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Hepatitis C virus in Mexican Americans: a population-based study reveals relatively high prevalence and negative association with diabetes

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SUMMARY

This study aimed to estimate the prevalence and risk factors for hepatitis C virus (HCV) infection in Mexican Americans living in South Texas. We tested plasma for the presence of HCV antibody from the Cameron County Hispanic Cohort (CCHC), a randomized, population-based cohort in an economically disadvantaged Mexican American community on the United States/Mexico border with high rates of chronic disease. A weighted prevalence of HCV antibody of 2·3% [$n = 1131$, 95% confidence interval (CI) 1·2–3·4] was found. Participants with diabetes had low rates of HCV antibody (0·4%, 95% CI 0·0–0·9) and logistic regression revealed a statistically significant negative association between HCV and diabetes (OR 0·20, 95% CI 0·05–0·77) after adjusting for sociodemographic and clinical factors. This conflicts with reported positive associations of diabetes and HCV infection. No classic risk factors were identified, but important differences between genders emerged in analysis. This population-based study of HCV in Mexican Americans suggests that national studies do not adequately describe the epidemiology of HCV in this border community and that unique risk factors may be involved.

Key words: Hepatitis C virus, infectious disease epidemiology, Mexican American, prevalence of disease, public health.

INTRODUCTION

Hepatitis C virus (HCV) is one of the main causes of chronic viral hepatitis [1]. Worldwide, the estimated prevalence of HCV is 2·2%, or about 130 million people [2]. In the United States, the prevalence has been decreasing since 1992, from 2·4% to ~1·6%, where it has remained relatively stable since 2006 [3, 4]. While the acute phase of HCV infection is not typically life-threatening, complications associated with chronic HCV – fibrosis, cirrhosis, and hepatocellular carcinoma – carry a poor prognosis and represent a significant societal and financial burden [5–7].

Despite the identification of HCV over 25 years ago, data on HCV epidemiology in minority groups are sparse [8]. It has been established, largely through the National Health and Nutrition Examination

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Survey (NHANES) that racial and ethnic disparities in HCV epidemiology exist, but little is known about prevalence in communities with the greatest health disparities, particularly those along the United States/Mexico border. Currently, passive surveillance of HCV infection is inadequate to estimate prevalence [9], so randomized population-based seroprevalence studies are a practical way to estimate the prevalence of HCV in particular communities in the United States .

To our knowledge, there are two data sources that have stratified HCV epidemiology in US Hispanics by ethnic subgroup. Kuniholm and co-workers used NHANES data to conduct stratified analysis of HCV epidemiology, comparing Mexican Americans to 'other Hispanic'. These data suggest that Mexican American Hispanics may have a decreased risk of HCV compared with non-Mexican Hispanics [8]. These data were supplemented using the Hispanic Community Health Study/Study of Latinos (HCHS/SOL), which recruited urban Hispanic/Latino participants from the Bronx, Miami, Chicago, and San Diego to participate in HCV research [8]. They found that Hispanics constitute a strikingly heterogeneous group in HCV epidemiology, with anti-HCV prevalence in Mexican Americans [1·9%, 95% confidence interval (CI) 1·1–3·4] falling between the low prevalence seen in South American Hispanics (0·4%, 95% CI 0·1–1·9) and the high prevalence seen in Puerto Rican Hispanics (11·6%, 95% CI 9·4–14·1) [8]. However, we have previously shown that national studies such as HCHS/SOL tend to underestimate the burden of disease in Mexican Americans in Cameron County, Texas [10, 11], and we sought to validate national Mexican American HCV prevalence studies in a discrete, homogenous population of Mexican Americans with high rates of obesity, diabetes, and other chronic disease [12]. Further, since we have previously observed high rates of cirrhosis with no known aetiology in Cameron County [11], it is urgent to fully characterize the unique risk factors and causes of chronic liver disease in this Mexican American community on the United States–Mexico border.

