Community Socioeconomic Deprivation Predicts Nonalcoholic Steatohepatitis

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In order to determine the relationship between socioeconomic deprivation and nonalcoholic fatty liver disease (NAFLD)/nonalcoholic steatohepatitis (NASH), we retrospectively reviewed the electronic medical records of 1,430 patients in a large tertiary health care network in New York. These patients underwent liver biopsy over a 10-year period and were included in our study if they had evidence of NAFLD/NASH on liver biopsy. Zip codes were used to obtain data necessary to derive the social deprivation index (SDI) from the US Bureau of the Census. The high-SDI group was compared to the low-SDI group. Univariate and multivariate logistic regressions were performed to assess association between socioeconomic factors and NAFLD parameters, including presence of NASH (NAFLD activity score >4), moderate to severe steatosis (>33%), and significant fibrosis (S2-S4). We included 614 patients with NAFLD/NASH; the median SDI was 31.5. Hemoglobin A1c values were higher in the high-SDI group compared to the low-SDI group (6.46 vs. 6.12, *P* = 0.02). Socioeconomic factors, such as private versus public health care, percentage being foreign born, percentage without a car, percentage with higher needs (<5 years old and >65 years old), and percentage currently living in renter-occupied and crowded housing units, showed statistically significant associations in predicting NASH. After adjusting for patient age, sex, race, body mass index, and diabetes, we saw a significant association between four or more socioeconomic parameters in predicting NASH (odds ratio [OR], 1.71; 95% confidence interval [CI], 1.099-2.856; *P* = 0.0190) and six or more socioeconomic parameters in predicting severe steatosis (OR, 1.498; 95% CI, 1.031-2.176; *P* = 0.0338) but no significant correlation between the number of socioeconomic parameters and significant fibrosis. *Conclusion:* Greater number of socioeconomic determinants (four or more) are associated with greater severity of NASH. Awareness of NAFLD/NASH needs to be raised in communities with high socioeconomic deprivation. (*Hepatology Communications* 2022;6:550-560).

Nonalcoholic fatty liver disease (NAFLD) has a current global prevalence of 24%, with nonalcoholic steatohepatitis (NASH) representing 25% of this population. NAFLD is expected to increase by approximately 30% globally, affecting 100 million people solely in the United States over the next decade.[1-4] This increase in prevalence of NAFLD will predominately affect areas of growing urbanization and decreasing population size.[4] The increasing clinical impact of NAFLD is already becoming obvious. In the 5-year period between 2012 and 2017, there was greater than a 20% and 15% increase in deaths related to liver cancer and cirrhosis, respectively, in patients initially diagnosed with NAFLD/NASH.[5] In addition, it is well known that people with NAFLD are also at risk for cardiometabolic disease, nonhepatocellular carcinoma, malignancy, lung disease, and diabetes.[6,7]

Globally, NAFLD stands as the number one cause of end-stage liver disease, and chronic liver disease

Abbreviations: ACS, American Community Survey; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CI, confidence interval; EHR, electronic health record; NAFLD, nonalcoholic fatty liver disease; NAS, nonalcoholic fatty liver disease activity score; NASH, nonalcoholic steatohepatitis; OR, odds ratio; S, stage of fibrosis; SDI, social deprivation index.

Received May 18, 2021; accepted September 8, 2021.

View this article online at wileyonlinelibrary.com.
DOI 10.1002/hep4.1831

Potential conflict of interest: Dr. Bernstein advises Novartis. The other authors have nothing to report.

has now become one of the world's leading causes of death.[8,9] In fact, as of 2019, cirrhosis of the liver was the tenth and eighth leading cause of death in low-income and lower-middle-income countries, respectively.[10] Traditionally, NAFLD was rarely seen in countries with lower income. However, their rates of NAFLD have steeply increased as these countries started experiencing higher rates of metabolic disease. Additionally, while such low-income countries have started to see higher rates of NAFLD, there has been a significantly larger growth in the prevalence of NAFLD in countries with a middle- to high-socioeconomic demographic index.[11]

The risk factors of NAFLD are still being explored. Known risk factors include obesity, type two diabetes mellitus, hypertriglyceridemia, and metabolic syndrome. Suspected risk factors include hypothyroidism, hypopituitarism, hypogonadism, obstructive sleep apnea, polycystic ovarian syndrome, total parenteral nutrition, excessive fructose consumption, rapid weight loss, and the presence of patatin-like phospholipase domain-containing 3 (*PNPLA3*) and transmembrane 6 superfamily 2 (*TM6SF2*) genes.[12,13] Other possible predictors of NAFLD are inadequate physical activity, sedentary behavior, high-calorie diets, food insecurity, and adoption of a westernized diet[14-17]

