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TITLE: NONALCOHOLIC STEATOHEPATITIS DIAGNOSED BY THE SERUM BIOMARKER CYTOKERATIN 18 IS FREQUENT IN HIV INFECTED PATIENTS AND IS ASSOCIATED WITH LIVER FIBROSIS BY TRANSIENT ELASTOGRAPHY

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AWARDS:

ABSTRACT BODY:

Aims: Nonalcoholic steatohepatitis (NASH) is a leading cause of end-stage liver disease and the third indication for liver transplantation in Canada. HIV infected patients are at high risk of NASH due to metabolic comorbidities, long-lasting use of antiretroviral medications, chronic inflammation related to HIV. Nevertheless, due to the invasiveness of liver biopsy, data on NASH in HIV mono-infected patients are scarce. No study has employed cytokeratin 18 (CK-18), a validated biomarker for the non-invasive diagnosis of NASH, and transient elastography (TE) with controlled attenuation parameter (CAP) to dissect prevalence and cofactors of NASH in HIV mono-infected patients without hepatitis B or C.

Methods: This was a prospective cohort study of consecutive HIV mono-infected persons enrolled at McGill University Health Centre. Patients with significant alcohol intake or coinfection with hepatitis B or C were excluded. NASH was diagnosed by CAP >232 dB/m and CK-18 level >246 U/L. Significant liver fibrosis and cirrhosis were defined as TE measurement >8 kPa and >13 kPa, respectively. A subgroup of patients with a non-invasive diagnosis of NASH underwent liver biopsy. Spearman's rho was used to investigate correlations between CK-18 and other factors. Cofactors associated with NASH were determined by multivariate logistic regression models.

Results : Overall, 122 HIV mono-infected persons (mean age 51.6 years, 80.8% men) were included. Median CK-18 levels were 90.7 U/L (IQR 54.9-138.2). Prevalence of NASH was 9.8%. Significant liver fibrosis and cirrhosis were found in 9.1% and 2.5% of cases, respectively. Liver histology was requested in 10 out of 12 patients with a non-invasive diagnosis of NASH and it confirmed such a diagnosis in all cases. Serum CK-18 levels correlated with CAP value ($r=0.21$, $p=0.02$), TE measurement ($r=0.34$, $p<0.001$) and ALT ($r=0.59$, $p<0.001$). After adjusting for age and BMI, elevated ALT (odds ratio=48.85, 95% CI 5.24-455.27; $p=0.001$) and TE measurement (odds ratio=1.31, 95% CI 1.02-1.69; $p=0.03$) were independent predictors of NASH. Moreover, after adjustments for BMI and albumin, NASH was an independent predictor of significant liver fibrosis (odds ratio=23.49, 95% CI 2.75-200.85; $p=0.004$).

Conclusions: NASH diagnosed by cytokeratin 18 and CAP is frequent in HIV mono-infected persons, particularly in those with elevated ALT and higher TE measurement. Importantly, NASH diagnosed by CK-18 and CAP is a predictor of significant liver fibrosis by TE. Longitudinal studies are needed to evaluate the impact of non-invasive screening strategies and interventions aimed at reducing morbidity and mortality due to liver disease in this population.

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Supervisor Letter-Core: