British HIV Association
BHIVA
20th Annual Conference

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Third Joint Conference

of the
British HIV Association (BHIVA)
with the
British Association for Sexual Health and HIV (BASHH)

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Arena and Convention Centre · Liverpool

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LEADING HIV CARE FOR BRIGHTON

Brighton and Sussex University Hospitals NHS Trust

Non- viral liver disease burden in HIV-positive individuals: An observational retrospective cohort study

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Introduction

- Liver disease is an important cause of morbidity and mortality amongst HIV-positive individuals

- Potent antivirals have significantly improved outcomes in chronic viral hepatitis B and C

Hypothesis

As HBV and HCV become increasingly treatable, other causes of liver disease likely to become increasingly prominent

- Alcohol
- Metabolic syndrome
- Antiretroviral agents

Objectives

- Assess prevalence, patient characteristics and predictors of non-viral related liver disease in patients with HIV
- Explore association, if any, between alcohol use, metabolic syndrome and antiretroviral treatment
- Provide data to assist HIV clinicians in managing patients with abnormal liver function tests

Methods

Inclusion Criteria	Exclusion Criteria
HIV-positive	Positive serology for Hepatitis B (HBV) or Hepatitis C (HCV)
Abnormal alanine aminotransferase (ALT) >1ULN on at least two occasions 6 months apart	Presence of biliary, autoimmune or congenital liver disease
Further investigation with one or more of: - Imaging (USS/CT/MRI) - Transient Elastography (Fibroscan) - Liver Biopsy	Incomplete data/notes not available

Methods

Chronic liver disease was defined as one or more of the following:

- > F1 (Metavir) fibrosis on liver biopsy and/or Fibroscan
- Imaging showing any one of the following:
  - Fatty liver
  - Heterogenous/ irregular liver
  - Ascites
  - Varices / abnormal portal venous flow
  - Splenomegaly >12cm (after excluding other causes)

