Vol. 10(6), pp. 83-95, October 2018
DOI: 10.5897/JAHR2018.0463
Article Number: 2113EBE59001
ISSN 2141-2359

http://www.academicjournals.org/JAHR

ACADEMIC JOURNALS
expand your knowledge

Journal of AIDS and HIV Research

Full Length Research Paper

Correlation of hepatobiliary ultrasonographic findings with cd4cell count and liver enzymes in adult hiv/aids patients in Jos

A. Angbalaga[1], C. C. Ani[1], D. Atsukwei[2], E. D. Eze[3*], A. M. Afodun[4], E. O. Igoh[1], S. C. Owoeye[1] and C. B. Ukaonu[1]

[1]Department of Radiology, Faculty of Medical Sciences, Jos University Teaching Hospital, Jos, Nigeria.
[2]Department of Radiology, Federal Medical Centre, Keffi, Nasarawa State, Nigeria.
[3]Department of Physiology, Faculty of Biomedical Sciences, Kampala International University, Western Campus, Ishaka-Bushenyi, Uganda.
[4]Department of Anatomy, Faculty of Biomedical Sciences, Kampala International University, Western Campus, Ishaka-Bushenyi, Uganda.

Received 8 April, 2018; Accepted 4 October, 2018

Hepatobiliary diseases occur commonly in patients with Human immunodeficiency virus (HIV) infection and are now the commonest cause of death in HIV positive patients on antiretroviral therapy (ART) in western countries. The hepatobiliary manifestations of AIDS are related to the levels of CD_4^+ count as well as liver enzymes. Abdominal ultrasound examination is easy to perform, non-invasive, inexpensive, readily available and provides valuable information about hepatobiliary findings in AIDS. The study was to evaluate hepatobiliary sonographic findings in HIV/AIDS adult patients and correlate with their CD_4^+ count and abnormal liver enzymes (ALP, ALT and AST) in Jos, Plateau State, Nigeria. A cross-sectional study of hepatobiliary ultrasound findings of 410 adult patients with HIV/AIDS was carried out over a period of six months. Two hundred and sixteen (52.7%) of the patients had normal hepatobiliary ultrasound findings while 194 (47.3%) patients had various abnormalities. The common abnormalities seen include enlarged gallbladder in 33.5%, increased liver parenchymal echogenicity in 26.3%, hepatomegaly in 23.7%, and thickened gallbladder wall in 7.8% patients. Other findings included gallbladder sludge and gall stone in 6.6 and 2.1% respectively. These findings correlated significantly with the patients' CD_4^+ count and liver enzymes (ALT, AST and ALP) with p value < 0.05 in both. Ultrasonography as a baseline imaging modality in HIV/AIDS patients, together with CD_4^+ count and liver enzymes are useful in the assessment of the disease state, monitoring of therapy and management of these patients.

Key words: Hepatobiliary ultrasonography, adult patients, CD4 cell count, HIV/AIDS, liver enzymes.

INTRODUCTION

Human immune deficiency virus (HIV) is a retrovirus that stores its genetic material as ribonucleic acid (RNA). Two strains of HIV are known to infect humans; HIV-1 and HIV-2. HIV-1 is by far the most common pathogen worldwide (Sebastian, 2002; Obajimi et al., 2008). In 2013, it was estimated that the number of people living

with HIV worldwide were more than 35 million; 70% of these individuals were in sub-Saharan Africa were in sub-Saharan Africa and the majority (61%) were women. Southern Africa is the worst affected region with the adult HIV prevalence exceeding 17.3% in eight southern African countries in 2011 (Igbinedion et al., 2009; Global Fact sheet, 2012; Worldwide AIDS and HIV statistics, 2011). The individuals who require antiretroviral therapy (ART) may not have access to it in sub-Saharan Africa thus worsening the morbidity and mortality. The prevalence of HIV infection in Plateau state is 4.9% while North Central Nigeria has the highest prevalence of 6.1%, the National prevalence is 4.4% (World Bank Nigeria Report, 2008; Federal Ministry of Health, 2005). Liver enzymes [alanine/aspartate transaminases (ALT/AST), and alkaline phosphatase (ALP)] abnormalities have been shown to be common in HIV/AIDS patients, probably due to direct inflammation induced by HIV virus on the liver cells and gall bladder or by other opportunistic agents (Ejilemele et al., 2007). Hepatobiliary disease is an increasingly important cause of morbidity and mortality in patients with HIV/AIDS (Gore et al., 1998). With the availability of highly active anti-retroviral therapy (HAART), there has been an observable change in the pattern of liver disease in these patients (Goldin et al., 2002). Although opportunistic infections and neoplasm are still seen, co-infection with hepatitis viruses, especially HCV, is now emerging as the most significant cause of liver disease in this group of patients (Guardaat el., 1983). In addition, drug-induced liver damage is becoming more prevalent due to the increased complexity and toxicity of the HAART regimens used (Goldin et al., 2002). Biliary disorders seen in AIDS patients can be classified into AIDS cholangiopathy (AC), acalculous cholecystitis (ACC) and non-HIV associated disease such as gallstones (Flum at el., 1997). Gallstone disease is the most commonly observed cause of acute cholecystitis in this population (Flum at el., 1997). While HIV related biliary disorders are rare, they are associated with significant morbidity when they occur. AC and ACC were first reported in 1983 by Guarda and Pitlik respectively (Guarda et al., 1983; Pitlik et al., 1983). The two diseases can occur concurrently with opportunistic infections. Bile ducts in AIDS patients appear to be uniquely susceptible to opportunistic infections (Enns et al., 2003). Since the advent of highly active antiretroviral therapy (HAART), the incidence of AIDS associated biliary disorders have been steeply declining (O'Hara et al., 2009; Ko et al., 2003). Distinct hepatobiliary sonographic findings have been reported in these patients and include hepatomegaly, altered liver echotexture, gall bladder sludge, gall bladder wall thickening, gallstones, AIDS Cholangitis and periportal lymphadenopathy (Pawar et al., 2013). CD_4 cell count is one of the baseline measurements and an important parameter used in the assessment of AIDS progression and follow-up of AIDS patients. CD_4 cell depletion in HIV-infected patients results from ongoing viral replication. Hepatobiliary diseases were initially thought to be associated with advanced immunosuppression (CD_4 cell counts < 200 cells/microlitre), but it was later recognized that the lesions associated with the disease can occur at any stage of HIV-1 infection, even before antibody seroconversion (Herman et al., 2003). The relationship of hepatobiliary sonographic findings with CD_4 cell count and liver enzymes has not been well exploited in this environment.

