Burden and correlates of significant liver fibrosis among HIV-infected and uninfected adults in urban Uganda

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ABSTRACT

Introduction: Following chronic inflammation and other disease specific factors, the risk of liver disease is believed to be higher among HIV-infected patients than in the general population despite shared risk factors. Understanding this differentiated burden and its drivers will inform policy and priority populations for intervention.

Methods: This was a cross sectional study among 516 adults attending care clinics in Kampala Uganda. Significant liver fibrosis (SLF) was defined as liver stiffness measurement ≥7.2 KPa identified by Fibroscan®. Data analyses were stratified by HIV status and we performed logistic regression performed to identify correlates.

Results: The prevalence of SLF was higher among HIV un-infected patients ((24% Vs 14%; p0.004). Overall HIV-uninfected patients were more likely to be overweight and or obese, with elevated serum cholesterol levels. Elevated measurement of fatty change in the liver (CAP scores >248 dB/m) was associated with SLF among HIV un-infected patients (OR 2.3 CI (1.0-5.2); *p* = 0.046). Low nadir CD4 counts (200cell/mm3) was predictive of SLF among HIV-infected patients (OR 3.3 CI (1.0-10.7); *p* = 0.05).

Conclusion: The prevalence of SLF was unexpectedly higher among HIV un-infected than HIV affected patients attending care clinics in urban Uganda. This observed burden is most likely driven by non-alcoholic fatty liver disease (NAFLD) resulting from metabolic syndrome.

1. Background

Liver disease is fast becoming of global health importance especially in resource limited countries, where there is little data to describe this condition [1]. Among the general population, a systematic review demonstrated an increase in morbidity resulting from liver disease over a span of 27 years, culminating in an estimated 1.23 million deaths attributable to liver cirrhosis in 2017 [2]. Advancements in HIV care have improved the life span of people living with HIV/AIDS, reducing the incidence of most opportunistic infections thus reducing mortality due to AIDS related complications. This has however switched the morbidity and mortality in this patient population towards non-HIV associated factors including liver diseases [3]. Liver disease-related death is 10 times more prevalent among HIV-infected persons and is the second leading cause of death in this population. Despite evidence of this considerable burden both in HIV-infected and uninfected persons, efforts in the prevention of Non Communicable Diseases (NCDs) are focused mainly around the four major NCDs (heart disease, diabetes, chronic obstructive pulmonary disease and cancer) at the detriment of those suffering from other emerging NCDs such as liver disease. This is despite the fact that liver disease causes increasing proportion of disability adjusted life years, negatively impacting families, and communities economically [2].

Risk factors for liver disease are generally similar regardless of HIV status. Viral hepatitis B and C account for 80% of the global burden of liver disease [4]. With changes in lifestyle, NCD risk factors are increasingly accounting for a considerable proportion of liver disease. These include harmful use of alcohol, obesity which increases risk for altered lipid and glucose metabolism and insulin resistance [5,6]. Elevated serum lipid levels facilitate deposition of fat into the liver, increasing the risk for hepatosteatosis and non-alcoholic fatty liver disease (NAFLD) [7]. Other NCD risk factors include drug-induced liver disease and damage from other toxins such as tobacco and certain herbs [6,8,9]. Regardless of the similarity in risk factors, HIV infection may accelerate progression to chronic and complicated forms of liver disease [3]. For example, co-infection with viral hepatitis, increases risk of viral replication of both viruses as well as progression to chronic HBV/HCV infection [10]. In addition, long term HIV infection is associated with a chronic inflammatory state resulting from increased levels of pro-inflammatory cytokines that stimulate increased

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production of collagen tissue in the liver and through insulin resistance lead to elevated serum levels of glucose and lipids [11,12]. In addition, HIV infection of the enterocytes compromises gut mucosa integrity allowing portal circulation of bacterial bi-products (mainly lipo-polysaccharides) that stimulate production of inflammatory cytokines [13]. Certain classes of ART drugs may also injure the liver tissue via various mechanisms, including mitochondrial toxicity, steatosis, hypersensitivity reactions, dysglycaemia, insulin insensitivity and dyslipidemia [14–17].

