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High prevalence of hepatic fibrosis, measured by Elastography, in a Population-based study of Mexican Americans

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Abstract

Background & Aims: Hepatic fibrosis is a primary risk factor for cirrhosis and hepatocellular carcinoma, which affect a disproportionate number of Hispanics in the United States. We aimed to determine the prevalence of significant fibrosis, measured by point shear-wave elastography (pSWE), and determine characteristics of hepatic fibrosis and simple steatosis in a population-based study of Mexican American Hispanics in south Texas.

Methods: Liver stiffness was measured by pSWE, performed by 2 separate operators, for 406 participants in the Cameron County Hispanic Cohort from 2015 through 2017. Significant fibrosis (F2–F4) was defined as median stiffness > 1.34 m/s. Steatosis was determined by ultrasound. All participants underwent a clinical examination that included a comprehensive laboratory analysis and standardized interview about their medical and social history. We calculated weighted prevalence of fibrosis and determined clinical and demographic associations with significant fibrosis (with or without steatosis) and simple steatosis with no/minimal fibrosis using multinomial logistic regression.

Results: Fifty-nine participants were excluded due to unreliable pSWE findings or inconclusive ultrasound results, for a final analysis of 347 participants. The prevalence of significant fibrosis was 13.8%; most of these participants (37/42, 88.1%) had no evidence of viral hepatitis or heavy drinking. Levels of liver enzymes were associated with fibrosis and simple steatosis. Indicators of metabolic health (insulin resistance, triglycerides, and cholesterol) were significantly associated with simple steatosis. Fibrosis, but not simple steatosis, was significantly associated with of antibodies against HCV in plasma (odds ratio, 18.9; P=.0138) and non-significantly associated with reduced platelet count (odds ratio, 0.8 per 50×10^3/μL; 95% CI, 0.5–1.1). Multivariable analyses, as well as sensitivity analyses removing F4 fibrosis and viral or alcoholic etiologies, confirmed our results.

Conclusion: We estimated the prevalence of fibrosis in a large population of Mexican American Hispanics using pSWE measurements. We found Mexican American Hispanics to have a higher prevalence of fibrosis compared to European and Asian populations, primarily attributable to metabolic disease.

Keywords

CCHC; US; obesity; minority

Introduction

The incidence of hepatocellular carcinoma (HCC) is increasing in the United States (US), particularly among Hispanics[1]. In south Texas, Hispanics now have among the highest rates

of HCC in the country (12.1 cases for 100,000 person-years *vs* 8.4 among Hispanics nationwide)[1,2] However the prevalence and characteristics of liver fibrosis—a key risk factor for cirrhosis and HCC—in this region is unknown.

Biopsy remains the gold standard for staging of liver fibrosis, but is not suitable for population screening due to the potential for complications, patient discomfort, and expense.[3] Therefore, point shear-wave elastography (pSWE), which has been validated against biopsy for the staging of liver fibrosis,[4,5] is a promising method for population fibrosis screening. pSWE integrates easily into standard B-mode ultrasonography, has good inter-operator reliability,[6,7] and has a lower failure rate than transient elastography in obese individuals.[8] Validation studies of pSWE against biopsy in diverse populations have reported excellent accuracy to detect F2 fibrosis (meta-analysis sensitivity = 85.0%, specificity = 94.4)[9] which is an ideal target for screening and HCC prevention.[10]

Despite robust clinical validation of pSWE, and the importance of early fibrosis detection, population-based applications of elastography are scant. Several European and Asian groups have used elastography in population-based studies[11–13], but in the US no studies have employed elastography to determine the burden and distribution of fibrosis in the general population.

In the current study we applied pSWE screening to the Cameron County Hispanic Cohort (CCHC), a population-based study of Mexican Americans in south Texas, US. We assessed a cross-sectional sample of CCHC participants to (1) determine the prevalence of significant fibrosis, (2) determine the clinical and sociodemographic correlates of fibrosis and simple steatosis, and (3) identify clinical characteristics that distinguish individuals with fibrosis from those with simple steatosis.

Methods

Patient Population and Setting

The CCHC is a population-based cohort with stratified two-stage cluster sampling design in Brownsville, Texas, initiated in 2004. The Census blocks of Brownsville are stratified by socioeconomic quartiles based on US Census data; within each stratum, census tracts are selected randomly for invitation to the study; all members of selected households (≥ 18 years of age) are invited in-person at the home to participate in the CCHC studies.[14] pSWE examinations began in 2015, with all participants invited to participate in the additional imaging studies (See Supplemental Figure 1). Greater than 95% of participants since 2015 have elected to undergo pSWE measurement. The study protocol was approved by the Committee for the Protection of Human Subjects of the University of Texas Health Science Center at Houston.