METHODOLOGY

Study design, period and setting

This was a hospital based cross-sectional study that spanned over the period of six months from November 2015 to April 2016 in the Department of Radiology, Jos University Teaching Hospital (JUTH), a tertiary health institution situated in the central part of Jos, Nigeria.

JUTH is one of the teaching hospitals in the North-Central Zone of Nigeria. The hospital provides medical and surgical care, gynaecology and obstetrics services along with radiology, emergency services and an outpatient clinic to the population of the city and neighboring states of Bauchi, Gombe, Benue, Kogi, Nasarawa, Taraba, Adamawa and parts of Kaduna State. The hospital has an outpatient daily clinic (Clinic II) for HIV/AIDS management.

Ethical approval and consent to participate

Ethical clearance was obtained from the Research and Ethical Committee of Jos University Teaching Hospital, Jos, Nigeria dated 27th March 2015 with authorization: JUTH/DCS/ADM/127/XIX/6074. In addition, informed consent was obtained from each enrolled participant.

Target population/study participants

The study population comprised patients aged 18 years and above confirmed with HIV who were referred for abdominal ultrasound scan from Clinic II located within the Jos University Teaching Hospital complex. Clinic II is a specialized clinic exclusively for the management of HIV/AIDS patient.

Study inclusion criteria

Participants in this study were those patients aged 18 years and above confirmed with HIV infection. Participants were selected

*Corresponding author. E-mail: daneze4@gmail.com.

Table 1. Demographic characteristics of HIV/AIDS patients in Jos.

Variables	Gender			χ^2/t-test	P
	Male (%)	Female (%)	Total (%)		
Age group					
≤30	26(18.6)	82(30.4)	108(26.3)	29.96	0.001
31-40	29(20.7)	100(37.0)	129(31.5)		
41-50	51(36.4)	53(19.6)	104(25.4)		
>50	34(24.3)	35(13.0)	69(16.8)		
Total	140(100)	270(100)	410(100)		
Mean age± SD	42.84±11.29	37.59±10.57	39.38±11.09	4.659	0.001

being informed of the nature of the study, the potential benefits and safety of the procedure, as well as the voluntary nature of the participation.

Study exclusion criteria

Participants who were pregnant HIV positive patients, HIV positive adults with confirmed co-infection with Hepatitis A, B or C viruses and HIV positive adults with co-existing medical conditions such as Diabetes mellitus, sickle cell disease and hypertension were excluded from the study.

Data collection procedure and analyses

Patients were prepared by asking them to fast for 6 to 8 h to reduce bowel gas and ensure gallbladder distension. Blood pressures were measured using a standard mercury sphygmomanometer to exclude hypertensive patients from the study. Western Blot and CD_4^+ results were obtained from patients' case files. All the patients were on Highly Active Antiretroviral Therapy (HAART). The time between CD_4^+ count and ultrasound findings were less or equal to six months. Five millilitres (5 ml) of blood sample was collected from each patient using a new syringe into a clean dry glass test tube and centrifuged to obtain the serum. This serum was analysed for liver enzymes (ALT, AST and ALP) by enzymatic method using spectrophotometer. The ultrasound scan examination was performed using a high resolution real time ultrasound scanner (ALOKA SSD-3500, Co. Ltd., Tokyo, Japan, 2007) equipped with 3.5 MHz curvilinear transducer and Doppler facility. Ultrasound scan is operator dependent; therefore, all scanning and measurements were done only by the researcher in order to minimize inter-observer error. All measurements were taken twice to reduce intra observer variability. The liver, gallbladder and biliary ducts were then examined sonographically using standard ultrasound scanning procedures.

Data preparation, management and analysis

At the end of the examinations, the hepatobiliary ultrasonographic findings and the data obtained were entered into a computer and processed using SPSS for window version 20.0 (Microsoft® Inc. Chicago, Illinois, USA. 2011). Mean ± standard deviation was used to summarize variables. The variables were tested for correlation via the Chi- square test, students' test and cross tabulations. P value of 0.05 or less was considered statistically significant.

RESULTS

Sex and age variables

A total of 410 HIV positive patients, who met the inclusion criteria were studied. This comprised 140 males (34.15%) and 270 females (65.85%) with male to female ratio of approximately 1:2. Majority of the male patients were within age range 41-50 years while most female patients presented at an earlier age range of 31-40 years. The mean age was significantly higher in males than females (Table 1).

CD4 count and liver enzymes analyses

The frequency of patients reduced with increasing severity of disease and decreasing CD_4^+ count from 47.6% for 'not significant' (≥500 cell/microlitre) to 9.3% for 'severe' (<200 cell/microlitre) CD_4^+count (Table 2). The result showed 69.8% of patients had normal serum ALT; while 30.2% had various degrees of elevated ALT. The highest abnormal frequency for ALT was seen in Grade 1 (19.8%) and the lowest (1.5%) in grade 3 (Table 2). Most patients (51.7%) had normal serum AST while 48.3% had abnormal levels of serum AST. The highest abnormal frequency for AST was also seen in Grade 1 (22.2%) and the lowest (1.5%) in grade 3 out of this 22.2% was seen in grade 1 (Table 2). Majority of patients (60.5%) had various grades of abnormal ALP with the highest abnormality seen in Grade 0 (32.4%) and the lowest in Grade 2 (2.5%) (Table 2). No patient had Grade 3 ALP abnormality.

Age and CD4 count analysis

The CD_4^+ count decreased with increasing age in all CD_4 classification groups, except for age range 31-40 years and >50years which showed no specific trend with CD_4^+count. There was significant negative correlation between age and CD_4^+ count (P=0.001) (Table 3).

Table 2. Distribution of patients in relation to CD_4^+ count and liver enzymes.

CD4+ count and liver enzymes	Frequency	Percentage
CD4+ classification		
Not significant(≥500)	195	47.6
Mild(350-499)	106	25.8
Advanced (200-349)	71	17.3
Severe(<200)	38	9.3
Total	410	100
ALT grade (IU/L)		
Normal (≤40IU/L)	286	69.8
0(<1.25 times ULN)	30	7.2
1(1.25-2.25 times ULN)	81	19.8
2(>2.25-5 times ULN)	7	1.7
3(>5.0-10 times ULN)	6	1.5
Total	410	100
AST grade (IU/L)		
Normal (≤40IU/L)	212	51.7
0(<1.25 times ULN)	80	19.5
1(1.25-2.25 times ULN)	91	22.2
2(>2.25-5 times ULN)	21	5.1
3(>5.0-10 times ULN)	6	1.5
Total	410	100
ALP grade (IU/L)		
Normal (21-92IU/L)	162	39.5
0(<1.25 times ULN)	133	32.4
1(1.25-2.25 times ULN)	105	25.6
2(>2.25-5 times ULN)	10	2.5
3(>5.0-10 times ULN)	-	-
Total	410	100

ULN = Upper Limit of Normal; ALT = Alanine Transaminase; AST = Aspartate Transaminase; ALP = Alkaline Phosphatase.

