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Research Article

Effects of Anti-Retroviral Drugs on Liver and Kidney function among HIV Patients Attending Gitwe District Hospital

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Abstract

Background: About 35.3 million people were living with HIV and AIDS worldwide by 2012 up from 33.4 million in 2008 and more than 25 million have died since the first cases were reported in 1981. Sub-Saharan Africa is the worst affected region with an estimated 25 million people (70.8%) of the global total. The population of Sub-Saharan Africa accounts for only 11-12% of the world's population. 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 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. 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.

Aim: the present study aimed to assess the effects of anti-retroviral drugs on liver and kidney function among HIV patients at Gitwe District Hospital.

Methodology: The study used both cross-sectional and retrospective study. A total number of 118 patients participated in the study. Blood samples were examined to assess the effect of HAART on liver and kidney.

Results: Prevalence of abnormal liver and renal analytes in HAART treated were 42.4%.

Conclusion: The study recommended that Gitwe District Hospital and Ministry of Health should establish stringent measures in investigating and screening liver and renal dysfunction by taking blood samples for full hemogram. There are also needs for improvement of diagnostic ability of organs among patients on HAART by the health workers. Routine screening should be encouraged as a prophylactic measure.

Keywords: Anti-Retroviral Drugs, human immune-deficiency virus, Liver function, Kidney function.

INTRODUCTION

The advent of antiretroviral therapy (ART) has revolutionized the treatment of HIV infection, transforming it from a once-fatal diagnosis to a manageable chronic condition. ART has played an integral role in reducing the viral load, preventing the progression to acquired immunodeficiency syndrome (AIDS), improving immune function, and significantly extending the lifespan of those living with HIV. As of 2023, over 38 million people worldwide live with HIV, and ART remains the cornerstone of their care[1]. Despite the immense benefits of ART, it comes with a spectrum of side effects, with the potential for long-term toxicity, particularly affecting vital organs such as the liver and kidneys.

The liver and kidneys are central to the metabolism and elimination of drugs, including antiretrovirals (ARVs). These organs are tasked with processing these medications to render them active or inactive and facilitate their excretion from the body. Consequently, the liver and kidneys are particularly susceptible to drug-induced damage. Hepatotoxicity and nephrotoxicity, or liver and kidney toxicity respectively, are among the most common adverse effects reported in HIV patients undergoing ART, especially with long-term use. While newer ARV agents have improved efficacy

and safety profiles, toxicity remains a concern due to the lifelong nature of treatment.

The liver is the primary organ for drug metabolism, with the cytochrome P450 enzyme system playing a critical role in the biotransformation of various ARVs. Hepatotoxicity in HIV patients can manifest in multiple ways, ranging from asymptomatic liver enzyme elevations to severe liver failure. This issue is particularly significant in patients with pre-existing liver diseases, such as those co-infected with hepatitis B (HBV) or hepatitis C (HCV). ART drugs like non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs) are frequently associated with liver toxicity. For example, nevirapine, a widely used NNRTI, has been implicated in severe hepatotoxicity, leading to life-threatening liver failure in rare cases[2]. This risk is heightened in individuals co-infected with HBV or HCV, where chronic liver disease accelerates the progression of liver fibrosis and cirrhosis, contributing to increased mortality[3].

Mitochondrial toxicity, caused primarily by nucleoside reverse transcriptase inhibitors (NRTIs), is another significant mechanism through which ARVs exert toxic effects on the liver. NRTIs, particularly older agents such as stavudine and zidovudine, can impair mitochondrial DNA synthesis by inhibiting mitochondrial polymerase gamma. This inhibition leads to decreased energy production and an accumulation of toxic by-products, which manifest clinically as hepatic steatosis (fatty liver), lactic acidosis, and in severe cases, liver failure[4]. Although newer NRTIs like tenofovir and lamivudine have shown reduced mitochondrial toxicity, patients with underlying liver conditions remain vulnerable to hepatic complications.

The kidneys play a crucial role in the excretion of many ARVs, particularly nucleoside and nucleotide analogs like tenofovir disoproxil fumarate (TDF) and protease inhibitors. Prolonged exposure to ARVs can impair renal function, causing nephrotoxicity, which may manifest as acute kidney injury (AKI), chronic kidney disease (CKD), or tubular dysfunction. Tenofovir, a cornerstone in ART regimens, is well-known for its association with proximal tubular toxicity, leading to conditions such as Fanconi syndrome. This disorder is characterized by the loss of essential substances like phosphate, glucose, and amino acids in the urine, eventually resulting in bone demineralization and renal insufficiency[5]. Long-term use of TDF has been associated with a significant decline in glomerular filtration rate (GFR), increasing the risk of CKD and end-stage renal disease (ESRD) in susceptible populations[6].