Clinical Examination

Participants arrived to the clinic 8 hours fasting and gave informed consent to participate in the clinical exam. Trained interviewers conducted in-depth interviews to capture sociodemographic parameters and social history, and completed a clinical exam, described elsewhere[14]. Hepatitis C Virus antibodies (anti-HCV) and Hepatitis B Virus surface antigen

(HBsAg) were assayed using the Ortho HCV Version 3.0 ELISA Test System and Abnova Hepatitis B surface antigen Elisa Kit, respectively. Positive viral hepatitis results were sent to an independent CLIA-certified laboratory for confirmation, and those not confirmed positive were considered to be negative. Drinking history was obtained by interview. “Heavy drinking” was defined as regular consumption of > 21 drinks per week for men, and > 14 drinks per week for women.[15]

Ultrasonography and Elastography

Liver steatosis was determined by liver ultrasonography performed by trained operators and read by a single board-certified gastroenterologist. Next, pSWE liver stiffness measurements were taken using the Siemens Acuson S3000 (Siemens AG, Mountain View, CA). One operator captured shear wave speeds until a total of 10 readings were made (study 1). This process was repeated by a second operator (study 2), blind to the location of the previous 10 readings. The median shear wave velocity was recorded for each study, and the higher of the two medians is used to determine fibrosis stage.

Quality Control for pSWE Measurement

Participants were excluded (1) if either study had a shear-wave IQR-to-median ratio > 0.3;[6] (2) if only one study was completed; (3) if either study had less than 7 valid readings;[4] or (4) if the difference between medians in study 1 and study 2 was greater than two standard deviations of the distribution of differences. In addition, we excluded participants with an inconclusive liver ultrasound. Supplemental Figure 1 describes the development of the analytical data set.

Inter-operator reliability

There were four trained operators from which two completed the pSWE studies for each participant. We divided the sample into six strata (corresponding to the six pairwise combinations of operators) and calculated stratum-specific and overall kappa and tested homogeneity of kappa statistics over the strata for detection of significant fibrosis. In addition, we determined if the operator was associated with staging of significant fibrosis using logistic regression.

Statistical Analysis

All analyses take into account the sampling design of the CCHC. In addition, age- and gender-adjusted weights were calculated to estimate population prevalence, and we accounted for possible clustering effects by census block and household. First, we divided the participants into three disease groups: healthy (no steatosis and fibrosis < F2); steatosis (steatosis on ultrasound and fibrosis < F2); and fibrosis (fibrosis ≥ F2 with or without steatosis). In these groups, we calculated mean and standard error (SE), or frequency and proportion, of variables of interest. *P*-values for differences between the groups were calculated by one-way analysis of variance for continuous variables, and Rao-Scott χ^2 test for categorical variables. Second, for parameters with a possible association with the disease groups (unadjusted $p < 0.25$), we used univariable multinomial logistic regression to estimate the odds ratio (OR) and 95% confidence interval (CI) for steatosis and fibrosis,

relative to the healthy, for each parameter. Finally, we calculated the OR and 95% CI for fibrosis relative to steatosis in the multinomial framework, and repeated the univariable analyses after adjustment for age and sex. Results significant at the $p < 0.05$ level after controlling for false discovery rate (using the Benjamini-Hochberg procedure) are marked with an asterisk. Multivariable models were developed by including the variables that were predictive in univariable analysis as well as age and sex.

Sensitivity analyses

First we assessed changes to the multinomial results after removing participants with alcoholic or viral etiologies. Second, we repeated the multinomial analysis excluding those with F4 fibrosis (m/s > 2.55). Percent changes in ORs, changes in direction of association, and changes in significance were examined. Finally, we repeated analyses using a binomial parameterization of the outcome (significant fibrosis *vs* no/minimal fibrosis, irrespective of steatosis).

SAS 9.4 (Cary, NC) was used to complete all analyses. Figures were developed in the *ggplot* package[16] of R Version 3.3.[17]

Results

Quality Control and Inter-Operator Reliability

Four hundred and six participants completed pSWE examinations between 2015 and 2017. We excluded 40 participants pursuant to our pSWE quality control criteria, and 19 participants with inconclusive liver ultrasound, for a final analytic sample of 347 (See supplementary Figure 1). For inter-operator reliability, the overall kappa statistic was 0.6, with 93.2% overall agreement between study 1 and study 2 for staging of significant fibrosis, and no evidence of heterogeneity across strata. There was no significant association between operator and fibrosis stage. Descriptive statistics of the analytic sample are given in Table 1; participant characteristics are similar to previous CCHC publications [14]

Population Prevalence and Characteristics of Significant Liver Fibrosis

The overall prevalence of significant (F2+) fibrosis was 13.6% (95% CI 8.2—18.9%). By F-stage, we found that 5.6% (95% CI 2.3 – 8.9) had F2 fibrosis, 5.8% (95% CI 2.3 – 9.4) had F3 fibrosis, and 2.1% (95% CI 0.4 – 3.8) had F4 fibrosis. Among the 42 participants with significant fibrosis, two reported chronic heavy drinking and three were positive for anti-HCV (one participant had evidence of both risk factors). No participants had confirmed presence of HBsAg. The remaining cases were classified as NAFLD if they had at least one characteristic of NAFLD: steatosis, obesity, elevated waist circumference, or metabolic syndrome (n = 30, 66.9%). We considered those with no evidence of viral hepatitis, heavy drinking, or risk factors for NAFLD to have “unknown” etiology (n = 7, 18.6%). No participants were taking medications known or suspected of causing drug-induced liver disease. Figure 1 displays the liver stiffness and etiology of each participant by F score.