METHODS

This study aimed to estimate the prevalence of, and determine the risk factors for, HCV in Mexican Americans in Cameron County, Texas, using data from a population-based cohort study, the Cameron County Hispanic Cohort (CCHC, $n = 3300$). This is a 'Framingham-like' cohort of a Mexican American community, recruited from households, active since 2004 [13]. Households are stratified by socioeconomic strata and randomly selected by census tract/block; all occupants aged $\geqslant 18$ years are invited to participate. Participants then visit our Clinical Research Unit, where extensive sociodemographic, clinical, and laboratory data are collected, and are followed-up at 5-year intervals [12]. In the present work, we designed a cross-sectional study of baseline data, accessing archived plasma samples from the CCHC. Plasma samples were selected sequentially, beginning with the first participant in the CCHC, thus preserving the two-stage sampling design.

We tested 1331 samples for the presence of hepatitis C Antibody (anti-HCV) using the ORTHO® HCV version 3.0 test system (Ortho-Clinical Diagnostics, USA). Plates were read in a Spectramax M5 spectrophotometer (Molecular Devices, USA) at a wavelength of 490 nm with a reference wavelength of 620 nm. Reactive and non-reactive results were determined according to the manufacturer's specifications. Results were then merged with the existing CCHC database for analysis.

Ethical standards

The study was approved by the Committee for the Protection of Human Subjects of the University of Texas Health Science Center at Houston as HSC-SPH-03-007-B.

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Definitions

Any participant with a positive HCV antibody assay was considered to be in the HCV group. In analysing diabetes mellitus (DM) results, 'diabetes status' was categorized into three groups in accordance with the American Diabetes Association's 2010 diagnostic criteria: normal, impaired fasting glucose (hereafter 'prediabetes') and diabetic (hereafter, 'DM') [14]. We considered participants to have a history of smoking if they had smoked more than 100 cigarettes in their life, and considered 'alcohol consumption' to be any participant that drinks at least occasionally (compared to not at all). Finally, when discussing liver function

tests (LFTs), we refer only to alanine transaminase (ALT) and aspartate aminotransferase (AST) levels.

Statistical methods

We conducted design-based analyses using age- and gender-adjusted sampling weights to scale the sample to the population and also accounted for the potential clustering effect in participants from the same household. For descriptive purposes of the sample, categorical variables for demographic and clinical characteristics were summarized in unweighted frequencies and weighted percentages, and continuous variables for demographic and clinical characteristics were summarized using weighted means and their standard errors. Of participants with HCV, we counted the number who reported taking any of the commonly prescribed anti-HCV medications in the United States and Mexico (peginterferon, ribavirin, and protease inhibitors, or any of their marketed names – including generics – in English and Spanish). Design-adjusted, weighted prevalence of HCV was calculated and analyses were conducted for various risk factors (1) in the entire sample and (2) in the sample stratified by gender. The Rao-Scott design-adjusted χ^2 test was used to test for equality of proportions across the risk factors groups. Odds ratios (ORs) with 95% Wald confidence limits were reported for dichotomous categorical variables, and P values were reported for non-dichotomous categorical variables. Univariable survey-weighted logistic regression analyses were performed to assess the effects of continuous variables on presence of HCV antibody.

Multivariable survey-weighted logistic regression analyses were performed to assess the independent effects of risk factors on HCV antibody detection, selected from the univariable analysis with moderate ($P < 0{\cdot}10$) association, in addition to demographic variables classically associated with HCV infection: age, gender, socioeconomic indicators, and smoking and drinking history. Harmful multicollinearity effects between the independent variables of interest in the survey-weighted logistic regression multivariable model were not observed (variance inflation factor < 1·5). Two-way multiplicative scale interaction effect between the independent variables were tested by including their product terms in the regression model and evaluating the Wald χ^2 test statistics of their coefficient estimates. A two-sided test with $P < 0{\cdot}05$ was considered significant for all analyses. The survey-weighted logistic regression model fit was evaluated with F-adjusted mean residual goodness-of-fit test using Stata v. 13 software (StataCorp LP, USA). All other weighted analyses were conducted using SAS v. 9·4 (SAS Institute Inc., USA).

