# Comparative Effects of Anti-Retroviral Drugs on Liver Enzymes

Adieboye George Oforibika[1] and Augustine Amadikwa Uwakwe [2]

[1]Department of Science Laboratory Technology, School of Science and Technology, Port Harcourt Polytechnic Rumuola, P.M.B. 5936, Port Harcourt, Rivers State
[2]Department of Biochemistry, Faculty of Science, University of Port Harcourt, East-West Road, P.M.B. 5323, Choba, 500004 Port Harcourt, Nigeria.
oforibikaa@yahoo.com

**Abstract:** This study was designed to evaluate the comparative effect of nevirapine (nevran), lamivudine and zidovudine on alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) activities of normal albino rats. A total of 63(sixty-three) albino rats were randomly divided into five groups labelled A, B, C, D and E and kept in a well ventilated room. Their environmental conditions were constant. Group A served as control and these rats were treated with distilled water. Rats in the groups B, C, D and E were treated with four different doses of the drugs (0.7, 1.4, 2.1 and 2.8mg/Kgbw) respectively. The drugs were administered once daily for 1,2,3,4 and 5 weeks consecutively, animals were sacrificed twenty four hours after the last treatment. Results obtained in this study revealed that AST levels were highest in Nevran at week 3 of grp B (178.00±1.15 IU/L) when compared to the control (122.6±8.45IU/L). Significant differences ($p<0.05$) were observed among the 3 drugs at group B of week 1 and there was no significant differences between any at group E of week 5. Lamivudine had the highest activity for ALT at group D of week 3(80.00±1.15IU/L) as compared to the control of (44.67±2.60IU/L). Nevran and zidovudine were significantly different ($p<0.05$) with the other drugs at group B of week 1 and group E of week 5 respectively. Mean ALP activity was greatest in Lamivudine at group C of week 1 (58.20±0.06IU/L) when compared to the control (46.73±3.54IU/L). When compared to each other there was no significant difference ($p>0.05$) between any drug at group B of week1 while at group E of week5 Lamivudine was significantly different ($p<0.05$) with the other two drugs. Treatment of HIV/AIDS with ARVs likely results to liver damage by hepatocellular injury by necrosis of the liver and this is due to prolonged treatment.
[Oforibika, G.A. and Uwakwe, A.A.. **Comparative Effects of Anti-Retroviral Drugs on Liver Enzymes.** *Biomedicine and Nursing* 2017;3(4): 50-54]. ISSN 2379-8211 (print); ISSN 2379-8203 (online). http://www.nbmedicine.org. 6. doi:10.7537/marsbnj030417.06.

**Keywords**: Nevirapine, lamivudine, zidovudine, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatise, HIV/AIDS, liver damage, hepatocellular injury.

## 1. Introduction

Limited attention has been given to the several dilemmas and side effects of Antiretroviral drugs (ARVs), including the balance between cost and toxicity as these are major ongoing challenges in resource limited settings in Africa.

Because of the limited availability, cost and convenience of fixed dose combinations, most patients receive first line regimen including Nevirapine, Zidovudine and Lamivudine without monitoring and considering side effects. HIV (Human Immunodeficiency Virus) is the virus which causes AIDS (Acquired Immunodeficiency Syndrome), a condition in humans in which progressive failure of the system allows life threatening opportunistic infections and cancers to thrive (Aktar *et al.,* 2008).

Since the first reported case of AIDS in the USA with 800, 00 new infections occurring daily, the disease has become a global pandemic. By the year 2006, AIDS had infected more than 65million people out of which 25million have died (Anonymous, 2008).

In Nigeria, the acclaimed heart beat of Africa, the prevalence of HIV infection has been increasing steadily from 1.8% in 1991 to 3.8% in 1993, 4.5% in 1996, 5.4% in 1999 and 5.8% in 2001. Recently at the American Conference on the treatment of HIV held in Denver Colorado on May 10 2014 it was stated that the absolute number of people living with HIV in Nigeria had increased by almost half a million in the three years (2010-2013).

It was stressed also that AIDS related mortality had also increased in the same time period to about 217,418. Until recently (with the advent of antiretroviral therapy), HIV infection was a death sentence, in most parts of the world it is still due to non-availability of the anti AIDS drugs, ignorance and financial incapacity (Macaltan, 1001).