The overall prevalence of fatty liver (irrespective of fibrosis) in the population was 43.4% (95% CI 37.6 – 49.2); among those with significant fibrosis, the prevalence of steatosis was

38.3% (95% CI 30.3 – 46.2), and among those with no/minimal fibrosis, it was 49.3% (95% CI 41.0 – 57.6). The 35 to 50 year age group had the greatest prevalence of both steatosis and fibrosis (Figure 2).

Comparison of parameter values in each of the phenotypic groups

Table 2 presents participant characteristics in each phenotypic group. The prevalence of diabetes was highest in the steatosis group (37.5%), followed by fibrosis (27.5%), and healthy (23.2%; overall $p = 0.1581$). Measures of liver enzymes were associated with the liver phenotypes, with the highest levels of aspartate aminotransferase (AST) in the fibrosis group ($p = 0.0228$), and the highest levels of alanine aminotransferase (ALT) in the steatosis group ($p = 0.0032$). Measures of adiposity (obesity and waist circumference) were elevated in the steatosis group, with overall significant associations ($p = 0.0006$, $p < 0.0001$, respectively). There was an increasing number of mean drinks per week from healthy (1.8 drinks) to steatosis (2.1 drinks) to fibrosis (5.4 drinks), although this association did not reach nominal statistical significance ($p = 0.1737$).

Univariable analysis comparing steatosis and fibrosis to healthy participants

After controlling the false discovery rate, several clinical variables were associated significantly only with steatosis (Table 3), including fasting blood glucose [odds ratio (OR) 1.1 per 10 mg/dL, 95% CI 1.0 – 1.2], triglycerides (OR 1.4 per 50 mg/dL, 95% CI 1.1 – 1.8), ALT levels (OR 1.5 per 10 units/L, 95% CI 1.2 – 1.8), obesity (OR 2.3, 95% CI 1.5 – 5.0) and insulin (OR 2.8 per 10 mg/dL, 95% CI 1.6 – 4.7). Both triglyceride levels and ALT levels were independently associated with steatosis, but not fibrosis, in the multivariable model (OR 1.3 per 10 mg/dL, 95% CI 1.0 – 1.7; and OR 1.5 per 10 units/L, 95% CI 1.0 – 2.2, respectively) after adjustment for age, sex, fasting glucose, waist circumference, platelet count, HCV positivity and number of drinks per week (Supplementary Table 5).

In contrast, few associations reached 5% significance only for fibrosis *vs* healthy. Fasting glucose had a similar (but non-significant) association with fibrosis (OR 1.1 per 10 mg/dL, 95% CI 1.0 – 1.2). There was a suggestive negative association with platelet count (OR 0.8 per 50×10^3/μL, 95% CI 0.6 – 1.1). Anti-HCV presence was strongly associated with fibrosis relative to healthy (OR 18.9, 95% CI 1.8 – 196.4), but did not reach corrected significance.

When comparing fibrosis to the steatosis reference, we found that reduced platelet count was borderline significantly associated with fibrosis relative to steatosis [OR 0.7 per 50×10^3/μL, 95% CI 0.4 – 1.0]. We also found that HDL cholesterol was slightly higher in the fibrosis group (OR per 10 mg/dL = 1.5, 95% CI 1.0 – 2.3). Neither association was significant after controlling the false discovery rate. Results were similar after adjusting for age and sex (Supplementary Table 1).

Sensitivity analyses

We then repeated the analysis in Table 3 excluding those with evidence of HCV infection or heavy alcohol consumption (n = 5; Supplementary Table 2), revealing only minor differences in measures of association and significance. Similar results were found after removing participants with F4 fibrosis (cirrhosis; Supplementary Table 3), and when using a

binomial parameterization of the outcome (significant fibrosis *vs* no/minimal fibrosis; Supplementary Table 4).

Discussion

We have estimated the population prevalence of significant liver fibrosis in a Mexican American population using an accurate and non-invasive method, pSWE.[18,19] Our results show that a large proportion (13.8%) of the Mexican American population in Texas, which is known to have a high incidence of liver cancer, has significant liver fibrosis.

