Age-stratified Analysis of Associations Between Participant's Characteristics and NAFLD

Syed H. Naqvi
University of Massachusetts Medical School
Anthony P. Nunes (Anthony.Nunes@umassmed.edu)
University of Massachusetts Medical School

Research Article

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Abstract

Background: Nonalcoholic fatty liver disease (NAFLD) is highly prevalent and a leading cause of liver transplantation. In clinical settings, diagnosis is often inferred based on patient attributes and generalized algorithms that haven't been tailored to patients' age. This study aims to understand age-dependent associations between NAFLD and patient characteristics.

Methods: Subjects were identified from the National Health and Nutrition Examination Survey (NHANES) 2007-2016. NAFLD status was established through the U.S. Fatty Liver Index in the absence of excessive alcohol consumption and viral etiology. Descriptive patient attributes' distributions are reported relying on the mean and standard deviation for continuous variables and proportions for categorical variables. Prevalence estimates and prevalence ratios for NAFLD are provided in the following age stratifications: 18 and younger, 19-49, 50-64, 65-74, and 75+.

Results: A total of 4,560 NHANES participants from 2007-2016 were included, with a mean age of 42.9. Prevalence ratios of NAFLD in the context of clinical/demographic characteristics varied between age groups. The NAFLD prevalence ratio for Mexican Americans compared to Non-Hispanic White was 3.44 in respondents 18 years old or younger (95%CI: 2.48-4.77) and 1.60 in respondents 75 or older (95%CI: 1.30-1.97). The magnitude of the association between albumin and NAFLD was negative. It ranged from a prevalence ratio of 0.32 (0.20 – 0.51) for respondents under 19 years of age to 1.15 (0.86-1.53) over the age of 74.

Conclusion: The significant differences between participant characteristics and NAFLD within different age groups suggest that age plays an essential role in the magnitude of the association between risk factors and NAFLD. This study highlights that the accuracy of a NAFLD diagnosis in the absence of imaging and histological conformation may depend on the patients' age. Additional work should evaluate the need for diagnostic and management guidelines formally tailored to patients' age.

Introduction

Nonalcoholic fatty liver disease (NAFLD) encompasses progressive histologically different diseases ranging from simple steatosis, marked by fat accumulation in the liver, to nonalcoholic steatohepatitis if inflammation develops. Approximately 85 million Americans have NAFLD, and NAFLD is the most common cause of chronic liver disease globally [1, 2]. NAFLD's progression can lead to liver fibrosis, cirrhosis, and hepatocellular carcinoma that can cause a decline in liver function or even liver failure. There has been a threefold increase in patients on the waitlist for a liver transplant due to NAFLD from 2004 to 2013 [2]. After controlling for comorbidities, NAFLD's presence was found to have increased overall healthcare costs by 26% [3].

Based on data from the National Health and Nutrition Examination Survey (NHANES), NAFLD's prevalence has increased from 20% in 1988–1994 to 31.9% in 2013–2016 [4]. NAFLD is most common in the elderly population, so most NAFLD research focuses on the aging population. However, it is expected

that NAFLD will be the most prevalent cause of liver complications and liver failure for children in the next decade. More importantly, NAFLD in children can be pathologically distinct from adults [5–7]. Age-specific variation exists in prevalence and all-cause mortality of NAFLD. Prior research has found that the highest prevalence rates of NAFLD are found in males between 50–60 years old, and people 75 years or older are at the highest risk of dying from NAFLD [8–10]. However, there is limited information about how NAFLD patients' demographic and clinical characteristics differ by age.

This study aims to understand how the demographic and clinical characteristics of participants with NAFLD differ by age. To this end, using data from NHANES, we examined age-specific differences in demographic characteristics (sex, ethnicity, etc.) and clinical characteristics (biometrics and liver-specific and non-liver specific laboratory values). Understanding the differences in participants' characteristics and the prevalence of NAFLD by age is of critical importance. Results from this study can inform the future development of age-specific NAFLD screening tools and research algorithms.