Additionally, protease inhibitors like indinavir and atazanavir are linked to nephrolithiasis (kidney stones), which can further exacerbate renal impairment. Atazanavir, in particular, has been implicated in the formation of kidney stones due to its poor solubility, especially in the acidic environment of the renal tubules[7]. The crystallization of these drugs within the renal system can cause obstructive uropathy, leading to AKI. Recurrent episodes of AKI can eventually lead to CKD, posing long-term health risks for HIV patients.

The development of liver and kidney complications in HIV patients is often multifactorial. Co-morbidities such as diabetes, hypertension, and co-infection with HBV or HCV significantly increase the risk of organ dysfunction. For instance, co-infected patients are at a higher risk of developing advanced liver fibrosis and end-stage liver disease (ESLD) due to the combined effects of viral replication, immune activation, and drug toxicity[8]. Moreover, the effects of aging on liver and kidney function further complicate the clinical picture, as older HIV patients are more likely to develop drug-induced organ damage due to decreased organ resilience and the cumulative toxicity of lifelong ART use.

Aging itself introduces challenges, as HIV patients often experience premature aging of the liver and kidneys due to chronic immune activation and inflammation. The presence of metabolic disorders, such as diabetes and dyslipidemia, commonly observed in older HIV patients, further exacerbates the risk of organ damage. In addition, ART can interact with other medications used to treat these co-morbidities, increasing the likelihood of drug-drug interactions and adverse effects. Therefore, clinical management must consider the multifactorial nature of liver and kidney dysfunction in HIV patients on ART[9].

The effects of antiretroviral drugs on liver and kidney function in HIV patients present a complex challenge in the management of HIV infection. While ART has been life-saving for millions of people worldwide, its long-term use is associated with significant risks of hepatotoxicity and nephrotoxicity. Understanding the mechanisms by which ARVs cause liver and kidney damage, recognizing the factors that increase susceptibility to these complications, and implementing effective clinical management strategies are crucial to optimizing treatment outcomes. As the population of HIV patients continues to age and live longer lives, ongoing research and clinical vigilance will be essential to mitigating the adverse effects of ART on vital organ function. Therefore, this study aimed at assessing the effects of antiretroviral drugs on liver and kidney function in HIV patients at Gitwe District Hospital.

METHODOLOGY

Study area and design

This research was carried out in the Laboratory department of Gitwe District Hospital which is located in the South Province of Rwanda, Ruhango district. It was retrospective and cross-sectional study.

Study population and sample size

A total of 118 patients (47 males and 71females) referred in the laboratory of Gitwe District Hospital from ARV service for testing of creatinine and ALT were concerned during the study period.

Blood sample collection

For each study participant, 4 mL of venous blood was collected into labeled dried tube. The samples for ALT and creatinine test in biochemistry were tested and after 2 hours the results were released.

Data collection

As the data of this study were received retrospectively and cross-sectional, the retrospective data of this study were collected from the laboratory records data of ALT and creatinine in log book of biochemistry unite. In addition, the cross-sectional data of this study were collected through the laboratory diagnoses of ALT and Creatinine for ARVs. In cross-sectional study, the specimens were collected from patients under ARV on the basis of clinical criteria. Patients under ARV, each participating individual provided blood sample in dry tube then were centrifuged. Clear serum sample was obtained used for dosage of quantity of ALT and creatinine.

Data analysis

The data was recorded and analyzed using the statistical package for the social sciences (SPSS) software program. Descriptive statistics and chi-square test was used to determine associations where a *P*-value ≤0.05 was considered as statistically significant. Results were presented using words, tables and graphs.

RESULTS

Demographic characteristics of patients

The table below represents the demographic characteristics of patients who were recruited in the present study.

Table 1: Demographic characteristic of study participants

Participants					
Retrospective study (N=80)			**Cross-sectional study (N=38)**		**Total (%)**
Age group (Years)	**Female (%)**	**Male (%)**	**Female (%)**	**Male (%)**	
[0-20[	15(18.07)	10(12.5)	6(15.72)	4(10.5)	35 (29.6)
[20-40[	20(25.0)	3(3.7)	6(15.7)	8(21.1)	37(31.35)
[40-60[	13 (16.25)	7 (8.75)	5(13.3)	4(10.5)	29(24.6)
≥60	3(3.7)	9(11.5)	3 (4.69)	2(5.30)	17(14.4)
Total	**51 (43.2)**	**29 (24.5)**	**20 (16.90)**	**18 (15.25)**	**118 (100)**

Table 1 represents demographic characteristics of patients. Females were 43.2% and 16.9% retrospectively and cross-sectional study respectively; while males were 24.5% and 15.25% for retrospective and cross section study respectively.

