Pharmaceutical Sciences & Analytical Research Journal
ISSN: 2640-6659

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Research Article *Volume 7 Issue 1*

Effects of Antiretroviral Therapy on Liver based Enzymes, AST, ALT, ALP and Total Bilirubin in HIV Patients Attending the Bamenda Regional Hospital

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Received Date: November 11, 2024; **Published Date:** January 08, 2025

Abstract

The introduction of antiretroviral therapy (ART) for use in management of HIV and AIDS, compounded with the routine use of CD4+ T-cell counts as surrogate markers of drug efficacy and disease progression significantly increased the life expectancy among HIV-infected patients. This study determined the pattern of, Aspartate Aminotransferase (AST), Alanine amino transaminase (ALT), Alkaline Phosphatase (ALP) and Total bilirubin (T.Bil) in HIV positive patients on above 6 months and less than 6 months antiretroviral therapy. Blood samples were collected from consented HIV positive individuals, who were sampled using convenience sampling in an institutional based cross sectional study design. The samples were collected in to sterile blank tubes, and immediately taken to the Bamenda Regional Hospital laboratory and analysed for levels of ALT, AST, ALP and T.Bil using the URIT 990 semi-automated biochemistry machine following standardised methods. SPSS version 23 was used for data analysis and statistical significance was considered if p value was less than 0.05. There was a statistically significant difference between the mean values of ALT in patients on ART above 6 months (13.04IU/L) and below 6 months (9.59IU/L) (p=0.011). However, the mean AST values indicated no statistically significant in patients on ART above 6 months (19.3IU/L) and below 6 months (16.01IU/L) (p=0.33). There was no statistically significant difference between the mean values of ALT in patients on ART above 6 months (13.04IU/L) and below 6 months (9.59IU/L) (p=0.27). With T.Bil, there was an observed statistically significant difference between the mean values of T.Bil in patients on ART above 6 months (0.7mg/dl) and below 6 months (0.5mg/dl) (p=0.02). The study indicated that the level of the analytes were statistically different in patients on ART above 6 months compared to those who had been on ART below 6 months except for AST and ALP. There is need for a closer follow up of patients on ART above 6 months for acute liver intoxication.

Keywords: AST; ALT; Bilirubin; ALP; Liver; Antiretroviral; Antiretroviral Therapy; HIV and AIDS; ART

Abbreviations

ART: Antiretroviral Therapy; ALT: Alanine Amino Transaminase; ALP: Alkaline Phosphatase; T.Bil: Total Bilirubin; AST: Aspartate Aminotransferase; HAART: Highly Active Antiretroviral Therapy; WHO: World Health Organization; IRB: Institutional Review Board.

Background

About 84.2 million people were living with HIV and AIDS worldwide by 2022 up from 40.1 million in 2008 and more than 25 million have died since the first cases were reported in 1981 [1]. Sub-Saharan Africa is the worst affected region with an estimated 25.0 million people [70.8%] of the global total. The population of Sub-Saharan Africa accounts for only 11-12% of the world's population [2]. The pandemic killed an estimated 1.4 million people in 2012 of which 1.2 million of the cases were from sub-Saharan Africa. The epidemic is more prevalent in low and middle income-countries where millions of people are infected each year [3]. About 2.3 million Cameroonians live with HIV/AIDS while an estimated 1.5 million have already died of the virus and each year, approximately 200,000 Kenyans develop the AIDS syndrome [4]. HIV and AIDS pandemic affect all regions and communities and it impacts negatively on households and economic growth of nations.

The introduction of antiretroviral therapy [ART] for use in management of HIV and AIDS, compounded with the routine use of CD4+ T-cell counts as surrogate markers of drug efficacy and disease progression significantly increased the life expectancy among HIV-infected patients. Between 1996 and 1999 the advent of highly active antiretroviral therapy [HAART] dramatically improved the survival of patients with HIV infection with unprecedented changes in disease progression and mortality seen first in the United States and European population [5]. World Health Organization [WHO] and other organizations are providing countries with ongoing guidance, tools and support in delivering and scaling up ART for HIV and AIDS within the public health sector.