Table 3. Relationship between age and CD_4^+ count of HIV/AIDS patients frequency (%).

Age group (years)	CD_4^+ classification				Total
	Not significant	Mild	Advanced	Severe	
≤30	67(62.0)	18(16.7)	15(13.9)	8(7.4)	108(100)
31-40	43(33.3)	52(40.3)	23(17.8)	11(8.6)	129(100)
41-50	53(51.0)	24(23.2)	13(22.1)	4(3.8)	104(100)
>50	32(46.3)	2(17.4)	10(14.5)	15(21.7)	69(100)
Total	195(47.6)	106(25.9)	71(17.3)	38(9.3)	410(100)

$\chi^2 = 44.507$, df = 9, P = 0.001.

Sex and CD4 count analysis

For both genders, the frequency of patients reduced with increasing severity of disease and decreasing CD_4^+ count. Most of the patients (47.6%) were in the 'not significant' disease group (Table 4).

Table 4. Relationship between gender and CD_4^+ count of HIV/AIDS patients frequency (%).

CD_4^+ classification (cell/microlitre)	Gender		Total
	Male	Female	
Not significant(≥500)	54(38.6)	141(52.2)	195(47.6)
Mild(350-499)	38(27.1)	68(25.2)	106(25.8)
Advanced (200-349)	37(26.4)	34(12.6)	71(17.3)
Severe(<200)	11(7.9)	27(10.0)	38(9.3)
Total	140(100)	270(100)	410(100)

Table 5. Relationship between age and Liver enzymes of HIV/AIDS patients.

Liver enzymes	Age (years)					χ^2	Df	P
	≤30	31-40	41-50	>50	Total			
ALT grade								
Normal	69(63.9)	96(74.4)	71(68.3)	50(72.5)	286(69.8)	20.248	12	0.063
0	4(3.6)	12(9.3)	8(7.7)	6(8.7)	30(7.3)			
1	29(26.9)	21(16.3)	18(17.3)	13(18.8)	81(19.8)			
2	3(2.8)	0(0.0)	4(3.8)	0(0.0)	7(1.7)			
3	3(2.8)	0(0.0)	3(2.9)	0(0.0)	6(1.5)			
Total	108(100)	129(100)	104(100)	69(100)	410(100)			
AST grade								
Normal	66(61.1)	64(49.6)	51(49.0)	31(44.9)	212(51.7)	21.324	12	0.018
0	17(15.7)	19(14.7)	21(20.2)	23(33.3)	80(19.5)			
1	19(17.6)	38(29.5)	22(21.2)	12(17.4)	91(22.2)			
2	3(2.8)	8(6.2)	7(6.7)	3(4.4)	21(5.1)			
3	3(2.8)	0(0.0)	3(2.9)	0(0.0)	6(1.5)			
Total	108(100)	129(100)	104(100)	69(100)	410(100)			
ALP grade								
Normal	46(42.6)	52(40.3)	42(40.4)	22(31.9)	162(39.6)			
0	36(33.3)	39(30.2)	35(33.7)	23(33.3)	133(32.4)	19.785	9	0.019
1	23(21.3)	38(29.5)	20(19.2)	24(34.8)	105(25.6)			
2	3(2.8)	0(0.0)	7(6.7)	0(0.0)	10(2.4)			
Total	108(100)	129(100)	104(100)	69(100)	410(100)			

Age, sex and liver enzymes analysis

Across all the age groups, ALT was normal in 69.8% of patients. Of these, the ALT abnormality was mostly Grade 1 seen in 19.8% and least frequent abnormality (1.5%) was grade 3. There was no significant association between patients age and serum ALT (P=0.063) (Table 5). About half (51.7%) of patients had normal AST and the proportion of patients with normal values decreased with increasing age group, this finding was statistically significant (P=0.018, Table 5). The most frequent AST abnormality was grade 1 and least grade 3 seen in 1.5% of subjects. Only about 40% of subjects had normal ALP and the proportion of patients with normal values decreased with increasing age group, this finding was statistically significant (P=0.019, Table 5). The most frequent ALP abnormality was grade 0 seen in 32.4% and least was grade 2 seen in 2.4% of subjects. In both genders and for all the enzymes, the frequency of patients generally reduced with increasing grade of liver enzymes abnormalities. This finding was not statistically significant (P=0.995, 0.97 and 0.970 respectively (Table 6).

Ultrasound findings

Two hundred and sixteen (52.7%) patients out of the 410

Table 6. Relationship between gender and Liver enzymes of HIV/AIDS Patients.

Liver enzymes	Gender			χ^2	Df	P
	Male (%)	Female (%)	Total (%)			
ALT grade						
Normal	112(70.0)	174(69.6)	286(69.8)	0.205	4	0.995
0	11(6.9)	19(7.6)	30(7.3)			
1	32(20.0)	49(19.6)	81(19.8)			
2	3(1.9)	4(1.6)	7(1.7)			
3	2(1.4)	4(1.6)	6(1.4)			
Total	160(100)	250(100)	410(100)			
AST grade						
Normal	80(50.0)	132(52.8)	212(51.7)	0.493	4	0.974
0	32(20.0)	48(19.2)	80(19.5)			
1	37(23.1)	54(21.6)	91(22.2)			
2	9(5.6)	12(4.8)	21(5.1)			
3	2(1.3)	4(1.6)	6(1.5)			
Total	160(100)	250(100)	410(100)			
ALP grade						
Normal	65(40.6)	97(38.8)	162(39.6)	0.243	3	0.97
0	52(32.5)	81(32.4)	133(32.4)			
1	39(24.4)	66(26.4)	105(25.6)			
2	4(2.5)	6(2.4)	10(2.4)			
Total	160(100)	250(100)	410(100)			

Table 7. Distribution of abnormal hepatobiliary ultrasound findings in HIV/AIDS patients.

Ultrasound findings	Frequency	Percentage
Enlarged GB	116	33.5
Increased liver Echogenicity	91	26.3
Hepatomegaly	82	23.7
Thickened GB wall	27	7.8
Gall bladder sludge	23	6.6
Gall stones	7	2.1
Total	*346	100.

GB=Gallbladder. *Some patients presented with more than one ultrasound findings.

studied had normal hepatobiliary ultrasound scan while the remaining 194 patients had various sonographic abnormalities (Table 7). The commonest hepatobiliary abnormality seen was enlarged gall bladder followed by increased liver Echogenicity and hepatomegaly (Figure 1) while the least frequent abnormal finding was gall stones (Figure 2) seen only in female patients. No significant association was seen between sonographic abnormalities and gender (P = 0.507) (Table 8).

