Published in final edited form as:

J Gastroenterol Hepatol. 2011 March ; 26(3): 501–509. doi:10.1111/j.1440-1746.2010.06443.x.

Nonalcoholic fatty liver disease across ethno-racial groups: Do Asian-American adults represent a new at-risk population?

James H. Tabibian^{*,†}, Mariana Lazo[‡], Francisco A. Durazo[†], Hsin-Chieh Yeh^{*,‡}, Myron J. Tong[†], and Jeanne M. Clark^{*,‡}

^{*}Department of Medicine, Johns Hopkins Hospital, Baltimore, Maryland, USA

[†]Dumont-UCLA Liver Transplant Center, Los Angeles, California, USA

[‡]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA

Abstract

Background and Aim—Nonalcoholic fatty liver disease (NAFLD) is increasingly common worldwide. We explored clinical, laboratory, and histological features of NAFLD as well as risk factors for histologically advanced disease among under-represented ethno-racial groups.

Methods—Patient records from one NAFLD clinic in California from 1998–2008 were reviewed. Biopsies were graded using Brunt criteria by a hepatopathologist blinded to clinical data. We used multivariate logistic regression to assess associations between ethno-racial group and histological severity of NAFLD, while controlling for other factors.

Results—We identified 90 biopsy-proven cases of NAFLD. Mean age was 49 years (standard deviation [SD] = 11.6), and half were female. 52% of patients were Caucasian, 20% Latino-American, 18% Asian-American, and 10% Middle Eastern-American. There were significant differences among groups with respect to age, weight, body mass index (BMI), and grade of hepatic steatosis (all $P < 0.05$). In multivariate analysis, older age was associated with severe (Brunt = 2) inflammation (odds ratio [OR] 1.1, $P = 0.002$) and severe (Brunt = 3) fibrosis (OR 1.2, $P = 0.001$), diabetes was associated with severe inflammation (OR 3.18, $P = 0.07$) and severe fibrosis (OR 8.81, $P = 0.002$), and increased BMI was associated with severe fibrosis (OR 2.43, $P = 0.07$). Additionally, compared to Caucasians, Asian-Americans showed a trend toward an association with severe (Brunt > 2) steatosis (OR 3.83, $P = 0.08$) and severe inflammation (OR 5.42, $P = 0.06$).

Conclusions—The findings from this ethno-racially diverse clinic-based cohort are consistent with prior studies and also suggest that Asian-Americans may be at risk for advanced NAFLD. This may have implications for the prevention, evaluation, and treatment of patients with NAFLD that merit further study.

Keywords

cirrhosis; ethnic groups; fatty liver; histopathology

Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of elevated aminotransferases among adults in the USA.^{1–3} It ranges in spectrum from simple hepatic steatosis to steatohepatitis (NASH), the latter of which can progress to hepatic cirrhosis, liver failure, and hepatocellular carcinoma. Clinical conditions commonly associated with NAFLD include those of the metabolic syndrome, particularly (central) obesity, insulin resistance and/or type 2 diabetes mellitus, and dyslipidemia, but the extent to which these or other factors may play a role in its pathogenesis is unclear.^{3–5} Nevertheless, as the prevalence and severity of these conditions continues to rise in the USA, the burden of NAFLD is predicted to become an even greater public health problem, doubling by the year 2025.^{1,3,6–8}

As with other chronic liver disease, heterogeneity in the development, clinical features, and progression of NAFLD and its associated conditions seems to be present between various ethno-racial groups.^{1,3,4,9–14} Despite the diversity of the US population, however, very few studies have examined NAFLD in the USA across ethno-racial groups, with data lacking particularly in Asian and Middle Eastern Americans, among other groups.^{1,3,10,11} Furthermore, the existing studies have also been limited by other factors, including the lack of a histological diagnosis of NAFLD and the use of permissive levels of allowable alcohol intake.^{1,3,11}

In this exploratory study, we compared the demographic, clinical, and laboratory characteristics of histologically-proven NAFLD across ethno-racial groups in the patients in our university fatty liver clinic, which is located in the diverse city of Los Angeles. Our objective was to better characterize the features of NAFLD in previously underrepresented ethno-racial groups and assess whether a particular group may be associated with having more severe NAFLD histology.

Methods

Study population and data collection

After appropriate institutional review board approval, a retrospective review of medical records was performed on all patients seen in the University of California, Los Angeles adult fatty liver clinic between 1998 and 2008 to confirm eligibility and obtain information pertinent to NAFLD. Data were gathered from the medical records by a single reviewer (JHT) using a standardized data collection form and consisted of a broad array of clinical (including demographic, anthropometric, and medico-historical), laboratory, and histological variables.

Exclusion criteria were as follows: (1) absence of a liver biopsy demonstrating (nonalcoholic) fatty liver disease; (2) any comorbid liver disease, including but not limited to

viral hepatitis, alcoholic liver disease, hemochromatosis, Wilson's disease, and alpha-1-antitrypsin deficiency; (3) present average intake of > 20 g of ethanol/day in men and > 10 g of ethanol/day in women or any history of heavy alcohol use; (4) use of medications, such as prednisone, amiodarone, or methotrexate, known to be associated with fatty liver, or other secondary causes of hepatic steatosis; (5) decompensated liver disease as evidenced by the presence of ascites on imaging or examination or albumin < 3 g/dL; and (6) unreported or unknown ethno-racial group. Data on ethanol intake (exclusion criterion 3) were gathered from patients, patient family members, and referring physicians. We chose to exclude decompensated liver disease (criterion 5) so as to not confound variables such as body mass index, diabetes, and lipids that often shift or decrease in severely ill patients.