Methods

Overview of Data

We performed a cross-sectional analysis of data from the 2007-2016 NHANES. NHANES is conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). The survey represents a nationally representative sample of the non-institutionalized population living in the United States. Participants' selection is guided by a stratified multistage probability design that oversamples certain ethnic and age groups. The data used for this analysis is aggregated from 5 consecutive two-year cycles that were carried out between 2007 and 2016. We included all NHANES respondents that had complete information to rule in or rule out NAFLD. The age was categorized into five groups: 18 years old or younger, 18-49 years old, 50-64 years old, 65-74 years old, and 75 years old or older.

Definition of NAFLD

NAFLD is clinically defined as the presence of liver fat accumulation exceeding five percent of hepatocytes in the absence of heavy alcohol consumption and viral infections [3]. We identified NAFLD within NHANES data relying on the United States Fatty Liver Index (USFLI) [11]. The USFLI is a parametric equation consisting of the following components: ethnicity, age, waist circumference, GGT, fasting insulin, and fasting glucose. The criteria to be categorized as having NAFLD included a USFLI score >=30, absence of excessive alcohol consumption (Avg. of ≤ 1 alcoholic drink per day for women & ≤ 2 alcoholic drinks per day for men), negative Hepatitis C antibody, and negative Hepatitis B surface antigen.

Co-variates

The following covariates were included to evaluate participants' characteristics that could be associated with NAFLD variability by age: sex, presence of fibrosis, ethnicity, BMI, waist to height ratio, liver

laboratory findings, other laboratory findings, and comorbidities. Ethnicity was recorded in the following classifications: Mexican American, other Hispanics, Non-Hispanic White, Non-Hispanic Black, other race (including multi-racial). BMI was presented as four categories: underweight (<18.5), normal weight (18.5-25), overweight (25-30), and obese (≥30). Waist to height ratio was grouped into quartiles based on our observed distributions in the overall NHANES population (32.1 <= Q1 < 47.8, 47.8 <= Q2 <54.3, 54.3 <= Q3 < 62.1, 62.1 <= Q4 < 113.7).

We evaluated the risk of liver-related complications from NAFLD by estimating cases of advanced fibrosis (AF). The severity of fibrosis is not reported in NHANES. To rule in the presence of advanced fibrosis, we used the NAFLD fibrosis score (NFS) used in previous work [12]. An NFS score greater than 0.676 was interpreted as the presence of AF.

Liver related laboratory findings included serum levels of albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, gamma-glutamyl transferase (GGT), lactate dehydrogenase, and total bilirubin. Other laboratory findings examined included serum glycohemoglobin, fasting glucose, fasting insulin, and total cholesterol. All lab values were collected by trained medical personnel in the mobile examination center. The estimated glomerular filtration rate (eGFR) was calculated using serum creatinine along with demographic data according to the CDK-EPI equation [13].

The presence of diabetes was identified via response to the question: “{Other than during pregnancy, have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?”. The metabolic syndrome was defined using the National Cholesterol Education Program’s Adult Treatment Panel III (ATP III) definition [14]. Cardiovascular disease was described as a self-reported coronary heart disease diagnosis, myocardial infarction, stroke, congestive heart failure, or angina pectoris.

Statistical Analyses

All analyses were conducted in STATA version 15.1. Demographic and clinical characteristics of respondents with NAFLD are presented by age group. We report percentages for categorical variables and the mean and standard deviation for continuous variables. The prevalence estimate of NAFLD is reported overall and by age group. Prevalence ratios and 95% confidence intervals were estimated, relying on the log-binomial model. In select instances where the log-binomial failed, we relied on Poisson regression to estimate the prevalence ratios and a 95% confidence interval.

Results

Among all NHANES respondents (n = 50,588), 14,623 had completed the survey components necessary for the USFLI, and NFS score calculations and were included in the analysis. The study population's mean age was 42.9 years, 51% were women, and 66% were non-Hispanic white.