Age and abnormal ultrasound findings

Hepatomegaly and increased liver echogenicity were the commonest abnormalities seen in majority of patients over >50 years while thickened gallbladder wall and gallbladder sludge were more frequent in age group 41-50 years. Enlarged gallbladder was seen commonly in younger age group of ≤30 years. There was statistically significant association between the abnormal ultrasound

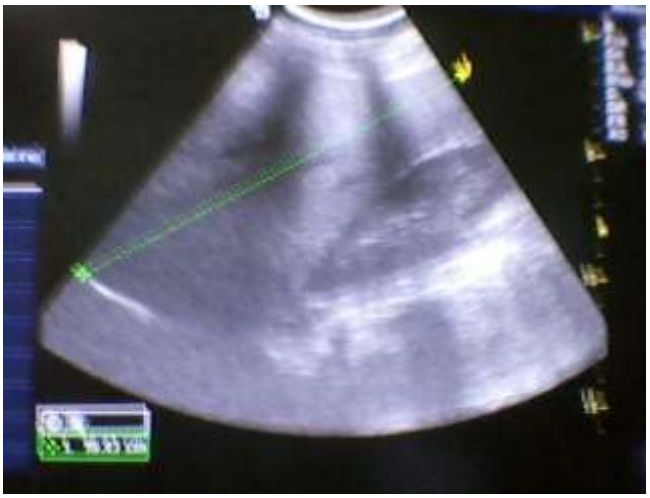

Figure 1. Longitudinal ultrasound image of the liver demonstrating increased liver echogenicity and hepatomegaly in a 43 year old female HIV positive patient.

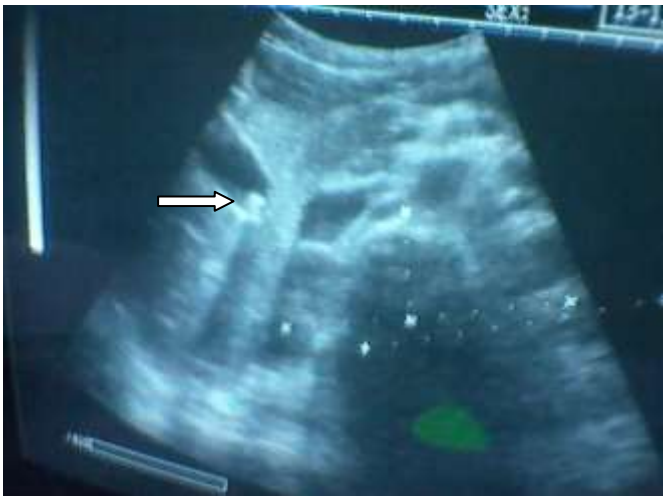

Figure 2. Longitudinal ultrasound image of the gallbladder (GB) showing a gallstone (White arrow) in a 39 year old HIV female positive.

Table 8. Distribution of Ultrasound findings in relation to gender.

Ultrasound findings	Gender		
	Male	Female	Total
Enlarged GB	25(32.1)	91(34.0)	116(33.5)
Increased liver Echogenicity	21(26.9)	70(26.1)	91(26.3)
Hepatomegaly	21(26.9)	61(22.8)	82(23.7)
Thickened GB wall	4(5.1)	23(8.6)	27(7.8)
Sludge	7(9.0)	16(6.0)	23(6.6)
Gall stone	0(0.0)	7(2.6)	7(2.1)
Total	78(100.0)	268(100.0)	*346(100.0)

*Some patients have multiple findings. GB = Gallbladder. $\chi^2 = 4.303$; df = 5. P = 0.507.

Table 9. Distribution of abnormal Ultrasound findings in relation to age group frequency (%).

Ultrasound findings	Age group (years)				
	≤30	31-40	41-50	>50	Total
Enlarged GB	35(38.9)	39(37.9)	30(28.6)	12(25.0)	116(33.5)
Increased liver echogenicity	22(24.4)	28(27.2)	26(24.8)	15(31.3)	91(26.3)
Hepatomegaly	22(24.4)	21(20.4)	24(22.9)	15(31.3)	82(23.7)
Thickened GB wall	7(7.8)	4(3.9)	13(12.4)	3(6.3)	27(7.8)
Sludge	4(4.4)	4(3.9)	12(11.4)	3(6.3)	23(6.6)
Gall stone	0(0.0)	7(6.8)	0(0.0)	0(0.0)	7(2.0)
Total	90(100)	103(100)	105(100)	48(100)	*346(100)

*Some patients have multiple findings. GB = Gallbladder. $\chi^2 = 32.507$; df = 15; P = 0.005.

Table 10. Relationship between ultrasound findings and CD_4^+ classification.

CD_4^+Classification	Ultrasound findings			χ2	df	P
	Normal frequency (%)	Abnormal frequency (%)	Total frequency (%)			
Not significant(≥500)	110(50.9)	85(43.8)	195(47.6)	37.023	3	0.001
Mild (350-499)	60(27.8)	46(23.7)	106(25.9)			
Advanced (200-349)	36(16.7)	35(18.0)	71(17.3)			
Severe (<200)	10(4.6)	28(14.4)	38(9.3)			
Total	216(100)	194(100)	410(100)			

Table 11. Distribution of Ultrasound findings in relation to CD_4^+ classification frequency (%).

Ultrasound findings	CD4+ classification					χ2	P
	Not Sig.	Mild	Advanced	Severe	Total		
Enlarged GB	63(35.8)	29(44.6)	17(30.4)	7(14.3)	116(33.5)	61.517	0.001
Increased liver echogenicity	41(23.3)	13(20.0)	13(23.2)	24(49.0)	91(26.3)	23.066	0.001
Hepatomegaly	41(23.3)	23(35.4)	14(25.0)	4(8.2)	82(23.7)	36.146	0.001
Thickened GB wall	14(8.0)	0(0.0)	6(10.7)	7(14.3)	27(7.8)	4.222	0.121
Sludge	10(5.7)	0(0.0)	6(10.7)	7(14.3)	23(6.6)	1.130	0.568
Gall stone	7(4.0)	0(0.0)	0(0.0)	0(0.0)	7(2.0)	-	-
Total*	176(100)	65(100)	56(100)	49(100)	*346(100)	-	-

*Some patients have multiple findings. GB = Gallbladder.

findings and age (P=0.005) (Table 9).

CD4 count and Ultrasound findings

Of the patients studied, 52.7% had normal ultrasound findings. In those with abnormal ultrasound findings, 43.8% were in the 'not significant' CD_4group and the frequency of abnormal ultrasound findingsreduced with decreasing CD_4^+ count and increasing disease severity, implying a negative correlation with disease severity (P = 0.001) (Table 10).