Liver biopsies were evaluated in a blinded fashion by a hepatopathologist using the Brunt criteria.¹⁵

Race and ethnicity

Subjects were divided into four anticipated major ethno-racial groups based on the overall demographic distribution of our fatty liver clinic patients: Asian-American (Asian), Caucasian American (Caucasian), Latino-American (Latino), and Middle Eastern American (Middle Eastern). We excluded the 'Other' category from further analysis since there were < 5 individuals with this designation. The term "ethno-racial" was used to encompass both hereditary and cultural factors that could influence disease development and progression.

Other variables

We collected information from the medical record on: age at the time of biopsy, sex, self-reported ethno-racial group, calculated body mass index (BMI), diabetes, hypertension, dyslipidemia, and use of angiotensin converting enzyme inhibitor (ACEI), statin drug, or peroxisome proliferator-activated receptor- γ (PPAR- γ) agonists. Diabetes was defined as it being listed as a diagnosis, hypoglycemic agent or insulin use, and/or glycated hemoglobin (HbA1c) > 6.5%.¹⁶ Dyslipidemia was based on it being listed as a diagnosis, lipidemic medication use, triglycerides > 150 mg/dL or low density lipoprotein (LDL) > 130 mg/dL or high density lipoprotein (HDL) < 40 in males and < 50 mg/dL in females.

We collected information from laboratory reports including: random glucose, HbA1c, HDL, LDL, triglycerides, triglyceride : HDL ratio, alanine aminotransferase (ALT), aspartate aminotransferase (AST), AST : ALT ratio, alkaline phosphatase (ALK), albumin, and total bilirubin. We defined high ALT as > 30 in males and > 19 in females and high AST as > 30 in males and > 19 in females.

We collected information from the medical record on family history of: nonalcoholic liver disease, alcoholic liver disease, diabetes, hypertension, cancer (not excluding hepatocellular carcinoma), or coronary artery disease.

Liver biopsies were evaluated using Brunt's criteria. For this study, we defined severe steatosis as Brunt score ≥ 2 , severe inflammation as Brunt score ≥ 2 , and severe fibrosis or cirrhosis as Brunt score ≥ 3 .

All time-sensitive data, such as BMI, medication history, and laboratory values, were from the time of or within 6 months prior to liver biopsy.

Data analysis

To compare differences in demographic, clinical, and laboratory features across ethno-racial groups, and to test factors univariately associated with histological severity, we used the χ^2 test or analysis of variance (anova) for categorical and continuous variables, respectively. Multivariate logistic regression was used to assess putative associations between ethno-racial background and histological severity of NAFLD, while adjusting for age, sex, BMI, diabetes, and dyslipidemia. For fibrosis, we further adjusted for use of ACEI. Tests of significance were two-tailed, with an alpha level of 0.05.

Analyses were performed using Stata (College station, TX, Version SE 9.0).

Results

Ninety-three patients with biopsy-proven NAFLD were identified. Three of these 93 patients belonged to an ethno-racial group other than the pre-identified ones (two African-American and one Native-American) and were excluded. The self-reported ethno-racial distribution of the remaining 90 patients was: 52% Caucasian, 18% Asian, 20% Latino, and 10% Middle Eastern. The mean age was 49.1 years (SD = 11.6) and 50% were female. The mean BMI was 30.9 Kg/m² (SD = 7). There were significant differences in univariate analysis among ethno-racial groups with respect to age, weight, BMI, AST : ALT ratio, family history of coronary artery disease, family history of cancer, and grade of hepatic steatosis. These and other variables are presented for the entire sample and with univariate comparisons across ethno-racial groups in Table 1. The histological characteristics of the sample are shown in Table 2.

In univariate analysis by histology (Table 3a–c), severe steatosis was significantly associated with female sex, AST, high AST, and lower bilirubin (all $P < 0.05$). Severe inflammation was significantly associated with increased age, diabetes, and PPAR- γ agonist use (all $P < 0.05$). Severe fibrosis was significantly associated with increased age, female sex, increased BMI, diabetes, random serum glucose, hypertension, dyslipidemia, high AST, AST : ALT ratio, and lower albumin (all $P < 0.05$).

In multivariate analysis, we found that: (i) severe steatosis showed a trend toward an association with female sex (adjusted odds ratio [OR] 3.13; 95% confidence interval [CI] 0.96, 10.26) and Asian background (OR 3.83; 95% CI 0.83, 17.63); (ii) severe inflammation was significantly associated with increased age (OR 2.86; 95% CI 1.29, 6.36), with a trend toward an association with Asian background (OR 5.42; 95% CI 0.96, 30.5) and diabetes (OR 3.18; 95% CI 0.93, 10.9); and (iii) severe fibrosis was significantly associated with increased age (OR 3.18; 95% CI 1.37, 7.38), increased BMI (OR 2.43; 95% CI 1.34, 4.42), and diabetes (OR 8.81; 95% CI 2.25, 34.48), with a trend toward a negative association with dyslipidemia (OR 0.28; 95% CI 0.07, 1.09) (Table 3a–c). These results are shown in greater detail in Figure 1a–c. Figure 2 demonstrates adjusted histological differences across ethno-racial groups from multivariate analyses.

