used for Pyruvate kinase enzyme assay and HIV Screening. All the tests were carried out according to manufacturer's instructions.

2.4 Statistical Analyses

The data obtained was analysed using Statistical Package for Social Sciences (SPSS version 20). Data were expressed as mean ± SD. The significance of differences in mean values between groups were analysed using t-test, while significance of the differences in mean values among different groups was evaluated using one-way ANOVA. $P<.05$ was considered statistically significant.

2.5 Laboratory Methods

2.5.1 Determination of HIV status

2.5.1.1 Determine HIV 1/2 assay

The abbot Determine™ HIV ½ is an in vitro test kit, visually qualitative immune assay for the detection of antibodies to HIV-1 and HIV-2 in human serum, plasma or whole blood.

2.5.2 Principle of the test

Determine HIV ½ is an immune chromatographic test for the qualitative detection of antibodies to HIV-1 and HIV-2. Sample migrates through the conjugate pad, it reconstitutes and mixes with the selenium colloid-antigen conjugate. This mixture continues to migrate through the solid phase to the immobilized recombinant antigens and synthetic peptides in HIV-1 or HIV-2. If HIV ½ were present in the sample, the antibodies bind to the antigen-selenium colloid and to the antigen at the patient window side. Whereas if the antibodies to HIV-1 and/or HIV-2 are absent, the antigen selenium colloid flows past the patient window and no red line are formed at the patient window site. To ensure assay validity, a procedural control bar is incorporated in the assay device.

2.5.3 Chembio HIV ½ stat-pak™ assay

2.5.3.1 Principle of test

The Chembio HIV ½ STAT PAK™ assay employs a unique combination of a specific antibody-binding protein, which is conjugated to colloidal gold dye particles and HIV ½

antigens which are bound to the membrane solid phase. The sample is applied through the sample well followed by the addition of running buffer. The buffer facilitates the lateral flow of the released products and promotes the binding of antibodies to the antigens. If present, the antibodies bind to the gold conjugate antibody-binding protein. In a reactive sample, the dye-conjugate immune complex migrates through nitrocellulose membrane and is captured by the antigens immobilized in the test (T) area. The sample migrates along the membrane and produces a pink/purple colour on the control (C) area containing immunoglobulin antigens. This control serves to demonstrate that specimens and reagents have been applied properly and have migrated through the device.

2.5.4 Glucose-6-phosphate dehydrogenase (G-6-PD) enzyme assay (as described by the manufacturers of the kit; randoxlaboratories LTD UK)

2.5.4.1 Principle of test

The enzyme activity is determined by measurement of the rate of absorbance change at 340nm due to the reduction of $NADP^+$

2.5.5 Pyruvate kinase enzyme assay (as described by the manufacturers of the kit; Sigma-Aldrich Co LTD US, 2012)

2.5.5.1 Principle of test

The Pyruvate Kinase Activity assay kit which provides a simple and direct procedure for measuring Pyruvate kinase activity determines the pyruvate concentration by a coupled enzyme assay, which results in a colorimetric (570nm) product that is proportional to the pyruvate present. One unit of Pyruvate kinase is the amount of enzyme that will transfer a phosphate group from Phospho-enolpyruvate (PEP) to ADP to generate 1.0 µmole of pyruvate per minute at 25℃.

2.5.6 Prothrombin time (PT)[17]

2.5.6.1 Principle of test

In the presence of calcium ions, tissue thromboplastin initiates the extrinsic coagulation pathway by the direct activation of factor VII to VIIa. This culminates in the conversion of soluble Fibrinogen to insoluble Fibrin by the direct action of Thrombin. Reduction in the concentration of clotting factors of the extrinsic or common pathway will result in the prolongation of the PT, the degree of which is proportional to the level of concentration reduction.

2.5.7 Activated partial thromboplastin time (APTT) [18]

2.5.7.1 Principle of test

It is a measure of the combined effect of the clotting factors of the Intrinsic and common coagulation pathways. It represents the ultimate refinement in which Platelet activity is standardised by the use of platelet substitute and contact activation is standardised by pre-incubation of the plasma with the Kaolin platelet substitute mixture for a standard time before re-calcification. It will reflect deficiencies of any of the factors of the intrinsic or common

clotting pathways (factors II, V, VIII, IX, X, XI, XII and Fibrinogen) and is therefore a valuable ancillary screening test.

2.5.8 Platelet count

Platelet count was done by automation using Sysmex automated haematology analyser KX 21N model manufactured by Sysmex Corporation Kobe, Japan.

2.5.8.1 Principle of test

The aspirated blood samples is measured to a predetermined volume, diluted at the specified ratio and then fed into each transducer chamber which has a minute aperture which also contains the electrodes in which direct current flows. Blood cells suspended in the diluent sample pass through the aperture causing direct current resistance to change between the electrodes and the blood cell size is detected as electric pulses. Blood cell count is calculated by counting the pulses and the histogram determined by the pulse sizes.