In those with abnormal ultrasound findings, patients with hepatomegaly and enlarged gallbladder were commoner in the mild CD_4^+ class while those with increased liver echogenicity, thickened gallbladder wall and sludge were most frequent in the severe CD_4^+ category. Gall stone was present only in the not significant CD_4^+class. Enlarged GB, increased liver echogenicity and hepatomegaly correlate significantly with CD_4^+ count (P = 0.001). However, thickened gallbladder wall and gallbladder sludge did not individually correlate significantly with CD_4^+ count (P = 0.12 and 0.57 respectively) (Table 11).

Liver enzymes and ultrasound findings

Majority (46.1%) of the patients who had normal ultrasound finding had normal serum liver enzymes however, some patients with normal serum liver enzymes also had abnormal ultrasound findings and vice versa. Hepatomegaly was seen in various grades of liver enzymes abnormalities except grade 2 ALT. It was most frequent in grades 3 for ALT and AST but in grade 1 for ALP. This finding was statistically significant (P = 0.001) (Table 12). Increased liver echogenicity varied with degree of elevated liver enzymes but was worse in grade 2 for ALT, grade 3 for AST and grade 2 for ALP. This finding was also statistically significant (P = 0.001, Table 12). Enlarged GB was seen in all grades of elevated liver enzymes and was most frequent in grade 2 for ALT, grade 3 for AST and grade 1 for ALP. This finding was statistically significant (P = 0.001, Table 12). Thickened GB wall was seen in grades 0 and 1 for ALT, and grades 0-2 for AST and ALP. The finding was statistically significant (P = 0.013 and 0.017 for ALT and AST respectively) (Table 12).

Among the three (3) liver enzymes studied, ALP has the highest sensitivity (68) to truly detect those patients with sonographic detectable hepatobiliary disease followed by AST (55.7). However, the ALT has the highest specificity (75.9) to detect correctly absence of hepatobiliary diseaseon ultrasound. ALT also has the highest positive predictive value implying those with abnormal ultrasound truly have the hepatobiliary disease while ALP has the highest negative predictive value implying that those with normal ultrasound truly have no hepatobiliary disease (Table 13).

Logistic analysis

Logistic regression shows that hepatomegaly was the most likely abnormal ultrasound finding (OR=4.08) to be seen in HIV/AIDS patients with advanced/severe CD_4 counts followed by enlarged gallbladder (OR=2.83) while increased liver echogenicity was the least probable. However these findings were not statistically significant with P = 0.08 or 0.48 (Table 14). Among the three (3) liver enzymes studied, abnormal ALP enzyme value (OR=1.3) was the most likely to be seen in patients with advanced/severe CD_4 counts followed by AST (OR=0.63). However these findings were also not statistically significant with P = 0.61 or 0.34) (Table 15).

DISCUSSION

The number of people living with HIV/AIDS worldwide was estimated to be 36.9 million at the end of 2014 according to World Health Organization (Worldwide AIDS and HIV statistics, 2011). The use of highly active antiretroviral therapy (HAART) has modified the disease pattern. Clinical and ultrasound findings in HIV/AIDS depend on the immune status of the patient as represented by their CD_4^+ count (Igbinedion et al., 2009). Abnormalities of liver enzymes are common in HIV/AIDS patients and these may be due to direct inflammation induced by HIV on the liver cells and gall bladder or due to complications of antiretroviral drugs (Ejilemele et al., 2007). A total of 410 HIV positive patients on HAART were studied, majority of the patients were females (65.8%) with male to female ratio of 1: 2. This is in agreement with a study done in South Western Nigeria by Obajimi et al. (2008) which documented a female preponderance of 66.5%. This finding is also similar to the report of the Joint United Nations Programme on HIV/AIDS (UNAID), 2010) which documented that the percentage of women living with HIV/AIDS increased from 43% in 1999 to 50% in 2010 and that Sub-Sahara African women comprised 59% of adults infected with HIV (Global Fact sheet, 2012). The sex ratio in this study was however at variance with the study documented in Sudan by Mahmoud et al. (2012) which showed a higher male preponderance of 66%. The finding of female preponderance in this study could be due to the fact that females' genital anatomy places them more at risk for sexually transmitted infections, compared to men (Center for Disease Control and Prevention Fact sheet, 2017). Females also have better health seeking behaviours and are routinely counseled during antenatal care for HIV testing leading to the discovery of their HIV status (Center for Disease Control and Prevention Fact sheet, 2017).

Approximately 83% of the patients were within the age range of 18 to 47years, thereby constituting the majority of the patients in this study population. This age range was described by Adeoye (2005) as the economically productive segment of Nigerian society and also the age group at the greatest risk of HIV/AIDS. However, there were few patients above 50 years old, possibly because most of the older populations are less sexually active (Adeoye, 2005). Finding is in agreement with a study done by Igbinedion et al. (2009) in Benin-Nigeria which documented about 89% of the patients to be between 18 to 47 years. The mean age for females and males were 37.59 years and 42.84 years respectively. This mean age was also consistent with the study done in South Western Nigeria by Obajimi et al. (2008) which documented mean age of female HIV patients to be 38.02 years. This may be due to the fact that females are sexually active at an early age compared to males (Abubakar et al., 2014).

Based on the World Health Organization (WHO, 2006) classification of CD_4^+ immunological profile in adult HIV infected patients, 73.4% of the patients had CD_4^+ count of350 cells/µl and above making up 47.6 and 25.8% for the "Not significant" and "Mild" categories respectively while only 9.3% were in the "Severe" category (that is CD4+ count<200cells/µl). This was at variance with the findings of Igbinedion et al (2009) who found almost half (46.3%) of the patients to be in the "Severe" CD4+ class.

Table 12. Distribution of Ultrasound findings in relation to liver enzymes classification.