As age increased, the proportion of NAFLD positive participants with fibrosis, metabolic syndrome, diabetes, and cardiovascular disease also increased (Table 1). The proportion of participants that were

women increased with advancing age, as did the proportion of participants identified as non-Hispanic whites. Participants that were categorized as overweight and obese based on BMI showed opposite trends. The proportion of NAFLD patients that were obese was highest in the younger population and decreased with advancing age, while the proportion of those who were overweight increased with age.

The mean value of albumin ranged from 4.4 g/dL in the youngest groups to 4.2 g/dL in those over the age of 18 with NAFLD. Mean values of alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase peaked at the 19–49 and 50–64 age groups then decreased. LHD and total bilirubin increased with increasing age, as seen in Table 2. The mean values of fasting glucose and HBA1C increased with increasing age, then stabilized for older age groups. The mean value for fasting insulin and eGFR was highest for the youngest age group, then trended down as age increased. Age groups 19–49 and 50–64 had the highest mean values for total cholesterol, LDL, and total triglycerides and lower HDL values.

The demographic and clinical components contributing to the USFLI (ethnicity and waist circumference) exhibited a marginal magnitude of association with NAFLD as defined by the USFLI equation. Although the USFLI equation defines the overall magnitude and directions of associations, we observed notable differences between age groups. The magnitude of the association between NAFLD and non-white ethnicities was observed to be the strongest in the younger population. For example, the prevalence ratio for Mexican Americans compared to Non-Hispanic White was 3.44 in respondents 18 years old or younger (95%CI: 2.48–4.77) and 1.60 in respondents 75 or older (95%CI: 1.30–1.97). The prevalence ratio for females was higher in older age groups, with a prevalence ratio of 0.74 (95%CI: 0.62–0.88) in respondents in those older than 74. The magnitude of association for obese and overweight participants was most substantial for the youngest group. Specifically, 18 years old or younger participants who were obese had a prevalence ratio of 46.8, which decreased to 6.73 for the oldest age group. Similar prevalence ratio and age trends were observed for participants with diabetes and metabolic syndrome, as seen in table 3. We observed an increased waist to height ratio was associated with an increased risk of NAFLD, without a clear trend across age groups.

The laboratory components of the USFLI (GGT, fasting glucose, and fasting insulin) were significantly associated with NAFLD across age groups. For GGT, the association was highest for those under the age of 19. For fasting glucose and fasting insulin, the magnitudes of association were similar across age groups. The magnitude of the association between albumin and NAFLD was negative. It ranged from a prevalence ratio of 0.32 (0.20–0.51) for respondents under 19 years of age to 1.15 (0.86–1.53) over the age of 74.

Similarly, bilirubin was negatively associated with NAFLD, with increasing prevalence ratios with increasing age. eGFR, total cholesterol, LDH, and triglycerides had similar associations with NAFLD, where the magnitude of associations was positive and higher for younger groups and neutral to negative for older age groups. The associations between NAFLD and HDL were negative, and the magnitude was highest for younger age groups.

Discussion

Assessing age differences in the magnitudes of the association between potential risk factors and NAFLD will provide critical clinical information pertinent to the diagnosis and prognosis of NAFLD. The importance of evaluating the variability of risk factors for NAFLD spans the age spectrum. NAFLD is the most common liver disease in children and the leading indicator for liver transplantation in adults over the past decade [15]. While prior studies have sought to assess risk factors and develop predictive models, none have evaluated the need for age-specific modeling. This study observed that the association between patient characteristics and NAFLD varies across the age spectrum. We observed a gradient of the magnitude of association with increasing age for several risk factors, suggesting that future work should carefully consider age as a modifier when building predictive or prognostic models. To our knowledge, this is the first descriptive study to look at whether an association between patient characteristics and NAFLD varies by age in a large, nationally representative sample of the US population.