Discussion

Similar to previous studies of NAFLD, we found associations between steatosis and female sex, inflammation and increased age and diabetes, and fibrosis and increased age, BMI, diabetes, and hypolipidemia (the lattermost likely representing a manifestation, not a predictor, of severe liver disease).^{10,11,13,17,18} Genetic variations may predispose to these associated variables and thus to more frequent and/or more severe NAFLD. For example, in large epidemiologic studies, Latinos had the highest rates of diabetes and hypertriglyceridemia; other studies have also shown that Latinos have a relatively high prevalence of NAFLD and increased risk of severe NASH among the pediatric population.¹⁰ However, the role of genetics in NAFLD seems to go beyond such associations. This point has been illustrated in African-Americans, who despite having a high prevalence of both obesity and insulin resistance, seem to have a relatively lower prevalence of NAFLD compared with other ethno-racial groups.^{1,3,10}

The findings of our study seem to support the latter notion. Asians in our sample had average or lower rates of typical NAFLD risk factors/markers including the lowest weight, BMI, hemoglobin A1c, diabetes prevalence, AST : ALT ratio, and family history of coronary artery disease^{19–27} Nevertheless, Asian background appeared to be independently associated with severe steatosis and with severe inflammation after controlling for the aforementioned variables in multivariate analysis (Fig. 2). Although an association between Asian background and fibrosis was not found in multivariate analysis, it is ostensible that one may actually exist (as suggested by the magnitude of the OR and 95% CI) but did not reach significance. Aside from small sample size, one potential reason could be that the effect of Asian background was confounded by dyslipidemia, which was negatively associated with severe steatosis but is highly prevalent in Asians (although not significantly different across ethno-racial groups).

The mechanism of genetic effects on NAFLD in Asians or other groups is not clearly understood. Possible explanations include differences in body fat distribution (with Asians being described as having more *visceral* adiposity^{3,7,10,18,28}), lipid metabolism,^{12,29} mechanisms against oxidative stress, hepatocyte apoptotic pathways,³⁰ and adipokine levels such as adiponectin and leptin.^{13,29,31,32} Furthermore, adoption of a North American lifestyle, with a paucity of exercise and typically unhealthy diet, may heighten or bring out such differences and resultant deleterious hepatic sequelae, as suggested in this study. Our findings seem to emphasize the importance of ethno-rationally tailored educational programs and management, particularly for high-risk groups.

This study has several strengths. We used rigorous criteria, including the need for histological data, to identify patients with NAFLD and exclude other liver disease. Biopsies were interpreted by a hepatopathologist masked to clinical information. These data represent one of the larger and more ethno-rationally diverse cohorts of exclusively *biopsy-proven* adult NAFLD cases,^{33,34} including previously under- or unrepresented populations, namely Asian and Middle Eastern *Americans*. The data were also relatively comprehensive with regard to breadth of clinical and laboratory variables collected and analyzed.

There are also limitations to our study. Our sample size was small. This limited statistical power and our ability to further examine the relationship between ethno-racial group and NAFLD severity. It may also explain why some variables, including the associations between Asian background and severe NAFLD histology, did not reach statistical significance despite relatively large ORs. The study design was retrospective. Data such as central obesity, body fat percentage, or homeostasis model assessment of insulin resistance were not available since we do not routinely measure these in our clinic. Information on diet and exercise was not consistently obtainable and therefore not included. Despite using several inputs to estimate ethanol intake, this value may be underestimated. Finally, although in our clinic we broadly offer liver biopsy and thus do not restrict it only to cases with diagnostic uncertainty, it is possible that there may be selection or referral bias. However, this type of bias may be a problem in general clinical practice independent of study design. With these limitations in mind, this study and the hypotheses generated herein may be regarded as exploratory.

In summary, the associations we found between NAFLD and its various risk factors in a sample composed of 48% minorities are consistent with prior studies. In addition, our preliminary findings add to a growing body of evidence supporting the presence of ethno-racial variations in NAFLD within the diverse US population and highlight the need for awareness and additional research of such. Importantly, Asian-Americans could be a group at increased risk of severe NASH and may therefore merit increased physician vigilance given that traditionally common risk factors, such as elevated BMI, AST : ALT ratio, and/or diabetes, do not seem to be as important or as sensitive among them. Furthermore, if diagnosed with NAFLD, Asian-Americans may benefit from more aggressive treatment of underlying metabolic syndrome, particularly dyslipidemia and *central* obesity, if present. More research, including genetic studies, is needed to further investigate the findings of this study and determine which clinical, laboratory, and underlying genetic factors account for variations in the development and progression of NAFLD. Such research may provide clues to NAFLD pathogenesis as well as the development of new therapeutic approaches.

Acknowledgments

Grant support: data analysis of this project was supported by the Johns Hopkins Osler Fund for Scholarship.

References

1. Browning JD, Szczepaniak LS, Dobbins R, et al. Prevalence of hepatic steatosis in an urban population in the United States: impact of ethnicity. *Hepatology*. 2004; 40:1387–95. [PubMed: 15565570]
2. Clark JM, Brancati FL, Diehl AM. The prevalence and etiology of elevated aminotransferase levels in the United States. *Am J Gastroenterol*. 2003; 98:960–7. [PubMed: 12809815]
3. Weston SR, Leyden W, Murphy R, et al. Racial and ethnic distribution of nonalcoholic fatty liver in persons with newly diagnosed chronic liver disease. *Hepatology*. 2005; 41:372–9. [PubMed: 15723436]
4. Angulo P. GI epidemiology: nonalcoholic fatty liver disease. *Aliment Pharmacol Ther*. 2007; 25:883–9. [PubMed: 17402991]