The goal of ART is to suppress viral replication and have impaired immunity restored but its major drawback is adverse effects accompanying its use. HAART toxicity has emerged as an important complication and eventually a major reason for ART switch and/or discontinuation [6]. Acute drug toxicities still exist, and although typically not life-threatening, they can affect the quality of life and patients' willingness to adhere to their treatment regimens [7]. Despite substantial benefits of HAART, a variety of short and long-term adverse effects have been associated with their use which reduces adherence and efficacy levels of the medication [8]. The frequency of drug toxicities is often described in clinical trials but not so thoroughly monitored and evaluated in clinics [3], observed that, 18 out of 31 drugs causing hepatotoxicity in humans showed toxicity in animal models and one-third of all drugs associated with hepatotoxicity in animals result in a rise in liver enzymes in humans. Drug-induced toxicity is often detected long after a drug enters the market because animal models cannot always predict human toxicity [6]. Detection of toxicities is done by measuring the levels of organ-specific surrogate markers in blood and/or urine samples then compared with established reference range values of a normalized population when making interpretations. HIV patients are more prone to develop adverse effects due to use of a cocktail of antiretroviral drugs. Such patients are at high risk of developing short and long-term complications such as hepatotoxicity, cardiovascular disorders and renal insufficiency among others. Hepatotoxicity is associated with many of the antiretroviral agents which make their use a double-edged sword [8]. These effects can be seen from the analysis of liver enzymes such as AST, ALT, ALP, and other tests like Bilirubin. Despite scaling up of HAART treatment in Cameroon, documented data and reports on the prevalence of liver derangements are still scanty. It is against this backdrop that this study evaluated the prevalence of abnormal liver function analysts in HIV positive patients on ART at the Regional Hospital Bamenda.

Methodology

The study was carried out at the Bamenda Regional Hospital involving 50 consented HIV positive patients on antiretroviral therapy, involving 25 HIV patients on ART below 6 months and 25 HIV patients who had been on ART for 6 months and above. Two millilitres of freshly collected venous blood were dispensed into plain bottles and centrifuged for the estimation of AST, ALT, ALP and Total Bilirubin using colorimetric enzymatic method [9]. All statistical analyses were done using SPSS version 21 (IBM SPSS Statistics, IBM Corporation, Chicago, IL). The data was analysed using the independent sample t-test (to compare significant differences between the means of two independent groups). $p<0.05$ was considered statistically significant. Ethical approval was obtained from the Institutional Review Board (IRB) of the Bamenda Regional Hospital.

Results

Socio-Demographic Characteristics of Respondents

Table 1 below presents the social-demographic characteristics of respondents in this study. Out of a total sample size of 50, a majority of 36% (n=18) reported to have been between the age range of 30-40 years old. These were closely followed by those who reported to be 40-50 making a total percentage score of 30% (n=15). 60% (n=30) of these

respondents reported to been married, and 40% (n= 20) had unmarried status. According to the Education levels60% (n=30) reported to reach primary education, 20% (n=10) reached secondary education, and 10% (n=5) reported to reach tertiary education.

A 100% (n=50) were reported to be not pregnant. Out of the total sample size, majority were female with a percentage of 70% (n=35) and a percentage of male being 30% (n=15). A 100% (n=50) were reported to be Christians in religion. 80% (n=40) of the sample size were self-employed with 10% (n=5) were Government/ Privately employed and 10% (n=5) were house wives.

