# *Original Research Article*

## TRANSAMINASES AND ALKALINE PHOSPHATASES ACTIVITIES IN HIV/AIDS PATIENTS ON HIGHLY ACTIVE ANTIRETROVIRAL THERAPY ATTENDING USMANU DANFODIYO UNIVERSITY TEACHING HOSPITAL, SOKOTO


## ABSTRACT

Background: HIV/AIDS causes life threatening opportunistic infections with increased morbidity and mortality. HAART intervention in HIV/AIDS patients has not only reduce morbidity and mortality but also cause hepatic injury and elevation of the liver enzymes.

**Aim:** To measure the liver enzymes in HIV/AIDS patients on highly active antiretroviral therapy (HAART) and HIV/AIDS negative subjects

**Methodology**: Seventy patients aged 20-50 years with asymptomatic HIV seropositive infection on HAART, 39 of whom are on first line drug and 31 on second line drug were assessed and 30 apparently healthy subjects (control) that tested negative for HIV 1 and 2 were recruited into this study. Venous blood was collected to determine the plasma levels of ALT, AST and ALP using kinetic method. Data were statistically analyzed using paired t-tests, $P<0.05$ was considered as statistically significant.

**Result**: The activities of serum ALT and AST observed in HIV infected asymptomatic patients on HAART (first line and second line drug) were significantly higher ($P<0.001$) than in the HIV negative (control) group. No significant difference was observed in ALP of HIV infected asymptomatic patient on HAART (those on second line drug) $P>0.05$ while there was a significant difference in those on first line drug ($P=0.0058$) when compared with the control.

**Conclusion**: Management of HIV/AIDS patients with HAART should be done with caution because hepatic injury may ensue due to the HAART.



KEY WORDS**:** HIV/AIDS, HAART, ALT, AST**,** ALP.




### 1. INTRODUCTION

'Human Immunodeficiency Virus (HIV)' is a retrovirus and the etiologic agent of acquired immunodeficiency syndrome (AIDS), leading to condition like tuberculosis, pneumonia, diarrhoea, meningitis and tumours such as kaposi's sarcoma e.t.c (1). HIV/AIDS causes life threatening opportunistic infection and it affects millions of population and geographic region, and once infected, individuals remain infected for life (2). HIV illness was first described in 1981, and HIV 1 was isolated by the end of 1983 (3). Within a decade, if left untreated, the vast majority of HIV-infected individuals develop fatal opportunistic infections as a result of HIV-induced deficiencies in the immune system. AIDS is one of the most important public health problems worldwide at the start of the 21$^{st}$ century (2). In Nigeria, the prevalence of HIV in 2019 reduced to 1.4% compared to the past (2.8%) while north-west is 0.6%, Sokoto state is put at 0.4 %.( 4)

The intervention of highly active antiretroviral therapy (HAART) in HIV/AIDS patients did not only reduce morbidity and mortality but therapy efficacy may be complicated by infection and drug induced liver injury (5). Antiretroviral drugs are medications for the treatment of infection by retroviruses, primarily HIV. When several such drugs, typically three or four, are taken in combination, the approach is known as highly active antiretroviral therapy (HAART). Antiretroviral treatment is always recommended to all patients with AIDS but due to the complexity of selecting and following a regimen, the severity of the side effects and the importance of compliance to prevent viral resistance however, patients are involved in therapy choice (6). The safety and efficacy of these regimens is often complicated by the presence of infectious hepatitis and occurrence of drug-induced liver injury. These complications manifest as mild laboratory abnormalities and exist without clinical consequence in most patients (5)

The liver is a key organ not only in normal homeostasis but in metabolism of drugs. Some of the drug metabolites is toxic in nature and predisposes the liver to injury. The toxic HAART metabolites in synergy with co-infection of the hepatitis virus, substance and/or alcohol abuse, or concomitant medication speed up the process of liver injury (7).

Liver injury leading to liver disease is often reflected by liver biochemical analytes among which is the elevation of liver enzymes aspartate aminotransferases (AST) and alanine ammotransferases (ALT) (8).

AST and ALT are found in the liver and their levels are a valuable aid primarily in the diagnosis of liver disease. They are also found in red blood cells, heart cells, muscle tissue and other organs, such as the pancreas and kidneys. They are associated with inflammation and/or injury to liver cells, a condition known as hepatocellular liver injury (9). Damage to the liver typically results in a leakage of AST and ALT into the bloodstream. High level of Alkaline phosphatase (ALP) hint a possible blockage of the bile duct, or of possible injury to, or inflammation of the bile ducts(10). This type of problem is characterized by an impairment or failure of bile flow which is known as cholestasis. This type of liver injury is known as cholestatic liver injury and liver disease

## 2. MATERIALS AND METHODS

### 2.1 SUBJECTS

A total of seventy patients aged 20-50 years, with asymptomatic HIV seropositive infection and thirty age-matched, apparently healthy subjects who tested negative for antibodies for HIV 1 and 2 were

recruited into the study as test and control group respectively. About 39 of the HIV/AIDS patients were on “first line” drugs while 31 of the patients were on “second line” drugs.