NAFLD is considered to be a hepatic manifestation of Metbaolic Syndrome. A large prospective observational study in Japan showed that people with metabolic syndrome at baseline were more likely to develop NAFLD and less likely to regress NAFLD.[18] Metabolic derangements, such as impaired fasting glucose, act as independent risk factors for death in patients with NAFLD.[19] This is concerning as the number of individuals in the United States with diabetes is expected to increase 165% by year 2050.[20] Metabolic syndrome and type 2 diabetes are two risk factors that tend to also be prevalent in more socioeconomically deprived areas.[21-23] Additionally, individuals consistently exposed to high community socioeconomic disadvantage were more likely to have diabetes, hypertension, obesity, and fatty liver disease compared to those who were consistently exposed to low community socioeconomic disadvantage.[24] Most studies imply but do not prove an association between socioeconomic status and NAFLD, because the risk factors of NAFLD are highly prevalent in societies of lower socioeconomic standing. There is no literature evaluating the direct association between the presence of individual socioeconomic factors and NAFLD/NASH in adults in the United States. Additionally, we lack data regarding the association between socioeconomic factors and severity of NAFLD/NASH. In the present study, we sought to determine the relationship between socioeconomic deprivation in a biospy proven cohort of NAFLD/NASH.

Materials and Methods

STUDY DESIGN

This is a retrospective study of compiled data from both the inpatient and outpatient electronic health records (EHRs) (Sunrise Clinical Manager; Allscripts,

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Chicago, IL) of 1,430 patients from a large health system in the New York City area. The data included records from 12 hospitals within the Northwell Health system in New York.

INCLUSION/EXCLUSION CRITERIA

Patients included in the study had a liver biopsy between the years 2015 and 2020, had at least 5% steatosis and a NAFLD activity score (NAS) of 1 or greater regardless of serologies, were at least 18 years old, and currently reside in the New York area. Those without recorded or accurate zip codes or had duplicated files in the EHRs were considered "incomplete data" and excluded from the study.

Patients with a history of other chronic liver diseases (n = 198), including viral hepatitis, primary biliary cholangitis, primary sclerosing cholangitis, hereditary liver disease, autoimmune liver disease, or alcohol-associated liver disease, were excluded from this study. Identifying patients with alcohol-associated liver disease was difficult and based on a patient's self-reporting. Using the Centers for Disease Control and Prevention guidelines for recommended daily intake of alcohol, we included women who reported drinking one drink or less per day and men who reported drinking two drinks or less per day.

Details of the inclusion and exclusion criteria adapted to obtain the final cohort of 614 patients with NAFLD/NASH are presented in Fig. 1.

SOCIAL AND ECONOMICAL DETERMINANTS OF HEALTH VARIABLES

The social deprivation index (SDI) is a measurement used to dictate the impoverishment of an area based on social, economic, and health factors. Scores range from 0 to 100, with higher scores indicating more disadvantage. The SDI is derived from features that include the percentage of population less than 100% of the federal poverty level or the percentage below the poverty estimate based on income in the past 12 months, percentage of the population 25 years or more with less than 12 years of education, percentage of nonemployed/unemployed, percentage of the population living in renter-occupied housing, percentage of the population living in crowded spaces indicated by greater than 1.01 to 1.50 occupants per room, percentage with no vehicle available, percentage of single-parent households with dependents less than 18 years old, percentage of the population that is non-Hispanic black, percentage that is Hispanic, and percentage of the population deemed to be high needs (which include people over the age of 65, under the age of 5, and women).[25]

The SDI was calculated by the Robert Graham Center and is based on data from the 5-year Summary File American Community Survey (ACS) from 2011 to 2015.[25] Additional social and economic factors included in the study were percentage of the population

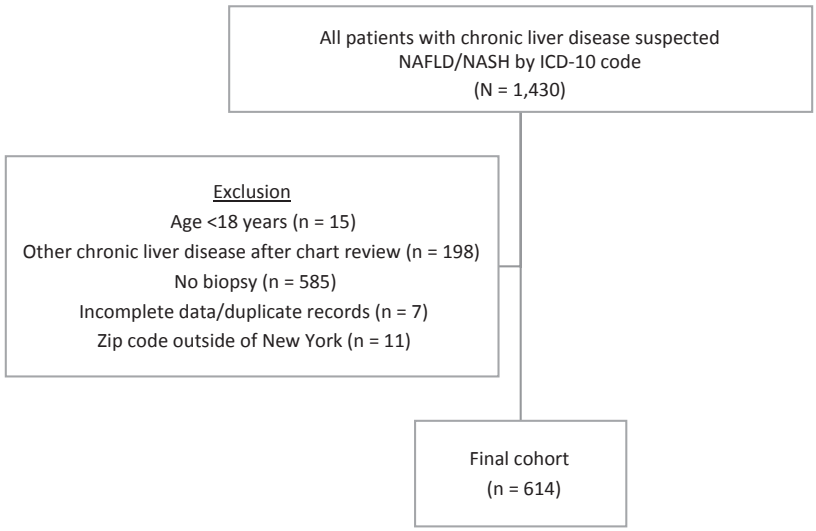

FIG. 1. Algorithm of inclusion and exclusion. Abbreviation: ICD-10, International Classification of Diseases, Tenth Revision.

unemployed; percentage of the population with a high school diploma as the highest level of education; percentage of the population with a bachelor's degree or higher; percentage of the population with private, public, or no health care; and percentage of the foreign-born population. This data was collected from the 5-year Summary File ACS from 2014 to 2018.[26,27]

