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Risk Factors for Cirrhosis in Contemporary Hepatology Practices—Findings from Texas Hepatocellular Carcinoma Consortium Cohort

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Background

Age-adjusted mortality from cirrhosis and hepatocellular carcinoma (HCC) continues to increase in the U.S.[1], as well as disproportionately affect racial/ethnic minorities. Understanding risk factors for cirrhosis is key to prevention but these have not been well described in contemporary hepatology practices. Several recent shifts may have changed cirrhosis and HCC epidemiology including improved access to highly efficacious hepatitis C virus (HCV) and[2] hepatitis B virus (HBV) treatments, increased prevalence of obesity and metabolic syndrome, and an increase in alcoholic liver disease[3].

We examined the distribution of risk factors in the Texas HCC Cohort (THCCC), a racial/ethnically and socioeconomically diverse prospective cohort of cirrhosis patients recruited from five Texas-based Hepatology practices.[4] Texas has the highest HCC incidence rates in U.S.[5], making it an ideal place to report the distribution of risk factors for cirrhosis overall and in different racial/ethnic subgroups.

Methods

THCCC cohort study was previously[4] described. Recruitment of patients with cirrhosis began December 21, 2016 from five institutions in three cities (Houston Veterans

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Administration and Baylor Clinic in Houston; University of Texas Southwestern and Parkland Hospital in Dallas; and University of Texas San Antonio in San Antonio). Cirrhosis diagnosis was based on liver histology, radiological features, liver elastography, or serum biomarkers. We excluded patients with uncontrolled hepatic decompensation, history of HCC, or current non-hepatic cancer. In addition to data extraction from the electronic medical record, patients completed data collection forms detailing medical history, alcohol and tobacco use and medications.

We analyzed risk factors including HCV infection [active, resolved, none], HBV infection [active, past, none], HIV, alcoholic liver disease, nonalcoholic fatty liver disease (NAFLD), metabolic syndrome (diabetes, obesity [BMI>30], dyslipidemia, hypertension) and other risk factors (alcohol drinking, tobacco use) (supplementary Table 1).

We compared cirrhosis risk factors among Hispanics, blacks and non-Hispanic whites. We calculated unadjusted and multivariate odds ratios and accompanying 95% confidence intervals using logistic regression models, where the dependent variables were groups based on race/ethnicity. We also constructed models where the dependent variables were groups based on HCV, NAFLD or ALD. Multivariate models included only variables with $p<0.1$ in univariate analyses.

Results

We enrolled 1717 participants as of January 30, 2019. The mean age was 60.1±10.1 years, and 582 (33.9%) were women. They included 50.0% non-Hispanic white, 25.9% Hispanics, 21.7% blacks, and 1.4% Asian. Among 445 Hispanics, 20 were born in Central America (4.5%), 8 in South America (1.8%), 5 in the Caribbean (1.1%), 122 in Mexico (27.4%), 282 (63.4%) in the United States, and 8 (1.8%) in other countries. Risk factors, in order of frequency, were resolved HCV (33.1%), alcoholic liver disease (30.6%), NAFLD (23.3%), active HCV (16.1%), and active HBV (2.5%). Diabetes was present in 55.5% of cirrhosis patients with NAFLD compared to 31.8%, 30.2%, and 35.4% of patients with active HCV, active HBV and alcoholic liver disease, respectively.

Hispanics were the youngest group with a mean age at time of diagnosis of 54 years (SD 10) compared with 58 (SD 10) in non-Hispanics. Alcoholic liver disease was the most common risk factor in Hispanics (35.5%), followed by NAFLD (34.2%) and resolved HCV (23.8%). In contrast, 53.6% of blacks had resolved HCV, 30.4% alcoholic liver disease and only 4.8% NAFLD. These 3 risk factors were equally distributed in non-Hispanic whites who also had the lowest proportions of diabetes or alcoholic liver disease (Table 1).

After adjusting for differences in demographics and other risk factors, Hispanics had higher odds of having obesity, diabetes, or NAFLD but lower odds of HBV or current smoking than non-Hispanics (Table 1). Blacks were more likely to have active or resolved HCV as well as alcoholic liver disease and tobacco smoking than Hispanics but less likely to have NAFLD. Analyses predicting HCV, NAFLD and ALD (supplementary Table 2), showed that black race was inversely associated with NAFLD, and Hispanic ethnicity was associated with ALD and NAFLD.

Discussion

The most common risk factors of cirrhosis and HCC have shifted from active viral hepatitis to resolved/treated viral hepatitis as well as alcoholic and non-alcoholic fatty liver disease. However, there are significant racial/ethnic differences in the distribution of risk factors, notably the high prevalence of metabolic syndrome and NAFLD in Hispanics and low prevalence of these risk factors in blacks. Blacks have high prevalence of alcoholic liver disease and heavy alcohol drinking. These findings portend a continued disproportionate burden of chronic liver disease in Hispanics[6] and possibly blacks. We excluded patients with decompensated cirrhosis, which affects the generalizability of the findings and opens the study to incidence-prevalence bias related to differential rate of decompensation or death.