5. Willner IR, Waters B, Patil SR, Reuben A, Morelli J, Riely CA. Ninety patients with nonalcoholic steatohepatitis: insulin resistance, familial tendency, and severity of disease. *Am J Gastroenterol*. 2001; 96:2957–61. [PubMed: 11693332]
6. Amarapurkar DN, Hashimoto E, Lesmana LA, Sollano JD, Chen PJ, KL G. Asia-Pacific Working Party on NAFLD. How common is non-alcoholic fatty liver disease in the Asia-Pacific region and are there local differences? *J Gastroenterol Hepatol*. 2007; 22:788–93. [PubMed: 17565631]
7. Chitturi S, Farrell GC, Hashimoto E, Saibara T, Lau GK, JD S. Asia-Pacific Working Party on NAFLD. Non-alcoholic fatty liver disease in the Asia-Pacific region: definitions and overview of proposed guidelines. *J Gastroenterol Hepatol*. 2007; 22:778–87. [PubMed: 17565630]
8. Seidell JC. Obesity, insulin resistance and diabetes—a worldwide epidemic. *Br J Nutr*. 2000; 83(Suppl. 1):S5–8. [PubMed: 10889785]
9. Struben VM, Hespeneheide EE, Caldwell SH. Nonalcoholic steatohepatitis and cryptogenic cirrhosis within kindreds. *Am J Med*. 2000; 108:9–13. [PubMed: 11059435]
10. Caldwell SH, Harris DM, Patrie JT, Hespeneheide EE. Is NASH underdiagnosed among African Americans? *Am J Gastroenterol*. 2002; 97:1496–500. [PubMed: 12094872]
11. Kallwitz ER, Kumar M, Aggarwal R, et al. Ethnicity and nonalcoholic fatty liver disease in an obesity clinic: the impact of triglycerides. *Dig Dis Sci*. 2008; 53:1358–63. [PubMed: 18347982]
12. Nonalcoholic SS. Fatty liver disease and obesity. *Nutr Clin Pract*. 2007; 22:1–10. [PubMed: 17242448]
13. Kemmer N, Neff GW. Ethnic variations in chronic liver diseases. *Dig Dis Sci*. 2008; 53:1339–44. [PubMed: 17934812]
14. Perry AC, Applegate EB, Jackson ML, et al. Racial differences in visceral adipose tissue but not anthropometric markers of health-related variables. *J Appl Physiol*. 2000; 89:636–43. [PubMed: 10926648]
15. Brunt EM, Janney CG, Di Bisceglie AM, Neuschwander-Tetri BA, Bacon BR. Nonalcoholic steatohepatitis: a proposal for grading and staging the histological lesions. *Am J Gastroenterol*. 1999; 94:2467–74. [PubMed: 10484010]
16. International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. *Diabetes Care*. 2009; 32:1327–34. [PubMed: 19502545]
17. Bacon BR, Farahvash MJ, Janney CG, Neuschwander-Tetri BA. Nonalcoholic steatohepatitis: an expanded clinical entity. *Gastroenterology*. 1994; 107:1103–9. [PubMed: 7523217]
18. Fan JG, Saibara T, Chitturi S, Kim BI, Sung JJ, Chutaputti A. Asia-Pacific Working Party for NAFLD. What are the risk factors and settings for non-alcoholic fatty liver disease in Asia-Pacific? *J Gastroenterol Hepatol*. 2007; 22:794–800. [PubMed: 17498218]
19. Prashanth M, Ganesh HK, Vima MV, et al. Prevalence of nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus. *J Assoc Physicians India*. 2009; 57:205–10. [PubMed: 19588648]
20. Shah AG, Lydecker A, Murray K, Tetri BN, Contos MJ, Sanyal AJ. Nash Clinical Research Network. Comparison of noninvasive markers of fibrosis in patients with nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol*. 2009; 7:1104–12. [PubMed: 19523535]
21. Georgescu EF. Angiotensin receptor blockers in the treatment of NASH/NAFLD: could they be a first-class option? *Adv Ther*. 2008; 25:1141–74. [PubMed: 18972077]
22. Park KS, Lee YS, Park HW, Seo SH, et al. Factors associated or related to pathological severity of nonalcoholic fatty liver disease. *Korean J Intern Med*. 2004; 19:19–26. [PubMed: 15053039]
23. Seo S, Maganti K, Khehra M, et al. *De novo* nonalcoholic fatty liver disease after liver transplantation. *Liver Transpl*. 2007; 13:844–7. [PubMed: 17029282]
24. Rafiq N, Bai C, Fang Y, et al. Long-term follow-up of patients with nonalcoholic fatty liver. *Clin Gastroenterol Hepatol*. 2009; 7:234–8. [PubMed: 19049831]
25. Choi DH, Park MO, Kang CD, Lee SJ, Lee JW, Cho BR. The relationship between nonalcoholic fatty liver disease and coronary artery disease; a prospective case-control study in a single center. *Hepatology*. 2009; 50:764A. abstract.
26. Rouvman Y, Alon M, Dvorin I, Deitzman M, Assy N. Fatty liver predict the presence of coronary plaques and early atherosclerosis independently by visceral fat accumulation. *Hepatology*. 2009; 50:768A. abstract.