CENSUS TRACKING

All socioeconomic values are based on patients' current zip codes collected from the EHRs. Information regarding the social and economic status of different areas in New York was extracted from the US Bureau of the Census from ACS reports from 2011 to 2015 and 2014 to 2018.[26,27]

CLASSIFICATION OF LIVER DISEASE SEVERITY

Liver histopathology data of the studied group were extracted from the EHR and the subjectes were classified based on degree of steatosis (steatosis: 0, <5%; 1, 5%-33%; 2, 33%-66%; 3, >66%), lobular inflammation (lobular inflammation: 0, none; 1, <2 foci per 200× field; 2, 2-4 foci per 200× field; 3, >4 foci per 200× field), ballooning (ballooning: 0, none; 1, few cells; 2, many cells), NAS (steatosis + lobular inflammation + ballooning), and fibrosis stage (S0-S4). A true NASH diagnosis was defined as NAS > 4.[28] Significant steatosis was defined as a steatosis grade of 1 or greater (>33%). Significant fibrosis was defined as fibrosis stage 2 or greater.

STATISTICAL ANALYSES

Patient-specific variables categorized as clinical, biochemical, and histologic and patient zip code-specific variables categorized as social/economic variables were analyzed for mean and median values. The median value of the SDI from 2015 (31.5) was used to dichotomize the cohort into high SDI (≥31.5) versus low SDI (<31.5). Univariate and multivariate logistic regression was performed to assess association between the SDI and NAFLD parameters, including presence of NASH (NAS > 4), moderate to severe steatosis (>33%), and significant fibrosis (S2-S4) in the population. We used two-sided tests with $\alpha = 0.05$. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

A total of 614 patients with biopsy-proven liver disease were divided into being from a low- or high-SDI area based on the median SDI of the entire cohort, which was 31.5. Comparison of clinical, biochemical, socioeconomic, and histologic factors are listed in Table 1. There were approximately twice as many women compared to men (400 vs. 214) and more non-Hispanic (72.8%) and white (60.20%) patients, most of whom were from low-SDI areas. In the high-SDI group, there was a higher number of Hispanic/Latino (100 vs. 33), multiracial (101 vs. 30), African American/black (51 vs. 8), and Asian (15 vs. 8) patients compared to the low-SDI group ($P < 0.0001$). Those from the high-SDI group were younger than those from the low -SDI group (mean ± SD, 50.64 ± 14.62 years vs. 53.14 ± 13.77 years; $P = 0.0297$). There was no significant difference in laboratory values between the groups in terms of platelet counts, alkaline phosphate, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, and international normalized ratio. Both groups had elevated AST, ALT, body mass index (BMI), and lipids at baseline. Approximately one-third of patients in our study have diabetes. Despite no significant difference in the prevelence of diabetes between low- vs. high-SDI groups, the high-SDI group had higher hemoglobin A1c (HbA1c) (mean ± SD, 6.46 ± 1.53 vs. 6.12 ± 1.14; $P = 0.0227$). Median values of socioeconomic factors were all significant as the groups were separated based on these factors ($P < 0.0001$).

Although there were no statistically significant differences in hepatic steatosis and fibrosis between high- versus low-SDI groups, the high-SDI group had more lobular inflammation (mean ± SD, 0.48 ± 0.68 vs. 0.38 ± 0.62; $P = 0.0622$) and higher NAS (mean ± SD, 2.4 ± 1.45 vs. 2.19 ± 1.36; $P = 0.0627$) compared to the low-SDI group. Further analysis showed that more patients had NASH (NAS > 4) in the high-SDI group (23.13% vs. 16.29%, $P = 0.0331$) (Fig. 2). Additionally, there was a trend toward higher rates of moderate to severe steatosis (>33%) in the high-SDI group (53.96% vs. 46.99%, $P = 0.0871$).

Certain social and economic determinants were found to predict significant fibrosis, NASH, and severe steatosis. Those living in areas where a high percentage of the population had acquired higher