Over 88% of participants had no evidence of viral or alcoholic etiologies of disease. Among these non-alcoholic, non-viral cases, 81% likely had NAFLD, but the remaining 19% had no known risk factors for fibrosis. This is expected as non-alcoholic steatohepatitis is the fastest-growing indication for liver transplantation in the US[20], and obesity and diabetes are common in south Texas.[14] In addition, liver fibrosis is significantly heritable, suggesting possible genetic predisposition to fibrosis among those with no known risk factors.[21] Therefore, baseline susceptibility to NAFLD among Hispanic populations in Texas,[22] combined with the rise of obesity and diabetes, may explain the high rates of HCC in south Texas[1]. However, to examine the hypothesis that aflatoxin B1 exposure contributes substantially to HCC in south Texas, we previously sequenced the *P53* R249S mutation (which is characteristic of aflatoxin B1 exposure) in the CCHC, and found no participants with the mutation[23]. These data call into question the assertion by Ramirez et al. that aflatoxin is an important etiology of disease in south Texas[24].

There are few population-based studies (none in the Americas) with which to compare our prevalence estimates. Two population-based studies using TE in European populations found prevalence of significant fibrosis equal to 5.6% and 9.0%.[11,25] Another group applied TE in a randomly selected Hong Kong Chinese population and found a 3.7% prevalence of significant fibrosis.[12] Many others have applied TE to selected clinical populations whose estimates are not generalizable to general populations. Despite the limited studies employing pSWE or TE in a population-based context, our results suggest that the burden of significant liver fibrosis is substantially greater in Mexican American Hispanic groups than in Europe or Asia.

Clinical characteristics of participants with steatosis only and those with significant fibrosis did not differ appreciably, highlighting the importance of imaging for liver disease risk stratification. Surprisingly, the younger age groups had a greater prevalence of significant fibrosis (Figure 2), possibly reflecting a cohort effect related to US nativity[26], which is associated with younger age in the CCHC (data not shown). This finding echoes previous studies in the CCHC which emphasized the need for chronic disease intervention in younger Mexican Americans, particularly men.[27,28] Indeed, the overall prevalence of fibrosis was higher in men (17.3%) than women (10.6%) in this study.

This study has several limitations. First, unlike clinical studies, this community-recruited study does not perform liver biopsy. This prevents an independent validation of pSWE against biopsy in this population. However, a recent meta-analysis showed that pSWE had

the greatest area under receiver operating characteristic curve for F2+ fibrosis compared to TE and biomarker measures, so misclassification is likely to be minor and nondifferential with respect to most clinical measures. Finally, our ultrasound measurement of liver steatosis may have limited sensitivity for the detection of steatosis < 30% of the liver, leading to an under-estimate of the prevalence of steatosis, particularly in the presence of fibrosis.[29]

In conclusion, hepatic fibrosis is a crucial phenotype for HCC risk stratification in Mexican American populations in the US. Published data show that liver fibrosis, regardless of NAFLD activity score or degree of steatohepatitis, is a primary predictor of liver-related mortality;[30,31] therefore, the detection of and intervention on liver fibrosis in this population has the potential to reduce morbidity and mortality of both cirrhosis and HCC. Overall, our results urge increased community health efforts to stem the burden of NAFLD among Mexican Americans, particularly in younger groups. Elastography—whether pSWE or TE—is an affordable, rapid, and practical screening modality for early liver disease in the general population, and has broad potential for detection and prevention of advanced liver disease in health disparity groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

ALT	alanine aminotransferase
ARFI	acoustic radiation force impulse elastography
AST	aspartate aminotransferase
AUROC	area under receiver operator curve
CCHC	Cameron County Hispanic Cohort
TE	transient elastography
NAFLD	non-alcoholic fatty liver disease