Prevalence of abnormal liver and renal analytes in HAART treated

Table 2: Prevalence of Liver and kidney abnormality of study participants

			N=118	
		Frequency of patients	Prevalence	Total (%)
Retrospective	Creatinine	45	18(22.5)	25.4
	ALT	35	12(15.0)	
Cross sectional	Creatinine	21	13(34.2)	16.9
	ALT	17	7(18.4)	
Average prevalence	ALT and Creatinine	Positive	50	42.4
	ALT and Creatinine	Negative	68	57.6

Table 2 represents the prevalence of organs abnormalities. In general, the average prevalence of liver and kidney disease based on their corresponding analytes was found to be 42.4% while the average prevalence of patients with normal organs was 57.6%.

Prevalence of patients with both liver and kidney abnormal under HAART

Table 3: Prevalence of patients with both liver and kidney abnormal under HAART

Analytes	Population Frequency	Prevalence	Percentages
CREATININE	66	31	26.2
ALT	49	19	16.1
BOTH ALT and Creatinine	3	3	2.54
Total	118	50	42.4

Table 3 represents the Prevalence of patients with both liver and kidney abnormality under HAART based on the analytes results where patients with abnormal creatinine were 26.2%, those with abnormal ALT were 16.1 and those with both abnormal ALT and creatinine level were 2.54%.

DISCUSSION

Prevalence of abnormal liver and renal analytes in HAART treated

The emergence of highly active antiretroviral therapy (HAART) has dramatically improved quality of life in prolonging survival of human immunodeficiency virus (HIV)-infected patients on treatment in developed as well as developing countries. However, the main shortcoming of HAART in long-term use is its potential to cause liver and kidney derangements that may be life threatening. The drugs are actively accumulated in the proximal renal tubule resulting in functional disturbance with mitochondrial injury being one of the most important targets recognized[10].

Therefore, the aim of this study was to assess the adverse effects of HAART on kidney and liver functions among HIV-infected patients attending Gitwe District Hospital. A total of 118 study subjects were included in the study. Of these, 60.1% were females, Male were 39.8% and the overall prevalence of kidney and liver disease were 42.4% among the study populations. This is supported by the findings from two studies in Ghana and one in Cameroon by Kuehn,who got prevalence of toxicity of 30.0%, another similar study also reported that renal and liver dysfunction as a side effect of HAART that has been associated primarily with the parent tenofovir, which is accumulated in proximal renal tubule.

Furthermore, CKD is the major problem in HAART patients and can lead to loss of kidney function, leading to complications and kidney failure, and development of also the current research findings are in line with the study conducted in Ghana but lower than that in studies conducted in Nigeria and Burundi with CKD prevalence of 47.6% and 45.7% among HIV patients, respectively.

Prevalence of patients with both liver and kidney abnormal under HAART

In present study, patients who took HAART for more years have shown a strong association with CKD, which is supported by a previous study, that indicates longer duration of treatment as significantly associated with CKD. Furthermore, another cross-sectional study has demonstrated that subjects who took HAART for longer periods showed strong association with renal and liver dysfunction[11]. Different studies in sub-Saharan Africa reported that long-term infection with HIV is associated with a wide spectrum of renal diseases with variable prevalence of these diseases in HIV-infected patients: 6% in South Africa, 38% in Nigeria, 26% in Côte d'Ivoire, 28% in Tanzania, 25% in Kenya, 20%–48.5% in Uganda, and 33.5% in Zambia and Nigeria[12]. Results from these histopathological studies also suggested that broader spectrum of tissue damage in HIV-associated kidney disease, exists in the African population than was previously thought, whereas in our study it did not show significant association (95% CI=0.52–3.57). The reason might be that a majority of the participants took HAART for a lower duration in the category that we used to explain the results.

CONCLUSION

The emergence of highly active antiretroviral therapy (HAART) has dramatically improved quality of life in prolonging survival of human immunodeficiency virus (HIV)-infected patients on treatment in developed as well as developing countries. However, the main shortcoming of HAART in long-term use is its potential to cause liver and kidney derangements that may be life threatening. The drugs are actively accumulated in the proximal renal tubule resulting in functional disturbance with mitochondrial injury being one of the most important targets recognized. Therefore, the aim of this study was to assess the adverse effects of HAART on kidney and liver functions among HIV-infected patients Gitwe District Hospital. The prevalence of nephrotoxicity and hepatotoxicity were high among patients who took HAAR. Stage 3 nephrotoxicity and Grade 2 hepatotoxicity had the highest incidences of the total toxicities, and the female gender was a risk factor for nephrotoxicity.

There is need for more stringent measures in investigating and screening of renal and liver dysfunction among patients on HAART by taking blood samples for analytes Measurements. Corrective measures should then be instituted immediately. There is also need for improvement of diagnostic ability of liver and renal by the health workers. Routine iron supplementation should be encouraged as a prophylactic measure. Further prospective studies are

recommended to determine the effect of HAART and contributing factors

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