

The prevalence of liver fibrosis in HIV infected patients with abnormal liver function tests

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Background

- Liver-related deaths are a leading cause of mortality in persons receiving continuous combination antiretroviral therapy for HIV infection¹.
- Liver fibrosis is a predictor of liver-related and non-liver-related mortality in non-alcoholic fatty liver disease (NAFLD)².
- Local screening for liver injury in persons living with HIV infection is largely based on inclusion of hepatobiliary enzymes as part of routine blood monitoring. However, liver function tests in isolation are not specific at diagnosing or excluding liver disease³.
- Data from a community population aged over 16 years suggests that whilst an abnormal ALT or AST was predictive of liver disease (hazard ratio = 4.2), only 3.9% of those with an abnormal value were diagnosed with significant liver disease within 5 years of the test⁴.
- The prevalence of liver fibrosis in people living with HIV who have abnormal liver function tests was evaluated.

Methods

- All registered patients living with HIV infection who had an abnormal alanine transferase (ALT) and/or aspartate aminotransferase (AST) and/or gamma-glutamyltransferase (GGT) between 1 January 2014 and 30 November 2017 were identified as part of a local audit.
- A retrospective review of the electronic patient record was performed to identify all patients with a documented FibroScan® assessment.
- Histological data was collected where liver biopsy had been performed.

Results Table 1: Overview of results

536 patients with abnormal ALT +/- AST +/- GGT between 01/01/2014 and 30/11/2017

150 patients (28%) with documented FibroScan® on retrospective review of the case notes

Patient characteristics	Number of patients	%
Male	124 / 150	82.7
Median age last attendance	48 (range 30 - 79)	
Patient on combination antiretroviral therapy*	84 / 150	56.0
VL <50 copies/mL	66 / 84	78.6
Abnormal ALT	99 / 150	66.0
Grade 1 (≤3 x ULN [^])	87 / 99	87.9
Grade 2 (>3-≤5x ULN)	7 / 99	7.0
Grade 3 (>5-≤10x ULN)	3 / 99	3.0
Grade 4 (>10x ULN)	2 / 99	2.0

*Combination antiretroviral therapy at time of abnormal liver function test
[^]ULN = upper limit normal

Median FibroScan® score: 5.4 kPa (range 2.8 – 72 kPa)

Results Table 2: Predicted fibrosis stage by FibroScan®

FibroScan® Value (kilopascals)*	Number of patients (%)	ALT at baseline (%)	Diagnosis (number patients)
<7.0 (F0 – F1 fibrosis)	110 / 150 (73.3)	Normal = 35 / 110 (31.8) Abnormal = 75 / 110 (68.2)	NAFLD (57) No cause identified (21) Viral hepatitis [^] (18) Alcohol (9) Antiretroviral therapy (4) Autoimmune hepatitis (1)
7-9 (F2 fibrosis)	23 / 150 (46.0)	Normal = 8 / 23 (34.8) Abnormal = 15 / 23 (65.2)	Viral hepatitis(10) NAFLD (6) No cause identified (3) Alcohol (1) Genetic haemochromatosis (1)
10-14 (F3 fibrosis)	7 / 150 (4.7)	Normal = 4 / 7 (57.1) Abnormal = 3 / 7 (42.9)	Viral hepatitis(5) NAFLD (4)
>14 (F4 fibrosis)	10 / 150 (6.7)	Normal = 3 / 10 (30.0) Abnormal = 7 / 10 (70.0)	Viral hepatitis (6) NAFLD (3) Alcohol (1)

*Liver stiffness cut-off values with FibroScan® vary by liver disease. Cut-offs provided are based on NAFLD
[^]Viral hepatitis = hepatitis B and/or C virus co-infection

Median FibroScan® score: 5.4 kPa (range 2.8 – 72 kPa)

Results Table 3: Fibrosis staging by liver biopsy (available for 21/150 patients)

FibroScan (kilopascals)	Clinical diagnosis	Histological diagnosis
6.5	NAFLD	Steatohepatitis , mild fibrosis
7.5	NAFLD	Moderate steatosis with features of steatohepatitis, moderate fibrosis
8.2	Genetic haemochromatosis	Haemochromatosis associated with mild to moderate fibrosis
4.9	NAFLD	Moderate steatosis with inflammatory changes amounting to steatohepatitis, minimal fibrosis
36.9	NAFLD	Steatohepatitis with severe fibrosis amounting to established cirrhosis
3.4	NAFLD	Mild steatosis only
6.1	NAFLD	Steatohepatitis , mild fibrosis
7.4	No cause identified	Resolving hepatitis ?cause, no significant fibrosis
17.5	Viral hepatitis	Moderately severe chronic hepatitis, mild fibrosis
10.7	NAFLD	Steatohepatitis , mild to moderate fibrosis
4.9	No cause identified	No fatty liver disease or fibrosis. No aetiological clues
10.1	NAFLD	Steatohepatitis, mild to moderate fibrosis
6.3	NAFLD	Mild fatty change, no significant fibrosis
16.9	NAFLD	Moderate fibrosis with bridging, underlying aetiology not readily evident
3.9	No cause identified	Minimal steatosis not amounting to steatohepatitis or fatty liver disease, no evidence chronic liver disease
6.1	Alcohol	Mild fibrosis, suggestion vascular architectural changes as might be seen with large vessel disease or drug reaction, fatty change very mild and not in pattern of fatty liver
8.7	NAFLD	Steatohepatitis, mild fibrosis
10.5	NAFLD	Steatohepatitis, mild to moderate fibrosis
6.0	NAFLD	Steatohepatitis, mild fibrosis
9.0	Biliary pathology	Mild fibrosis, paucity of bile ducts
16.5	NAFLD	Mild steatosis, very mild fibrosis

Summary

- 26.7% of this small cohort with abnormal liver function tests had significant liver fibrosis predicted by FibroScan® (≥7.0kPa).
- ALT correlated poorly with presence of significant liver fibrosis.
- Viral hepatitis and NAFLD were the most common causes of significant liver fibrosis
 - 53.8% (21/39) of patients with viral hepatitis had significant liver fibrosis
 - 18.6% (13/70) of patients with NAFLD had significant liver fibrosis.
- 14/21 (66.7%) patients undergoing liver biopsy had a clinical diagnosis of NAFLD
 - 71.4% (10/14) had steatohepatitis on liver biopsy and were at risk of progression to liver cirrhosis
 - 75.0% (6/8) of patients with significant liver fibrosis predicted by FibroScan® had steatohepatitis on biopsy
 - 66.7% (4/6) of patients with a normal FibroScan® score had steatohepatitis on liver biopsy.
 - 57.1% (8/14) were predicted to have significant liver fibrosis by FibroScan® of which 7 (87.5%) had at least mild fibrosis confirmed on liver biopsy

Conclusion

- The prevalence of significant liver fibrosis in our HIV cohort with abnormal liver function tests was 26.7%. ALT appeared to correlated poorly with presence of liver fibrosis and significant and reversible liver disease may be missed if fibrosis assessment tools are not included in screening algorithms.

References

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