OR odds ratio

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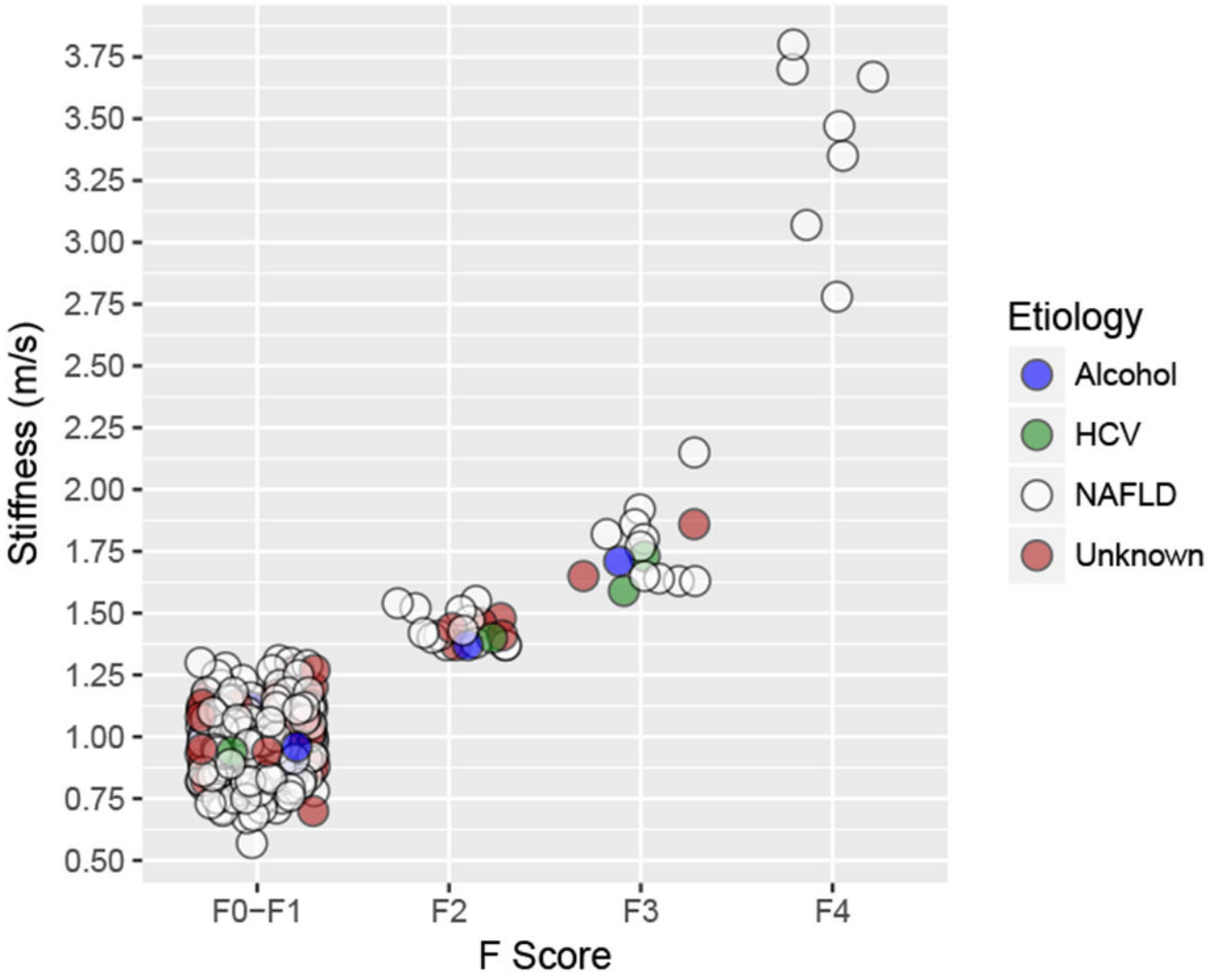

Figure 1. Liver stiffness measurements by point shear-wave elastography with etiologies, Cameron County Hispanic Cohort (2015-2017)

Disease etiology is represented by fill color. Most (78%) of participants with F2-F4 disease had non-viral, non-alcoholic etiologies.