Ultrasound findings	Liver enzymes grading						χ2	P
	Normal	0	1	2	3	Total		
	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)		
				ALT				
Normal	164(43.6)	11(23.9)	41(33.9)	0(0.0)	0(0.0)	216(38.4)	-	-
Hepatomegaly	45(12.0)	11(23.9)	23(19.0)	0(0.0)	3(25.0)	82(14.6)	48.927	0.001
Increased liver echogenicity	57(15.2)	8(17.4)	16(13.2)	4(57.1)	6(50.0)	91(16.2)	107.956	0.001
Enlarged GB	76(20.2)	8(17.4)	26(21.5)	3(42.9)	3(25.0)	116(20.6)	67.709	0.001
Thickened GB wall	16(4.3)	4(8.7)	7(5.8)	0(0.0)	0(0.0)	27(4.8)	8.667	0.013
Sludge	15(4.0)	4(8.7)	4(3.3)	0(0.0)	0(0.0)	23(4.1)	10.522	0.005
Gall stone	3(0.8)	0(0.0)	4(3.3)	0(0.0)	0(0.0)	7(1.2)	0.143	0.705
Total	376(100)	46(100)	121(100)	7(100)	12(100)	*562(100)	-	-
				AST				
Normal	126(45.7)	41(39.4)	39(28.7)	10(29.4)	0(0.0)	216(38.4)	-	-
Hepatomegaly	30(10.9)	15(14.4)	31(22.8)	3(8.8)	3(25.0)	82(14.6)	46.293	0.001
Increased liver echogenicity	36(13.0)	20(19.2)	18(13.2)	11(32.4)	6(50.0)	91(16.2)	28.615	0.001
Enlarged GB	55(19.9)	19(18.3)	32(23.5)	7(20.6)	3(25.0)	116(20.6)	76.586	0.001
Thickened GB wall	13(4.7)	3(2.9)	8(5.9)	3(8.8)	0(0.0)	27(4.8)	10.185	0.017
Sludge	9(3.3)	6(5.8)	8(5.9)	0(0.0)	0(0.0)	23(4.1)	0.609	0.738
Gall stone	7(2.5)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	7(1.2)	-	-
Total	276(100)	104(100)	136(100)	34(100)	12(100)	*562(100)	-	-
				ALP				
Normal	100(49.0)	68(33.7)	45(32.8)	3(15.8)	-	216(38.4)	-	-
Hepatomegaly	23(11.3)	33(16.3)	23(16.8)	3(15.8)	-	82(14.6)	23.171	0.001
Increased liver echogenicity	28(13.7)	39(19.3)	17(12.4)	7(36.8)	-	91(16.2)	25.176	0.001
Enlarged GB	26(12.7)	46(22.8)	41(29.9)	3(15.8)	-	116(20.6)	38.552	0.001
Thickened GB wall	10(4.9)	10(5.0)	4(2.9)	3(15.8)	-	27(4.8)	6.333	0.096
Sludge	13(6.4)	3(1.5)	7(5.1)	0(0.0)	-	23(4.1)	6.609	0.037
Gall stone	4(2.0)	3(1.5)	0(0.0)	0(0.0)	-	7(1.2)	0.143	0.705
Total	204(100)	202(100)	137(100)	19(100)	-	*562(100)	-	-

*Some patients have multiple findings. GB = Gallbladder; ALT = alanine transaminase; AST = aspartate transaminase; ALP = alkaline phosphatase.

Table 13. Sensitivity, Specificity, Positive predictive value and Negative predictive value using ultrasound as outcome variables.

Parameters	ALT	AST	ALP
Sensitivity	37.1	55.7	68.0
Specificity	75.9	58.3	48.3
Positive predictive value	58.1	54.5	53.2
Negative predictive value	57.3	59.4	61.7

ALT = alanine transaminase; AST = aspartate transaminase; ALP = alkaline phosphatase.

The higher CD4+ count and thus milder/not significant disease in this study maybe due to incessant public enlightenment, with resultant decreased stigmatization, earlier diagnosis and follow up as well as improved availability of anti retroviral drugs unlike in the past when most patients were well stigmatized, presented late and were unable to access or procure anti retroviral medications. This might also indicate the improved

Table 14. Logistic regression abnormal ultrasound findings and advanced/severe CD_4 counts.

Findings	Odd Ratio (OR)	95% C.I. for OR	P
Hepatomegaly	4.08	0.86-19.37	0.077
Increased liver echogenicity	0.63	0.17-2.28	0.483
Enlarged GB	2.83	0.70-11.51	0.143
Thickened GB wall	1.00	0.21-4.67	1.000
Sludge	1.00	-	-

GB = Gallbladder. C.I = Confidence Interval.

Table 15. Logistic regression liver enzymes and advanced/severe CD_4 counts

Findings	Odd ratio (OR)	95% C.I. for OR	P
ALT	0.187	0.07-0.48	0.060
AST	0.63	0.24-1.63	0.342
ALP	1.30	0.48-3.53	0.610

ALT = alanine transaminase; AST = aspartate transaminase; ALP = alkaline phosphatase. C.I = Confidence Interval.

effectiveness of government interventions such as public health education, Voluntary Confidential Counseling and Testing (VCCT), and availability of free Antiretroviral Drugs (ARVS).

Based on the grading system developed by the Acquired Immune Deficiency Syndrome (AIDS) Clinical Trials Group (CTG) in assessing the serum level of liver enzymes of infected individuals. In this study, 53.7% of the patients had normal liver function tests while 46.3% of the patients had various abnormalities of their liver enzymes (ALT, AST and ALP). This is not in agreement with the study done by Ejilemele et al. (2007) in Port Harcourt Nigeria who documented a higher (87.6%) abnormal liver enzyme. This study is also at variance with the finding of Savita et al. (2015) in India which also documented a higher (63%) abnormal liver function tests (LFT). In this study, out of the patients with abnormal (46.3%) liver enzymes, 39.4% were classified as hepatocellular liver (elevated AST and ALT) injury while 60.6% were classified as cholestatic liver (elevated ALP) injury. This is not in agreement with the study done by Ejilemele et al. (2007) in Port Harcourt Nigeria who recorded a lower (14.5%) cholestatic liver injury and a higher (85.5%) hepatocellular injury (Ejilemele et al (2007). This study is also not in agreement with the finding of Savita et al (2015) in India which documented 63% of their patients with abnormal liver function tests (LFT). They recorded a lower (6%) cholestatic liver injury, a higher (29%) hepatocellular injury and 28% had a mixed pattern of liver injury. The reason for the higher prevalence of abnormal liver function tests in the Port Harcourt and India studies is most likely due to the fact that the patients studied were both not on antiretroviral therapy at the time of data collection.