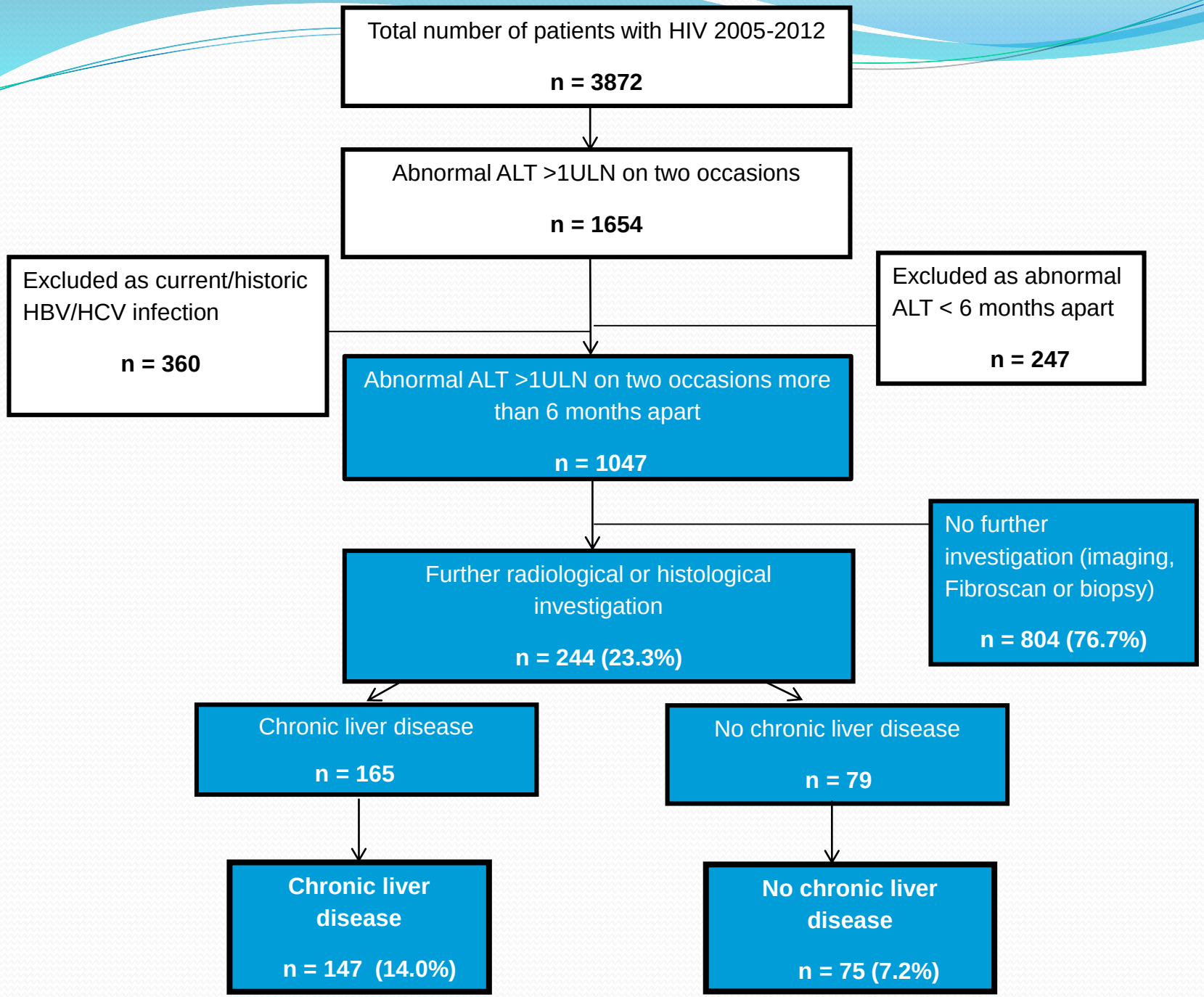
Methods

Data collected:

- Demographics, ARV history, LFTs, lipids, glucose
- Investigation results (imaging, Fibroscan, liver biopsy)
- Alcohol consumption and evidence of binge drinking

Categorised into three groups

- Alcohol - consuming >weekly limit
- Metabolic syndrome - presence of any one of the metabolic syndrome features
- Antiretroviral - use of didanosine, stavudine, nevirapine, efavirenz (>median)


Total number of patients with HIV 2005-2012
n = 3872
Abnormal ALT >1ULN on two occasions
n = 1654
Excluded as current/historic HBV/HCV infection
n = 360
Excluded as abnormal ALT < 6 months apart
n = 247
Abnormal ALT >1ULN on two occasions more than 6 months apart
n = 1047
No further investigation (imaging, Fibroscan or biopsy)
n = 804 (76.7%)
Further radiological or histological investigation
n = 244 (23.3%)
Chronic liver disease
n = 165
No chronic liver disease
n = 79
Chronic liver disease
n = 147 (14.0%)
No chronic liver disease
n = 75 (7.2%)

Population characteristics (n=222)

Age (years)	Mean 47.56 ± 10.10
Males	208 (93.7%)
Ethnicity (Caucasian)	186 (83.8%)
Duration of HIV (years)	Median 10.0 (6-17)
Body Mass Index (BMI)	Mean 26.67 ± 5.41

Investigations		
USS	198	(89.2%)
CT	43	(19.4%)
MRI	8	(3.6%)
Fibroscan	16	(7.2%)
Liver biopsy	42	(18.9%)

Investigation results

Radiological findings *n = 176*		
Fatty liver	105	(47.3%)
Splenomegaly	30	(13.5%)
Heterogeneous/ irregular liver	21	(9.5%)
Varices/ portal venous flow	11	(5.0%)
Ascites	9	(4.1%)

Fibroscan findings *n=16*		
<F2 fibrosis	11	(68.8%)
≥F2 fibrosis	5	(21.2%)

Biopsy findings *n=42*			
Steatosis :	Normal	18	(42.9%)
	Mild	5	(11.9%)
	Moderate	13	(31.0%)
	Severe	6	(14.3%)
Fibrosis	F0	13	(31.0%)
	F1	16	(38.0%)
	≥F2	13	(31.0%)