Variable	Characteristic	Frequency	Percentage
Age range (Years)	20-30	2	4
	30-40	18	36
	40-50	15	30
	50-60	14	20
	60-70	1	2
Total		50	100
Pregnancy	Pregnancy	0	
	Not Pregnant	50	
Total		50	100
Sex	Male	15	30
	Female	35	70
Total		50	100
Education Level	Primary	30	60
	Secondary	15	30
	University	5	10
Total		50	100
Religion	Christian	50	100
	Muslem	0	0
	Others	0	0
Total		50	100
Occupation	Self-Employed	40	80
	Government Employed	5	10
	House Wife	5	10
Total		50	100
Duration of ART	0-6 Month	25	50
	6 Month and Above	25	50
Total		50	100

Table 1: Descriptive characteristic of respondent.

Presentation of liver parameters analysed.

The maximum ALT, AST, ALP and TBil values observed in this study were 33IU/L, 36IU/L, 91 IU/L, and 4mg/dl respectively. The mean±SD values of the above measured parameters gotten in the study were 11.3±7.6IU/L, 17.65±11.59IU/L, 48.72±17.58IU/L and 0.62±0.59mg/dl respectively as shown in Table 2 below.

	ALT	AST	ALP	TBil
N	50	50	50	50
Mean	11.312	17.656	48.722	0.622
Std. Deviation	7.61734	11.68537	17.57908	0.59154
Minimum	0.3	0.8	2.9	0.1
Maximum	33	46.6	91	4

NV: ALT 1 - 40IU/L, AST 1 - 40IU/L, ALP 35 - 110 IU/L, TBil 0.1 - 1.2mg/dl

Table 2: General description of ALT, AST, ALP and TBil level (0 to above 6months).

Effect of Art on the Liver of HIV Positive Patients based on the Enzymes ALT, AST, ALP and Bilirubin on Treatment for more than 6 Months

The mean±SD of ALT, AST, ALP and TBil in this study was observed to be 13.03±6.6IU/L, 19.30±11.99IU/L, 46.65±16.26IU/L and 0.68±0.77mg/dl respectively. With the maximum values observed at 31.1IU/L, 46.6IU/L, 91.0IU/L and TBil of 4mg/dl respectively. The values were within normal values except for AST which one patient had up to 46.6IU/L and TBil where one patient had up to 4mg/dl as shown in Table 3 below.

	ALT	AST	ALP	TBil
N	25	25	25	25
Mean	13.036	19.296	46.648	0.676
Std. Deviation	6.63676	11.99321	16.25518	0.76772
Minimum	2.6	0.9	11.2	0.1
Maximum	31.1	46.6	91	4

NV: ALT 1 - 40IU/L, AST 1 - 40IU/L, ALP 35 - 110 IU/L, TBilirubin 0.1 - 1.2mg/dl

Table 3: Description of ALT, AST, ALP and TBil levels in HIV patients on ART >6months.

For the 25 patients on ART above 6 months, each of their ALT, AST, ALP and TBil values are presented in Figure 1 below.

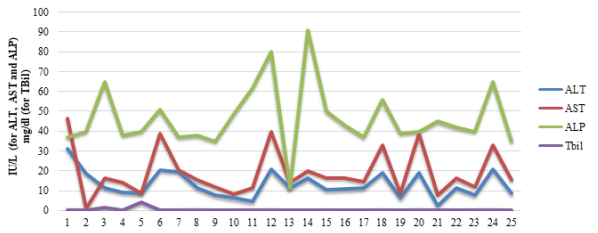

Figure 1: Presentation of ALT, AST, ALP and TBil levels in HIV patients on ART >6months.

Effect of Art on the Liver of HIV Positive Patients Based on the Enzymes ALT, AST, ALP and Bilirubin on Treatment for Less than 6 Months

The mean±SD of ALT, AST, ALP and TBil in this this study was observed to be 9.59±8.26IU/L, 16.01±11.37IU/L 50.80±18.91IU/L and 0.57±0.34mg/dl respectively. With the maximum values observed at 33IU/L, 45.7IU/L, 91IU/L and TBil of 1.2mg/dl respectively. The values were within normal values except for AST which one patient had up to 45.7IU/L as shown in Table 4 below.