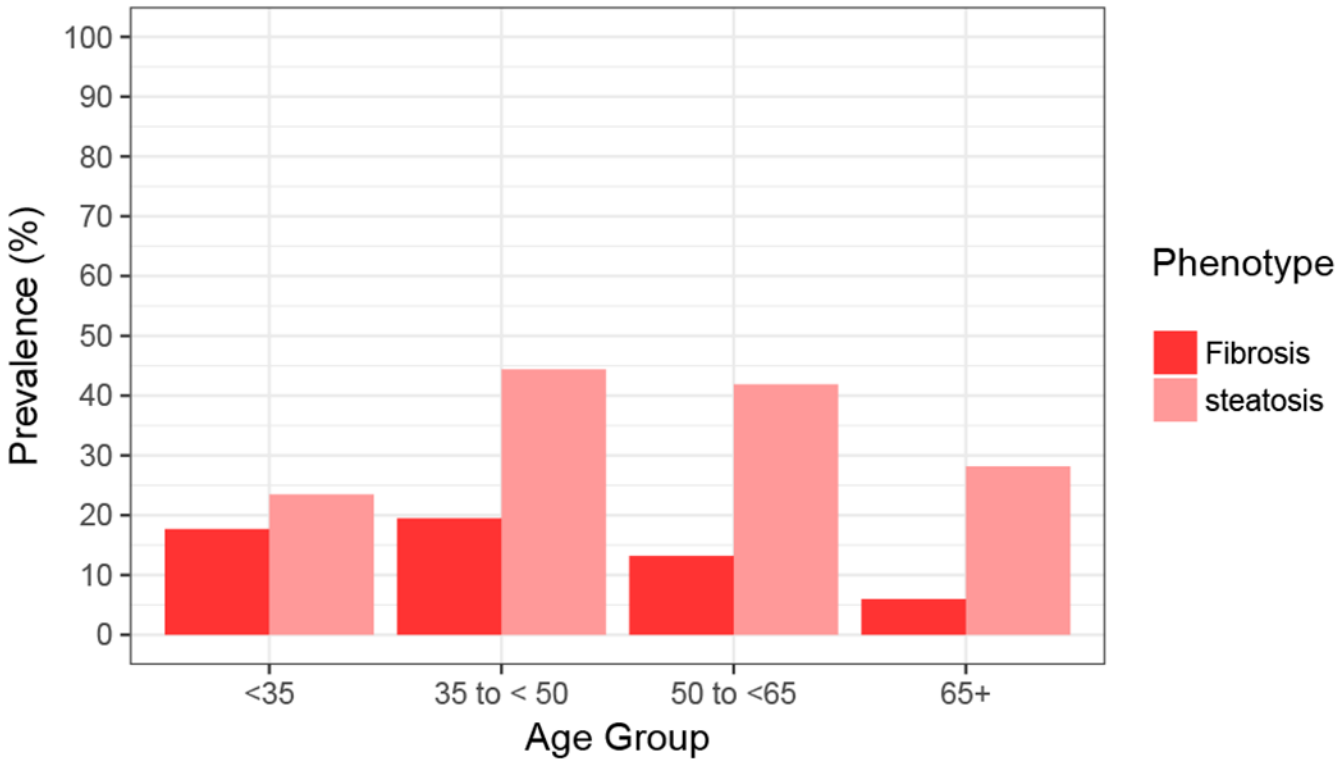

Figure 2. Prevalence of steatosis (without significant fibrosis) and significant fibrosis (with or without steatosis), Cameron County Hispanic Cohort (2015-2017)

The prevalence of significant fibrosis (F2 – F4) was greatest in the younger two age groups. The presence of fibrosis and steatosis in young Mexican Americans highlights the need for effective community health interventions for younger individuals in the region.

Table 1.

Descriptive statistics of the analytic data set, Cameron County Hispanic Cohort

Variable	Count	%
Age Group		
<35	47	16.8
35 to <50	85	26.1
50 to < 65	134	28.9
65 +	99	28.2
Male Sex	131	43.9
No Insurance	191	51.4
No Insurance (< 65 yrs) [n = 265]	174	67.9
Place of Birth [n = 357]		
United States	102	27.6
Mexico	255	72.4
Receives Public Assistance [n = 362]	84	19.6
Diabetes[a]		
No	251	71.4
Yes, Diagnosed	78	20.2
Yes, Undiagnosed	27	8.4
Hypertension[b]	160	41.9
Body Mass Index (BMI) Categories		
Normal Weight (BMI < 25)	63	16.1
Overweight (25 ≤ BMI < 30)	134	42.2
Obese (30 ≤ BMI < 40)	157	39.3
Morbidly Obese (BMI ≥ 40)	10	2.5
Elevated waist circumference[c]	246	65.0
Anti-HCV Positive	9	1.8
HBsAg Positive	0	0
Heavy Drinking[d]	8	3.5

Abbreviations. HCV, hepatitis C Virus. HBsAg, Hepatitis B Surface Antigen.

[a]Diabetes status is determined according to the American Diabetes Association 2010 diagnostic guidelines.

[b]Hypertension is defined as systolic blood pressure > 135 mmHg or diastolic blood pressure > 85 mmHg or taking antihypertensive medication

[c]Defined as waist circumference > 102 cm for men, and > 88 cm for women

[d]Defined as self-reported drinks > 21 for men and > 14 for women

Table 2.

Characteristics of participants with normal liver, steatosis, and F2 fibrosis, Cameron County Hispanic Cohort