The introduction of Highly Active Antiretroviral Therapy (HAART), a cocktail of nucleoside and non-nucleoside analogues capable of inhibiting reverse transcriptase and proteases in industrialized countries during the mid 1990's led to a well documented

reduction in the risk of AIDS-defining illnesses and AIDS related mortality.

Although antiretroviral treatment is not a cure for HIV/AIDS, it can significantly prolong and improve the lives of HIV infected people by suppressing viral loads to non-detectable levels, improving immune status and reducing the incidence of opportunistic infections. However people taking antiretroviral drugs are likely to experience some side effects during their treatment.

Some of which are: dyslipidemia, lipodystrophy, lactic acidosis, severe liver problems, anaemia, renal tubular disorders etc. In the bid to save lives, as many patients as possible are put on potent ART but limited attention has been given to the side effects. There is usually unavailability of proper laboratory monitoring.

Antiretroviral drug related liver injury (ARLI) is defined by elevations in liver enzymes in plasma or serum, with alanine aminotransferase (ALT) characteristically greater than aspartate aminotransferase (AST). It is among the major causes of treatment discontinuation in HIV-infected patients (Nune *et al.,* 2006). Recent surveys have shown that there is an increase in the occurance of hepatic injury in HAART treated patients. Also life threatening hepatotoxic events and end-stage liver disease has been seen in most patients on HAART.

As the use of HAART increases, coupled with the new antiretroviral medications that have been made available, ARLI has come into the limelight due to its negative impact on clinical outcomes. Drug associated hepatotoxicity creates an extra economic burden on already strained medical budgets, as there will be additional visits and hospital admissions are usually needed for proper patient care and management (Nune *et al.,* 2006).

Drug discontinuation hinders maintenance of HIV suppression. Many of the HAART treatment regimens are hepatotoxic. The liver is among the important organs needed in the metabolism of these drugs and also detoxification. Thus the liver must be monitored closely. Also those HAART regimens that have shown signs of toxicity should be identified and adjustments made immediately to improve the patient treatment.

## 2. Materials And Methods

The three antiretroviral drugs samples namely Lamivudine, Zidovudine and Nevran used in this study were obtained from Barata Pharmaceutical Stores which is NAFDAC approved and located at Rumuokuta junction along Ikwerre Road Port Harcourt, Rivers State, Nigeria. Zidovudine (300mg) manufactured by CIPA Ltd Plot No. L. 139 Verna Goa 403922 India for Evans Medical PLC, KM 32 Lagos-Ibadan Expressway. Batch No: K82625. MDF: 01/2011. EXP: 12/2013. NAFDAC Reg No.: 04-6915. Nevran 300mg: manufactured by Ranbaxy laboratories LTD, Paonta Sahib, Dist Simour. Batch No: 235556. MDF: 12/2011. EXP: 11/2013. NAFDAC Reg No: 04-2708.

Lamivudine 300mg: manufactured by Cipla LTD, Plot No L-139 Verna, Goa 403722, India for Evans Medical PLC, Km 32 Lagos-Ibadan Expressway, Lagos State. Batch No: E120365. MDF: 03/2012. EXP: 02/2014. NAFDAC Reg No: 04-7521. Specimen (animal) used for the experiment: sixty-three albino rats were purchased from the department of Human Physiology, University of Nigeria, Enugu Campus (UNEC) and acclimatized for one week in the animal house of Biochemistry Department, University of Port Harcourt.

During acclimatization, the animals were fed with rat pellets, water and libitum. Chemicals and reagents: all chemicals and reagents used in this study were obtained from Randox Laboratories UK. Preparation of Drug solution for administration: based on the daily requirement, 1 tablet each of Nevran, Lamivudine and Zidovudin were ground to a fine powder and dissolve in 100ml of distilled water to make a therapeutic dose concentration of 0.6g (4.29mg/KgBW) which served as the stock solution from which four other concentrations prepared.

Four other concentrations of the three drugs are prepared from the stock solutions which are 0.1g (0.7mg/KgBW), 0.2g (1.4mg/KgBW), 0.3g (2.1mg/KgBW), 0.4g (2.8mg/KgBW) which are 16.7ml, 33.3ml, 50.0ml and 66.7ml of the stock solution respectively. These are then made up to 100ml by dilution with distilled water.