TABLE 1. DEMOGRAPHIC, BIOLOGICAL, AND SOCIOECONOMIC FACTORS BETWEEN HIGH- VERSUS LOW-SDI AREAS

Main Class	Parameter	All Patients	SDI <31.5	SDI ≥31.5	*P* Value
Clinical	Male (n; %)	214; 34.85	119; 38.76	95; 30.94	0.0421
	Female (n; %)	400; 65.15	188; 61.24	212; 69.06	
	Hispanic or Latino (n; %)	133; 21.66	33; 10.75	100; 32.57	<0.0001
	Not Hispanic or Latino (n; %)	447; 72.80	265; 86.32	182; 59.28	
	Unknown (n; %)	34; 5.54	9; 2.93	25; 8.14	
	Asian (n; %)	23; 3.78	8; 2.64	15; 4.92	<0.0001
	White (n; %)	366; 60.20	249; 82.18	117; 38.36	
	Black or African American (n; %)	59; 9.70	8; 2.64	51; 16.72	
	Other/multiracial (n; %)	131; 21.55	30; 9.90	101; 33.11	
	Unknown (n; %)	29; 4.77	8; 2.64	21; 6.89	
	Age (n; % ± SD)	614; 51.89 ± 14.24	307; 53.14 ± 13.77	307; 50.64 ± 14.62	0.0297
	Diagnosed with type 2 diabetes mellitus (n; %)	181; 29.48	93; 30.3	88; 28.7	0.6581
Biochemical	BMI, kg/m^2 (n; mean ± SD)	597 ; 37.31 ± 8.53	299; 37.87 ± 8.42	298; 36.75 ± 8.61	0.1082
	Hemoglobin, g/dl (n; mean ± SD)	591; 13.10 ± 1.73	299; 13.25 ± 1.65	292; 12.95 ± 1.79	0.0343
	Platelet count, x10^9 per liter (n; mean ± SD)	591; 245.02 ± 73.37	299; 240.49 ± 72.53	292; 249.65 ± 74.06	0.1292
	ALP, U/L (n; mean ± SD)	436; 108.88 ± 156.10	207; 104.70 ± 90.42	229; 112.66 ± 197.67	0.5831
	AST, U/L (n; mean ± SD)	436; 60.80 ± 80.09	207; 58.57 ± 70.77	229; 62.81 ± 87.78	0.5777
	ALT, U/L (n; mean ± SD)	436; 84.75 ± 155.82	207; 77.58 ± 106.63	229; 91.23 ± 189.64	0.3490
	Tbil, mg/dL (n; mean ± SD)	435; 0.93 ± 2.03	207; 0.87 ± 1.56	228; 0.99 ± 2.38	0.5493
	Albumin, g/dL (n; mean ± SD)	572; 4.04 ± 0.52	288; 4.07 ± 0.47	284; 4.02 ± 0.57	0.3165
	Cholesterol, mg/dL (n; mean ± SD)	299; 185.13 ± 49.08	150; 185.17 ± 46.44	149; 185.10 ± 51.76	0.9907
	HDL, mg/dL (n; mean ± SD)	298; 47.01 ± 14.25	150; 46.91 ± 13.79	148; 47.11 ± 14.75	0.9031
	LDL, mg/dL (n; mean ± SD)	295; 109.01 ± 42.19	147; 108.51 ± 40.86	148; 109.51 ± 43.60	0.8386
	Triglycerides, mg/dL (n; mean ± SD)	299; 154.17 ± 86.06	150; 158.93 ± 89.89	149; 149.37 ± 82.05	0.3375
	Hemoglobin A1c, whole blood % (n; mean ± SD)	326; 6.29 ± 1.35	168; 6.12 ± 1.14	158; 6.46 ± 1.53	0.0227
	INR, ratio (n; mean ± SD)	527; 1.13 ± 0.30	267; 1.11 ± 0.15	260; 1.15 ± 0.41	0.1457
Factors of SDI (2011-2015)	SDI 2015 (n; mean ± SD)	614; 36.90 ± 29.88	307; 11.43 ± 8.41	307; 62.37 ± 20.40	<0.0001
	Living in poverty (n; mean ± SD)	614; 26.74 ± 23.12	307; 8.57 ± 5.67	307; 44.90 ± 19.40	<0.0001
	Single-parent household (n; mean ± SD)	614; 34.52 ± 29.34	307; 12.74 ± 10.18	307; 56.30 ± 25.87	<0.0001
	Black non-Hispanic (n; mean ± SD)	614; 49.47 ± 27.01	307; 33.59 ± 19.95	307; 65.34 ± 23.61	<0.0001
	High school dropout (n; mean ± SD)	614; 45.59 ± 28.29	307; 22.95 ± 13.50	307; 68.23 ± 19.82	<0.0001
	Without a car (n; mean ± SD)	614; 59.94 ± 28.39	307; 38.92 ± 18.93	307; 80.95 ± 19.23	<0.0001
	Renters (n; mean ± SD)	614; 34.44 ± 31.61	307; 12.02 ± 13.13	307; 56.86 ±28.65	<0.0001
	Overcrowding housing unit (n; mean ± SD)	614; 52.48 ± 32.00	307; 25.02 ± 17.15	307; 79.93 ± 15.62	<0.0001
	Nonemployed (n; mean ± SD)	614; 40.87 ± 20.17	307; 30.94 ± 13.72	307; 50.80 ± 20.71	<0.0001
	Unemployed (n; mean ± SD)	614; 40.87 ± 20.17	307; 30.94 ± 13.72	307; 50.80 ± 20.71	<0.0001
	High-needs population (<5 years old, women and ≥65 years old) (n; mean ± SD)	614; 42.02 ± 25.96	307; 34.90 ± 23.78	307; 49.14 ± 26.13	<0.0001
	Hispanic (n; mean ± SD)	614; 63.51 ± 18.64	307; 50.34 ± 13.65	307; 76.67 ± 12.73	<0.0001
	Foreign born (n; mean ± SD)	614; 74.84 ± 18.60	307; 61.41 ± 14.29	307; 88.27 ± 11.26	<0.0001