	ALT	AST	ALP	TBil
N	25	25	25	25
Mean	9.588	16.016	50.796	0.568
Std. Deviation	8.25996	11.37298	18.91381	0.34487
Minimum	0.3	0.8	2.9	0.1
Maximum	33	45.7	91	1.2

NV: ALT 1 - 40IU/L, AST 1 - 40IU/L, ALP 35 - 110 IU/L, TBilirubin 0.1 - 1.2mg/dl

Table 4: Description of ALT, AST, ALP and TBil levels in HIV patients on ART <6months.

For the 25 patients on ART below 6 months, each of their ALT, AST, ALP and TBil values are presented in Figure 2 below.

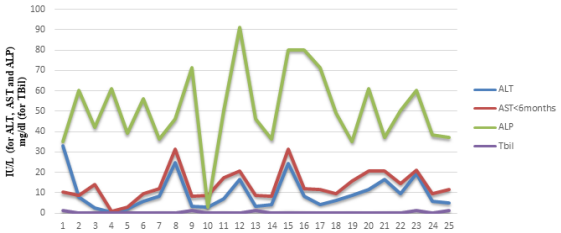

Figure 2: Presentation of ALT, AST, ALP and TBil levels in HIV patients on ART <6months.

Statistical Difference Between ALT, AST, ALP and Tbil Values in HIV Patients on Art below and above 6 Months

ALT (IU/L)

Using the independent sample t test, there was a statistically significant difference between the means of ALT in patients on ART above 6 months (13.04IU/L) and below 6 months (9.59IU/L) with a p value of 0.011. It can as well be seen in figure 3 below that patients who were on ART above 6 months had slightly elevated ALT values.

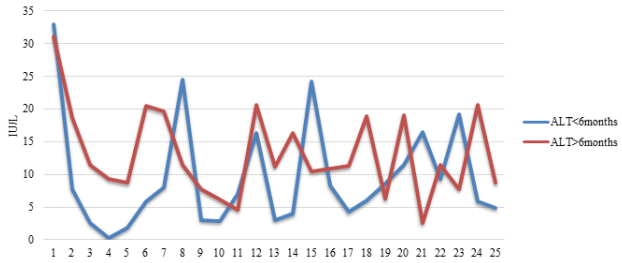

Figure 3: Statistical difference in ALT values in HIV patients on ART below and above 6 months.

AST (IU/L)

There was no statistically significant difference between the means of AST in patients on ART above 6 months (19.3IU/L) and below 6 months (16.01IU/L) with a p value of 0.33. Even though it can be seen in Figure 4 below that patients who were on ART above 6 months had slightly elevated AST values, there was no statistically significant difference between the AST means in this case.

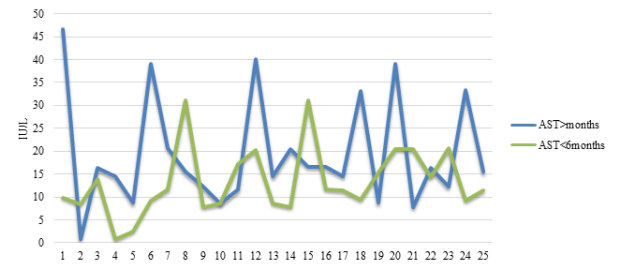

Figure 4: Statistical difference in AST values in HIV patients on ART below and above 6 months.

ALP (IU/L)

There was no statistically significant difference between the means of ALP in patients on ART above 6 months (46.6IU/L) and below 6 months (50.8IU/L) with a p value of 0.27.

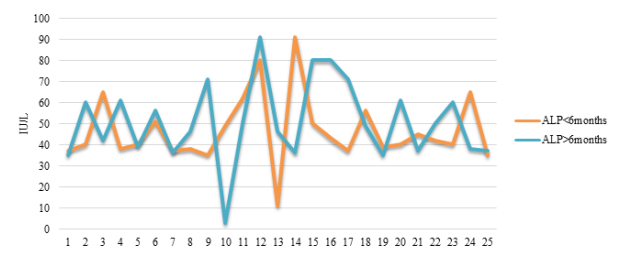

Figure 5: Statistical difference in ALP values in HIV patients on ART below and above 6 months.