### 2.1 Experimental Procedure

A total of sixty-three (63) albino rats of weight range (124-194g/BW) were randomly divided into five groups labelled A, B, C, D and E where group A served as control and rats (n=5 rats/dose) were treated with distilled water. Rats in groups B, C, D and E (n=5rats/dose) were orally treated with 4 different doses (0.7, 1.4, 2.1 and 2.8) of the three drugs for 5weeks. Animals were sacrificed twenty-four (24) hours after last treatment.

### 2.2 Experimental Design

Drug administration to rats: 0.25ml of drug solution was administered at the different concentrations to the animals in the groups.

### 2.3 Collection of Blood and Preparation of Serum

The rats were withdrawn from the cages in each of the group twenty four hours after the last administration of the drugs for 1, 2, 3, 4, and 5 weeks and placed in a desiccator containing cotton wool soaked in chloroform to anaesthetize the rats. The

blood was obtained by cutting the jugular vein of the rat on the neck.

## 3. Results And Discussion

The results from Table 1 showed that mean plasma aspartate amino transferase (AST) activity significantly decreased when compared to the mean control value of 122.67±8.45 for rats treated with Nevran. In Table 2, there were significant decreases along the weeks in groups D and E for the drug Zidovudine. Lamivudine followed similar trend as Nevran. When compared with each other there were significant differences ($P<0.05$) among all group B of week 1 while there were no significant differences between any two drugs at group E of week5.

For ALT, Nevran had significant decreases ($p< 0.05$) at week 5 for all groups while Zidovudine had significant increases ($p<0.05$) when both were compared to the control. Lamivudine also had the same trend as Zidovudine except for weeks 4 and 5. Nevran was significantly different ($P<0.05$) with the other two drugs at group B of week 1. In week 5 at group E, it was observed that Zidovudine was significantly different ($P<0.05$) with both of the other drugs.

Nevran had significant increases at groups D and E when compared to the mean control value (46.73±3.54) for ALP. Zidovudine followed this trend. Lamivudine had significant increases in all the weeks. In drug to drug comparison there was no significant difference between the drugs at group E of week 5.

In the face of global AIDS pandemic, advancement in the treatment of the disease has been strikingly impressive. For example, patients on antiretroviral therapy now live for more than a decade than those without (chevrria *et al.,* 1993). But problems still remain since hapatotoxicity has been a major side effect of antiretroviral drugs limiting their use in treatment regimens (Oforibika and Essien, 2017; Morisco *et al.,* 2008).

ALT is present in higher concentrations in the liver and to a lesser extent in the kidneys, heart, skeletal muscle, pancreas, spleen and lung. Increased levels of ALT are generally as a result of liver disease linked to hepatic necrosis such as cirrhosis, carcinoma, viral or toxic hepatitis and obstructive jaundice. Typically ALT is generally higher than AST in acute viral or toxic hepatitis, whereas for most patients with chronic hepatic disease, ALT levels are generally lower than AST levels.

Elevated ALT levels have also been found in extensive trauma, muscle disease, hypoxia, myocardial infarction, circulatory failure and also shock and haemolytic disease (Gray *et al.,* 1985). Elevated activities of these enzymes indicate cell damage which might have resulted from several mechanisms which include metabolic host mediated injury, hypersensitivity reactions, mitochondrion toxicity and immune reconstitution. All the nucleoside and non-nucleoside analogues have been implicated although the degree varies from one drug to the other. The three drugs used in this study – Nevran (NNRTI), Zidovudine and Lamivudine (NRTI) exhibit this but hypersensitivity is more prevalent in Nevran (NNRTIs) than Zidovudine and Lamivudine (NRTIs) as seen in the research work. This is also supported (Clark *et al.,* 2002).

This is because both drug classes NRTIs and NNRTIs inhibit the same target, the reverse transcriptase enzyme. NRTIs bind at the active site thus inhibiting the DNA polymerase γ from the host cell while their counterpart NNRTIs bind on the enzyme thus changing its shape and also inhibiting the DNA polymerase γ (Dacie and Lewis, 1991).

ALP is a nonspecific enzyme which hydrolyses aliphatic, aromatic or heterolytic phosphate compounds. ALP is produced by osteoroblast of bones. Moderate increase in ALP levels is seens in hepatic diseases such as infective hepatitis, alcoholic hepatitis or hepatocellular carcinoma (Zee *et al.,* 2002; Oforibika and Uwakwe, 2017).