Different hepatobiliary sonographic abnormalities such as enlarged gallbladder (GB), increased liver echogenicity, hepatomegaly, thickened GB wall, gallbladder sludge and stone were observed in this study which were comparable with those documented by other authors (Obajimi et al (2008); Igbinedion et al (2009); Pawar et al. (2013); Mahmoud et al (2012). Some of these abnormal ultrasound findings (enlarged GB, increased liver echogenicity and hepatomegaly) correlated significantly with CD_4^+ count (P = 0.001). The "Not significant" CD_4^+ class recorded 43.8% abnormal hepatobiliary ultrasound findings as compared to 14.4% noted in the "severe" CD_4^+ class. In a similar study, Pawar et al. (2013) documented 43.3% abnormal hepatobiliary ultrasound findings in the "Not significant" CD_4^+ (>350 cells/µl) category and 56.7% in the "Significant" CD_4^+ (≤350 cells/µl) class. This was in contrast with the finding of Igbinedion et al. (2009) who documented a higher abnormal abdominal ultrasound finding of 85.7% in the "Not significant" CD_4^+ class and 89.9% in the "severe" CD_4^+ category. Hepatomegaly was the third most common abnormal hepatobiliary sonographic findings in this study as seen in 23.7% patients. Different studies had documented figures such as 13.3, 39.0, 40.0, 35.0 and 41.0% respectively for hepatomegaly; (Obajimi et al., 2008; Igbinedion et al., 2009; Javier et al., 2005; Tshibwabwa et al., 2000; Grumbach et al., 1989). According toIgbinedion et al. (2009), hepatomegaly in these patients could be due to infections, non specific response to infective hepatitis, fatty infiltration or neoplastic infiltration from lymphoma or Kaposi sarcoma. Increased liver echogenicity was the second most common finding as seen in 26.3% patients. Grumbach et al. (1989) documented a higher finding of

45.5%. Both hepatomegaly and increased liver echogenicity negatively correlate with CD_4^+ count (Both P = 0.001). This was also in contrast with the study of Igbinedion et al. (2009), whose finding (hepatomegaly and increased liver echogenicity) did not correlate with CD_4^+ count. Increased liver echogenicity in HIV could be due to fatty infiltration, chronic hepatitis, drug and alcoholic induced liver diseases as in the general population (Valentina and Giuseppe, 2012). Gallbladder enlargement was noted in 33.3% of patients while thickened gallbladder wall, gallbladder sludge and gallbladder stones were noted in 7.8, 6.6 and 2.1% of the patients respectively. In similar studies, Igbinedion et al. (2009) documented thickened gallbladder wall in fewer patients (7.3%) and gall stones in a higher proportion (4.7%) of the patients. Pawar et al. (2013) who recorded thickened gallbladder wall and gall stones in a higher proportion(9.0%) and (4.0%) of the patients respectively and gallbladder sludge in fewer patients(6.0%) which did not correlate with CD_4^+ count. Obajimi et al. (2008) recorded gall stones in only 1.3% of their patients. Grumbach et al. (1989) recorded thickened gallbladder wall in 55%, dilated gallbladder in 18%, biliary sludge in 23% and gall stones in 5% of the patients. This difference (lower values in this study) in gallbladder abnormal findings may be attributed to the fact that there is better awareness on HIV/AIDS. Therefore, most patients present early coupled with the availability of HAART and early treatment. Thickened gallbladder wall in HIV could be due to cholecystitis, hepatitis, sepsis and tuberculosis (HIV infection and Gallstones-Risk factors, 2017).

The major risk factors for developing gallstones in HIV include male sex, increasing age (>40years), those on Norvir therapy and high blood pressure (Romano et al., 1988). Gallbladder sludge in HIV is associated with opportunistic infection, cholecystitis and hepatitis (HIV infection and Gallstones-Risk factors, 2017). Hepatomegaly was the most likely abnormal ultrasound finding in HIV/AIDS patients with advanced/severe CD_4 counts while increased liver echogenicity was the least probable. However these findings were not statistically significant (P=0.77 and 0.48 respectively) using logistic regression test. No specific reason could be adduced for this finding and further studies would be required in this regard. Aspartate and Alanine transaminases are excellent markers of hepatobiliary injury while Alkaline Phosphatase is a marker of biliary diseases; however, none of the enzymes are specific for hepatobiliary diseases as similar elevation of these enzymes may be encountered in myocardial infarction and some muscle injuries (Ocama et al., 2008).

In this study, the prevalence of abnormal liver enzymes (ALT, AST and ALP) and ultrasound abnormalities (hepatomegaly, increased liver echogenicity, enlarged GB, thickened GB wall, GB sludge and stone) in adult HIV positive patients was 47.3%. This was lower than in earlier reported studies done by Igbinedion et al. (2009), Pawar et al. (2013) and Mahmoud et al. (2012) which recorded 66.6, 96.0 and 93.3% respectively. This low prevalence may be due to the fact that all the patients at the time of conducting this study were already on regular Highly Active Antiretroviral Therapy (HAART).Some patients with normal liver enzymes had abnormal ultrasound findings and vice versa; an average of 46.3% of the patients had various grades of liver enzymes abnormalities.This was not in agreement with a study done by Savita et al 2015 in India which documented a higher (63%) abnormal liver function tests (LFT). In this study, 47.3% of the patients had various abnormal hepatobiliary ultrasound findings and this was in agreement with the study of Savita et al. (2015) who recorded 47% of various abnormal ultrasound findings in their patients. In this study, increased liver echogenicity was seen in 27.0% which is inconsistent with the finding of Savita et al. (2015) who recorded a higher percentage of 46.3%. This study recorded hepatomegaly in 27.1% of the patients which is also in contrast with a study done by Savita et al. (2015) who recorded 15.5%. In this study, both increased liver echogenicity and hepatomegaly significantly correlate individually with liver enzyme. There was however no correlation between LFTs (ALT, AST and ALP) and ultrasound findings in the study done by Savita et al. (2015). Infection by HIV increases activities of the three enzymes, which may be due to liver cells apoptosis caused by HIV infection, or immune response to HIV replication which subsequently leads to hepatocellular necrosis and inflammation (Housset et al., 1990; Hufert et al., 1993; Gendrault et al., 1991). Low frequency of abnormal liver function tests and various abnormal hepatobiliary ultrasonographic findings in this study could be due to early diagnosis and treatment with readily available antiretroviral therapy. Elevated serum alkaline phosphatase was the most likely liver enzyme abnormality in patients with advanced/severe CD_4 counts followed by aspartate transaminases as indicated by logistic regression analysis but this was not statistically significant (P = 0.61).

Conclusion

Ultrasonography is a versatile tool for evaluating hepatobiliary organs affected by HIV/AIDS. Most abnormal sonographic hepatobiliary findings in patients with HIV/AIDS correlated significantly with CD_4^+ count and liver enzyme levels. Therefore, ultrasound scan could be introduced as part of management/follow-up of HIV/AIDS patients as it may improve management out come in these patients. Ultrasound is easy to perform, non invasive, inexpensive and readily available in this part of the world where HIV/AIDS is most prevalent. Among the liver enzymes studied, ALP has the highest sensitivity to truly detect those patients with sonographic Detectable hepatobiliary disease and highest negative

predictive values implying those with negative abnormal ultrasound truly have no hepatobiliary disease.