TABLE 1. CONTINUED

Main Class	Parameter	All Patients	SDI <31.5	SDI ≥31.5	*P* Value
Additional socioeconomic factors (2014-2018)	Unemployment (n; mean ± SD)	614; 3.22 ± 1.17	307; 2.70 ± 0.68	307; 3.73 ± 1.33	<0.0001
	High school degree only (n; mean ± SD)	614; 24.96 ± 8.15	307; 23.03 ± 7.44	307; 26.88 ± 8.39	<0.0001
	Bachelor or higher(n; mean ± SD)	614; 39.32 ± 15.68	307; 46.82 ± 13.38	307; 31.83 ± 14.17	<0.0001
	Private health care(n; mean ± SD)	614; 74.95 ± 12.61	307; 85.06 ± 4.33	307; 64.84 ± 9.73	<0.0001
	Public health care (n; mean ± SD)	614; 30.62 ± 7.76	307; 25.71 ± 4.00	307; 35.53 ± 7.50	<0.0001
	No health care (n; mean ± SD)	614; 6.12 ± 4.02	307; 3.05 ± 1.48	307; 9.19 ± 3.36	<0.0001
	% Foreign born (n; mean ± SD)	614; 23.73 ± 14.54	307; 13.40 ± 7.20	307; 34.06 ± 12.55	<0.0001
Histologic findings*	Steatosis (n; mean ± SD)	614; 1.55 ± 0.70	307 1.50 ± 0.68	307; 1.60 ± 0.71	0.1051
	Lobular inflammation (n; mean ± SD)	614; 0.43 ± 0.65	307; 0.38 ± 0.62	307; 0.48 ± 0.68	0.0622
	Ballooning (n; mean ± SD)	614; 0.32 ± 0.54	307; 0.31 ± 0.53	307; 0.33 ± 0.56	0.5533
	NAS (n; mean ± SD)	614; 2.30 ± 1.41	307; 2.19 ± 1.36	307; 2.40 ± 1.45	0.0627
	Fibrosis stage (n; mean ± SD)	614; 0.80 ± 1.18	307; 0.76 ± 1.17	307; 0.84 ± 1.18	0.4306

Abbreviations: ALP, alkaline phosphate; HDL, high-density lipoprotein; INR, international normalized ratio; LDL, low-density lipoprotein; n, number of patients; Tbili, total bilirubin.
*Steatosis (0, <5%; 1, 5%-33%; 2, 33%-66%; 3, >66%), lobular inflammation (0, none; 1, <2 foci per 200× field; 2, 2-4 foci per 200× field; 3, >4 foci per 200× field), ballooning (0, none; 1, few cells; 2, many cells), NAS; fibrosis stage (0-4).

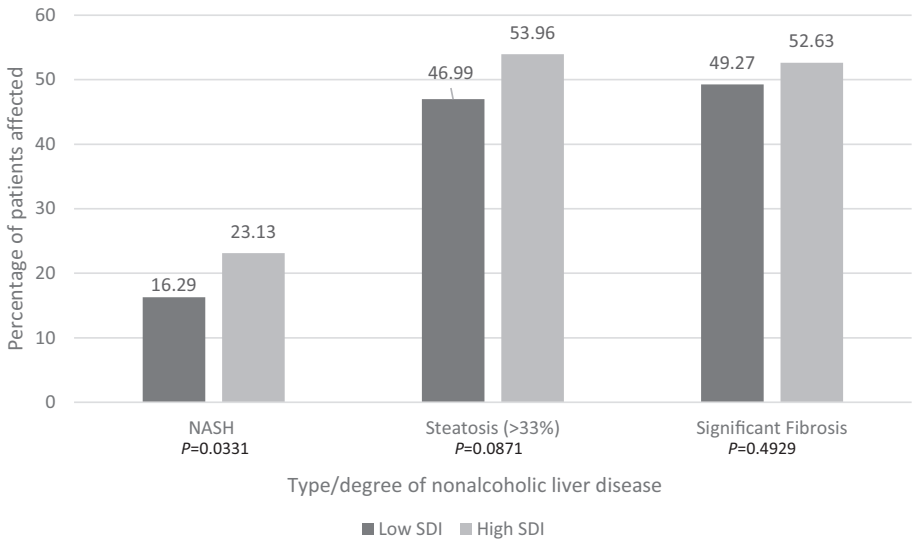

FIG. 2. Degree and severity of liver injury between high- versus low-SDI groups. NASH (NAS > 4), *P* = 0.0331; significant steatosis, *P* = 0.0871; significant fibrosis ≥2, *P* = 0.4929.

levels of education were associated with significant fibrosis (odds ratio [OR], 1.016; 95% confidence interval [CI], 1.002-1.031; *P* = 0.0291), and those earning solely a high school diploma had lower odds of having fibrosis (OR, 0.969; 95% CI, 0.941-0.997; *P* = 0.0315) (Table 2). No other variables were associated with significant fibrosis. The social and economic factors that were found to be associated with NASH included percentage of foreign-born residents, percentage with public health care, percentage without a car, and percentage of high-needs people in the area (Table 3). There was a strong association between having NASH and living in an area with a greater number of people with public health care (OR, 1.026; 95% CI, 1.001-1.052; *P* = 0.0395), whereas living in an area where more people had private health care