27. Angulo P, Keach JC, Batts KP, Lindor KD. Independent predictors of liver fibrosis in patients with nonalcoholic steatohepatitis. *Hepatology*. 1999; 30:1356–62. [PubMed: 10573511]
28. Fan JG, Peng YD. Metabolic syndrome and non-alcoholic fatty liver disease: Asian definitions and Asian studies. *Hepatobiliary Pancreat Dis Int*. 2007; 6:572–8. [PubMed: 18086620]
29. Aouizerat BE, Bambha K, Unalp-Arida A, Ferrell L, Bass NM. Genetic variation in hormone sensitive lipase and adiponectin confers susceptibility to nonalcoholic fatty liver disease. *Hepatology*. 2009; 50:768A. abstract.
30. Younossi ZM, Jarrar M, Nugent C, et al. A novel diagnostic biomarker panel for obesity-related nonalcoholic steatohepatitis (NASH). *Obes Surg*. 2008; 18:1430–7. [PubMed: 18500507]
31. Bambha K, Aouizerat BE, Unalp-Arida A, Ferrell L, Bass NM. Genetic variation in adiponectin confers susceptibility to nonalcoholic fatty liver disease in Latino Caucasians. *Hepatology*. 2009; 50:771–772A. abstract.
32. Muñoz LE, Cordero P, Torres L, Saucedo AY, Flores JP, Segura JJ. Adipokines in a group of Mexican patients with nonalcoholic steatohepatitis. *Ann Hepatol*. 2009; 8:123–8. [PubMed: 19502655]
33. Miele L, Vallone S, Cefalo C, et al. Prevalence, characteristics and severity of non-alcoholic fatty liver disease in patients with chronic plaque psoriasis. *J Hepatol*. 2009; 51:778–86. [PubMed: 19664838]
34. Hossain N, Afendy A, Stepanova M, et al. Independent predictors of fibrosis in patients with nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol*. 2009; 7:1224–9. 1229.e1–2. [PubMed: 19559819]

Figure 1.

(a) Factors associated with severe steatosis. Key: Multivariate analysis. Adjusted odds ratio (95% confidence interval). (•) Asian, (•) Latino, and (•) Middle Eastern. (b) Factors associated with moderate-severe inflammation. (c) Factors associated with severe fibrosis or cirrhosis. ACEI, angiotensin converting enzyme inhibitor; BMI, body mass index.

Figure 2. Adjusted odds ratio for more severe histology in: Asians, Latinos and Middle Easterners versus Caucasians. Key: Multivariate analysis. Adjusted odds ratio (OR) (95% confidence interval [CI]).

Table 1

Characteristics of sample overall and by ethno-racial group

	All n = 90	Caucasian n = 47	Asian n = 16	Latino n = 18	Middle Eastern n = 9	P-value
Demographic						
Age (years)	49.1 (11.6)	51.6 (9.4)	49.4 (10.1)	41.6 (13.2)	48.9 (15.5)	0.02
Sex, female	50%	53.2	37.5	61.1	33.3	0.42
Anthropometric						
Weight (pounds)	192.9 (48.3)	200.9 (46.2)	161.8 (42.4)	203.4 (53.2)	191.9 (36.4)	0.03
BMI (kg/m ²)	30.9 (7.0)	32.3 (7.5)	26.1 (5.9)	32.3 (6.1)	29.5 (4.6)	0.02
Clinical						
Diabetes [†]	37.8%	38.3%	31.3%	38.9%	44.4%	0.92
Dyslipidemia [‡]	66.7%	68.1%	81.3%	50.0%	66.7%	0.28
Hypertension [§]	38.9%	42.6%	43.8%	38.9%	11.1%	0.28
ACEI use	19.9%	14.9%	37.5%	11.1%	22.2%	0.16
Statin use	15.6%	19.2%	6.3%	5.6%	33.3%	0.15
PPAR-γ use	8.9%	10.6%	6.3%	11.1%	0%	0.89
Laboratory						
Random glucose (mg/dL)	124.3 (51.6)	120.9 (39.3)	103.4 (23.5)	133.7 (67.9)	166.5 (96.9)	0.05
HbA1c (%)	6.3 (1.2)	6.2 (0.96)	6.0 (0.77)	6.5 (0.94)	7.1 (2.2)	0.3
HDL (mg/dL)	47.6 (15.9)	49 (20.4)	47.3 (11.8)	44.4 (11.6)	49.8 (10.1)	0.66
LDL (mg/dL)	124.2 (51.6)	119.7 (33.4)	119.6 (35.9)	123 (39.2)	150.5 (38.9)	0.31
Triglycerides (mg/dL)	161 (111, 218)	137 (113, 206)	204 (92, 251)	172 (116, 305)	119 (95, 170)	0.57
Triglyceride : HDL ratio	3.6 (2.2, 5.9)	3.4 (2.4, 4.9)	3.8 (2.0, 6.6)	3.7 (3.2, 7.4)	2.9 (1.8, 4.1)	0.47
ALT (U/L)	53 (33, 79)	52 (27, 72)	70 (41, 104.5)	55.5 (43, 101)	51 (48, 57)	0.25
High ALT [¶]	90.0%	82.9%	93.8%	100%	100%	0.12
AST (U/L)	43 (29, 59)	44 (28, 60)	44.5 (38.5, 58.5)	43 (29, 59)	38 (34, 60)	0.93
High AST [¶]	86.70%	87.20%	87.50%	83.30%	88.90%	0.97
AST : ALT ratio	0.8 (0.6, 1.1)	0.90 (0.75, 1.2)	0.6 (0.5, 0.9)	0.7 (0.5, 1)	0.7 (0.5, 0.9)	0.04
ALK (U/L)	80 (65, 108)	78 (65, 119)	79.5 (59.5, 105)	93 (70, 120)	87 (68, 92)	0.7
Albumin (mg/dL)	4.1 (0.52)	4.1 (0.4)	4.2 (0.5)	3.9 (0.8)	4.5 (0.5)	0.08
Total bilirubin (mg/dL)	0.7 (0.6, 0.9)	0.7 (0.6, 0.8)	0.9 (0.8, 1.1)	0.65 (0.5, 0.7)	0.9 (0.6, 1.1)	0.21

	All n = 90	Caucasian n = 47	Asian n = 16	Latino n = 18	Middle Eastern n = 9	P-value
Family history						
Liver disease	15.6%	21.3%	12.5%	11.1%	0%	0.22
Alcoholic liver disease	6.7%	4.3%	0%	16.7%	11.1%	0.17
Diabetes	34.4%	38.3%	31.3%	27.8%	33.3%	0.4
Hypertension	10.0%	8.5%	18.8%	11.1%	0%	0.24
Cancer	31.1%	42.6%	25.0%	5.6%	33.3%	0.03
CAD	25.6%	38.3%	0%	16.7%	22.2%	0.02

Values reported as percentage or mean (standard deviation [SD]) or median (interquartile range). *P* < 0.10 bolded.