3.RESULTS AND DISCUSSION

The comparison of the mean values of G-6-PD, PK, APTT, PT and PLT between male and female subjects on ART, not on ART and controls shows no significant difference (P> .05).

Table 1shows that there are a total of 181 subjects, comprising 95 female and 86 male subjects. Out of the 95 females 30 (31.6%) were on ART, 35 (36.8%) were non-ART and 30 (31.6%) were control subjects. Similarly, of the 86 males 30 (34.9%) were on ART, 25 (29.1%) were non-ART, and 31 (36%) were control subjects.

Table 2 shows that G-6-PD activity was significantly higher in both ART and non-ART group when compared with the corresponding values in the control (P< .05). Similarly, APTT were significantly higher in ART and non-ART compared with the control (P< 0.05). Moreover, Prothrombin time (PT) was also significantly higher in ART and non-ART compared with the control (P<.05). Likewise, G-6-PD was significantly higher in ART compared with non-ART (P<.05). Similarly PT in ART was significantly higher than the corresponding value in non-ART (P<.05). However, no significant difference was observed in the mean values of Pyruvate kinase (PK) and Platelets (PLT) between ART, non-ART and the control group (P>.05).

Table 3 shows that G-6-PD was significantly higher in ART duration of >8 – 17 years compared to ART durations of >5 – 8 years and <1 – 5 years(P<.05). Group comparison showed that the mean value of those with ART duration of <1 – 5 was significantly lower compared with ART duration of >8 – 17 years (P<.05) while that of >5 – 8 years was also significantly lower compared with >8 – 17 years (P<.05), but comparison of group <1 – 5 years and >5 – 8 years showed no statistical significant difference (P>.05). The mean ± SD of PK, APTT, PT and PLT for ART duration of <1 – 5 years, > 5 – 8 years and > 8 – 17 years showed no statistical significant difference (P<.05).

Table 4 shows that G-6-PD was significantly lower in ART subjects with HIV duration of <1 – 5 years and >5 – 8 years when compared with the >8 – 17 years group (P<.05). However, comparison of G-6-PD activity for subjects with duration <1 – 5 years and >5 – 8 years showed no significant difference (P>.05). Moreover, no significant difference was observed

among <1– 5 years, >5–8 years and >8–17 years duration in PK, APTT, PT and PLT (*P*> .05).

Table 5 shows that G-6-PD was significantly higher in non-ART subjects with HIV duration of >3 -6 years and>6 – 11 years compared with <1 – 3 years (*P*<.05) while the mean values of PLT was significantly higher in <1 – 3 years duration than >6 - 11 years duration (*P*<.05). However, no difference was observed in the mean values of PK, APTT and PT among <1 – 3 years, >3 – 6 years and >6 – 11 years respectively (*P*> .05).

Table 1. Sex demographic characteristics of the HIV seropositive on ART, not on ART and HIVnegative control subjects

Group	Females		Males		Total number
	Number	Frequency (%)	Number	Frequency(%)	
ART	30	31.6	30	34.9	60
Non-ART	35	36.8	25	29.1	60
Control	30	31.6	31	36	61
Total	95	100	86	100	181

Table 2. Mean ± SD of red cell enzymes and coagulation parameters compared among HIV seropositive on ART, not on ART and HIV negative control subjects

Groups	G-6PD(mU/10^9 RBC)	PK (mU/ml)	APTT(Sec)	PT(Sec)	PLT(X 10^9/L)
(A) ART(n=60)	430.28±396.95	38.80±16.55	42.37±2.60	19.45±2.29	271±143
(B) Non-ART(n=60)	282.63±181.47	41.13±13.20	41.15±3.68	18.22±1.76	284±116
(C) Control(n=61)	82.90±61.47	44.20±15.90	37.07±2.00	16.54±1.77	246±140
F (P) Values	28.57(.00*)	1.90 (.15)	57.98(.00*)	33.88(.00*)	1.22 (.30)
A vs. BP values	.03*	.67	.10	.00*	.85
A vs. CP-values	.00*	.17	.00*	.00*	.61
B vs. CP-values	.00*	.48	.00*	.00*	.25

**Significant at P < .05Key:F (P) value = Mean ± SD of parameters compared among HIV seropositive on ART, not on ART and HIV negative control subjects using ANOVA.A vs. B: (P) value = Mean ± SD of parameters compared between HIV seropositive on ART and not on ART using t-test.A vs. C: (P) value = Mean ± SD of parameters compared between HIV seropositive on ART and HIV negative control subjects using t-test.B vs C: (P) value = Mean± SD of parameters compared between HIV seropositive not on ART and HIV negative control subjects*

Table 3. Mean ± SD of parameters compared for the seropositive on ART based on duration of antiretroviral therapy