Total Bilirubin (mg/dl)

Using the independent sample t test, there was a statistically significant difference between the means of TBil in patients on ART above 6 months (0.7mg/dl) and below 6 months (0.5mg/dl) with a p value of 0.02. It can as well be seen in Figure 6 below that patients who were on ART above 6 months had slightly elevated TBil values.

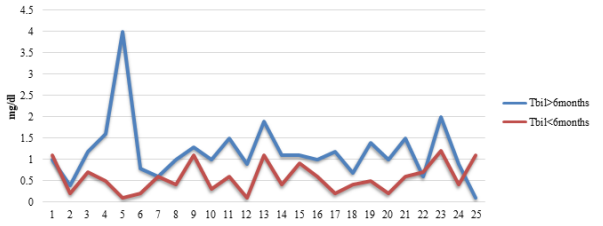

Figure 6: Statistical difference in TBil values in HIV patients on ART below and above 6 months.

Discussion

In 2004 Cameroon was still in the context of generalized HIV epidemic, with a prevalence of 5.5% of which 6.8% were women and 4,1% were men. Groups identified to have high risk behaviours included mostly men and women in uniform, commercial sex workers, truck drivers and populations living along the Chad – Cameroon pipeline project area. Youths around 20 years of age were found to be the most vulnerable. The major mode of transmission was through non – protected heterosexual activity, even if mother to child transmission remained a preoccupation [3]. These are reasons why the study population sample included only HIV positive individuals. Despite of the benefits of ART, it may come with adverse effects [3], hence the question of discontinuation or alteration of treatment may come to play [4].

According to Melashu, et al. [10] and Abongwa, et al. [11], Studies showed that the prevalence of liver enzyme elevation among HIV-positive individuals on ART ranged from 14 to 26.7% [10,11]. AST and ALT are frequently sensitive biomarkers of liver cell injury and are used for the detection of hepatocellular disorders. Different studies found that retroviral-infected patients on HAART had exhibited elevated levels of AST and ALT [12].

In this present study, there was a statistically significant difference between the means of ALT in patients on ART above 6 months (13.04IU/L) and below 6 months (9.59IU/L) with a p value of 0.011 compared to AST in which there was no statistically significant difference between the means of AST in patients on ART above 6 months (19.3IU/L) and below 6 months (16.01IU/L) with a p value of 0.33. This may be attributable to the direct acute inflammation of hepatocytes by HIV through apoptosis, mitochondrial dysfunction, and permeability alteration in the mitochondrial membrane that stimulates an inflammatory response [13,14], especially as majority of the patients with higher ALT values were just slightly above 6 months. This may be an explanation behind the acute liver damage that suggests no statistical difference in the mean AST/ALP and a statistical difference in the mean ALT values when the 2 groups of study are compared.

there was a statistically significant difference between the means of TBil in patients on ART above 6 months (0.7mg/dl) and below 6 months (0.5mg/dl) with a p value of 0.02. This does not fall in line with the observations of Kolgiri, et al. [15] who reported that the mean serum total bilirubin was moderately high in ART-naive HIV-positive patients than ART first-line and ART second-line HIV-positive patients. According to them, moderately high total bilirubin might act as an antioxidant agent against increased oxidative stress in ART-naive HIV-positive patients.

Conclusion

This study revealed a statistically significant differences in mean ALT and T.bil values in patients on ART below 6 months and those who had been on ART above 6 months on ART, except that for ALP and AST even though ALP/AST values were significantly higher in HIV participants on long term ART and short-term ART.

Acknowledgments

We wish to thank the Bamenda Regional Hospital authorities for granting us permission to carry out the work. Special thanks go to the patients who gave us the consent to work with them and on their samples.

Conflict of Interests

The authors declare that they have no competing interests

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