Predictive Risk Score for Nonalcoholic Steatohepatitis Among Patients in the US Department of Defense Population

Onur Baser, MA, MS, PhD[1,2,3]; Erdem Baser, MA, MS, PhD[4]; Nehir Yapar, MS[4]; Gabriela Samayoa, MD, MPH[4]; Anna Budhu, MPH[4]

[1]Graduate School of Public Health, City University of New York, New York, NY, USA; [2]Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA; [3]Department of Economics, Bogazici University, Istanbul, Turkey; [4]Columbia Data Analytics, New York, NY, USA

BACKGROUND

Non-alcoholic steatohepatitis (NASH) is underdiagnosed and imposes a substantial burden on patients, providers, and payers and can lead to the development of end-stage liver disease, cirrhosis, or hepatocellular carcinoma. Although NASH is a leading risk factor for end-stage liver disease and cardiometabolic diseases, the condition often goes undiagnosed in clinical practice because of the need for direct imaging assessments.[1]

The non-specific nature of NASH symptoms creates a challenge to diagnose the condition using routine laboratory tests or clinical examination.[2] Despite underdiagnosis, NASH prevalence is rapidly increasing alongside the global epidemics of obesity and diabetes.[1]

In clinical practice and experimental trials, liver biopsy is currently the standard for diagnosis and staging of NASH.[2] The treatment is invasive and carries certain risks, including bleeding and pain after the surgery as well as additional expenses.[2]

OBJECTIVES

This study aimed to measure the impact of risk factors and create a predictive risk score on NASH that can help the management of the disease and increase the likelihood of early diagnoses.

METHODS

- **Data Source:** US Department of Defense (DoD) data
- **Study Period:** 01JAN2019 - 01OCT2022
- **Sample Size:** 10,551 patients with NASH; 6,413,061 non-NASH patients
- **Key Independent Variable:** NASH diagnosis
- **Outcome Variable:** Impact of risk factors on NASH

Inclusion Criteria

Patients were included if they:

a. had at least 1 diagnosis of NASH during the identification period (01JAN2020-01OCT2022)

b. were ≥18 years of age

Exclusion Criteria

a. Patients with nonalcoholic fatty liver disease and cirrhosis were excluded.

RESULTS

Descriptive Analysis

We identified 10,551 patients with NASH and 6,413,061 non-NASH patients. The mean age for the NASH population was 61.28 years, and 55.84 years (p<0.0001) for the non-NASH population.

NASH-related baseline comorbidities including hypertension (48.86% vs 21.90%, p<0.0001) and type 2 diabetes (39.16% vs 10.50%, p<0.0001) were significantly higher among patients with NASH.

RESULTS (cont'd)

Table 1. Baseline Characteristics of Patients with vs without NASH (DoD Population)

	NASH (N = 10,551)		Non-NASH (N = 6,413,061)			
	N/Mean	%/SD	N/Mean	%/SD	p-value	Std. Diff.
Age (years)	61.28	14.51	55.84	20.14	<0.0001	0.2701
Age Group: 18-45	1,583	15.00%	2,093,624	32.65%	<0.0001	0.3764
Age Group: 46-54	1,466	13.89%	726,115	11.32%	<0.0001	0.0812
Age Group: 55-64	2,371	22.47%	975,763	15.22%	<0.0001	0.202
Age Group: ≥65	5,131	48.63%	2,617,559	40.82%	<0.0001	0.159
Gender						
Male	4,404	41.74%	2,765,767	43.13%	0.004	0.028
Female	6,147	58.26%	3,647,294	56.87%	0.004	0.028
US Region						
Northeast	1,889	17.90%	1,245,246	19.42%	<0.0001	0.0383
South	4,598	43.58%	2,427,181	37.85%	<0.0001	0.1182
Midwest	2,047	19.40%	1,333,127	20.79%	0.0005	0.0342
West	1,800	17.06%	1,241,509	19.36%	<0.0001	0.0582
Other	217	2.06%	165,998	2.59%	0.0006	0.0335
Comorbidities						
Obesity	2,179	20.65%	412,758	6.44%	<0.0001	0.5785
Hypertension	5,155	48.86%	1,404,621	21.90%	<0.0001	0.6515
Type 2 Diabetes	4,132	39.16%	673,783	10.51%	<0.0001	0.9333
Dyslipidemia	3,216	30.48%	890,459	13.89%	<0.0001	0.4796
Triglyceridemia	1,690	16.02%	373,750	5.83%	<0.0001	0.4344
Abnormal AST/ALT	270	2.56%	11,427	0.18%	<0.0001	0.5586
Abnormal Ferritin Levels	818	7.75%	96,690	1.51%	<0.0001	0.5109
Abnormal Liver Results	913	8.65%	28,758	0.45%	<0.0001	1.2115
Depressed HDL Cholesterol	34	0.32%	4,604	0.07%	<0.0001	0.0932

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HDL, high-density lipoprotein; NASH, non-alcoholic steatohepatitis; SD, standard deviation; Std. Diff., standardized difference

Logistic Regression Analysis

Increased age (odds ratio [OR]=1.99, 95% confidence interval [CI]=1.85-2.14 for ages 46-54; OR=2.04, 95% CI=1.91-2.18 for ages 55-64; reference: age 18-45), baseline abnormal AST/ALT level (OR=4.46, 95% CI=3.91-5.10), and abnormal liver tests (OR=10.01, 95% CI=9.29-10.79) were associated with increased odds of NASH, among other factors.

RESULTS (cont'd)

Table 2. Association of Demographics and Comorbid Conditions and NASH

	NASH			
	Odds Ratio	Z-value	95% Confidence Limits	
			Lower	Upper
Age (years)				
Age Group: 46-54	1.9923	0	1.8535	2.1416
Age Group: 55-64	2.0368	0	1.9063	2.1763
Age Group: ≥65	1.4025	0	1.3192	1.4909
Sex				
Male	0.8326	0	0.8008	0.8658
US Region				
Northeast	0.9723	0.698	0.8438	1.1205
South	1.1463	0.052	0.9989	1.3155
Midwest	1.0063	0.93	0.8737	1.159
West	0.991	0.901	0.8597	1.1424
Baseline Comorbidities				
Hypertension	1.5473	0	1.4722	1.6261
Type 2 Diabetes	3.3549	0	3.2021	3.515
Dyslipidemia	1.0964	0	1.0443	1.151
Triglyceridemia	1.3335	0	1.2608	1.4104
Abnormal AST/ALT	4.4631	0	3.9069	5.0985
Abnormal Ferritin Levels	2.2516	0	2.0854	2.4311
Abnormal Liver Results	10.0142	0	9.2936	10.7908
Depressed HDL Cholesterol	2.1378	0	1.5141	3.0183

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HDL, high-density lipoprotein; NASH, non-alcoholic steatohepatitis

CONCLUSION

In the US DoD population, comorbid abnormal AST/ALT and abnormal liver results were associated with the highest odds of NASH.

REFERENCES

1. Haas ME, Pirruccello JP, Friedman SN, et al. Machine learning enables new insights into genetic contributions to liver fat accumulation. *Cell Genom.* 2021;1(3):100066.

2. Docherty M, Regnier SA, et al. Development of a novel machine learning model to predict presence of nonalcoholic steatohepatitis. *J Am Med Informatics Assoc.* 2021;28(6):1235-41.