Very high activity of serum ALP than normal maybe noticed in extrahepatic obstruction or cholestasis. Increases in ALT and AST with lesser increases or normal ALP favours cell necrosis and are common symptoms of hepatotoxicity while increases in ALP and γ glutamyl transpeptidase were indicative of cholestasis (Oforibka and Uwakwe, 2017).

In this study γ glutamyl transpeptidase and serum bilirubin wasn't tested. At the clinical level, the mitochondria deficiency is responsible for the adverse effects such as life threatening lactic acidosis, hepatic steatosis and possible fat redistribution syndrome which is grouped as NRTI induced mitochondrial cythopathy (Sulkwoski *et al.,* 2000; Morisco *et al.*, 2008; Lee, 2003).

**Summary and Conclusion**

In summary, the researchers discovered that the overall incidence of severe hepatic injury was not significantly different between NRTIs and NNRTIs. Zidovudine has been involved in cases of fatal hepatic failure in advanced AIDS patients. These patients developed massive hepatomegalysis and microvesicular steatosis which progressed to fulminant hepatic failure (Tun *et al.,* 1993). Zidovudine cam also causes acute hepatitis due to hypersensitivity which resolved itself exactly 10 days after cessation of therapy. In such patients Zidovudine is usually replaced with didanosine.

**Table 1: Effect of Antiretroviral Drugs (Zidovudine Nevran and Lamivudine on (AST) Levels (iu/1) treated for 5 weeks.**

| DRUG TREATMENT/CONTROL GROUPS M±SEM | WEEKS OF TREATMENT WK4 | WK5 | WKI | WK2 | WK3 |
|---|---|---|---|---|---|
| | Group A (control Distil water) | | | | |
| | 122.67±8.45 | | | | |
| ZIDOVUDINE | (0.7mg/kgBW) | | 105.00±1.15$^{abbb}$ | 108.00±1.15$^{a}$ | |
| | 96.00±1.15$^{a}$ | 136.00±1.15$^{a}$ | 136.00±1.15 | | |
| | (1.4mg/kgBW) | 108.00±1.15$^{a}$ | 105.00±1.15 | 108.00±1.15$^{a}$ | |
| | 67.00±1.15$^{a}$ | 136.00±1.15$^{a}$ | | | |
| | (2.1mg/kgBW) | 112.00±1.15$^{a}$ | 102.00±1.15 | | |
| | 136.00±1.15$^{a}$ | 89.00±1.15$^{a}$ | 36.00±1.15$^{a}$ | | |
| | (2.8mg/kgBW) | 130.00±1.15 | 120.00±1.15$^{a}$ | | |
| | 126.00±1.15$^{a}$ | 108.00±1.15$^{a}$ | 41.00±1.15$^{a}$ | | |
| NEVRAN | (0.7mg/kgBW) | 130.00±1.15$^{abbb}$ | 141.00±1.15$^{a}$ | | |
| | 178.00±1.15$^{a}$ | 76.00±1.15$^{a}$ | 23.00±1.15$^{a}$ | | |
| | (1.4mg/kgBW) | 130.00±1.15 | 148.00±1.15$^{a}$ | | |
| | 112.00±1.15a | 76.00±1.15$^{a}$ | 67.00±1.15$^{a}$ | | |
| | (2.1mg/kgBW) | 141.00±1.15$^{a}$ | 156.00±1.15$^{a}$ | | |
| | 125.00±1.15 | 89.00±1.15$^{a}$ | 76.00±1.15$^{a}$ | | |
| | (2.8mg/kgBW) | 141.00±1.15$^{a}$ | 130.00±1.15$^{a}$ | | |
| | 108.00±1.15$^{a}$ | 98.00±1.15$^{a}$ | 36.00±1.15$^{a}$ | | |
| LAMIVUDINE | (0.7mg/kgBW) | 165.00±0.58$^{abbb}$ | 112.00±1.15 | | |
| | 148.00±1.15$^{a}$ | 89.00±1.15$^{a}$ | 94.00±1.15$^{a}$ | | |
| | (0.14mg/kgBW) | 148.00±1.15$^{a}$ | 148.00±1.15$^{a}$ | | |
| | 141.00±1.15$^{a}$ | 59.00±1.15$^{a}$ | 59.00±1.15$^{a}$ | | |
| | (2.1mg/kgBW) | 156.00±1.15$^{a}$ | 136.00±1.15$^{a}$ | | |
| | 148.00±1.15$^{a}$ | 89.00±1.15$^{a}$ | 36.00±1.15$^{a}$ | | |
| | (2.8mg/kgBW) | 136.00±1.15$^{a}$ | 130.00±1.15$^{a}$ | | |
| | 141.00±1.15$^{a}$ | 67.00±1.15$^{a}$ | 41.00±1.15$^{a}$ | | |