CLD vs no CLD

Parameter	CLD n = 147 (66.2%)	No CLD n=75 (33.8%)	OR	P value
Age (years)	49.03 ±9.69	44.08 ±9.80	1.062	<0.001
Duration of HIV (years)	12.8 ±8.25	8.2 ±4.73	1.137	<0.001
No. of patients diagnosed pre-1996	36 (97.3%)	1 (2.7%)	24.00	0.002
Body mass index (BMI)	26.80 ± 4.57	25.40 ±4.40	1.080	0.043
Weight (kg)	78.18 ±14.37	73.41 ±12.24	1.022	0.039
Cholesterol (≤5mmol/L)	5.50 ±1.32	5.17 ±1.04	1.284	0.040
Triglycerides (<2mmol/L)	2.5 (5-15.5)	1.80 (5-9)	1.238	0.015
FBG (mmol/L) (4-5.9)	5.79 ±2.03	5.19 ±0.19	1.359	0.021
Weekly intake alcohol initially(units)	21.0 (1.3-57.5)	10.0 (2-30)	1.011	0.024
Weekly intake alcohol on last clinic visit (units)	10.0 (0- 24.8)	0 (0-18.8)	1.023	0.024
Didanosine	52 (35.6%)	8 (10.5%)	4.893	<0.001
Stavudine	40 (27.4%)	5 (65.8%)	5.545	<0.001
Nevirapine	37 (25.3%)	10 (13.2%)	2.312	0.032
PI-based therapy	91 (62.0%)	37 (48.7%)	1.727	0.049

No significant difference between LFTs in CLD and no CLD

Univariate logistic regression of patients with chronic liver disease versus patients without chronic liver disease

Multivariate logistic regression for CLD

	Sig.	OR	95% C.I.for OR	
			Lower	Upper
HIV duration (yrs)	.067	1.119	.992	1.263
PI-based therapy	.221	1.959	.667	5.753
Didanosine	.899	1.123	.186	6.792
Stavudine	.141	4.397	.613	31.543
BMI	.011	1.192	1.040	1.365
Nevirapine	.753	.789	.180	3.462
Triglyceride	.024	1.581	1.061	2.358
FBG	.726	1.088	.678	1.747
Weekly alcohol intake at last clinic visit (units)	.011	1.044	1.010	1.080

Lifestyle factors significant

Aetiology

Aetiology Category	Subgroup category	CLD – no of patients n=147	Weekly intake alcohol (units)	Clinically significant liver disease n=28
Single aetiological factor	Alcohol	12 (8.2%)	45 (30-70) ←	0
	Antiretroviral	20 (13.6%)	1 (0-6)	3 (12.5%)
	metabolic	14 (9.5%)	0 (0-7)	0
	Total	**46 (31.3%)**	**6 (0-31)**	**3 (10.7%)**
2 aetiological factors	Alcohol and ARV	13 (8.8%)	67 (30-70) ←	2 (7.1%)
	Alcohol and metabolic	10 (6.8%)	63 (38-90) ←	2 (7.1%)
	ARV and metabolic	46 (31.3%)	6 (0-13)	14 (50%)
	Total	**71 (48.3%)**	**15 (0-41)**	**18 (64.3%)**
3 aetiological factors	Alcohol, ART and metabolic	**30 (20.4%)**	**40 (27-73)** ←	**7 (25.0%)**

Alcohol implicated in 65 patients (45.5%)
Metabolic syndrome implicated in 99 patients (67.8%)
Antiretroviral treatment implicated in 108 patients (74.0%)

Limitations

- Retrospective
- Investigations for abnormal ALT was HIV physician dependant - unable to capture detailed reasoning behind further investigation or referral
- Data in the ~800 individuals not investigated unknown
- Data for patients without abnormal LFTs

Conclusions

- In our study, 27% of HIV-positive individuals have a persistently abnormal ALT
  - <25% of whom had an ALT elevation requiring further investigation
- High rates of CLD in patients investigated
  - 12.6% ≥F2 fibrosis
  - Underlying aetiology multifactorial → lifestyle a key factor
  - 68.7% more than one risk factor
- Non-viral liver disease burden needs to be addressed in HIV-positive individuals and should be investigated more aggressively
- Future research?

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