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LETTER TO EDITOR
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Estimated time from clinical presentation to the development of cirrhosis in non-cirrhotic adult patients with non-alcoholic fatty liver disease

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Dear Editor:

The natural history of non-alcoholic fatty liver disease (NAFLD) has yet to be fully defined.[1] In the few relevant studies reported to date, repeat liver biopsies were performed in highly selected, predominantly non-alcoholic steatohepatitis (NASH) patients who may not reflect the general NAFLD population.[2,3] Although newly developed, non-invasive means of documenting hepatic fibrosis will play an important role in providing natural history data, prospective studies implementing these techniques will take years and likely decades to complete. In the present study we employed reversal of serum alanine to aspartate aminotransferase (ALT/AST) > 1 ratios to determine the time from initial presentation to development of advanced fibrosis/cirrhosis in adult NAFLD patients referred to our outpatient liver program between the years 1992-2012.

A total of 343 subjects (51% female, mean ages 46 years [range: 18-84 years]) with radiologic evidence of fatty infiltration of the liver, elevated serum aminotransferase levels, ALT/AST > 1 and no evidence of concurrent liver disease were followed in a tertiary care, outpatient clinic with standard liver enzyme and function testing every six months for a mean of 3.1 years (range: 1.0-20 years). In addition to patient demographics, risk factors for NAFLD (obesity, diabetes, hyperlipidemia and hypertension), liver function tests (albumin, bilirubin and international normalized ratio for prothrombin times) and complete blood cell counts (hemoglobin, white cell and platelet counts) were documented at baseline to identify variables that might predict progression to advanced fibrosis/cirrhosis.

Fifty-two patients (15%) reversed their ALT/AST > 1 ratio during the follow-up period. The mean ± SD time interval to this outcome in these individuals was 2.01 ± 1.87 years (range: 0.1-8.2 years). Logistic regression analysis revealed that high BMI scores and low serum albumin at presentation were the only predictor variables of ratio conversion. However, these variables served to explain only 20% of cases ($R^2 = 0.12$).

The results of this study provide an approximation of the percent of subjects (15%) and time interval (2 years) between when presumably non-cirrhotic NAFLD patients present to a tertiary care centre outpatient clinic for evaluation and the subsequent development of advanced fibrosis/cirrhosis. Although these findings are of practical value, they must be interpreted in the context of certain important limitations. For example, the data set did not distinguish between patients with simple steatosis (with elevated serum aminotransferase levels) and non-alcoholic steatohepatitis (NASH). The findings also do not account for patients presenting at different stages in the course of their disease. Although therapeutic interventions that might alter the course of NAFLD (vitamin E or thiazolidinediones) were limited to less than 5% of the study population, the effects of dieting and other life style changes that were advocated could not be ascertained.[4] Finally, although commonly employed as a non-invasive marker of progression to advanced fibrosis/cirrhosis, the ALT/AST ratio has limitations with respect to sensitivity and specificity.[5,6]

Despite the above limitations, the results of this study provide preliminary data to suggest the mean time from presentation of presumably non-cirrhotic NAFLD patients to a tertiary care centre for evaluation of their liver disease to the development of advanced fibrosis/cirrhosis can be relatively short and baseline BMI determinations and serum albumin levels might serve to identify which patients are at highest risk of developing such an outcome within that time frame.

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