Most literature on liver disease is derived from North American and European populations whose risk profile may differ considerably from other regions, including sub-Saharan Africa [18]. In order to address the projected growing burden of liver disease in sub Saharan Africa, it is important to understand the extent of liver disease and the contextual factors. We set out to compare the prevalence and factors associated with SLF among HIV-infected and HIV-uninfected adults attending out-patient care clinics at Mulago Hospital, Kampala Uganda.

2. Study methods

Study design and setting: We conducted a cross-sectional study between January 2015 and March 2020 involving 260 HIV-infected and 256 HIV-uninfected adults attending outpatient clinics within the National Referral Hospital in Kampala. The HIV-infected and HIV-uninfected patients were identified from the Adult Infectious Diseases Clinic (AIDC) and Ear Nose and Throat (ENT) outpatient clinics, respectively. The AIDC is a model center of excellence for the care and management of HIV-infected adults and is well described elsewhere [19,20]. The ENT clinic is government supported sub-specialized surgical out-patient clinic that receives stable patients seeking related services mainly as self-referrals as well as consultative referrals.

Ethical considerations: The study was conducted in accordance with the principles of the Declaration of Helsinki. The H2U study (the study from which the HIV-infected population was obtained) was approved by the School of Medicine Research Ethics Committee (SOMREC REF 2015-149), Uganda National Council of Science and Technology (UNCST) (HS 1984) and the John Hopkins School of Medicine Institutional Review Board (IRB 00086055). The study enrolling the HIV-negative participants was approved by the SOMREC (#REC REF 2017-165) and the UNCST (HS 1794 & ADM 154/212/01). Written informed consent was obtained from all study participants for study participation, sample storage and permission to review clinical records.

2.1. Study population

2.1.1. HIV-infected participant enrolment

We sampled our participants from already collected data for a prospective study, the HIV and Hepatocellular carcinoma in Uganda (H2U) at the AIDC, a study that aims to determine the prevalence and correlates of pre-malignant liver cirrhosis. Using a randomly generated computer list, we selected 260 HIV-infected study participants from a pool of 2000 participants in the H2U database. We included participants with complete records on liver stiffness measurement (LSM) done by Fibroscan®, information on relevant clinical study variables (use of alcohol, tobacco, herbs, hepatitis serology, liver chemistry) and availability of an adequate serum sample in storage.

2.1.2. HIV-uninfected participants

Using age and gender information from the HIV-infected participants, we enrolled the HIV-uninfected participants at the ENT clinic frequency-matched by gender and age group. We accessed the daily clinic register, identified and approached potential participants requesting initial consent to participate in the study and screen for HIV serology in accordance with the national guidelines [21]. Patients that tested HIV seronegative were then taken through a detailed informed consent process in the language of their preference. Adults who had no known history of chronic liver and heart disease were eligible to participate in the study. Pregnant women

and persons with implanted medical devices were excluded from participation due to the contraindication for elastography performance.

2.2. Study procedures

The data collection processes (interviews, phlebotomy and liver stiffness measurements) were identical for both HIV-infected and HIV-uninfected participants. Data collection for the HIV-infected participants was drawn from an existent database having previously been collected by the H2U study team, including blood samples placed in a repository. Data from the HIV-uninfected participants was actively collected.

Socio-demographic and clinical information: We designed a standardized questionnaire to collect similar information from both groups of participants from both clinics. This information included socio-demographic (age and gender); lifestyle habits (self-reported use of alcohol, tobacco and herbal medicines, consumption of fruits and vegetables).

Information for the HIV-infected participants was searched for and retrieved from the H2U database. At the ENT clinic, data was collected from participants using an interviewer administered questionnaire. HIV-infected participants' clinical information (ART drug use and duration, HIV viral load counts, nadir CD4 counts and anthropometric measurements) were obtained from H2U or AIDC database.

2.2.1. Physical measurements

(i) *Anthropometric information:* This included measurement of participant weight and height. All anthropometric measurements for both groups of participants were done using Seca 761 mechanical scale to the nearest 1 kg and a Seca Leicester stadiometer to the nearest 0.1 cm for weight and height respectively. BMI was calculated as weight (kg)/height (m)^2. Participant categorization using BMI was as follows; BMI ≤18.5 'underweight', BMI 18.5–24.9 'normal weight', BMI 25–29.9 'overweight' and BMI ≥30 'obese'.

(ii) *Transient Elastography:* Liver stiffness measurements (LSM) for participants from both clinics were done using Fibroscan® (Echosens, Paris France). The median result of ten Fibroscan® readings with the IQR <30% and accuracy of ≥60% was considered as the final result [22]. LSM for HIV-infected participants were retrieved from the H2U data base and LSM for non HIV-infected participants were measured at time of enrolment into the study. At the time of enrolment for the HIV-infected participants under the H2U study, the only available Fibroscan® probe was the M-probe and Fibroscan® software limited to LSM measurements. In contrast during the time of enrolment of the HIV-negative participants the Fibroscan® was upgraded to have both an M and XL probe and upgraded to include software for measurement of steatosis (CAP scores). The XL probe being suitable for LSM in persons with BMI ≥30 and the M-probe being suitable for persons with BMI less than 30. Significant liver fibrosis was defined as LSM ≥7.2 KPa and presence of steatosis was defined as CAP score ≥248 dB/m (indicating ≥11% fat accumulation in the liver to include stages S1–S3 of steatosis).

Blood sampling: For HIV-uninfected participants, phlebotomy was performed under aseptic technique and samples transported under suitable conditions within 4 h to the laboratory. Stored blood samples for the HIV-infected participants were retrieved for the purposes of conducting tests that were not conducted under the H2U study (lipid profile testing) and for tests done results were retrieved from the database (liver function tests, hepatitis serology and complete blood counts).

All blood testing was done at the Infectious Disease Institute, a CAP certified laboratory. Complete blood count was done using a Beckman Coulter AcT 5diff analyser and liver biochemistry was analysed using Hitachi Cobas C311. Hepatitis B serology was performed using an enzyme immunoassay (Monolisa HBsAg Ultra 3; Bio-Rad). Hepatitis C antibody testing was done using 3rd generation enzyme immunoassay (Bio-rad Monolisa Anti-HCV PLUS). Lipid profile analysis was done using the enzymatic colorimetric assay by the Cobas Integra 400 Plus.

Table 1
Baseline socio-demographic and clinical characteristics of HIV-infected participants stratified by study site.