Duration (years)	G-6PD(mU/10^9 RBC)	PK(mU/ml)	APTT(Sec)	PT(Sec)	PLT(X 10^9/L)
(A)< 1 – 5(n =23)	439.99±71.70	38.35±15.39	42.43±2.27	19.22±2.32	278.78±59.71
(B)> 5 – 8(n =25)	418.00±255.13	40.00±17.40	42.12±3.06	19.72±2.53	281.12±58.32
(C)> 8 – 7(n=12)	759.83±380.24	37.17±18.14	42.75±2.26	19.33±1.78	233.83±52.57
F (P) Values	7.25 (.00*)	0.13 (.88)	0.25 (.78)	0.30 (.74)	0.49 (.62)
A vs. B:P-values	.36	.94	.91	.75	1.00
A vs. C:P- values	.01*	.98	.92	.99	.45
B vs. C:P- values	.03*	.90	.76	.85	.38

**Significant at P< .05Key:F (P) value = Mean ± SD of parameter compared within Seropositive on ART based on duration of antiretroviral therapy using ANOVA.A vs. B: (P) value = Mean ± SD of parameters compared between Seropositive patients on ART with < 1 – 5 years and > 5 – 8 years on antiretroviral therapy using t-test.A vs. C: (P) value = Mean ± SD of parameters compared between Seropositive patients on ART with < 1 - 5 years and > 8 – 17 years on antiretroviral therapy using t-test.B vs. C: (P) value = Mean ± SD of parameters compared between Seropositive patients on ART with < 5 – 8 years and > 8 – 17 years on antiretroviral therapy using t- test*

Table 4. Mean±SD of red cell enzymes and coagulation parameters compared for HIV seropositive on art based on duration of HIV infection

Duration (years)	G-6PD (mU/10^9RBC)	PK (mU/ml)	APTT (Sec)	PT (Sec)	PLT (X 10^9/L)
(A) < 1 – 5(n =17)	430.85±270.29	36.94±16.10	42.35±2.42	19.41±2.29	277±179
(B) > 5 – 8(n = 26)	340.08±307.52	41.69±16.70	42.12±2.60	19.15±2.43	279±159
(C) > 8 – 17(n = 17)	728.24±336.04	36.24±17.06	42.76 ± 2.86	19.94±2.11	252±62
F (P) Values	8.60 (.00*)	0.70 (.50)	0.31 (.73)	0.60 (.55)	0.21 (.81)
A vs. B:P-values	.83	.62	.95	.93	1.00
A vs. C:P-values	.01*	.99	.89	.77	.85
B vs. C:P-values	.00*	.56	.73	.50	.70

**Significant at P< .05Key:F(P)-value = Mean ± SD of parameters compared within HIV seropositive on ART based on duration of HIV infection using ANOVA.A vs. B: (P) value = Mean ± SD of parameters compared between HIV seropositive on ART whose duration of infection is < 1 – 5 years and > 5 – 8years using t-test.A vs. C: (P) value = Mean ± SD of parameters compared between HIV seropositive on ART whose duration of infection is < 1 – 5 years and > 8 – 17 years using t-test.B vs. C: (P) value = Mean ± SD of parameters compared between HIV seropositive on ART whose duration of infection is > 5 – 8 years and > 8 – 17 years using t-test*

Table 5. Mean ± SD of red cell enzymes and coagulation parameters compared for HIV seropositive not on ART based on duration of HIV infection

Duration (years)	G-6PD (mU/10^9RBC)	PK (mU/ml)	APTT (Sec)	PT (Sec)	PLT (X 10^9/L)
(A) < 1 – 3(n = 31)	155.32±98.70	43.39±14.26	41.26±3.43	18.35±1.87	308±117
(B) > 3 – 6(n = 19)	403.21±125.15	39.26±11.29	41.58±3.39	18.16±1.74	269±131
(C) > 6 – 11(n = 10)	448.20±187.36	37.70±13.14	40.00±4.99	17.90±1.52	236±57
F(P) Values	33.71 (.00*)	0.98 (.38)	0.62 (.54)	0.26 (.77)	1.73 (.19)
A vs. B:P-values	.00*	.45	.94	.93	.54
A vs. C:P-values	.00*	.49	.74	.72	.04*
B vs. C:P-values	.78	.95	.65	.91	.62

**Significant at P< .05Key:F (P) value = Mean ± SD of parameters compared within HIV seropositive not on ART based on duration of HIV infection using ANOVA.A vs. B: (P) value = Mean ± SD of parameters compared between HIV seropositive not on ART whose duration of infection is < 1 – 3 years and > 3 – 6 years using t-test.A vs. C: (P) value = Mean ± SD of parameters compared between HIV seropositive not on ART whose duration of infection is < 1 – 3 years and > 6 - 11 years using t-test.B vs. C: (P) value = Mean ± SD of parameters compared between HIV seropositive not on ART whose duration of infection is > 3 – 6 years and > 6 – 11 years using t-test*