TABLE 2. SOCIAL AND ECONOMIC DETERMINANTS PREDICTING CLINICALLY SIGNIFICANT FIBROSIS

Social/Economic Variables (year of data collection)	OR (95% CI)	*P* Value
Unemployed (2018)	0.986 (0.805-1.208)	0.8930
Only high school diploma (2018)	0.969 (0.941-0.997)	0.0315
Bachelor's degree or higher (2018)	1.016 (1.002-1.031)	0.0291
Private health care (2018)	0.998 (0.980-1.017)	0.8596
Public health care (2018)	1.004 (0.975-1.035)	0.7771
No health care (2018)	0.995 (0.938-1.055)	0.8623
Foreign born (2018)	1.003 (0.987-1.019)	0.7463
SDI (2015)	1.001 (0.993-1.008)	0.8886
Poverty (2015)	1.003 (0.993-1.013)	0.5222
Single parent (2015)	0.996 (0.988-1.005)	0.3815
Black non-Hispanic (2015)	0.994 (0.985-1.003)	0.2013
High school dropout (2015)	0.996 (0.988-1.005)	0.3784
No car (2015)	1.004 (0.995-1.012)	0.3795
Nonemployment (2015)	1.000 (0.989-1.012)	0.9431
High needs (2015)	1.007 (0.998-1.016)	0.1191
Hispanic (2015)	0.998 (0.985-1.010)	0.7262
Foreign born (2015)	0.999 (0.987-1.012)	0.8952

TABLE 3. SOCIAL AND ECONOMIC DETERMINANTS PREDICTING NASH

Social/Economic Variables (year of data collection)	OR (95% CI)	*P* Value
Unemployed (2018)	0.845 (0.700-1.020)	0.0799
Only high school diploma (2018)	0.995 (0.971-1.020)	0.6917
Bachelor's degree or higher (2018)	1.001 (0.989-1.014)	0.8329
Private health care (2018)	0.984 (0.969-0.999)	0.0411
Public health care (2018)	1.026 (1.001-1.052)	0.0395
No health care (2018)	1.034 90.985-1.085)	0.1792
Foreign born (2018)	1.025 (1.012-1.039)	0.0003
SDI (2015)	1.006 (1.000-1.013)	0.0617
Poverty (2015)	1.006 (0.998-1.015)	0.1461
Single parent (2015)	1.001 (0.994-1.008)	0.7688
Black non-Hispanic (2015)	0.999 (0.991-1.006)	0.7313
High school dropout (2015)	1.007 (0.999-1.014)	0.0695
No car (2015)	1.012 (1.005-1.019)	0.0014
Nonemployment (2015)	0.999 (0.989-1.009)	0.8098
High needs (2015)	1.011 (1.004-1.019)	0.0034
Hispanic (2015)	1.008 (0.997-1.019)	0.1343
Foreign born (2015)	1.026 (1.014-1.039)	<0.0001

reduced the odds of having NASH (OR, 0.984; 95% CI, 0.969-0.999; P = 0.0411). Interestingly, the percentage of foreign-born people in the area was associated with significant steatosis (OR from 2015, 1.012; 95% CI, 1.003-1.021, P = 0.0087; OR from 2018, 1.015; 95% CI, 1.004-1.026; P = 0.0085) (Table 4).

TABLE 4. SOCIAL AND ECONOMIC DETERMINANTS PREDICTING MODERATE TO SEVERE STEATOSIS

Social/Economic Variables (year of data collection)	OR (95% CI)	*P* Value
Unemployment (2018)	0.983 (0.858-1.127)	0.8055
Only high school diploma (2018)	0.996 (0.977-1.016)	0.6910
Bachelor's degree or higher (2018)	1.000 (0.990-1.011)	0.9358
Private health care (2018)	0.991 (0.978-1.003)	0.1454
Public health care (2018)	1.007 (0.987-1.028)	0.5042
No health care (2018)	1.030 (0.990-1.072)	0.1442
Foreign born (2018)	1.015 (1.004-1.026)	0.0085
SDI (2015)	1.004 (0.999-1.009)	0.1414
Poverty (2015)	1.005 (0.998-1.012)	0.1712
Single parent (2015)	1.002 (0.996-1.007)	0.5722
Black non-Hispanic (2015)	1.000 (0.994-1.006)	0.9701
High school dropout (2015)	1.004 (0.998-1.009)	0.1961
No car (2015)	1.005 (1.000-1.011)	0.0695
Nonemployment (2015)	1.000 (0.992-1.008)	0.9685
High needs (2015)	1.003 (0.997-1.009)	0.3402
Hispanic (2015)	1.006 (0.997-1.014)	0.2046
Foreign born (2015)	1.012 (1.003-1.021)	0.0087

Individually, the SDI and other socioeconomic factors have varying associations with liver disease. However, grouping certain numbers of socioeconomic variables can predict the odds of having NASH and steatosis. Having four or more socioeconomic variables and six or more socioeconomic factors was found to be associated with increased odds of having NASH (having NAS > 4) and steatosis (>33%), respectively (Table 5). The greatest likelihood of having NASH is having five socioeconomic parameters present (OR, 1.689; 95% CI, 1.106-2.579; P = 0.0152). When adjusting for age, sex, race, BMI, and diabetic status, these odds increased to 1.946 (95% CI, 1.205-3.140; P = 0.0064) (Table 6). Analysis of the adjusted data shows that as the number of socioeconomic factors present increased, the odds of having NASH or steatosis increased. The accumulative number of socioeconomic factors did not predict fibrosis (S2-S4) even when the data was adjusted for age, sex, race, and BMI.