Previous studies of age and NAFLD have generally focused on age-specific trends in prevalence or age-restricted analyses. NAFLD prevalence in the US from 1988 to 1994 was reported as ~ 19.0% in the general population aged 20–74 years, based on NHANES respondents [16]. Individual studies have studied the prevalence of NAFLD within different age groups. In a study limited to older participants, researchers found the prevalence rates were ~ 40.3% for those between the age of 60 and 74 years old and ~ 39.2% for those over the age of 74 years [17]. Another study with patients between 28–70 (mean age: 54.6) years found the NAFLD prevalence to be ~ 46% [18]. These studies highlight an association between NAFLD and age but do not address whether NAFLD prognosis or risk factors vary. A study looked at the prevalence of NAFLD in children aged 9–17 years with obesity. They found that one-third of boys and one-fourth of girls had NAFLD [19].

Publications from the early 2000s discussed gender influences on NAFLD; their conclusion had variable NAFLD prevalence in males and females. However, males consistently had a higher prevalence than females in these studies [20–25]. Our results were consistent with the literature where males had a higher prevalence than females. However, our calculated NAFLD prevalence ratio for males and females increased with increasing age. The increase in prevalence ratio suggests an increase in NAFLD prevalence of males and females with increasing age was not proportional. A possible explanation for the observation can be that pre-menopausal women may benefit from estrogen's protective effects when it comes to developing NAFLD. Recent research has shown that the prevalence of NAFLD is higher in males than in females during reproductive years. After menopause, females are suggested to have a higher prevalence than males [26].

Obesity has been considered a significant risk factor for NAFLD [27]. Results from our study show a unique relationship between body weight, NAFLD, and age. Studies have suggested that the epidemic of pediatric obesity is driving the pediatric NAFLD prevalence [7, 28]. Participants who were younger than the age of 19 and obese had 47 times higher risk of developing NAFLD than normal-weight participants of

the same age. For other age groups, the prevalence ratio continued to be the highest obese participants. Our results are consistent with the literature suggesting that obesity is a significant risk factor for NAFLD. However, a recently published study concluded that nonobese NAFLD patients carry a higher mortality than obese NAFLD patients [29]. This suggests that it is essential to screen high-risk groups, even if obesity is not present.

Our results showed serum albumin was 4.4 g/dL for those younger than 18 and 4.2 g/dL for those over 18. In the literature, serum albumin is reported to decrease in patients with hepatic fibrosis. One study showed that serum level for albumin in patients with mild fibrosis was 4.4g/dL and albumin level for patients with intensive fibrosis was 4.2 g/dL [30, 31]. Serum bilirubin has been studied for its cytoprotective effects and reducing the risks of NAFLD. Our findings were consistent with the notion that total bilirubin may be protective against NAFLD [32].

NAFLD is associated with liver-related morbidity, cardiovascular disease, diabetes mellitus, and adulthood mortality in adults. Though the short term morbidity and mortality due to NAFLD are attenuated in the younger population, the increased lifetime consequences of chronic NAFLD with childhood-onset them at a higher risk of complications during their lifetime [33]. Younger populations have vulnerabilities to environmental influences and have exposures that are unique opportunities for interventions and modification of risks. For example, maternal preconception obesity/gestational diabetes and early feeding practices like high sugar consumption during vulnerable developmental stages are susceptibilities unique to early life. NAFLD present in children and adolescents also may differ histologically from adults [34]. For example, Type 2 NAFLD is more commonly found in children/young people and is associated with more significant fibrosis and progressive disease. Type 2 NAFLD refers to the periportal distribution of steatosis, inflammation, and fibrosis. In comparison, Type 1 NAFLD refers to steatosis, inflammation, and fibrosis surrounding the central vein [34].