4. DISCUSSION

HIV infection is characterised by alteration in enzyme activity, haematological and coagulation parameters in both antiretroviral therapy (ART) and non-antiretroviral therapy (non-ART) patients. The results of this study showeda normal Pyruvate kinase enzyme activity coupled with a significant increase in Glucose-6-Phosphate Dehydrogenase enzyme activity in HIV seropositive subjects compared with the control subjects Table 2. The increase was in association with HIV infection duration >8-17years (ART), >3-11 years (non-ART) and ART duration of >8-17years Tables 3-5. Reticulocytes has been demonstrated to have an increased G-6-PD enzyme activity [19], thus in the absence of reticulocytosis, the increased activity of G-6-PD seen in this study could be a compensatory response to the deficiencies of the erythrocyte antioxidant system in HIV infection. This plays an important role in the cell defence against oxidative damage to the cell by modulating intracellular redox status. This is supported by the discovery of an increase in oxidative stress and altered glutathione ratio (GSH/GSSG) in HIV infection [20], coupled with reduction in glutathione and glutathione peroxidase enzyme activity leading to disruption of redox balance [21]. This places an unbearable burden on the antioxidant system mediated by glutathione and other antioxidant enzymes. In erythrocytes this depends heavily on NADPH produced by G-6-PD for their antioxidant activities. Thus with this increased heavy burden of oxidants, G-6-PD activity could have increased to meet up with the perceived deficiencies and restore the redox balance. Also, increased expression of similar enzymes like Catalase [22] and superoxide dismutase [23] due to oxidative stress during HIV infection has also been documented.

The significant increase in G-6-PD activity also seen in seropositive subjects on ART compared with seropositive not on ART Table 2 could also be attributed to an increased oxidative stress. Antiretroviral therapy has been found to generate reactive Oxygen specie (ROS) which provokes the onset of more oxidative stress in HIV infection [24]. Increased G-6-PD activity in those on ART was observed to be associated with HIV infection duration of>8-17years and ART duration of >8-17years suggesting an increased oxidative stress Tables 3-4.

Activated Partial Thromboplastin time (APTT) and Prothrombin time (PT) were significantly higher in HIV seropositive subjects when compared with the control subjects (Table 2). This signifies that both the intrinsic and extrinsic coagulation pathways are deranged in HIV infection. This is in conformity with the earlier findings in HIV patients [25]. The higher PT and APTT values could be due to various abnormalities seen in HIV patients especially antiphospholipid antibody [26]. Antiphospholipid antibodies have been detected in HIV patients and are found to be directed against phospholipid moieties, and thus interfere in vitro with the action of the thromboplastin used in the test [27]. Deficiencies of coagulation factors, majority of which are produced in the liver, are detected using APTT and PT test. APTT and PT values were also significantly increased in HIV seropositive subjects on antiretroviral therapy compared to the control subjects (Table 2). This could be due to hepatotoxicity of some antiretroviral drugs such as Nevirapine [28], which formed part of the drug regimen for some of the research subjects recruited. PT was also significantly increased in HIV seropositive subjects on ART than those not on ART (Table 2). This agrees with previous findings [29]. This could be as a result of acquired factor VII deficiency secondary to liver damage, since factor VII is the only coagulation factor deficiency that PT detects which cannot be detected by APTT.

Platelet count was found to be decreased in non-ART seropositive subjects with HIV infection duration >6-11years (Table 5). This could be linked to previous findings which reported a predominance of thrombocytopenia due to increased platelet destruction and decreased platelet production in HIV subjects [16]. No significant difference was observed when values for G-6-PD, Pyruvate kinase, PT, APTT and Platelet count were compared between the male and female ART, non-ART and control subjects.

5. CONCLUSION

The result of this research work showed that Glucose-6-phosphate Dehydrogenase enzyme activity was significantly increased in HIV seropositive patients in association with HIV infection duration of >8-17years (ART), >3-11years (non-ART) and ART duration of >8-17years.Moreso, a significant increase was observed in HIV seropositive subjects on ART when compared with HIV seropositive not on ART. Pyruvate kinase enzyme activity was not significantly affected in HIV subjects in comparison with the seronegative subjects (control). Both the intrinsic and extrinsic haemostatic mechanisms were negatively affected.

6. FUNDING

This research did not receive any specific grant from any funding agency in the public, commercial, or non-profit sector.

CONSENT

The aim and details of the study was explained to the subjects and a written informed consent obtained before they were recruited for the study.

ETHICAL APPROVAL

Ethical approval was sought and obtained from the Nnamdi Azikiwe University Teaching Hospital ethics committee (NAUTHEC) before the commencement of the study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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