Values are expressed in means±standard error of the mean (M±SEM)
Superscript a: Indicates significant difference ($p<0.05$) with control.
Superscript b: Indicates significant difference ($p<0.05$) at 0.7mg/Kgbw of week 1
Superscript c: Indicates significant difference ($p<0.05$) at 2.8mg/Kgbw of week 5

**Table 2: Effect of Antiretroviral Drugs (Zidovudine Nevran and Lamivudine on Alanine Amino Transferase Levels (IU/L) Treated for 5 Weeks.**

| DRUG TREATMENT/CONTROL GROUPS M±SEM | WEEKS OF TREATMENT WK4 | WK5 | WKI | WK2 | WK3 |
|---|---|---|---|---|---|
| | Group A (control Distil water) | | | | |
| | 44.67±2.60 | | | | |
| ZIDOVUDINE | (0.7mg/kgBW) | | 45.00±1.15$^{bb}$ | 43.00±1.15 | |
| | 52.00±1.15$^{a}$ | 49.00±1.15 | 49.00±1.15$^{a}$ | | |
| | (1.4mg/kgBW) | 45.00±1.15$^{a}$ | 36.00±1.15$^{a}$ | 52.00±1.15$^{a}$ | |
| | 34.00±1.15$^{a}$ | 73.00±1.15$^{a}$ | | | |
| | (2.1mg/kgBW) | 74.00±1.15 | 45.00±1.15 | | |
| | 50.00±1.15 | 20.00±1.15$^{a}$ | 24.00±1.15$^{a}$ | | |
| | (2.8mg/kgBW) | 49.00±1.15 | 47.00±1.15 | | |
| | 56.00±1.15$^{a}$ | 34.00±1.15$^{a}$ | 36.00±1.15$^{accc}$ | | |
| NEVRAN | (0.7mg/kgBW) | 64.00±1.15$^{abbb}$ | 43.00±1.15 | | |
| | 47.00±1.15 | 38.00±1.15 | 22.00±1.15$^{a}$ | | |
| | (1.4mg/kgBW) | 50.00±1.15 | 45.00±1.15 | | |
| | 40.00±1.15a | 62.00±1.15$^{a}$ | 25.00±1.15$^{a}$ | | |
| | (2.1mg/kgBW) | 49.00±1.15 | 45.00±1.15 | | |
| | 49.00±1.15 | 38.00±1.15 | 27.00±1.15$^{a}$ | | |
| | (2.8mg/kgBW) | 44.00±1.58 | 49.00±1.15 | | |
| | 60.00±1.15$^{a}$ | 38.00±1.15 | 17.00±1.15$^{acc}$ | | |
| LAMIVUDINE | (0.7mg/kgBW) | 44.00±0.58$^{abbb}$ | 38.00±1.15 | | |
| | 40.00±1.15 | 25.00±1.15$^{a}$ | 30.00±1.15$^{a}$ | | |
| | (0.14mg/kgBW) | 54.00±1.15$^{a}$ | 64.00±1.15$^{a}$ | | |
| | 66.00±1.15$^{a}$ | 20.00±1.15$^{a}$ | 23.00±1.15$^{a}$ | | |
| | (2.1mg/kgBW) | 56.00±1.15$^{a}$ | 72.00±1.15$^{a}$ | | |
| | 80.00±1.15$^{a}$ | 28.00±1.15$^{a}$ | 23.00±1.15$^{a}$ | | |
| | (2.8mg/kgBW) | 52.00±1.15$^{a}$ | 45.00±1.15 | | |
| | 75.00±1.15$^{a}$ | 40.00±1.15 | 23.00±1.15$^{acc}$ | | |

Values are expressed in means±standard error of the mean (M±SEM)
Superscript a: Indicates significant difference ($p<0.05$) with control.
Superscript b: Indicates significant difference ($p<0.05$) at 0.7mg/Kgbw of week 1
Superscript c: Indicates significant difference ($p<0.05$) at 2.8mg/Kgbw of week 5

**Table 3: Effect of Antiretroviral Drugs (Zidovudine Nevran and Lamivudine) on Alkaline phosphatase (ALP) Levels Treated for 5 Weeks.**

| DRUG TREATMENT/CONTROL GROUPS M±SEM | WEEKS OF TREATMENT WK4 | WK5 | WKI | WK2 | WK3 |
|---|---|---|---|---|---|
| | Group A (control Distil water) | | | | |
| | 46.73±3.54 | | | | |
| ZIDOVUDINE | (0.7mg/kgBW) | | 47.20±0.12 | 56.27±0.09 | |
| | 56.30±1.15 | 33.60±0.12 | 33.60±0.12$^{a}$ | | |
| | (1.4mg/kgBW) | 50.00±1.15 | 53.10±0.06 | 53.10±1.15 | |
| | 53.0±0.09 | 28.70±0.12$^{a}$ | | | |
| | (2.1mg/kgBW) | 44.40±0.12 | 56.20±0.06 | | |
| | 56.30±1.15 | 41.20±0.12$^{a}$ | 39.50±0.12$^{a}$ | | |
| | (2.8mg/kgBW) | 47.70±0.12 | 56.23±0.07 | | |
| | 56.30±1.15 | 42.77±1.43 | 28.90±0.12$^{acc}$ | | |
| NEVRAN | (0.7mg/kgBW) | 44.40±0.23 | 46.90±0.00 | | |
| | 46.87±0.15 | 44.10±0.12 | 28.90±0.12$^{a}$ | | |
| | (1.4mg/kgBW) | 41.70±0.12 | 45.50±1.15$^{a}$ | | |
| | 44.13±0.19 | 44.10±0.12 | 29.60±0.12$^{a}$ | | |
| | (2.1mg/kgBW) | 55.30±0.15 | 50.00±1.15 | | |
| | 50.13±0.19 | 55.90±0.12$^{a}$ | 26.30±0.12$^{a}$ | | |
| | (2.8mg/kgBW) | 50.00±1.15 | 53.10±0.06 | | |
| | 53.10±0.12 | 55.90±0.12$^{a}$ | 30.30±0.12$^{acc}$ | | |
| LAMIVUDINE | (0.7mg/kgBW) | 52.50±0.21 | 56.30±0.06 | | |
| | 56.57±0.12 | 50.00±0.12 | 34.90±0.12$^{a}$ | | |
| | (0.14mg/kgBW) | 58.20±0.06 | 50.00±1.15 | | |
| | 50.10±0.21 | 50.00±0.12 | 41.40±0.12$^{a}$ | | |
| | (2.1mg/kgBW) | 38.70±0.12 | 50.00±1.15 | | |
| | 50.00±0.12 | 44.10±0.12 | 44.10±0.12 | | |
| | (2.8mg/kgBW) | 41.70±0.12 | 56.30±0.06 | | |
| | 56.30±0.12 | 52.90±0.12$^{a}$ | 20.60±0.12$^{acc}$ | | |

Values are expressed in means±standard error of the mean (M±SEM)
Superscript a: Indicates significant difference ($p<0.05$) with control.
Superscript b: Indicates significant difference ($p<0.05$) at 0.7mg/Kgbw of week 1
Superscript c: Indicates significant difference ($p<0.05$) at 2.8mg/Kgbw of week 5

Less report has been gotten on Lamivudine causing hepatic toxicity as compared to Zidovudine and Nevran on short term duration of administration These may be due to the low affinity of Lamivudine for mitochondria DNA polymerase γ. However Lamivudine is widely used and considered to be the best tolerated among the three drugs. Long term administration of Nevran can cause life threatening liver hepatotoxicity especially on women with high $CD_4^+$ counts but newer NNRTIs (efavirenz) have been produced with lesser effect. These findings suggest that greater increases in ALT than ALP maybe associated with hepatocellular injury.