[†]Diabetes defined as being documented in medical records, use of diabetes medications, and/or HbA1c > 6.5%.

[‡]Dyslipidemia defined as being documented in medical records, triglycerides > 200 mg/dL, or LDL-C > 130 mg/dL or HDL-C < 40 mg/dL and < 50 mg/dL for men and women, respectively, or eulipidemic medication use.

[§]Hypertension defined as being documented in medical records.

[¶]High ALT defined as > 60 U/L in males, > 40 U/L in females; high AST defined as > 50 U/L in males, > 35 U/L in females.

ACEI, angiotensin converting enzyme inhibitor; ALK, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; coronary artery disease (CAD); HDL, high density lipoprotein; LDL, low density lipoprotein; PPAR- γ , peroxisome proliferator-activated receptor- γ .

Table 2
Histologic characteristics of sample overall and by ethno-racial group

	All <i>n</i> = 90	Caucasian <i>n</i> = 47	Asian <i>n</i> = 16	Latino <i>n</i> = 18	Middle Eastern <i>n</i> = 9	<i>P</i> -value
Steatosis						0.04
Brunt score 1, < 33%	32%	25.50%	31.30%	50%	33.30%	
Brunt score 2, 33–66%	40%	48.90%	25.00%	16.70%	66.70%	
Brunt score 3, > 66%	27.80%	25.50%	43.80%	33.30%	0%	
Inflammation						0.12
Brunt score 0, none	8.90%	6.40%	12.50%	5.60%	22.20%	
Brunt score 1, mild	66.70%	65.90%	50%	83.30%	66.70%	
Brunt score 2, moderate	22.20%	27.70%	31.30%	5.60%	11.10%	
Brunt score 3, severe	2.20%	0%	6.30%	5.60%	0%	
Fibrosis						0.57
Brunt score 0, none	30%	21.30%	31.30%	38.90%	55.60%	
Brunt score 1, mild	25.60%	27.70%	37.50%	16.70%	11.10%	
Brunt score 2, moderate	8.90%	8.50%	6.30%	11.10%	11.10%	
Brunt score 3, severe	21.10%	21.30%	12.50%	27.80%	22.20%	
Brunt score 4, cirrhosis	14.40%	21.30%	12.50%	5.60%	0%	

Analysis of variance (ANOVA) test for overall differences across ethnoracial groups. *P* < 0.10 bolded.

Table 3a

Factors associated with severe steatosis (Brunt score 3, > 66%)

	Steatosis 2 n = 65	Steatosis > 2 n = 25	Bivariate Unadjusted OR (95% CI)	P-value	Multivariate Adjusted OR (95% CI)	P-value
Demographic						
Age (per 10 years)	48.9 (10.7)	48.8 (13.6)	0.99 (0.9, 1.0)	0.97	0.97 (0.53, 1.76)	0.91
Sex, Female	28 (43.1%)	17 (68%)	2.81 (1.1, 7.4)	0.04	3.13 (0.96, 10.26)	0.06
Ethno-racial group						
Caucasian	35 (53.9%)	12 (48%)	Ref	Ref	Ref	
Asian	9 (13.9%)	7 (28%)	2.27 (0.7, 7.4)	0.18	3.83 (0.83, 17.63)	0.08
Latino	12 (18.5%)	6 (24%)	1.46 (0.5, 4.7)	0.53	1.65 (0.38, 7.16)	0.5
Middle Eastern	9 (13.9%)	0 (0%)	—	—	—	
Anthropometric						
Weight (pounds)	193.9 (44.3)	192.1 (57.4)	0.99 (0.9, 1.0)	0.87		
BMI (per 5 units)	30.7 (6.6)	31.8 (7.9)	1.02 (0.9, 1.1)	0.52	1.19 (0.78, 1.81)	0.43
Clinical						
Diabetes [‡]	25 (38.5%)	9 (36%)	0.9 (0.4, 2.3)	0.83	0.92 (0.29, 2.91)	0.88
Dyslipidemia [‡]	42 (64.6%)	18 (72%)	1.41 (0.51, 3.87)	0.51	1.64 (0.51, 5.32)	0.41
Hypertension [§]	23 (35.4%)	12 (50%)	1.82 (0.7, 4.7)	0.21		
ACEI use	12 (18.5%)	5 (20.8%)	1.16 (0.4, 3.7)	0.80		
Statin use	10 (15.4%)	4 (16.7%)	1.10 (0.3, 3.7)	0.88		
PPAR- γ use	7 (10.8%)	1 (4%)	0.34 (0.04, 2.9)	0.32		
Laboratory						
Random glucose (mg/dL)	124.2 (49.8)	120.8 (54.8)	0.99 (0.9, 1.0)	0.79		
HbA1c (%)	6.3 (1.3)	6.3 (0.8)	0.96 (0.5, 1.7)	0.89		
HDL (mg/dL)	48.4 (18.0)	46.3 (10.5)	0.99 (0.9, 1.0)	0.62		
LDL	127.2 (35.5)	115.8 (37.1)	0.99 (0.9, 1.0)	0.23		
Triglycerides (mg/dL)	133 (107, 206)	170 (134, 251)	1.42 (0.5, 3.8)	0.49		
Triglyceride : HDL ratio	3.21 (2.2, 4.4)	3.81 (2.6, 6.3)	1.02 (0.9, 1.2)	0.80		
ALT (U/L)	49 (33, 73)	67 (50, 106)	2.1 (0.9, 4.4)	0.06		
High ALT [¶]	32 (49.2%)	17 (68%)	2.19 (0.8, 5.8)	0.11		
AST (U/L)	38 (29, 56)	53 (43, 77)	3.6 (1.3, 9.5)	0.01		