RESULTS

We tested a sample of the CCHC consisting of 1331 subjects for the presence of anti-HCV. Their average age was 48·7 years, and 40·7% were male. The sample did not differ significantly in age or gender from the cohort from which it was sampled. The majority (61·2%) were born in Mexico, 50·6% were overweight or obese, 26·3% had diabetes, and 31·2% had abnormal LFTs (Table 1). Nearly half (46·8%) of those with diabetes had not been previously diagnosed (data not shown).

Thirty out of 1331 participants' plasma tested positive for anti-HCV. This generated a weighted prevalence of 2·3% (95% CI 1·2–3·4).

A range of sociodemographic variables were tested for univariable association with HCV. Variables for gender, age, income, education level, nativity, and socioeconomic status had no significant association with HCV. Similarly, proxies for risky behaviour (smoking history and alcohol consumption) did not yield significant associations.

In univariable analyses of clinical and biological variables, there was a significant association between the three categories of diabetes status (normal, pre-diabetes, DM) and HCV ($P < 0{\cdot}005$). The HCV rate was 0·4% (95% CI 0·0–0·9) in participants with DM, 4·0% (95% CI 1·6–6·6) in participants with pre-diabetes, and 1·1% (95% CI 0·02–2·2) in normal participants. Elevated ALT and AST levels were significantly associated with HCV (OR 1·02, 95% CI 1·00–1·03; OR 1·03, 95% CI 1·01–1·05, respectively) (Table 2). None of the participants with HCV reported taking any anti-HCV medication, and only 4/30 (12·2%, 95% CI 5·3–18·1) participants with HCV reported any history of viral hepatitis.

In gender-stratified univariable analysis, increased age was associated with HCV in females (OR 1·04, 95% 1·01–1·06), but not in males. The average age of women with HCV was significantly higher than the average age of men with HCV (57·4 *vs.* 44·5, $P < 0{\cdot}005$). Further, there was a significant association between diabetes classification and HCV in females ($P < 0{\cdot}005$), with an HCV prevalence of 0·6% (95% CI 0–1·3) in participants with DM, 4·4% (95% CI 1·5–7·3) in participants with pre-diabetes, and 1·1%

Table 1. *Descriptive statistics for selected categorical and continuous variables, Cameron County Hispanic Cohort (2004–2012)*

Characteristic	Sample ($n = 1331$)
Sex, n[a] (%)[b]	
Women	938 (59·3)
Men	393 (40·7)
Place of birth, n (%)	
Mexico	908 (61·2)
United States	407 (37·1)
Other	16 (1·7)
Health insurance[c], n (%)	
Yes	401 (36·2)
No	929 (63·8)
Obese[d], n (%)	
No	651 (49·4)
Yes	680 (50·6)
Diabetes[e], n (%)	
No	540 (39·6)
Pre-diabetes	435 (34·1)
Yes	356 (26·3)
Abnormal LFT[f]	
No	983 (68·8)
Yes	348 (31·2)
Age, mean[g] (S.E.)	48·7 (0·8)
Household income, US$, mean[g] (S.E.)	21 433 (1462·4)
Years pre-college education, mean[g] (S.E.)	7·4 (0·3)

LFT, Liver function test; S.E., standard error.
[a] All frequencies reflect unweighted data.
[b] All percentages reflect weighted data.
[c] Includes any type of public or private health coverage.
[d] Defined as body mass index $\geqslant 30$.
[e] According to the 2010 diagnostic criteria of the American Diabetes Association.
[f] Defined as abnormal alanine transaminase or abnormal aspartate aminotransferase levels.
[g] Weighted mean.

(95% CI 0·02–2·2) in normal participants. The association was not significant in males ($P = 0·1765$). A history of smoking was significantly associated with HCV in males (OR 5·3, 95% CI 1·1–25·1), but not in females. Alcohol consumption in males had a significant *positive* association with HCV (OR 15·2, 95% CI 1·8–130·5), and a significant *negative* association with HCV in females (OR 0·2, 95% CI 0·1–0·7). Finally, ALT and AST levels were associated with HCV in females (OR 1·03, 95% CI 1·01–1·05; OR 1·05, 95% CI 1·02–1·07, respectively), but not in males (Table 3).