### 3.2 Recommendations

Antiretroviral treatment with NRTIs and NNRTIs may be associated with hepatocellular injury. There should be close monitoring of liver enzymes to prevent life threatening events. Also, there should be inclusion of hepatoprotective agents in the treatment regimen.

**Corresponding author:**
Dr. (Mrs.) Oforibika, George Adieboye
Department of Science Laboratory Technology, School of Science and Technology, Port Harcourt

Polytechnic Rumuola, P.M.B. 5936, Port Harcourt, Rivers State. Telephone: +2348073249805
E-mail: oforibikaa@yahoo.com

**References**


1. Aktar M, Mathieson K, Arey B. Post, J. Prevette R, Hilleer A., Patel, R., Ram, L. P., Van Thiel, D.H., Nardir, A., (Dec. 2008). Hepatic – Histopathology and Clinical Characteristics Associated with Antiretroviral Therapy in HIV Patients without viral Hepatitis. Eur. F. Gastroenterol Hepatol 22:1194-1204.
2. Anonymous (2003). Study confirms effectiveness of antiretroviral drugs for HIV patients' lancet, 362:1267-1274.
3. Clark, S. Creighton, S. Portmann, B., Taylor, C., Inendon, J. & Cramp, M. (2002). Acute Liver Failure Associated with Antiretroviral Treatment for HIV A Report of Six Cases: *Journal of Heaptology* 36:295 – 30.
4. Dacie, J.V. and Lewis, S.M., (1991). Practical Hematology. 7th edn Edinburgh, Churchill Livingstone England, pp.37-85.
5. Echevrria, P.S., Jonnalagadda, S.S. Hopkin S. B.L. and Rosenbloom, C.A. (1993). Perception of Quality of life of persons with HIV/AIDS and maintenance of nutritional parametus while on protease inhibitors AIDS patient care and STDs. 13(7):33427-33.
6. Gray, C.H., Howorth, P.J.N. and Rinsler, M.G. (1985). *In*: Plasma Protein and immunoglobine. Clinical/Chemical Pathology 10th edn. Edward Arnold (Publishers) LTD Bedford London. pp.73-89.
7. Lee, W.M. (2003). Drug indused hepatotoxicity. New Eng. J. Med, 349; 474-485. Morisco F., Votaglione, O., Amoruso, D., Russo B., Fogaliano V., and Caporaso, N., (2008). Foods & liver health, Molecular Aspects of Med. 29:144-150.
8. Macaltan, D.C. (1991). Wasting in HIV infection and AIDS. *J. Nutem.* 129:2385-2425.
9. Morisco F., Votaglione, O., Amoruso, D., Russo B., Fogaliano V., & Caporaso, N., (2008). Foods & liver health, Molecular Aspects of Med. 29:144-150.
10. Nune Z.M.J., Martin Carbonew, L. Moreno, Valencia, E. Grarcia Samanugo J., & Gonzale, ZCastilho,J. (2006): Impact of antiretroviral AIDS, 22:825-829.
11. Oforibika, G.A. and Uwakwe, A.A. (2017). Hepatotoxicity Of Nevirapine On The Liver. *Biomedicine and Nursing*, 3(2): 80-84.
12. Oforibika, G.A. and Essien, E.B. (2017). Hepatotoxicity Effect of Zidovudine on the Liver. *Academia Arena,* 9(6):27-30.
13. Oforibika, A.G. and Ezekiel, T. (2017). Hepatotoxicity of Lamivudine on the Liver. *Biomedicine and Nursing,* 3(2):49-52.
14. Sulkwoski, M.S., Thomas, D.L., Charsson, R.E., & Moore, R.D. (2000): hepatotoxicity associated with antiretroviral therapy in adults infected with HIV and the role of Hepatitis C or B virus infection, Jama. 283:74-80.
15. Tun, O.H., Okerhiolm, R.A. and Guengerich, E.P. (1993): Oxidation of the Antistamine Drug Terfernadrine in Human Liver microsomes. Role of Cytochrome p450 3A4 in N-d ealkylation and C-hydroxylation of Drug metab. *Dispose*, 21:403-409.
16. Zee, N. S., Dohjima, T., Bauer G., Ehasane, A., Solvaterra P. & Rossi, J. (2002): Experssion of Small interfering RNAS, Targeted Agaisnt HIV Rev Transcript in Human cells. *Nat Biotechnol.*20:500-505.


12/25/2017