Characteristic	HIV-uninfected participants	HIV-Infected Participants	Overall	P-value
	n (%)	n (%)	N (%)	
	256	260	516	
Gender				
Female	142(55.5)	145(55.8)	287(55.6)	0.95
Male	114(44.5)	115(44.2)	229(44.4)	
Mean age (years SD ±)	44.4(10.2)	44.9(10.3)	44.6(10.3)	0.58
Mean BMI (years SD ±)	26.7(10.6)	23.1(4.5)	24.9(8.3)	<0.001
Consume fruits	206(49)	214(51)	420(82)	0.654
Consume vegetables	219(50)	216(50)	435(85)	0.435
Alcohol consumption				
No	144(56.3)	154(59.2)	298(57.7)	0.49
Yes	112(43.7)	106(40.8)	218(42.3)	
Ever used tobacco products				
No	212(82.8)	220(84.6)	432(83.7)	0.58
Yes	44(17.2)	40(15.4)	84(16.3)	
Ever used herbal medicines				
No	171(66.8)	195(75.0)	366(70.9)	**0.04**
Yes	85(33.2)	65(25.0)	150(29.1)	
HBsAg				
Negative	249(97.3)	224(86.1)	473(91.7)	**<0.001**
Positive	7(2.7)	36(13.9)	43(8.3)	
HCV antibody				
Negative	248(96.9)	253(97.3)	501(97.1)	0.77
Positive	8(3.1)	7(2.7)	15(2.9)	
Median ALT (IQR)	17 (13–24)	20(14–26)	18(14–26)	**0.001**
Normal range (0-35)U/L				
Median AST (IQR)	21(17–26)	23(18–29)	22(18–27)	0.08
Normal range (0 − 32)U/L				
Median GGT (IQR)	24.8 (17.6–42.3)	44.1(24.5–74.3)	32.3(19.3–54.7)	**<0.001**
Normal range (0-40)U/L				
Median PLT (IQR)	253 (212–290.5)	243.5 (198.5–292.5)	250(20.5–291)	0.50
Median TC (IQR)	175.5 (159.3–200.3)	162.1 (132.6–190.1)	172.8 (146.9–195.8)	**<0.001**
Median LDL-C (IQR)	102(87–122.2)	96(69.6–112.3)	98(77.3–119.6)	**<0.001**
Median TG (IQR)	117.7 (85.5–164.3)	118.6 (83.1–160.3)	117.7 (84.4–161.4)	0.53
Median HDL-C (IQR)	46.6 (40.2–55.9)	39.7 (31.1–48.1)	44.2 (34.8–52.6)	**<0.001**
Detectable HIV RNA (≥1000copies/ml)				
Suppressed		194(74.6)		
Detectable		5(1.9)		
Missing		61(23.5)		
Nadir CD4 Count				
<200cells/mm^3		127(49)		
≥ 200 cells/mm^3		45(17)		
Missing		88(34)		
Duration on ART				
<10 years		43(17)		
≥ 10 years		156(60)		
Missing		61(23)		
Steatosis				
<248 dB/m	115(45)			
≥ 248 dB/m	58(23)			
Missing	83(32)			
Liver fibrosis				
No	194(75.8)	223(85.8)	417(80.8)	**0.004**
Yes	62(24.2)	37(14.2)	99(19.2)	

Cut-off values for the different lipid parameters representative of dyslipidemia were as follows; total cholesterol (TC) >5.2 mmol/l, triglycerides (TG) >2.3 mmol/l, low density lipoproteins (LDL-C) >3.4 mmol/l and high density lipo-proteins (HDL—C) <1.04 mmol/l-male, <1.3 mmol/l-female. To evaluate for hepatic toxicity, we applied the AIDS Clinical Trials Group (ACTG) classification for hepatic toxicity using the serum ALT level increase from the upper limit of normal (ULN) as elaborated; grade 0 1.25 × ULN; grade 1 1.25–2.5 × ULN; grade 2 2.6–5 × ULN; grade 3 5.1–10 × ULN and grade 4 > 10 × ULN [23,24].

2.3. Data analyses

Based on differences in the distribution of some risk factors for liver fibrosis by HIV status, findings on testing for interaction, the discriminate opportunity to apply certain testing (CAP measures) to one study population, we conducted stratified analyses [25,26]. To control for gender as an effect modifier it was included in the model as a variable. Significant liver fibrosis was categorized as binary outcome defined as LSM >7.1 KPa, a cutoff similar to prior studies for purposes of comparison and also in correspondence to stage ≥ F2 METAVIR staging for liver fibrosis [27]. In describing participant characteristics, continuous variables were summarized as means and medians and categorical variables were summarized as proportions. For comparison of characteristics between the two groups, continuous data were compared using *t*-test for means, Wilcoxon rank-sum test for medians and chi square test for proportions. In univariate analysis, all factors with *p*-value ≤ 0.2 were included in the final model. Factors at univariate analysis with p-value >0.2, but which in prior literature have been shown to impact or influence the development of liver fibrosis were retained in the final model (gender, use of alcohol, viral hepatitis).

To determine correlates of SLF, logistic regression was performed with estimation of odds ratios (OR) and 95% confidence intervals (CI) and variables with a *p*-value ≤ 0.05 were considered statistically significant. Analyses were performed using STATA 16 statistical package.