Parameters	Healthy[a] Estimate[b] (95% CI)	Steatosis Estimate (95% CI)	Fibrosis Estimate (95% CI)	*p*-value
Age (years)	51.8 (48.0 - 55.6)	52.5 (48.5 - 56.5)	45.1 (38.9 - 51.4)	0.1245
Male Sex	42.2 (33.4 - 51.0)	39.5 (28.0 - 51.0)	55.9 (39.6 - 72.3)	0.2908
No Insurance (< 65 years)	57.5 (46.8 - 68.3)	61.8 (49.9 - 73.7)	68.6 (49.1 - 88.2)	0.5859
Born in US	28.5 (20.3 - 36.7)	22.9 (14.4 - 31.3)	35.2 (15.5 - 55.0)	0.4247
Family History of Diabetes	29.1 (20.5 - 37.7)	33.7 (22.7 - 44.7)	21.6 (6.6 - 36.6)	0.4243
Diabetes[c]	23.2 (13.7 - 32.7)	36.6 (26.8 - 46.5)	27.5 (12.0 - 42.9)	0.1581
Fasting Glucose (mg/dL)	104.0 (97.4 - 110.6)	124.8 (107.8 - 141.7)	111.9 (87.9 - 135.8)	0.0839
Hemoglobin A1C (%)	6.1 (5.8 - 6.5)	6.7 (6.2 - 7.2)	6.4 (5.7 - 7.2)	0.1951
Insulin	9.4 (8.3 - 10.5)	14.7 (12.6 - 16.9)	10.5 (7.6 - 13.4)	0.0001*
HOMA-IR	2.4 (2.1 - 2.7)	4.4 (3.5 - 5.3)	2.8 (1.8 - 3.8)	0.0003*
Hypertension[d]	40.2 (30.1 - 50.2)	43.0 (27.6 - 58.4)	40.1 (20.1 - 60.1)	0.9465
Systolic BP (mmHg)[e]	117.9 (114.4 - 121.3)	120.2 (116.5 - 123.8)	116.5 (108.0 - 125.1)	0.5526
Diastolic BP (mmHg)	70.5 (68.8 - 72.3)	73.1 (71.2 - 75.0)	71.2 (66.6 - 75.9)	0.0931
Triglycerides (mg/dL)	127.7 (116.4 - 139.0)	161.9 (148.3 - 175.6)	134.2 (94.5 - 173.9)	0.0009*
Total Cholesterol (mg/dL)	178.5 (170.0 - 187.0)	180.6 (173.5 - 187.8)	172.4 (155.5 - 189.4)	0.6737
LDL Cholesterol (mg/dL)	107.3 (101.2 - 113.3)	104.5 (97.9 - 111.1)	97.4 (87.2 - 107.7)	0.2879
HDL Cholesterol, mean (mg/dL)	47.7 (45.7 - 49.8)	41.9 (40.1 - 43.6)	46.1 (42.1 - 50.2)	<0.0001*
AST (units/L)	21.3 (19.6 - 23.0)	27.7 (22.0 - 33.5)	34.2 (19.5 - 48.9)	0.0313
ALT (units/L)	29.3 (26.2 - 30.3)	44.5 (32.4 - 56.6)	39.5 (28.7 - 50.4)	0.0053*
AST/ALT Ratio	0.77 (0.73 - 0.82)	0.72 (0.61 - 0.83)	0.83 (0.74 - 0.92)	0.2464
Obese (BMI ≥ 30)	29.5 (21.4 - 37.5)	56.2 .0(45 - 67.3)	39.1 (22.9 - 55.3)	0.0006*
BMI (kg/m^2)	28.6 (27.9 - 29.4)	31.5 (30.7 - 32.4)	28.1 (26.2 - 29.9)	<0.0001*
Elevated waist circumference[f]	57.2 (47.8 - 66.5)	77.0 (65.8 - 88.2)	58.5 (40.6 - 76.4)	0.0234
Waist Circumference (cm)	97.9 (95.5 - 100.3)	104.8 (102.6 - 106.9)	98.7 (93.9 - 103.5)	<0.0001*
Platelet count ($10^3/\mu L$)	236 (224 - 248)	241.4 (228.3 - 254.4)	219.2 (200.5 - 238.0)	0.1374
Albumin (mg/dL)	3.9 (3.8 - 4.0)	4.9 (3.9 - 4.0)	3.9 (3.8 - 4.0)	0.5477
Total Bilirubin (mg/dL)	2.2 (0.0 - 5.2)	0.7 (0.4 - 1.0)	0.7 (0.4 - 1.0)	0.5936
Anti-HCV Positive	0.3 (0.0 - 1.0)	2.6 (0.0 - 5.3)	5.7 (0.0 - 12.5)	0.0157
HBsAg Positive	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	N/A
Drinks per week	1.8 (0.7 - 2.9)	2.1 (0.8 - 3.4)	5.4 (1.8 - 8.9)	0.1737
Heavy Drinking[g]	2.5 (0.0 - 6.9)	1.8 (0.0 - 4.5)	12.4 (0.0 - 27.1)	0.0639

Abbreviations: CI, confidence interval; HOMA-IR, homeostatis model of insulin resistance; LDL, low-density lipoprotein; HDL, high-density lipoprotein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BMI, Body Mass Index; Anti-HCV, hepatitis C Virus antibody; HBsAg, Hepatitis B Surface Antigen.

Note. Statistical tests significant at the 5% level after correction for false discovery rate are marked with an asterisk.

[a]Healthy indicates no evidence of steatosis and liver stiffness ≤ 1.34; steatosis indicates evidence of steatosis and liver stiffness ≤ 1.34 m/s; fibrosis indicates liver stiffness > 1.34 m/s with or without steatosis

[b] For continuous variables, mean; for categorical variables, proportion. *P*-values calculated from ANOVA for continuous variables and from Rao-Scott χ^2 test for categorical variables

[c] According to American Diabetes Association 2010 Diagnostic Guidelines

[d] Systolic Blood Pressure > 135 or Diastolic Blood Pressure > 85 or taking antihypertensive medication.

[e] Blood pressure analyses are adjusted for self-reported use of antihypertensive medication

[f] Defined as waist circumference > 102 for men and > 88 for women

[g] Defined as self-reported consumption of >21 drinks per week for men, and >14 drinks per week for women.

Table 3.

