

Increasing Metabolic Co-morbidities Are Associated With Higher Risk of Advanced Fibrosis in Nonalcoholic Steatohepatitis

Background

- Nonalcoholic fatty liver disease (NAFLD) is the accumulation of fat in the liver in people who drink little to no alcohol. Nonalcoholic steatohepatitis (NASH) is the most severe form; it is characterized by inflammation of the liver and can progress to cirrhosis or cancer.
- Among NASH patients, liver fibrosis is a strong indicator of liver-related complications and death.^{1,2} Prevalence estimates of NASH with advanced fibrosis are based on studies that are limited by study type (cohort-type or survey) or the likely underdiagnosis of NASH (due to defining criteria).
- A better understanding of the prevalence and metabolic risk factors for advanced fibrosis is important for effectively targeting preventive care.
- **Objective:** In this Quest Diagnostics Health Trends study, the investigators examined the prevalence of advanced fibrosis across a large US adult population. They also evaluated the association of metabolic co-morbidities with advanced fibrosis.

Methods

- Deidentified clinical laboratory data of adults (≥18 years old) were obtained from the Quest Diagnostics clinical laboratory database (10/1/2017-9/30/2018).
 - Patients were excluded if they had hepatitis B or C, alcoholic liver disease, or evidence of pregnancy.
- The proportions of patients with stage F3 and F4 fibrosis were evaluated using the fibrosis 4 (FIB-4) score; 5 sets of cutoffs were used to define the stages (eg, F3/F4 defined as FIB-4>2.67).³
- The following metabolic co-morbidities were assessed: decreased high-density lipoprotein (<40 mg/dL men, <50 mg/dL women), high triglycerides (≥150 mg/dL), elevated hemoglobin A1c (≥6.5%), and hypertension (by ICD-9/10 codes).
- A parallel analysis was performed using deidentified data from patients with NAFLD or NASH (determined by ICD-9/10 codes from 10/1/2013-9/30/2018). Multivariate logistic regression models were used to evaluate predictors of advanced (F3/F4) fibrosis.

Results

- The overall study population included 20,204,004 patients (mean age: 54.6 years; 57.4% female). With FIB-4 >2.67 as a threshold, 3.12% had advanced (F3/F4) fibrosis.
- Among NAFLD/NASH patients (n=208,749), 4.35% to 6.90% (depending on criteria) had advanced fibrosis and 2.52% to 3.67% had cirrhosis.
- Among NAFLD/NASH patients, co-morbidities were associated with greater risk of advanced fibrosis. The odds of advanced fibrosis were significantly higher for those with 1 (odds ratio [OR]=1.18), 2 (OR=1.28), 3 (OR=1.34), or 4 (OR=1.56) co-morbidities compared to those with none (all P<0.001).

Conclusions

- The prevalence of advanced fibrosis among NASH patients was as high as 6.9%. Thus, NASH with advanced fibrosis may affect up to 5.18 million people (based on an estimate of 75 million US patients with NAFLD).
- Higher numbers of metabolic comorbidities are associated with increased odds of advanced fibrosis.

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