The test groups were HIV–positive individuals attending ARV clinic in UDUTH while the control group were students in School of Medical Laboratory Science, Usmanu Danfodiyo University, Sokoto.

**2.2 SAMPLE COLLECTION AND STORAGE**

Venipuncture was used to collect 5ml of blood samples into a plain container and it was allowed to clot. Thereafter, it was centrifuged at 4000 revolution per minute (rpm) for 5 minutes to obtain the sera. The separated clear sera were transferred into sterile bottles and were stored at -20$^0$C until analysis. Written informed consent was obtained from all the subjects and ethical approval (UDUTH/ADM/PER/VOL1/25) was obtained from the management of Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto before the commencement of the study.

**2.3 SAMPLE ANALYSIS**

Serum AST and ALT was estimated using Reitman and Frankel (1975) method while Reichling and Kaplan (1988) method was used to estimate ALP.

**2.4 STATISTICAL ANALYSIS**

Data obtained were analyzed using paired t-test and the results were expressed as mean ± Standard Deviation (±SD). A p-value less than 0.05 ($p<0.05$) was considered as statistically significant.

**ETHICAL APPROVAL**

The authors hereby declare that all experiments have been examined and approved by Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki

**3.0 RESULT AND DISCUSSION**

**TABLE 1: Serum AST Between HIV Patients on HAART and HIV Negative Subjects (Control)**

| GROUP | N | $\bar{X}$ | S.D | p-value | Remark |
|---|---|---|---|---|---|
| HIV Negative(control) VS First line drugs | 15<br>39 | 20.15<br>36.59 | ±9.54<br>±32.23 | p<0.0001 | Significant |
| HIV Negative(control) VS Second line drugs | 15<br>31 | 17.82<br>33.5 | ±11.63<br>±17.82 | p<0.0001 | Significant |

Key:
n = number of subjects
$\bar{X}$ = mean
S. D= Standard deviation

**TABLE 2: Serum ALT Between HIV Patients on HAART and HIV Negative Subjects (Control)**

| GROUP | n | $\bar{X}$ | S.D | p-value | Remark |
|---|---|---|---|---|---|
| HIV Negative(control) | 15 | 45.8 | ±12.46 | | |

| | | | | | |
|---|---|---|---|---|---|
| VS | | | | p<0.0001 | Significant |
| First line drugs | 39 | 45.92 | ±15.93 | | |
| HIV Negative(control) | 15 | 15.35 | ±7.41 | | |
| VS | | | | p<0.0001 | Significant |
| Second line drugs | 31 | 35.28 | ±31.59 | | |

Key:
n = number of subjects
$\bar{X}$= mean
S.D= Standard deviation

**TABLE 3 Comparison of Serum ALP Between HIV Patients On HAART And HIV Negative Subjects (Control)**

| GROUP | N | $\bar{x}$ | S.D | p-value | Remark |
|---|---|---|---|---|---|
| HIV Negative(control) | 15 | 137.12 | ±45.01 | | |
| VS | | | | P= 0.0058 | Significant |
| First line drugs | 39 | 143.21 | ±86.3 | | |
| HIV Negative(control) | 15 | 122.46 | ±45.00 | | |
| VS | | | | p>0.05 | Not Significant |
| Second line drugs | 31 | 151.232 | ±67.85 | | |

Chronic liver disease is common among HIV-infected patients, and is increasingly a cause of mortality and morbidity as effective ART allows persons with HIV to live longer. The result of this study shows that there is a significant increase in the serum transaminases in both first line drugs and second line drugs (HAART) (P<0.001) when compared with the HIV negative subjects (controls) This results was in agreement with the report of (11, 12). These may be due to the active involvement of liver in the metabolism of HAART and probably due to the occurrence of hepatic injury.

There was no observable statistically significant difference in the level of ALP especially in those on second line drugs (p>0.05) when compared with the HIV negative subjects while there is a slight significance when compared with HIV patients on first line (P=0.0058). This is in agreement with the work of (13) while those on first line drug shows slight significant increase, which concord with the work of (14) who reported significant increase based on duration (first three month and a progressive fall to normal in 12 months).

However, den-Brinker *et al.,* 2000 indicates that the contribution of hepatitis B and/or hepatitis C virus in liver enzyme elevation of HIV patients on HAART is significant in hepatotoxicity (13). Hepatotoxicity appears to be related to the concurrence of HAART and to viral hepatitis infection. The increase in the liver enzymes AST and ALT may be due to the release of cellular contents of dead or injured cells into the surrounding medium of which enzymes constitutes 20%, an event that takes place in HIV infection.

**4.0 CONCLUSION**

Discerning the role of HAART in hepatotoxic reactions of HIV patients may be diffcult due to frequent preexisting liver pathology, such as that arising from infection with hepatitis B or C virus. Moreover, polypharmacy is common in HIV-infected individuals, and a very large number of medications are

known to have effects on liver function and drug metabolism. Management of HIV/AIDS patients with HAART should be done with caution because hepatic injury may ensue due to the HAART.

Acknowledgement: We appreciate the staff and management of antiretroviral clinic Sokoto, UDUTH for allowing us collect sample from their facility, we also appreciate our subjects for consenting to participate in the study.

**REFERENCES**

1. Greene, W. C., (2007). A history of AIDS: Looking back to see ahead. *Eur J Immunol,* 37(**1**): S94–S102
2. Brooks, G.F., Carnoll, K.C., Janet, S., Butel, Morse, S.A., Mietne, T.A., (2010):"Jawetz, Melnick S Adelberg's Medical Microbiology" McGraw-Hill Companies North American. 25th Edition. pp406-407
3. Rehana Basri and Wan Mohamad Wan Majdiah, 2013. Neurological Manifestations of HIV-1 Infection and Markers for HIV Progression, *Current Perspectives in HIV Infection,* Shailendra K. Saxena, IntechOpen, DOI: 10.5772/54026.
4. Nigerian HIV/AIDS Indicator and Impact Survey NAIIS (2019). National Summary Sheet Preliminary Findings. Available at: https://naca.gov.ng
5. Neff, G. W., Jayaweera D., and Sherman K. E., (2006). Drug-Induced Liver Injury in HIV Patients *Gastroenterology & hepatology*, *2*(**6**), 430–437.
6. Núñez, M., Lana, R., Mendoza, J., Martín-Carbonero, L., Soriano, V., (2001). Risk factors for severe hepatic injury following the introduction of HAART. *Journal of Acquired Immune Defficiency Syndrome* 27:426–431.
7. Neff, G.W., O'Brien, C., Montalbano, M., (2004): "Consumption of dietary supplements in a liver transplant population". *Liver Transplant*. 10:881-885.
8. Núñez, M., Lana, R., Mendoza, J., Martín-Carbonero, L., Soriano, V., (2001). Risk factors for severe hepatic injury following the introduction of HAART. *Journal of Acquired Immune Defficiency syndrome Syndr,* 27:426–431.
9. Shiferaw, M.B., Ketema, T.T., Zegeye, A.M., and Wubante, A. A., (2016): Liver enzyme abnormalities among highly active antiretroviral therapy experienced and HAART naïve HIV-1 infected patients at Debre Tabor Hospital,North West Ethiopia: A comparative cross-sectional study. *AIDS Research and Treatment,* 2016:7
10. Huang Xing-Jiu, Choi Yang-Kyu, Im Hyung-Soon, Yarimaga Oktay, Yoon Euisik and Kim Hak-Sung (2006): Aspartate Aminotransferase (AST/GOT) and Alanine Aminotransferase (ALT/GPT) *Detection Techniques Sensors* **6**:756-782
11. Burtis C. A and Ashwood E.R. (1999). Clinical Chemistry 3rd Edition
12. Wit F. W. N. M., Weverling, G. J., Weel. J, Jurriaans S., and Lange, J. M. A., (2002): Incidence of and risk factors for severe hepatotoxicity associated with antiretroviral combina-tion therapy. *J Infect Dis.* 186:23-31.

13. den Brinker M., Wit F. W., and Wertheim-van Dillen (2000): PM Hepatitis B and C virus co-infection and the risk for hepatotoxicity of highly active antiretroviral therapy in HIV-1 infection. *AIDS* **14**:2895-2902.
14. Maduka C., Ignatius E., Neboh E., Ikekpeazu EJ., Ureme S., Umeh C. and Ejezie E. (2009): "Assessment of Liver Enzymes in Asymptomatic HIV-Seropositive Patients" *Research Journal of Biological Sciences* 4(**3**): 360-362