3. Results

We enrolled a total of 516 adults into the study, 56% were female and the mean age was 44 years. The HIV un-infected participants had higher body mass indices, higher serum TC and LDL-C levels. The HIV infected participants had almost seven times higher prevalence of chronic hepatitis B infection, elevated liver transaminases and lower serum levels HDL—C. Majority of the HIV infected participants had undetectable HIV viral load (75%), were on ART for more than 10 years (60%) and had history of severe immunosuppression at the start of therapy (49%) (Table 1).

The prevalence of SLF among the HIV-uninfected participants was higher than that among HIV-infected participants (24% Vs 14%; p0.004) (Table 1). Among the HIV-infected participants, those with increasing platelet count and current fruit consumption had a lower possibility of SLF with an odds ratio of 0.9 (CI 141 (0.98–0.99); p0.013) and 0.3 (CI (0.09–0.79); p0.018) respectively. HIV infected participants with CD4 counts less than 200cells/mm3 (OR 3.2 CI (1.00–10.47); p0.05) at start of ART and increasing serum gamma glutamyl transferase (GGT) levels (OR 1.0 CI (1.00–1.01); p0.049) were more likely to have SLF respectively (Table 2).

Among the HIV-uninfected participants, those who consumed vegetables (OR 0.3 CI (0.11–0.90); p0.032) were less likely to have SLF. Participants with CAP scores>248 dB/m (≥11% of fat infiltration in the liver) had two times the odds of having SLF (OR 2.3 CI (1.01–5.17); p0.046) (Table 3).

4. Discussion

Our study found that SLF was more prevalent among HIV-uninfected adults compared to their HIV-infected counterparts (24% Vs 14%; p-0.004). This finding is contrary to most existing literature that suggests HIV-infected persons are at higher risk of SLF and even differs from findings of a recent study conducted in rural Uganda (HIV-infected Vs HIV-uninfected 17% Vs11%) [27]. From literature, viral hepatitis accounts for a significant proportion of liver disease globally [6]. In our study the HIV-infected patients despite having a higher prevalence of chronic hepatitis B infection (12% Vs 3%; *p* < 0.001) had less individuals with SLF. In the last 2 decades of HIV management in Uganda, there has been introduction of better treatment guidelines and use of more efficacious ART regimens that have antiviral activity against HBV infection as well. Since over 90% of our HIV-infected patients were ART experienced (majority on tenofovir and lamuvide based regimens), it is likely that this provided long term HBV therapy, reducing risk for HBV disease progression and possibly reversing fibrosis in some HIV/HBV co-infected patients. In addition, other studies have demonstrated that patients on long term ART use more likely suppress the pro-fibrotic effect of uncontrolled HIV infection on the liver [28]. The finding of a higher prevalence of SLF with lower HBV prevalence among the HIV-uninfected patients would possibly suggest that for each equivalent age and gender, HIV-uninfected patients may have other comorbidities that account for this burden and these may be missed diagnoses and or poorly managed conditions in comparison to HIV-infected patients in regular care.

HIV-uninfected persons may not have similar opportunities to interface regularly with health providers especially for wellness and maintenance of good health. They often present at stages of established and or complicated disease since most of the early symptoms of disease are often silent. For example, in our study we found that HIV-uninfected patients were more likely to have higher BMI and higher serum levels of both total and low density

Table 2
Factors associated with significant liver fibrosis among HIV-infected persons attending AIDC clinic at Mulago National Referral Hospital.