Discussion

Our study suggests an association between socioeconomic factors and severe steatosis and NASH in adults in a diverse population in the United States. Higher SDI regions were found to have significantly

TABLE 5. ASSOCIATION OF NUMBERS OF SDIS AND RISK OF NASH, MODERATE TO SEVERE STEATOSIS (>33%), OR SIGNIFICANT FIBROSIS (S2-S4), USING UNADJUSTED LOGISTIC REGRESSION ANALYSIS

Number of Socioeconomic Parameters	OR (95% CI)	*P* Value
Predictors of NASH (NAS > 4)		
1+	1.197 (0.587-2.441)	0.6203
2+	1.095 (0.696-1.723)	0.6956
3+	1.497 (0.968-2.317)	0.0700
4+	1.554 (1.018-2.374)	0.0412
5+	1.689 (1.106-2.579)	0.0152
6+	1.607 (1.071-2.411)	0.0221
Predictors of steatosis (>33%)		
1+	1.003 (0.581-1.731)	0.9928
2+	1.131 (0.788-1.623)	0.5038
3+	1.236 (0.883-1.730)	0.2180
4+	1.246 (0.897-1.730)	0.1896
5+	1.219 (0.880-1.688)	0.2339
6+	1.332 (0.967-1.836)	0.0798
Predictors of fibrosis (S2-S4)		
1+	1.363 (0.670-2.773)	0.3923
2+	1.048 (0.678-1.619)	0.8327
3+	1.283 (0.850-1.938)	0.2357
4+	1.159 (0.779-1.723)	0.4665
5+	1.212 (0.817-1.799)	0.3395
6+	1.218 (0.828-1.792)	0.3161

TABLE 6. ASSOCIATION OF NUMBERS OF SDIS AND RISK OF NASH, MODERATE TO SEVERE STEATOSIS (>33%), OR SIGNIFICANT FIBROSIS (S2-S4), USING LOGISTIC REGRESSION ANALYSIS ADJUSTED FOR AGE, SEX, RACE, BMI, AND DIABETES

Number of Socioeconomic Parameters	OR (95% CI)	*P* Value
Predictors of NASH (NAS > 4)		
1+	1.249 (0.598-2.611)	0.5536
2+	1.075 (0.657-1.760)	0.7736
3+	1.608 (0.989-2.614)	0.0552
4+	1.771 (1.099-2.856)	0.0190
5+	1.946 (1.205-3.140)	0.0064
6+	1.748 (1.097-2.786)	0.0189
Predictors of steatosis >33%		
1+	1.096 (0.617-1.927)	0.7657
2+	1.243 (0.839-1.843)	0.2778
3+	1.372 (0.940-2.002)	0.1015
4+	1.398 (0.962-2.032)	0.0786
5+	1.343 (0.925-1.950)	0.1207
6+	1.498 (1.031-2.176)	0.0338
Predictors of fibrosis (S2-S4)		
1+	1.415 (0.664-3.018)	0.3684
2+	1.106 (0.675-1.813)	0.6901
3+	1.542 (0.955-2.490)	0.0766
4+	1.422 (0.891-2.268)	0.1400
5+	1.495 (0.938-2.384)	0.0910
6+	1.491 (0.937-2.375)	0.0922

higher levels of poverty, single-parent households, black and Hispanic populations, high school dropouts, renters, overcrowded housing units, nonemployed and unemployed, high-needs population, publicly insured, uninsured, and foreign-born residents. While most of these socioeconomic variables are specific to zip codes and not individuals, the purpose of this study is to show that living in a certain area may predispose or increase the odds of having higher severity of fatty liver disease (i.e., NASH or significant steatosis).

There is a significant correlation between obesity and NAFLD/NASH.[29] In our study, we found that in both high- and low-SDI subgroups, the mean BMI was above 35, which categorizes our average population of patients with NAFLD as class 2 obese. This is not unexpected as a previous study showed that when BMI starts to increase over 23 kg/m^2, the risk of fatty liver disease significantly increases in a nonlinear fashion with a 1-kg/m^2 increase in BMI.[30] Elevated BMI, most commonly due to central obesity, is regarded as an important risk factor because it may indicate advanced NAFLD and faster rates of progression to fibrosis.[31,32] Regarding diabetes, our population's mean HbA1c test (A1C) level (6.29) was below the diabetic range but within the prediabetic range. We found there was no statistically significant difference in the percentage of people diagnosed with diabetes in high- versus low-SDI regions. However, there was a statistically significant higher A1C level in higher SDI groups compared to lower SDI groups. These data may imply better glucose control in areas with less socioeconomic stressors. Our results can be due in part to the high burden of food insecurity, high rates of avoidance coping and depression, poor access to pharmacies and transportation, and greater financial impact of medication cost that are seen in low-socioeconomic areas.[33,34]