Unadjusted association of sociodemographic and clinical parameters with healthy liver, steatosis, and liver fibrosis, Cameron County Hispanic Cohort

	Steatosis *vs* Healthy[a]		Fibrosis *vs* Healthy		Fibrosis *vs* Steatosis	
Variable	**OR (95% CI)[b]**	***p*-value**	**OR (95% CI)**	***p*-value**	**OR (95% CI)**	***p*-value**
Age (years)	1.0 (0.8 - 1.3)	0.7975	0.8 (0.6 - 1.0)	0.0671	0.8 (0.6 - 1.0)	0.0475
Male Sex	0.9 (0.5 - 1.7)	0.7313	1.7 (0.8 - 3.7)	0.1473	1.9 (0.8 - 4.6)	0.1259
Diabetes[c]	1.9 (1 - 3.8)	0.0654	1.3 (0.5 - 3.2)	0.6361	0.7 (0.3 - 1.6)	0.3371
Fasting Glucose (per 10 mg/dL)	1.1 (1.0 - 1.2)	0.0156	1.1 (0.9 - 1.2)	0.4311	1.0 (0.8 - 1.1)	0.4818
Hemoglobin A1c (%)	1.2 (0.9 - 1.5)	0.3242	1.1 (0.9 - 1.5)	0.4220	1.0 (0.8 - 1.2)	0.7178
Insulin (10 mg/dL)	2.8 (1.6 - 4.7)	0.0002*	1.4 (0.7 - 2.6)	0.3294	0.5 (0.2 - 1.1)	0.0832
HOMA-IR	1.4 (1.2 - 1.7)	<0.0001*	1.1 (0.9 - 1.4)	0.3072	0.8 (0.6 - 1.1)	0.1047
Diastolic BP (mmHg)[d]	1.4 (1.0 - 2.0)	0.0375	1.1 (0.6 - 2.0)	0.7770	0.8 (0.4 - 1.5)	0.4540
Hypertension[e]	1.1 (0.5 - 2.4)	0.7585	1.0 (0.4 - 2.6)	0.9979	0.9 (0.3 - 2.5)	0.8260
Triglycerides (per 50 mg/dL)	1.4 (1.1 - 1.8)	0.0033*	1.1 (0.6 - 1.9)	0.7381	0.8 (0.4 - 1.4)	0.3992
HDL Cholesterol (mg/dL)	0.6 (0.4 - 0.8)	0.0003*	0.9 (0.6 - 1.3)	0.5098	1.5 (1.0 - 2.3)	0.0421
AST (per 10 units/L)	1.4 (1.1 - 1.9)	0.0176	1.5 (1.1 - 2.0)	0.0080	1.1 (1.0 - 1.1)	0.2640
ALT (per 10 units/L)	1.5 (1.2 - 1.8)	0.0005*	1.4 (1.2 - 1.8)	0.0014*	1.0 (0.9 - 1.1)	0.5715
AST/ALT Ratio	0.5 (0.1 - 3.5)	0.4546	1.9 (0.7 - 5.6)	0.2227	4.2 (0.5 - 38.4)	0.2016
Obese[f]	3.0 (1.7 - 5.5)	0.0001*	1.5 (0.7 - 3.4)	0.2828	0.5 (0.2 - 1.2)	0.1039
Waist Circumference (per 10 cm)	1.0 (1.0 - 1.0)	0.0002*	1.0 (1.0 - 1.0)	0.7556	0.7 (0.5 - 1.0)	0.0408
Platelets (per $50\times10^3/\mu L$)	1.1 (0.8 - 1.4)	0.5600	0.8 (0.6 - 1.1)	0.1680	0.7 (0.4 - 1.0)	0.0649
Anti-HCV	8.4 (0.9 - 79.4)	0.0646	18.9 (1.8 - 196.4)	0.0138	2.3 (0.4 - 11.7)	0.3285
Drinks per week	1.0 (0.9 - 1.1)	0.7294	1.1 (1.0 - 1.2)	0.0358	1.1 (1.0 - 1.1)	0.0505
Heavy Drinking[g]	0.7 (0.1 - 7.6)	0.7913	5.5 (0.6 - 52.3)	0.1368	7.6 (1.0 - 56.8)	0.0493

Abbreviations: OR, Odds Ratio; CI, confidence interval; HOMA-IR, homeostasis model of insulin resistance ; BP, blood pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; NAFLD, non-alcoholic fatty liver disease;

Note. Statistical tests significant at the 5% level after correction for false discovery rate are indicated with an asterisk.

[a] Healthy indicates no evidence of steatosis and liver stiffness ≤ 1.34; steatosis indicates evidence of steatosis and liver stiffness ≤ 1.34 m/s; fibrosis indicates liver stiffness > 1.34 m/s

[b] OR, 95% CI and *P*-value obtained from survey-based multinomial logistic regression

[c] According to American Diabetes 2010 Diagnostic Guidelines

[d] Blood pressure analyses are adjusted for self-reported use of antihypertensive medication

[e] Systolic Blood Pressure > 135 or Diastolic Blood Pressure > 85 or taking antihypertensive medication

[f] BMI ≥ 30

[g] For men, greater than 21 self-reported drinks per week; for women, greater than 14 drinks per week.