Algorithms have been developed to identify and characterize NAFLD relying on diagnoses, laboratory measures, biometrics, and demographics. These algorithms use different data inputs and thresholds to rule out potential NAFLD cases [35]. For example, the Fatty Liver Index (FLI) is used to predict fatty liver in the general population by using parameters like BMI, triglycerides (TG); waist circumference (WC); and gamma-glutamyl transferase levels [36]. The Hepatic Steatosis Index (HSI) is an alternative algorithm relying on aspartate aminotransferase, alanine aminotransferase; BMI; and diabetes mellitus [37]. Other algorithms include the lipid accumulation product, visceral adiposity index, and triglyceride and glucose index, which use a combination of parameters like gender; TG; WC; glucose; BMI, and HDL [38–40]. These algorithms have a sensitivity that ranges from 46–96% and specificity that ranges from 40–92%, depending on the cut-off point and algorithm used [35]. There has been work done to improve the algorithms to fit the population. For example, USFLI adds to the FLI to predict hepatic steatosis more accurately in the multiethnic U.S. population [11, 36]. By accounting for additional parameters like race, age, insulin, and glucose, they improved the algorithm's sensitivity and specificity. For USFLI, the diagnostic accuracy of ≥ 30 cut-point was 62% sensitivity, 88% specificity, 5.2 likelihood ratio of positive, and 0.43 likelihood ratio of negative [11]. Despite the differences seen between younger and older NAFLD

patients, the algorithms commonly used to identify NAFLD have not taken age into account as an effect modifier.

Our study's main strength was the dataset used, which contained both self-reported data and laboratory collected value to assess the relationship between individual characteristics and NAFLD. Additionally, our population-based estimates of prevalence are representative of the U.S. non-institutionalized population and collected in standardized ways by trained professionals. Along with using a robust data source, we used a validated algorithm for NAFLD diagnosis. One of the study's limitations is that the data used does not represent the institutionalized U.S. population who may have a different prevalence of NAFLD. The USFLI algorithm is a validated algorithm that accurately predicts the presence of steatosis but does not predict the severity of NAFLD. While algorithms are used to indicate NAFLD's presence, they are not the gold standard diagnostic tool. Future studies should utilize biopsy or imaging confirmed NAFLD cases. Lastly, the study design is cross-sectional, limiting us from analyzing NAFLD progression in individuals over time.

Declarations

- **Guarantor of the article:** Anthony P. Nunes, PhD
- **Ethics approval and consent to participate:** NHANES was approved by the Centers for Disease Control and Prevention NCHS Research Ethics Review Board (ERB). All NHANES participants provided written consent to participate.
- **Consent for publication:** Not applicable
- **Availability of data and materials:** The data analyzed during the current study is publicly available through the Centers for Disease Control and Prevention's National Center for Health Statistics. [https://www.cdc.gov/nchs/nhanes/index.htm]
- **Competing interests:** The authors have no conflict of interests to declare regarding this work.
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- **Authors' contributions:**
    - Syed H. Naqvi: Responsible for implementation of analysis and drafting of the manuscript.
    - Anthony P. Nunes: Responsible for the design of analysis and drafting of the manuscript.
    - Both authors have reviewed and approved the final draft.

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Tables

Table 1
Demographic characteristics of participants with NAFLD, by age categories, among NHANES respondents from year to year