	Steatosis 2 n = 65 27 (41.5%)	Steatosis > 2 n = 25 19 (76%)	Bivariate Unadjusted OR (95% CI)	P-value	Multivariate Adjusted OR (95% CI)	P-value
High AST ^f					4.46 (1.57, 12.6)	0.005
AST : ALT ratio	0.76 (0.6, 1.0)	0.85 (0.58, 1.3)		1.11 (0.5, 2.7)		0.82
ALK (U/L)	91.7 (65, 102)	91.1 (57, 119)		0.99 (0.98, 1.01)		0.94
Albumin (g/dL)	4.1 (0.5)	4.1 (0.5)		0.78 (0.3, 1.8)		0.57
Total Bilirubin (mg/dL)	0.7 (0.6, 1)	0.6 (0.4, 0.8)		0.26 (0.08, 0.79)		0.02

Values reported as n (%) or mean (standard deviation [SD]) or median (interquartile range). *P* < 0.10 bolded.

^fDiabetes defined as being documented in medical records, use of diabetes medications, and/or HbA1c > 6.5%.

^gDyslipidemia defined as being documented in medical records, triglycerides > 200 mg/dL, or LDL-C > 130 mg/dL or HDL-C < 40 mg/dL and < 50 mg/dL for men and women, respectively, or eulipidemic medication use.

^hHypertension defined as being documented in medical records.

ⁱHigh ALT defined as > 60 U/L in males, > 40 U/L in females; high AST defined as > 50 U/L in males, > 35 U/L in females.

ACEI, angiotensin converting enzyme inhibitor; ALK, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CI, confidence interval; HDL, high density lipoprotein; LDL, low density lipoprotein; OR, odds ratio; PPAR-γ, peroxisome proliferator-activated receptor-γ.

Table 3b
Factors associated with severe inflammation (Brunt score 2)

	Inflammation < 2 n = 68		nInflammation 2 n = 22		Bivariate Unadjusted OR (95% CI)		P-value		Multivariate Adjusted OR (95% CI)		P-value	
Demographic												
Age (per 10 years)	46.8 (11.3)		55.5 (9.9)									
Sex, Female	33 (48.5%)		12 (54.6%)									
Ethno-racial group												
Caucasian	34 (50%)		13 (59.1%)									
Asian	10 (14.7%)		6 (27.3%)									
Latino	16 (23.5%)		2 (9.1%)									
Middle Eastern	8 (11.8%)		1 (4.6%)									
Anthropometric												
Weight (pounds)	194.99 (6.7)		188.7 (54.3)									
BMI (per 5 units)	30.99 (6.71)		30.87 (7.9)									
Clinical												
Diabetes [‡]	20 (29.4%)		14 (63.6%)									
Dyslipidemia [‡]	48 (70.6%)		12 (54.6%)									
Hypertension [§]	26 (38.8%)		9 (40.9%)									
ACEI use	11 (16.4%)		6 (27.3%)									
Statin use	12 (17.9%)		2 (9.1%)									
PPAR- γ use	3 (4.4%)		5 (22.7%)									
Laboratory												
Random glucose	117.6 (47.3)		139.04 (57.9)									
HbA1c	6.3 (1.2)		6.3 (0.94)									
HDL	46.4 (11.7)		51.9 (25.3)									
LDL	126.8 (39.3)		115 (23.4)									
Triglycerides	158 (112, 224)		163.5 (101, 182)									
Triglyceride : HDL ratio	3.5 (2.3, 6.3)		3.6 (2.0, 4.9)									
ALT (U/L)	53.5 (40, 79.5)		49.5 (33, 77)									
High ALT [¶]	38 (55.9%)		11 (50.0%)									
AST (U/L)	43 (28.5, 59)		44.5 (31, 60)									

	Inflammation < 2 n = 68	nflammation 2 n = 22	Bivariate Unadjusted OR (95% CI)	P-value	Multivariate Adjusted OR (95% CI)	P-value
High AST [¶]	33 (48.5%)	13 (59.1%)	1.53 (0.58, 4.1)	0.39		
AST : ALT ratio	0.74 (0.54, 1.05)	0.89 (0.67, 1.36)	1.66 (0.69, 3.9)	0.26		
ALK (U/L)	89.9 (65, 102)	96.5 (68, 119)	1.0 (0.99, 1.01)	0.51		
Albumin (g/dL)	4.1 (0.57)	4.0 (0.39)	0.66 (0.28, 1.57)	0.35		
Total Bilirubin (mg/dL)	0.7 (0.6, 0.9)	0.7 (0.6, 0.9)	0.86 (0.33, 2.28)	0.77		

Values reported as n (%) or mean (standard deviation [SD]) or median (interquartile range). *P* < 0.10 bolded.

[‡]Diabetes defined as being documented in medical records, use of diabetes medications, and/or HbA1c > 6.5%.

[‡]Dyslipidemia defined as being documented in medical records, triglycerides > 200 mg/dL, or LDL-C > 130 mg/dL or HDL-C < 40 mg/dL and < 50 mg/dL for men and women, respectively, or eulipidemic medication use.

[§]Hypertension defined as being documented in medical records.