In the regression analysis, DM (compared to 'normal') was independently negatively associated with HCV (OR 0·20, 95% CI 0·05–0·77) after controlling for age, gender, socioeconomic quartile, employment status, obesity, ALT and AST levels, and smoking and drinking history. Pre-diabetes was not significantly associated with HCV (compared to 'normal'). No other significant effects emerged in the model, and no interaction effects were found to contribute significantly to the fit of the model (Table 4). As an alternative analysis, we ran the same regression, but used DM as the reference value instead of 'normal'. Here, pre-diabetes (compared to DM) was significantly positively associated with HCV (OR 8·93, 95% CI 2·48–32·15), as was 'normal' (compared to DM) (OR 5·30, 95% CI 1·30–21·54) (data not shown).

DISCUSSION

The Centers for Disease Control and Prevention (CDC) estimated that there were 16 000 new cases of HCV in the United States in 2009 [15], most of which will go undiagnosed and many of which will progress to chronic infection. Klevens and co-workers consider injection drug users to be the 'center of the current hepatitis C epidemic' [4]. There are few data on injection drug use in the United States/Mexico border region, although one population-based study showed that the lifetime prevalence of injection drug use is low (1·0%) in Cameron County [16].

The prevalence of HCV in this population (2·3%) is similar to the national population-based rate found in Mexican Americans in NHANES (2·1%) and HCHC/SOL (1·9%) [8]. However, this community differs from previous studies of HCV in Mexican Americans. First, the region is dominated by the Brownsville metropolitan area (population 400 000, 85% Mexican American), a network of small cities and towns on the United States–Mexico border, considered among the poorest in the United States [17–19]. As such, this is not a scattered urban population sample like that in HCHC/SOL, but rather a single non-urban population. It is also tightly integrated with Matamoros, Tamaulipas, Mexico, so it was important to consider the prevalence of HCV in northern Mexico. It is thought that the nationwide prevalence of HCV in Mexico is lower (1·0–1·4) than in the United States [20, 21], but that the northern Mexican states have a slightly higher rate at 1·7% [22]. It therefore appears that the rate of HCV in Cameron County is slightly higher than the rate in northern Mexico, and similar to that of Mexican Americans in the United States.

We have previously quantified poor health outcomes and high rates of undiagnosed chronic disease

Table 2. *Weighted univariable analysis of HCV by categorical and continuous variables, Cameron County Hispanic Cohort (2004–2012)*

Variable	Level	HCV/total (%)[a]	OR (95% CI)
Gender	Female	18/938 (1·7)	Reference
	Male	12/393 (2·8)	1·4 (0·6–3·6)
Marital status	Unmarried	15/533 (2·6)	Reference
	Married	15/794 (2·1)	0·8 (0·3–2·0)
Socioeconomic status	Lower 50%	16/580 (2·9)	Reference
	Upper 50%	14/751 (1·8)	0·6 (0·2–1·7)
Obese	No (BMI <30)	16/651 (2·7)	Reference
	Yes (BMI ⩾30)	14/680 (1·9)	0·7 (0·3–1·7)
School	⩽8 years	12/520 (2·2)	Reference
	>8 years	18/809 (2·4)	1·1 (0·5–2·6)
Finished high school	No	20/755 (2·4)	Reference
	Yes	10/574 (2·2)	0·9 (0·3–2·5)
Majority school years	Mexico	22/837 (2·7)	Reference
	USA	8/438 (2·0)	0·7 (0·2–2·3)
Diabetes[b]	Normal	11/540 (2·0)	$P = 0·0030$
	Pre-diabetes	15/435 (4·0)	
	Diabetic	4/356 (0·4)	
Insured[c]	Yes	8/401 (2·9)	Reference
	No	22/929 (2·0)	0·7 (0·3–1·8)
Employment status	Employed	17/640 (2·8)	Reference
	Not employed	13/691 (1·8)	0·6 (0·2–1·6)
History of smoking[d]	No	20/963 (1·8)	Reference
	Yes	10/368 (3·5)	2·0 (0·8–5·2)
Alcohol consumption	No	16/705 (2·1)	Reference
	Yes	14/626 (2·4)	1·1 (0·4–2·6)
Age (years)[e]		48·7 (0·8)	1·0 (0·99–1·03)
Years in Cameron County[e]		24·6 (1·0)	0·99 (0·98–1·01)
Years of pre-college education[e]		7·4 (0·3)	1·04 (0·93–1·15)
ALT[f] (U/l)[e]		40·9 (1·0)	1·02 (1·00–1·03)*
AST[f] (U/l)[e]		35·1 (0·9)	1·03 (1·01–1·05)*