	Age Groups				
	≤ 18 years old	19–49	50–64	65–74	≥ 75 years old
Observations	**291**	**1736**	**1309**	**751**	**473**
Population Size	**2,858,076**	**31,739,358**	**22,290,051**	**10,558,081**	**5,331,015**
Fibrosis	0%	2.3%	10.2%	16.8%	26.9%
Sex					
Male	62.6%	61.2%	55.3%	54.1%	47.9%
Female	37.4%	38.8%	44.7%	45.9%	52.1%
Ethnicity					
Mexican American	34.8%	19.9%	9.4%	6.6%	4.8%
Other Hispanic	8.6%	7.7%	5.7%	4.5%	3.4%
Non-Hispanic White	42.9%	59.4%	72.6%	78.5%	86.6%
Non-Hispanic Black	8.0%	7.0%	7.1%	4.5%	2.3%
Other Race - Including Multi-Racial	5.7%	6.0%	5.2%	5.9%	2.9%
BMI					
Underweight	N/A	N/A	N/A	N/A	N/A
Normal Weight	6.0%	2.5%	4.7%	4.0%	8.6%
Overweight	17.4%	20.7%	23.9%	29.0%	39.5%
Obese	76.6%	76.8%	71.4%	67.0%	51.8%
Waist to Height Ratio (WHR)					
Q1 - (32.1 < = WHR < 47.8)	1.5%	0.16%	0.33%	N/A	N/A
Q2 (47.8 < = WHR < 54.3)	9.5%	5.0%	3.9%	1.5%	2.4%
Q3 (54.3 < = WHR < 62.1)	27.0%	29.4%	27.3%	22.4%	23.7%
Q4 (62.1 < = WHR < 113.7)	62.0%	65.4%	68.5%	76.0%	73.9%
Comorbidities					
Metabolic syndrome	7.2%	45.5%	67.7%	75.4%	75.7%

	Age Groups				
Diabetes	2.0%	9.6%	26.3%	34.0%	30.7%
CVD	N/A	3.8%	13.9%	27.9%	39.7%
N/A = insufficient numbers to obtain estimates					

Table 2
Clinical characteristics of participants with NAFLD, by age categories, among NHANES respondents from year to year

	Age Groups				
	≤ 18 years old	19–49	50–64	65–74	≥ 75 years old
Observations	291	1736	1309	751	473
Population Size	2,858,076	31,739,358	22,290,051	10,558,081	5,331,015
Liver Labs	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
Albumin (g/dL)	4.4 (4.3–4.4)	4.2 (4.2–4.3)	4.2 (4.2–4.2)	4.2 (4.2–4.2)	4.2 (4.2–4.2)
Alanine aminotransferase (U/L)	31.4 (28.8–34.0)	37.8 (36.2–39.4)	31.6 (30.3–32.9)	27.3 (25.3–29.3)	21.6 (20.8–22.4)
Aspartate aminotransferase (U/L)	26.3 (25.0-27.7)	29.6 (28.3–30.8)	28.9 (27.6–30.1)	27.2 (25.7–28.7)	25.2 (24.5–26.0)
Alkaline phosphatase (U/L)	138.6 (127.3–150.0)	72.4 (70.6–74.2)	73.6 (71.8–75.4)	69.8 (67.6–72.0)	71.4 (68.7–74.1)
Gamma glutamyl transferase (U/L)	24.2 (21.8–26.7)	41.2 (39.0-43.5)	45.5 (42.1–48.9)	36.6 (32.6–40.5)	33.8 (29.6–37.9)
Lactate dehydrogenase (U/L)	138.7 (134.4-142.9)	127.6 (126.1-129.1)	132.6 (130.8-134.4)	134.2 (131.2-137.2)	140.9 (137.9-143.9)
Total bilirubin (mg/dL)	0.63 (0.59–0.66)	0.68 (0.66–0.70)	0.71 (0.68–0.73)	0.72 (0.69–0.75)	0.80 (0.76–0.84)
Other Labs					
Fasting HbA1C	5.2 (5.1–5.3)	5.6 (5.5–5.8)	6.1 (5.9–6.3)	6.1 (5.9–6.2)	6.1 (5.9–6.3)
Fasting Glucose (mg/dL)	103.0 (96.0-110.0)	113.4 (111.5-115.4)	125.5 (122.2-128.9)	125.0 (121.7-128.3)	125.0 (121.4-128.5)
Fasting Insulin (Pmol/L)	205.0 (190.3-219.6)	150.1 (142.9-157.3)	129.1 (122.5-135.6)	131.9 (118.9–145.0)	114.9 (105.9-123.9)
eGFR (mL/min/1.73 m^2)	139.8 (136.9-142.7)	106.7 (105.7-107.7)	88.0 (86.8–89.1)	75.0 (73.4–76.6)	61.5 (59.6–63.5)