Other biochemical findings, such as slightly elevated liver enzymes (AST and ALT), have been widely studied in patients with NAFLD. While there may be moderate elevations in AST and ALT, many patients with NAFLD can present with normal values.[35,36] We also found that our patients with

NAFLD had high levels of low-density lipoprotein and triglycerides. Hyperlipidemia is a component of metabolic disease that has been proven to be strongly associated with NAFLD.[37]

When reviewing individual socioeconomic factors, we found that a higher percentage of people with no health care or public health care lived in more deprived regions of New York. Analysis of our study population showed that people living in areas with a high percentage of publicly insured people had an increased likelihood of having NASH, whereas the opposite was seen regarding people living in areas with a high percentage of people privately insured. We also found that people living in highly deprived areas seemed to present to clinic at earlier ages than those living in less-deprived regions. The high-SDI group's average age of diagnosis was about 3 years earlier than those in the low-SDI group, which is more likely due to disease arising at earlier ages than patients simply seeking out medical attention sooner. Similar results were found in research conducted by Orkin et al.[38] in a small pediatric population.

The socioeconomic factor that seemed to have the greatest impact on NASH and significant steatosis was the percentage of foreign-born residents in a given area. Areas with many foreign-born residents tended to have more people with NASH, and most of these areas also tended to be high-SDI regions. Considering the global effect of NASH and its high incidence in countries with high SDIs compared to the United Sates, it raises suspicion for a cultural or genetic component to NASH/steatosis.[5,39] One study conducted by Bambha et al.[40] suggests that socioeconomic factors in people with NASH differ depending on ethnicity; this is possibly due to differences in diets and customs, which can have large effects on individuals' metabolic profiles and contribute to the risk of developing NAFLD.

Two socioeconomic factors correlated with the degree of fibrosis. People with solely a high school diploma had lower odds of having significant fibrosis, whereas people with a bachelor's degree or higher had higher odds of having significant fibrosis. These values fail to consider the people with no education and those who did not graduate high school and therefore do not have a high school diploma. Arguably, those with a high school diploma would be able to obtain substantial jobs that may be more labored (skilled worker vs. desk job), requiring more working hours compared to the jobs of those with college degrees. Another explanation for these findings is that the 4 years spent in college can promote unhealthy lifestyle habits, such as eating fatty and sugary food/drinks, drinking alcohol, experimenting with drugs, and poor sleep hygiene, which are some known and suggested risk factors of liver disease.

Our data suggest that people living in high-SDI regions are at greater odds of having NASH. The definition of NASH in our study is NAS > 4.[28] This feature-based scoring system developed by the NASH Clinical Research Network considers the amount of surface area involved in steatosis, extent of lobular inflammation, and degree of hepatocyte ballooning.[41] While we did not see individual differences in the rates of these factors between the high- and low-SDI groups, when the NAS was calculated, we did see a greater percentage of people with NAS > 4 in the higher SDI subgroup. These data differ from the results of a study performed in Iran that found that people of low- and moderate-socioeconomic classes had a lower risk of developing NAFLD.[42] However, that study differed from ours in that the researchers used only a three-variable combination (income, occupation, and education) to determine socioeconomic status; they also used ultrasound, arguably one of the less-sensitive and less-specific modalities, especially in patients with high BMIs to diagnose liver disease, to confirm a diagnosis of NAFLD.[43]

The combination of different socioeconomic factors predicts levels on NASH as well as steatosis. When patients present in areas with four or more socioeconomic parameters that put them in a more disadvantaged group (higher SDI), they tend to have higher odds of having NASH. When these results are adjusted for age, sex, race, BMI, and diabetes, then there is a more significant correlation between socioeconomic factors and NASH and an association between socioeconomic factors and steatosis. Therefore, people living in places with more components of a social and economic deprivation have a greater likelihood of having NASH or severe steatosis. These regions may benefit from increased NAFLD screening and management starting at a younger age to combat the growing NAFLD epidemic.

A major limitation of our study was the inability to correlate exactly which socioeconomic parameters were combined to determine which area was at higher odds of having NASH/steatosis. Our data only

analyzed the number of factors that needed to be present to put people in certain regions at higher odds of having liver disease. Another limitation we faced was the inability to track how long patients included in our study were living in their recorded zip code region. To our advantage, while people may not live in the same area or location for an extended period, they rarely jump up or down in socioeconomic class at a rapid rate. This notion would increase the chances that even if patients were not living in their said location for a long time, they were most likely residing in an area of similar SDI. Additionally, the liver biopsies were read by multiple pathologists; however, we used the NASH Clinical Research Network scoring system to rescore for uniformity and eliminate any bias. Despite these limitations, the strength of our study is the inclusion of a relatively large population size of patients with biopsy-proven NAFLD.[44]

In conclusion, social and economic factors in each area are associated with NASH and moderate to severe steatosis (>33%) but not significant fibrosis. Several social and economic components, especially percentage of the foreign-born population, have a significant influence in predicting NAFLD. Additionally, there is a significant association between numbers of social and economic parameters and risk of developing NASH and severe steatosis.

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