Characteristic	Unadjusted model			Adjusted model		
	Odds Ratio	[95% Conf. Interval]	P > z	Odds Ratio	[95% Conf. Interval]	P > z
Gender						
Male	1.6	0.8–3.1	0.21	0.5	0.16–1.49	0.207
Age	1.0	0.97–1.03	0.819			
Body mass Index						
Underweight	0.4	0.1–2.0	0.294			
Overweight	1.0	0.5–2.2	0.953			
Lifestyle characteristics						
Ever consumed alcohol	1.3	0.64–2.59	0.477	0.6	0.21–1.92	0.419
Ever consumed tobacco	1.4	0.55–3.37	0.501			
Used herbal medicine in last year	0.9	0.44–2.21	0.965			
Currently consumes fruits	0.4	0.20–0.99	**0.048**	0.4	0.20–0.99	**0.048**
Currently consumes vegetables	0.9	0.36–2.13	0.763			
Clinical characteristics						
HBSAg positive	1.6	0.64–3.97	0.319	1.1	0.26–4.95	0.16
HCV antibody test positive	1.0	0.11–8.32	0.979			
Hepatotoxicity present	3.1	1.09–8.66	**0.034**	0.5	0.03–6.07	0.548
Serum alanine transferase level (U/L)	1.0	1.00–1.04	**0.013**	1.0	0.97–1.07	0.430
Serum aspartate transferase level (U/L)	1.0	1.01–1.05	**0.011**	1.0	0.98–1.05	0.602
Serum GGT level	1.0	1.00–1.00	**0.015**	1.0	1.00–1.01	**0.030**
Platelet count	1.0	0.98–0.99	**0.027**	1.0	0.98–0.99	**0.015**
Serum total cholesterol level	1.0	0.99–1.00	**0.074**			
Serum LDL level	1.0	0.98–1.00	0.126	1.0	0.99–1.05	0.187
Serum triglyceride level	1.0	0.99–1.00	0.983			
Serum HDL level	1	0.97–1.01	0.725			
Atherogenic risk (log10 triglceride/HDL)						
Present	1.9	0.59–6.25	0.278	3.5	0.48–25.97	0.215
ART related variables						
cART use	0.5	0.22–1.29	0.163	0.5	0.14–2.04	0.355
Low nadir CD4count (<200cells/mm3)	2.5	1.00–6.03	**0.048**	3.3	1.00–10.71	**0.050**
Detectable HIV RNA (>1000copies/mm3)	4.3	0.67–26.54	0.124	7.7	0.73–81.75	0.09

Table 3

Factors associated with significant liver fibrosis among HIV-uninfected participants attending OPD clinics at Mulago National Referral Hospital.

Characteristic	Unadjusted model			Adjusted model		
	Odds Ratio	[95% Conf. Interval]	P > z	Odds Ratio	[95% Conf. Interval]	P > z
Gender						
Male	1.2	0.69–2.18	0.483	1	0.43–2.14	0.912
Age	1.0	0.97–1.03	0.892			
Body mass Index						
Underweight	1.6	0.33–8.05	0.538			
Overweight	1.3	0.27–6.39	0.738			
Lifestyle characteristics						
Ever consumed alcohol	1	0.56–1.76	0.971	0.5	0.22–1.17	0.111
Ever consumed tobacco	0.9	0.42–1.96	0.800			
Used herbal medicine in last year	1.1	0.63–2.09	0.661			
Currently consumes fruits	0.4	0.19–0.74	**0.004**	0.7	0.22–1.74	0.365
Currently consumes vegetables	0.3	0.15–0.63	**0.001**	0.3	0.11–0.90	**0.032**
Clinical characteristics						
HBSAg positive						
HCV antibody test positive	0.4	0.05–3.59	0.438			
Hepatotoxicity present	2.6	0.68–10.03	0.163	5.8	5.22–64.45	0.152
Serum alanine transferase level (U/L)	1	0.98–1.03	0.597			
Serum aspartate transferase level (U/L)	1	0.99–1.03	0.162	1.0	0.98–1.02	0.842
Serum GGT level	1	0.99–1.00	0.477			
Platelet count	1	0.99–1.00	0.863			
Serum total cholesterol level	1	0.99–1.00	0.317			
Serum LDL level	1	0.98–1.00	0.102	1.0	0.98–1.00	0.100
Serum triglyceride level	1	0.99–1.00	0.629			
Serum HDL level	1	0.99–1.03	0.206	1.0	0.99–1.05	0.271
Atherogenic risk (log10 triglceride/HDL)						
Present	1	0.21–5.31	0.958			
Cap Score						
≥248 dB/m	1.8	0.84–3.64	0.133	2.3	1.01–5.17	**0.046**