	Age Groups				
Total Cholesterol (mg/dL)	165.6 (154.9-176.4)	203.6 (197.7-209.5)	201.7 (194.9-208.6)	180.9 (172.8-188.9)	189.4 (178.1-200.7)
HDL (mg/dL)	44.3 (41.0-47.6)	43.1 (41.8–44.5)	46.0 (44.4–47.6)	47.9 (45.7–50.2)	51.7 (48.4–54.9)
LDL (mg/dL)	97.0 (92.0-102.0)	120.8 (118.7–123.0)	119.8 (116.9-122.8)	103.1 (99.5-106.7)	103.9 (99.7–108.0)
Triglycerides (mg/dL)	116.7 (108.6-124.9)	172.3 (165.0-179.6)	173.5 (164.9–182.0)	150.0 (142.6-157.6)	152.8 (142.7-162.9)

Table 3

Prevalence ratio of NAFLD by age group and categories of clinical and demographic characteristics

	Age Group				
	≤ 18 years old	19–49	50–64	65–74	≥ 75 years old
Sex	Prevalence Ratio (95% CI)	Prevalence Ratio (95% CI)	Prevalence Ratio (95% CI)	Prevalence Ratio (95% CI)	Prevalence Ratio (95% CI)
Male	1 (-)	1 (-)	1 (-)	1 (-)	1 (-)
Female	0.62 (0.46–0.84)	0.64 (0.578–0.717)	0.75 (0.66–0.85)	0.76 (0.65–0.88)	0.74 (0.62–0.88)
Ethnicity					
Mexican American	3.44 (2.48–4.77)	1.78 (1.60–1.98)	1.65 (1.48–1.83)	1.496 (1.31–1.71)	1.6 (1.3–1.97)
Other Hispanic	1.66 (1.05–2.60)	1.1 (0.95–1.29)	1.14 (0.99–1.32)	1.14 (0.96–1.35)	1.16 (0.87–1.56)
Non-Hispanic White	1 (-)	1 (-)	1 (-)	1 (-)	1 (-)
Non-Hispanic Black	0.73 (0.45–1.17)	0.59 (0.50–0.70)	0.62 (0.53–0.72)	0.53 (0.42–0.67)	0.39 (0.24–0.62)
Other Race - Including Multi-Racial	1 (0.54–1.87)	0.72 (0.59–0.88)	0.79 (0.61–1.02)	0.82 (0.59–1.12)	0.91 (0.58–1.43)
BMI					
Underweight	0.62 (0.46–0.84)	0.2 (0.03–1.46)	0 (0)	0 (0)	0 (0)
Normal Weight	1 (-)	1 (-)	1 (-)	1 (-)	1 (-)
Overweight	8.5 (3.93–18.40)	8.36 (5.47–12.78)	3.59 (2.46–5.22)	4.68 (3.12–7.02)	3.74 (2.49–5.62)
Obese	46.8 (22.78–96.12)	28.8 (19.15–43.34)	8.68 (6.09–12.38)	10.22 (7.02–14.9)	6.73 (4.55–9.94)
Waist to Height Ratio (WHR)					
Q1 - (32.1 < = WHR < 47.8)	0.064 (0.01–0.38)	0.04 (0.02–0.13)	0.28 (0.06–1.25)	0 (0)	0 (0)
Q2 (47.8 < = WHR < 54.3)	1 (-)	1 (-)	1 (-)	1 (-)	1 (-)
Q3 (54.3 < = WHR	4.35 (2.46–	5.16 (3.83–	3.82 (2.56–	6.96 (3.52–	4.38 (2-9.53)