OR, Odds ratio; CI, confidence interval; BMI, body mass index; ALT, alanine transaminase; AST, aspartate aminotransferase; S.E., standard error.

[a] All percentages weighted.

[b] According to the 2010 diagnostic criteria of the American Diabetes Association.

[c] Includes any type of public or private health coverage.

[d] Defined as ever having smoked more than 100 cigarettes.

[e] Continuous variable: mean (S.E.) and OR (95% Wald CI) estimates are given.

* Statistically significant with $P < 0·05$.

in Cameron County. For instance, the prevalence of DM is 30·7% (49·7% undiagnosed), hypercholesterolaemia, 48·2% (48·7% undiagnosed) and hypertension, 30·5% (16% undiagnosed) [12]. In the present study, at least 87·8% of those with HCV had no known history of viral hepatitis. For comparison, current national estimates suggest that between 50% and 75% of those infected with HCV are unaware of their infection [23]. This suggests that HCV may be more often undiagnosed, and therefore untreated, in Cameron County than in the rest of the country. This is not surprising, considering 65·1% of the CCHC has no insurance of any kind, and the rates of undiagnosed chronic disease are high [10–12].

It is surprising that certain risk factors seen in previous HCV studies did not emerge in this work. We hypothesized that the risk factors seen in HCHS/SOL (male gender and US nativity, for instance) would present in our data, but there were no significant associations with these variables. In gender-stratified analysis, there were several associations – marital status, age, ALT levels, and AST levels – that emerged only in females. This is partially attributable to the low unweighted sample size of males ($n = 393$),

Table 3. *Weighted univariable analysis of HCV by categorical and continuous variables, stratified by gender, Cameron County Hispanic Cohort (2004–2012)*