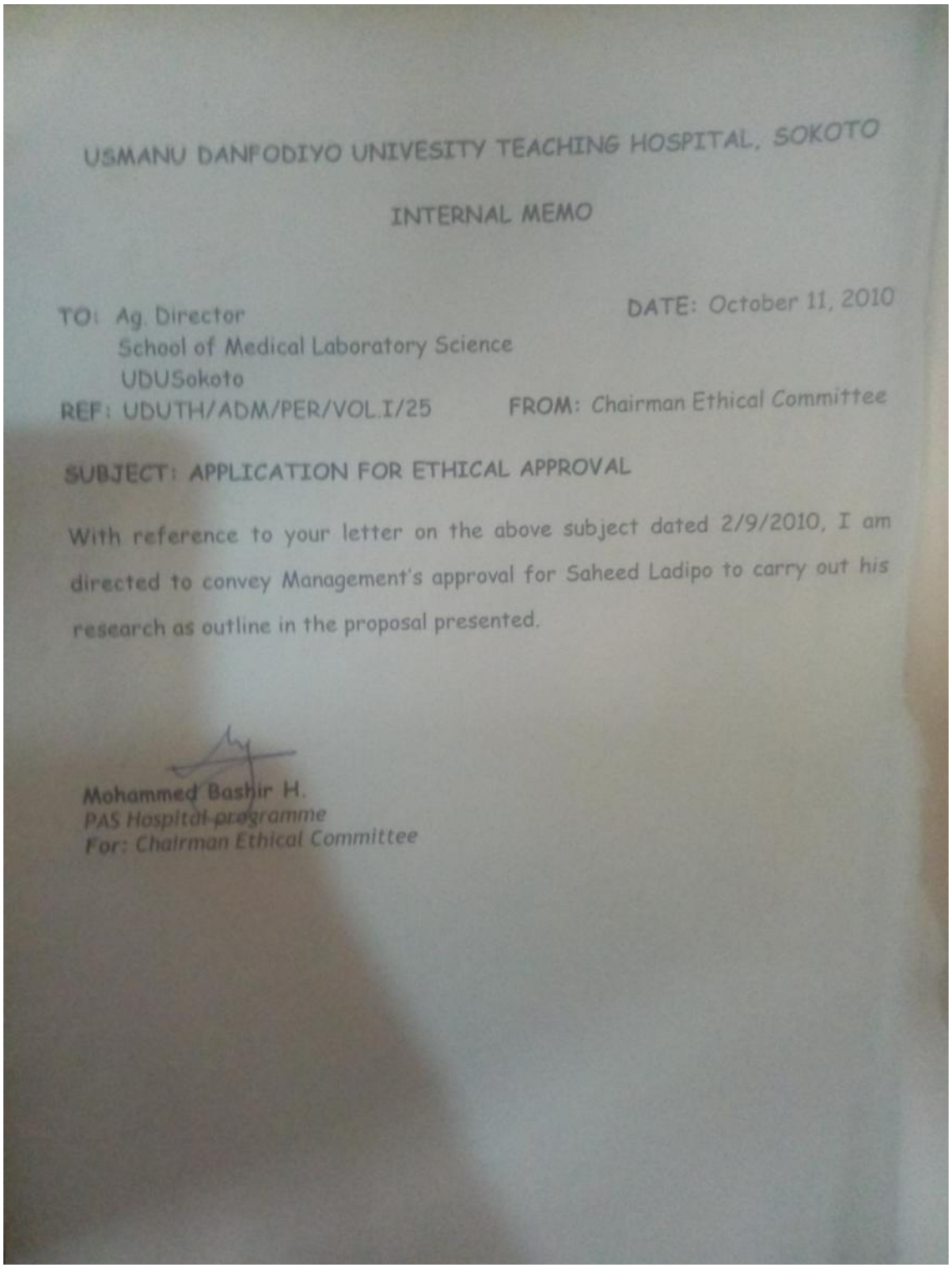
**ETHICAL APPROVAL**

The authors hereby declare that all experiments have been examined and approved by Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

**Patients' consent**

As per university standard guideline participants' consents have been collected and preserved by the authors.

**Ethical Approval letter**



USMANU DANFODIYO UNIVESITY TEACHING HOSPITAL, SOKOTO

INTERNAL MEMO

TO: Ag. Director
School of Medical Laboratory Science
UDUSokoto

DATE: October 11, 2010

REF: UDUTH/ADM/PER/VOL.I/25

FROM: Chairman Ethical Committee

SUBJECT: APPLICATION FOR ETHICAL APPROVAL

With reference to your letter on the above subject dated 2/9/2010, I am directed to convey Management's approval for Saheed Ladipo to carry out his research as outline in the proposal presented.

Mohammed Bashir H.
PAS Hospital programme
For: Chairman Ethical Committee