< 62.1)	7.69)	6.96)	5.71)	13.75)	
Q4 (62.1 < = WHR < 113.7)	16.1 (9.62–26.94)	13.42 (10.09–17.84)	8.90 (6.07–13.06)	17.24 (8.94–33.26)	12.01 (5.65–25.5)
Comorbidities					
Metabolic syndrome	11.91 (9.14–15.5)	6.04 (5.40–6.75)	4.68 (3.96–5.54)	4.15 (3.28–5.25)	4 (3.04–5.26)
Diabetes	3.96 (1.46–10.72)	2.65 (2.35–2.99)	1.88 (1.68–2.11)	1.72 (1.50–1.97)	1.62 (1.36–1.92)
CVD	N/A	1.75 (1.29–2.19)	1.53 (1.33–1.77)	1.28 (1.09–1.50)	1.32 (1.11–1.58)
Liver Labs					
Albumin (g/dL)	0.32 (0.20–0.51)	0.53 (0.46–0.61)	0.65 (0.54–0.78)	0.76 (0.58–0.99)	1.15 (0.86–1.53)
Alanine aminotransferase (U/L)	1.14 (1.08–1.20)	1.06 (1.03–1.08)	1.09 (1.05–1.13)	1.06 (1.03–1.09)	1.22 (1.08–1.37)
Aspartate aminotransferase (U/L)	1.27 (1.17–1.39)	1.03 (1.02–1.04)	1.05 (1.02–1.09)	1.06 (1.02–1.10)	1.08 (0.98–1.21)
Alkaline phosphatase (U/L)	1 (0.99–1.01)	1.1 (1.07–1.14)	1.07 (1.05–1.09)	1.04 (1.01–1.07)	1.01 (0.98–1.03)
Gamma glutamyl transferase (U/L)	1.23 (1.15–1.31)	1.05 (1.03–1.06)	1.03 (1.02–1.04)	1.07 (1.05–1.08)	1.05 (1.03–1.07)
Lactate dehydrogenase LDH (U/L)	1.08 (1.04–1.13)	1.02 (1.01–1.04)	1 (0.98–1.02)	1 (0.97–1.03)	0.98 (0.95–1.01)
Total bilirubin (mg/dL)	0.3 (0.19–0.49)	0.6 (0.49–0.72)	0.78 (0.62–0.98)	0.82 (0.63–1.07)	1.24 (0.95–1.61)
Other Labs					
Fasting HbA1C	1.02 (0.78–1.34)	1.35 (1.25–1.46)	1.15 (1.10–1.21)	1.2 (1.08–1.34)	1.24 (1.05–1.46)
Fasting Glucose (mg/dL)	1.09 (1.06–1.12)	1.09 (1.08–1.10)	1.06 (1.05–1.07)	1.07 (1.05–1.08)	1.09 (1.06–1.12)
Fasting Insulin (Pmol/L)	1.09 (1.07–1.10)	1.01 (1.01–1.02)	1.01 (1.01–1.02)	1.02 (1.01–1.02)	1.02 (1.01–1.03)
eGFR (mL/min/1.73 m^2)	1.12 (1.04–1.20)	0.97 (0.94-1.00)	0.98 (0.94–1.01)	0.97 (0.93–1.01)	0.95 (0.91-1.00)

Total Cholesterol (mg/dL)	1.07 (0.97–1.19)	1.08 (1.04–1.11)	0.98 (0.94–1.01)	0.92 (0.89–0.96)	0.98 (0.94–1.02)
HDL (mg/dL)	0.46 (0.31–0.68)	0.56 (0.51–0.62)	0.68 (0.63–0.75)	0.67 (0.59–0.75)	0.82 (0.70–0.94)
LDL (mg/dL)	1.13 (1.08–1.19)	1.07 (1.06–1.09)	0.98 (0.97-1.00)	0.95 (0.93–0.97)	0.97 (0.95-1.00)
Triglycerides (mg/dL)	1.08 (1.06–1.11)	1.01 (1.01–1.01)	1.01 (1.01–1.02)	1.03 (1.03–1.05)	1.04 (1.03–1.05)