		Males		Females	
Variable	Level	HCV/total (%)[a]	OR (95% CI)	HCV/total (%)	OR (95% CI)
Marital status	Unmarried	2/124 (1·2)	Reference	13/409 (3·2)	Reference
	Married	10/268 (3·3)	2·8 (0·4–18·6)	5/526 (1·0)	0·3 (0·1–0·9)*
SES	Lower 50%	6/181 (3·4)	Reference	10/399 (2·6)	Reference
	Upper 50%	6/212 (2·3)	0·7 (0·1–3·2)	8/539 (1·4)	0·5 (0·2–1·6)
Obese	No (BMI < 30)	8/213 (4·1)	Reference	8/438 (1·6)	Reference
	Yes (BMI ⩾ 30)	4/180 (1·4)	0·3 (0·1–1·6)	10/500 (2·3)	1·4 (0·5–4·3)
School	⩽8 years	5/126 (3·3)	Reference	7/394 (1·7)	Reference
	>8 years	7/266 (2·6)	0·8 (0·2–3·8)	11/543 (2·1)	1·3 (0·4–3·9)
Finished high school	No	8/187 (3·6)	Reference	12/568 (1·9)	Reference
	Yes	4/205 (2·3)	0·7 (0·1–3·1)	6/369 (2·1)	1·1 (0·4–3·4)
Majority school years	Mexico	8/218 (2·9)	Reference	14/619 (2·5)	Reference
	USA	4/161 (2·8)	1·0 (0·2–4·6)	4/277 (1·2)	0·5 (1·2–1·8)
Diabetes[b]	Normal	6/149 (3·9)	$P = 0·1765$	5/391 (1·1)	$P = 0·0009$
	Pre-diabetes	5/136 (3·7)		10/299 (4·4)	
	Diabetes	1/108 (0·3)		3/248 (0·6)	
Insured[c]	Yes	3/158 (3·0)	Reference	5/243 (2·7)	Reference
	No	9/235 (2·6)	0·9 (0·2–4·5)	13/694 (1·6)	0·6 (0·2–1·8)
Employment status	Employed	9/257 (3·3)	Reference	8/383 (2·2)	Reference
	Not employed	3/136 (1·6)	0·5 (0·1–2·8)	10/555 (1·8)	0·8 (0·3–2·4)
History of Smoking[d]	No	4/188 (0·9)	Reference	16/753 (2·1)	Reference
	Yes	8/205 (4·6)	5·3 (1·1–25·1)*	2/163 (1·2)	0·6 (0·1–2·8)
Alcohol consumption	No	1/84 (0·3)	Reference	15/607 (2·3)	Reference
	Yes	11/309 (3·7)	15·2 (1·8–130·5)*	3/331 (0·5)	0·2 (0·1–0·7)*
Age (years)[e]		48·9 (1·5)	0·98 (0·95–1·01)	48·5 (0·8)	1·04 (1·01–1·06)*
Years in Cameron County[e]		26·5 (1·6)	0·99 (0·96–1·01)	23·3 (1·0)	1·00 (0·98–1·02)
Pre-college education (years)[e]		7·9 (0·6)	1·02 (0·91–1·15)	7·1 (0·2)	1·05 (0·88–1·24)
ALT (U/l)[e]		47·0 (2·2)	1·01 (0·99–1·02)	36·7 (0·6)	1·03 (0·01–1·05)*
AST (U/l)[e]		38·4 (1·8)	1·01 (0·96–1·05)	32·8 (0·6)	1·05 (1·02–1·07)*

OR, Odds ratio; CI, confidence interval; SES, socioeconomic status; BMI, body mass index; ALT, alanine transaminase; AST, aspartate aminotransferase; S.E., standard error.

[a] All percentages weighted.

[b] According to the 2010 diagnostic criteria of the American Diabetes Association.

[c] Includes any type of public or private health insurance.

[d] Defined as ever having smoked more than 100 cigarettes.

[e] Continuous variable: mean (S.E.) and OR (95% Wald CI) estimates are given.

* Statistically significant with $P < 0·05$.

which limited statistical power for gender-stratified tests. It also suggests that significant epidemiological differences between men and women in this cohort exist. For example, the proportion of male participants with abnormal LFTs is significantly higher than the proportion of female participants with abnormal LFTs (38·6% *vs.* 26·1%, $P < 0·005$).

Most marked, however, was the strong negative association between DM and HCV. As shown, the prevalence of HCV was highest in those with pre-diabetes, and lowest in those with DM. While we do not propose that diabetes is protective, *per se*, for HCV in this population, our results do indicate a negative association between HCV and DM, even after controlling for a variety of sociodemographic and clinical factors. There is considerable controversy surrounding this relationship, as many researchers have previously found *positive* associations between DM and HCV. There is both epidemiological [24, 25] and direct experimental evidence [26] that suggests that DM may predispose HCV infection, and that HCV might play a role in the progression of DM, although these interactions have been contested [27, 28]. In one systematic review of this association,

Table 4. *Multivariable logistic regression analysis of predictors of anti-HCV in serum, Cameron County Hispanic Cohort (2004–2012)*

Variable	OR (95% CI)
Male gender	0·85 (0·43–1·70)
Increased age[a]	1·02 (1·00–1·05)
Higher SES	0·64 (0·23–1·78)
Unemployed	0·76 (0·27–2·12)
Obese[b]	0·67 (0·22–2·07)
ALT (U/l)[a]	1·01 (0·99–1·03)
AST (U/l)[a]	1·02 (0·99–1·05)
Alcohol consumption	0·78 (0·43–1·40)
Smoking history[c]	2·36 (0·98–5·68)
Diabetes[d,e]	0·20 (0·05–0·77)*
Pre-diabetes[e,f]	1·69 (0·55–5·14)