RECOMMENDATIONS

Hepatobiliary ultrasound scan should be made an initial routine examination in all HIV clinics for better management of these patients.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

REFERENCES

Abubakar MG, Abduljalil MM, Nasiru YI (2014). Changes in the liver enzymes of HIV/AIDS patients treated with antiretroviral drugs (ARVS) in Specialist Hospital, Sokoto. Nigeria. Nigerian Journal of Basic and Applied Science 21(3&4):87.

Adeoye S (2005). Sexual behaviour, perception of HIV/AIDS and condom use among commercial motorcyclists in Benin City. Nigerian Postgraduate Medical Journal 12(4):262-265.

Center for Disease Control and Prevention Fact sheet. Availabe at: https://www.cdc.gov

Chen XM, La Russo NF (2002). Cryptosporidiosis and pathogenesis of AIDS cholangiopathy. Seminars in Liver Disease 22(3):277-289.

Ejilemele AA, Nwauche CA, Ejele O (2007). A pattern of abnormal liver enzymes in HIV patients presenting at a Nigeria Tertiary Hospital-Port Harcourt. Nig. Postgrad med. J. 14(4):306-309.

Enns R (2003). AIDS cholangiopathy: “An Endangered Disease”. The American Journal of Gastroenterology 98(10):2111-2112.

Federal Ministry of Health National HIV/Syphilis Sero-prevalence Sentinel Survey (2005). Available at: https://www.medbox.org

Flum DR, Steinberg SD, Sarkis AY, Pacholka JR, Wallack MK (1997). The Role of Cholecystectomy in Acquired Immunodeficiency Syndrome. Journal of the American College of Surgeons 184(3):233-239.

Global Fact sheet, joint United Nations programme on HIV and AIDS (2012). Available at: https://www.unaids.org

Goldin RD, Lloyd J (2002). HIV and hepatobiliary disease. Current Diagnostic Pathology 8(3):144-151.

Gore RM, Miller FH, Yaghmai V (1998). Acquired Immune Deficiency Syndrome of the abdominal organs: Imaging features. Semin ultrasound. CT. MR19:175-189.

Gendrault JL, Steffan AM, Schmitt MP, Jaeck D, Aubertin AM, Kirn A (1991). Interaction of cultured human Kupffer cells with HIV-infected CEM cells: an electron microscopic study. Pathobiology 59:223-226.

Guarda LA, Stein SA, Cleary KA Ordonez NG (1983). Human Cryptosporidiosis in the Acquired Immune Deficiency Syndrome. Archives of Pathology and Laboratory Medicine 107(11):562-566.

Grumbach K, Coleman BG, Gal AA, Argar PH, Mintz MC (1989). Hepatic and biliary tract abnormalities in patients with AIDS. Sonographic-pathologic correlation. Journal of Ultrasound in Medicine 8(5):247-254.

Herman ES, Klotman PE (2003). HIV-associated nephropathy: epidemiology, pathogenesis, and treatment. Seminars in Nephrology 23:200-208.

Housset C, Boucher O, Girard PM, Leibowitch J, Saimot AG,Bréchot C (1990). Immunohistochemical evidence for human immunodeficiency virus-1 infection of liver Kupffer cells. Human Pathology 21:404-408.

Hufert FT, Schmitz J, Schreiber M, Schmitz H, Rácz P, von Laer DD (1993). Human Kupffer cells infected with HIV-1 in vivo. Journal of Acquired Immune Deficiency Syndromes 6:772-777.

Igbinedion BO, Marchie TT, Ogbeide E (2009). Trans-abdominal ultrasound findings correlated with CD_4^+ counts in adult HIV- infected patients in Benin Nigeria. South African Journal of Radiology 13(2):34-40.

Javier L, Luis E, Soto R, Jorge LP, Misael U (2005). Hepatobiliary Diseases in Patients with Human Immunodeficiency Virus (HIV) Treated with Non Highly Active Anti- Retroviral Therapy: Frequency and Clinical Manifestations. Annals of Hepatology 4(3):188-191.

Ko WF, Cello JP, Rogers SJ, LecoursA (2003). Prognostic factors for the survival of Patients with AIDS Cholangiopathy. The American Journal of Gastroenterology 98(10):2176-2181

Mahmoud MZ, Alsafi AA, Ala MA (2012). AIDS effects in liver and biliary tract by ultrasound in Sudan. Afro-Egyptian Journal of Infectious and Endemic Diseases 2(4):133-139.

Savita M, Sudaga RB, Vengadakrishnan K, Damodharan J (2015). Liver Function Abnormalities in Human Immunodeficiency virus Positive Individuals and its Correlation with Disease Severity. International Journal of Scientific Study 3(8):15-18.

Obajimi MO, Atalabi MO, Adeniyi-Sofoluwe AT, Agunloye AM, Adekanmi AJ, Osuagwu YU (2008). Abdominal ultrasonography in HIV/AIDS Patients in Southwestern Nigeria. BMC Medical Imaging 8:5-10.

Ocama P, Katwere M, Piloya T, Feld J,Opio KC (2008). The spectrum of liver diseases in HIV infected individuals at an HIV treatment clinic in Kampala, Uganda. African Health Sciences 8(1):8-12.

O’Hara SP, Small AJ, Gajdos GB, Badley AD, Chen XM, Larusso NF (2009). HIV-1 Tat Protein Suppresses Cholangiocyte toll-like Receptor 4 Expression and Defense against Cryptosporidium parvum. The Journal of Infectious Diseases 199(8):1195-1204.

Pawar SS, Biradar SP, Gajbhiye MI, Khadse GJ (2013). Correlation of hepatobiliary ultrasound findings with CD_4^+ Count and liver function tests in HIV Positive Patients. Medical journal of western India 41(1):86-88.

Pitlik SD, Fainstein V, Rios A, Guarda L,Mansell P W (1983). Cryptosporidial Cholecystitis. The New England Journal of Medicine 308(16):127-129.

Sebastian L (2002). The pathology of HIV infection. Leprosy review 73:64-71.

Tshibwabwa ET, Mwaba P, Bogle-Taylor J, Zumla A (2000). Four-year study of abdominal ultrasound in 900 Central African adults with AIDS Referred for Diagnostic Imaging. Abdominal Imaging 25(3):290-296.

World Bank Nigeria (2008). Report final CHASE Bank14 July 08.doc. Available at: https://www.info.com

Valentina LV, Giuseppe M (2012). Prospective evaluation of hepatic steotosis in HIV infected patients with or without hepatitis c virus co-infection. Internal Journal of infectious Disease 16(5):397-402.

World Health Organization (2006). WHO Case Definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-Related Disease in Adults and Children. Geneva: World Health Organization, 16.

Worldwide AIDS and HIV statistics, Global epidemic (2011). Available at: https://www.who.int