cholesterol, common NCD risk factors that are modifiable. High BMI and elevated serum lipids are constituents for metabolic syndrome, which is a risk factor for NAFLD which when poorly managed progresses to liver fibrosis [29,30]. In our study we found that HIV-uninfected patients with steatosis on elastography (which is the hallmark of NAFLD) had two time the odds (OR 2.3 CI (1.01–5.17); p0.046) of having SLF. HIV-infected patients are more likely to interface with health care givers as they are expected to make regular follow-up visits at care clinics. This increases their chances for continuous screening for common ailments (including screening for obesity and related complications) and counseling on prevention of the same.

The findings of our study seem to suggest that the consumption of fruits and vegetables have a protective effect against significant liver fibrosis. We found that among HIV-infected patients who consumed fruit had 0.2 times the odds of presenting with SLF (OR 0.2 CI (0.08–0.73); p0.012) and HIV-uninfected patients who consumed vegetables had 0.3 times the odds of presenting with SLF (OR 0.3 CI (0.1–0.9); p0.036). Studies conducted among persons with NAFLD have shown that healthy diet (including fruits and vegetables) independent of physical exercise, lowers risk of liver fibrosis [31]. A typical Ugandan diet is often very starchy, the proportion of vegetables on the plate is low in comparison to other food groups and fruits are rarely eaten and often left for children. Studies done on nutrition in Uganda have identified several factors that hinder consumption of healthier foods such as certain foods not being in constant supply because of seasonality (plant based foods and vegetables), expense coupled with low income, ignorance of what healthy foods are and quantities in which they should be consumed and transition to fast foods often fried for convenience and time saving. In addition, for persons engaged in the growing and or raring of most of these food products, priority is given to the selling of the same to generate income and not for home consumption [32,33].

In our study among HIV-infected participants we found that those who had a CD4 count of less than 200cells/mm3 at initiation of ART (OR 3.2 CI (1.00–10.47); p0.05) and increasing serum GGT level (OR 1.0 CI (1.00–1.01); p0.049) had higher odds of having SLF. This finding is similar to other studies that have shown that a low absolute CD4 cell count is an independent risk factor for liver disease progression among HIV-infected patients [34]. Persons with a detectable HIV viral load had almost eight times the odds of having SLF; however, this was not statistical significant and could be explained by the low numbers in this cell. However, other this is an agreement with other studies done among HIV-infected persons have shown that detectable HIV virus is a risk factor for progression of liver fibrosis [34].

Our study had some limitations. We were not able to measure the CAP score on participants with HIV infection. The machine that had capacity to perform this score came after these patients were already recruited. We also had a considerable proportion of HIV-infected participants with a missing HIV viral load result. However, this study demonstrated the risk factors for hepatic fibrosis in the 2 population groups highlighting the role of certain non-infectious risk factors in the current burden of observed SLF.

Key finding: The burden of SLF appears to be higher among HIV-uninfected adults in contrast to previous literature and may be driven mainly by NAFLD. HIV-infected patients with a nadir CD4count less than 200 cells/mm3 and uncontrolled HIV infection are more likely to present with SLF.

Recommendation: We recommend that the screening of SLF be inculcated into usual practice in the care of both HIV-infected and uninfected individuals. Among the HIV-infected persons' specific focus should be placed towards those that started ART at very low CD4 counts and have uncontrolled HIV infection. HIV un-infected persons that are overweight or obese, with elevated serum cholesterol levels and evidence of NAFLD should be the primary target for screening of SLF. We also recommend for more advocacy in creating awareness of the impact of NCD risk factors (dietary and weight control) that are largely modifiable and advocate for the adoption of better lifestyle choices.

Declaration of Competing Interest

None declared.

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