OR, Odds ratio; CI, confidence interval; SES, socioeconomic status; ALT, alanine aminotransferase; AST, aspartate transaminase.
[a] Continuous variable.
[b] Defined as body mass index $\geqslant 30$.
[c] Defined as ever having smoked more than 100 cigarettes.
[d] According to the 2010 diagnostic criteria of the American Diabetes Association.
[e] Compared to non-diabetic, non-impaired fasting glucose.
[f] According to the 2010 criteria of the American Diabetes Association, definition for 'impaired fasting glucose'.
* Statistically significant with $P < 0·05$.

researchers found 45 out of 46 studies proposed a *positive* association between DM and HCV [29]. On the other hand, there are two studies that report a result of low prevalence of HCV in diabetics [27, 30], although these studies were not population-based and do not account for ascertainment bias. More recently, Ruhl and co-workers, using NHANES data, were unable to demonstrate a relationship between DM and HCV [28]. Instead, the authors suggest that elevated liver enzymes had a non-negligible effect on the association between DM and HCV [28]. In the present work, we have shown that DM is independently negatively associated with HCV even when controlling for ALT and AST. The widely varying prevalence of HCV in the three categories of DM, and the result of an independent effect of DM status on HCV in multivariable regression modelling, together suggest an important association in this population. The literature on this association, however, especially the recent work by Ruhl and co-workers using NHANES, urges caution in interpreting these findings, and further study is needed to examine the effect of liver enzymes on this association.

Additionally, there are important differences between the CCHC and NHANES, although both are population-based cohort studies. CCHC is an ethnically homogenous study population, which allows for detailed analysis of Mexican Americans in particular, whereas NHANES samples from a heterogeneous national population. Other distinctions between this study and the recent NHANES work are that the prevalence of diabetes is much higher in this cohort (26·8% *vs.* 10·5%), and this study is community-based, rather than national. These differences, especially the much higher prevalence of diabetes in Cameron County, allow for the possibility of a DM–HCV association that is present in this community but not detectable at the national level.

The high rate of HCV in those with pre-diabetes (4·0%) is cause for some concern. Obesity, insulin resistance, and diabetes are associated with a more rapid progression of fibrosis in HCV-infected individuals [31–33]. Higher levels of insulin resistance are also associated with a poorer response to antiviral therapy for HCV [34]. Moreover, because this community suffers high rates of insulin resistance [35], diabetes, obesity, and all-cause liver disease, it may be prudent to incorporate HCV screening efforts into pre-diabetes and DM education and outreach already in place.

Finally, there are some limitations to this study. This cohort does not contain data on risky behavior (such as illicit drug use, risky sexual practices, tattoos, or unhygienic medical procedures), which are often significant in HCV epidemiology. Despite this, the CCHC provides the only available large population-based data on community-dwelling Mexican Americans in the country, and the present study has effectively shown that the epidemiology of HCV in this population differs from that of existing national studies. Second, an anti-HCV assay does not provide data on the burden of active disease, and as such the burden of acute or chronic HCV remains unknown in this region. Using an HCV antibody test, however, allowed us to compare prevalence estimates with other studies, like NHANES and HCHS/SOL, which also used anti-HCV to estimate prevalence.

In conclusion, this study may be seen as preliminary work in understanding the unique epidemiology of HCV in a border-dwelling Mexican American community with severe health disparities. Our results – particularly the low prevalence of HCV in participants with diabetes, despite overall elevated prevalence of HCV and rampant diabetes – contrast with a large

body of previous work. Moving forward, it will be important to: (1) explore risk factors for HCV exposure unique to Cameron County, and (2) determine the genotype and seroprevalence of HCV RNA, in order to characterize the burden of active disease in this community. We have shown, much like previous studies, that diabetes is an important consideration in the epidemiology of HCV. In a Mexican American population with high prevalence of diabetes, obesity, and non-alcoholic liver disease, it is critical to characterize any factors, such as chronic viral hepatitis, that might further insult the health of the liver.

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DECLARATION OF INTEREST

None.

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