[¶]High ALT defined as > 60 U/L in males, > 40 U/L in females; high AST defined as > 50 U/L in males, > 35 U/L in females.

ACEI, angiotensin converting enzyme inhibitor; ALK, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CI, confidence interval; HDL, high density lipoprotein; LDL, low density lipoprotein; OR, odds ratio; PPAR-γ, peroxisome proliferator-activated receptor-γ.

Table 3c
Factors associated with severe fibrosis and cirrhosis (Brunt score 3)

	Fibrosis < 3 n = 58		Fibrosis 3 n = 32	Bivariate Unadjusted OR (95% CI)	P-value	Multivariate Adjusted OR (95% CI)	P-value
Demographic							
Age (per 10 years)	46.5 (10.3)	53.3 (12.4)		1.06 (1.01, 1.11)	0.01	3.18 (1.37, 7.38)	0.007
Sex, Female	24 (41.4%)	21 (65.6%)		2.70 (1.1, 6.6)	0.03	1.35 (0.38, 4.77)	0.65
Ethno-racial group							
Caucasian	27 (46.6%)	20 (62.5%)		Ref		Ref	
Asian	12 (20.7%)	4 (12.5%)		0.45 (0.13, 1.60)	0.22	3.22 (0.50, 20.82)	0.22
Latino	12 (20.7%)	6 (18.8%)		0.68 (0.22, 2.11)	0.49	0.57 (0.10, 3.34)	0.53
Middle Eastern	7 (12.1%)	2 (6.3%)		0.39 (0.07, 2.1)	0.27	0.34 (0.03, 4.10)	0.39
Anthropometric							
Weight (pounds)	187.8 (43.9)	204.0 (53.5)		1.01 (0.9, 1.02)	0.13		
BMI (per 5 units)	29.7 (6.63)	33.1 (7.11)		1.1 (1.01, 1.2)	0.03	2.43 (1.34, 4.42)	0.004
Comorbidities							
Diabetes [‡]	13 (22.4%)	21 (65.6%)		6.6 (2.5, 17.2)	<0.001	8.81 (2.25, 34.48)	0.002
Dyslipidemia [‡]	42 (72.4%)	18 (56.3%)		0.49 (0.19, 1.21)	0.12	0.28 (0.07, 1.09)	0.07
Hypertension [§]	18 (31.0%)	17 (54.8%)		2.69 (1.1, 6.64)	0.03		
ACEI use	9 (15.5%)	8 (25.8%)		1.89 (0.65, 5.54)	0.24	0.67 (0.14, 3.1)	0.61
Statin use	10 (17.2%)	4 (12.9%)		0.71 (0.20, 2.49)	0.59		
PPAR- γ use	3 (5.2%)	5 (15.6%)		3.39 (0.75, 15.3)	0.11		
Laboratory							
Random glucose	111.1 (43.7)	143.5 (55.9)		1.01 (1.0, 1.03)	0.02		
HbA1c	6.1 (1.1)	6.7 (1.2)		1.59 (0.88, 2.86)	0.13		
HDL	48.5 (17.4%)	46.1 (13.2)		0.99 (0.95, 1.03)	0.56		
LDL	127.8 (36.5)	115 (34.6)		0.99 (0.98, 1.00)	0.17		
Triglycerides	152 (107, 219)	173 (116, 217)		1.13 (0.43, 3.02)	0.80		
Triglyceride : HDL ratio	3.5 (2.2, 5.9)	3.6 (2.6, 5.2)		1.02 (0.86, 1.21)	0.85		
ALT (U/L)	53.5 (40, 77)	53.5 (40, 80)		0.88 (0.45, 1.72)	0.71		
High ALT [¶]	30 (51.7%)	19 (59.4%)		1.36 (0.57, 3.27)	0.49		
AST (U/L)	37.5 (28, 57)	53.5 (36, 60.5)		2.21 (0.92, 5.36)	0.08		

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

	Fibrosis < 3 n = 58	Fibrosis 3 n = 32	Bivariate Unadjusted OR (95% CI)	P-value	Multivariate Adjusted OR (95% CI)	P-value
High AST ^f	23 (39.7%)	23 (71.9%)		3.89 (1.52, 9.89)		0.004
AST : ALT ratio	0.72 (0.5, 1.0)	0.91 (0.72, 1.3)		2.98 (1.2, 7.5)		0.02
ALK (U/L)	89.7 (65, 102)	94.9 (68, 121)		1.00 (0.99, 1.01)		0.56
Albumin (g/dL)	4.2 (0.5)	3.9 (0.5)		0.24 (0.08, 0.66)		0.006
Total Bilirubin (mg/dL)	0.7 (0.6, 0.8)	0.75 (0.6, 1.2)		1.22 (0.52, 2.9)		0.65

Values reported as n (%) or mean (standard deviation) or median (interquartile range). *P* < 0.10 bolded.

^fDiabetes defined as being documented in medical records, use of diabetes medications, and/or HbA1c > 6.5%.

^gDyslipidemia defined as being documented in medical records, triglycerides > 200 mg/dL, or LDL-C > 130 mg/dL or HDL-C < 40 mg/dL and < 50 mg/dL for men and women, respectively, or eulipidemic medication use.

^hHypertension defined as being documented in medical records.

ⁱHigh ALT defined as > 60 U/L in males, > 40 U/L in females; high AST defined as > 50 U/L in males, > 35 U/L in females.

ACEI, angiotensin converting enzyme inhibitor; ALK, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CI, confidence interval; HDL, high density lipoprotein; LDL, low density lipoprotein; OR, odds ratio; PPAR-γ, peroxisome proliferator-activated receptor-γ.