Further, the shift from uncommon risk factors that carry a considerable increase risk of cirrhosis and HCC (active HCV, HBV) to more common but weaker risk factors (alcohol, NAFLD) is likely to result in a larger pool of chronic liver disease patients at risk for developing cirrhosis and HCC. However, it may become increasingly difficult to define the highest risk groups in need of interventions or monitoring. There is a clear need for risk stratification tools for cirrhosis and HCC among patients with HCV sustained virological response, adequate HBV suppression[7], alcoholic liver disease, and NAFLD[8].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Demographic and risk factors among different ethnic/racial groups. Statistical comparisons are made between Hispanic vs. non-Hispanic, and between Hispanics vs. blacks.

		Race/Ethnic Groups				Hispanic vs. Non-Hispanic		Hispanic vs. Black	
Variable	**Subgroups**	**Hispanic or Latino N = 445**	**Black: N = 371**	**Non-Hispanic White N = 858**	**Not Hispanic or Latino: N = 1245**	**Multivariate* Adjusted Odds Ratio**	**Multivariate* P Value**	**Multivariate* Adjusted Odds Ratio**	**Multivariate* P Value**
Age (years)	[20,58]	254 (57.08%)	87 (23.45%)	295 (34.38%)	391 (31.41%)	Reference	Reference	Reference	Reference
	[58,65]	113 (25.39%)	152 (40.97%)	258 (30.07%)	416 (33.41%)	0.49 (0.36, 0.69)	<0.001	0.53 (0.32, 0.86)	0.01
	[65,87]	78 (17.53%)	132 (35.58%)	305 (35.55%)	438 (35.18%)	0.41 (0.29, 0.58)	<0.001	0.57 (0.33, 0.96)	0.04
HCV	Negative	283 (63.6%)	79 (21.29%)	483 (56.29%)	571 (45.86%)	Reference	Reference	Reference	Reference
	Active	56 (12.58%)	92 (24.8%)	126 (14.69%)	218 (17.51%)	1.03 (0.67, 1.57)	0.90	0.55 (0.31, 0.10)	0.05
	Resolved	106 (23.82%)	200 (53.91%)	249 (29.02%)	456 (36.63%)	1.17 (0.83, 1.66)	0.37	0.54 (0.33, 0.87)	0.01
HBV	Neg/Unknown	407 (91.46%)	231 (62.26%)	734 (85.55%)	969 (77.83%)	Reference	Reference	Reference	Reference
	Past Infection	36 (8.09%)	128 (34.5%)	104 (12.12%)	235 (18.88%)	0.61 (0.39, 0.96)	0.034	0.47 (0.27, 0.79)	0.01
	Chronic	2 (0.45%)	12 (3.23%)	20 (2.33%)	41 (3.29%)	0.09 (0.02, 0.43)	0.003	0.11 (0.02, 0.83)	0.03
NAFLD	No	293 (65.84%)	353 (95.15%)	637 (74.24%)	999 (80.24%)	Reference	Reference	Reference	Reference
	Yes	152 (34.16%)	18 (4.85%)	221 (25.76%)	246 (19.76%)	1.65 (1.21, 2.26)	0.002	7.43 (3.87, 14.26)	<0.001
Alcoholic liver disease	No	287 (64.49%)	258 (69.54%)	616 (71.79%)	887 (71.24%)	Reference	Reference	Not included	Not included
	Yes	158 (35.51%)	113 (30.46%)	242 (28.21%)	358 (28.76%)	1.43 (1.03, 1.99)	0.03	Not included	Not included
Diabetes	No	221 (49.66%)	215 (57.95%)	544 (63.40%)	767 (61.61%)	Reference	Reference	Reference	Reference
	Yes	224 (50.34%)	156 (42.05%)	314 (36.60%)	478 (38.39%)	1.84 (1.38, 2.45)	<0.001	1.42 (0.94, 2.15)	0.09
High Cholesterol	No	358 (80.45%)	286 (77.09%)	676 (78.79%)	972 (78.07%)	Not included	Not included	Not included	Not included
	Yes	87 (19.55%)	85 (22.91%)	182 (21.21%)	273 (21.93%)	Not included	Not included	Not included	Not included
BMI	Normal	44 (9.89%)	85 (22.91%)	144 (16.78%)	236 (18.96%)	Reference	Reference	Reference	Reference
	Overweight	122 (27.42%)	131 (35.31%)	280 (32.63%)	412 (33.09%)	1.46 (0.91, 2.32)	0.11	1.46 (0.76, 2.80)	0.25
	Obese	272 (61.12%)	150 (40.43%)	415 (48.37)	573 (46.02%)	2.41 (1.56, 3.74)	<0.001	2.23 (1.20, 4.13)	0.01
High BP	No	241 (54.16%)	110 (29.65%)	407 (47.44%)	533 (42.81%)	Reference	Reference	Reference	Reference
	Yes	204 (45.84%)	261 (70.35%)	451 (52.56%)	712 (57.19%)	0.69 (0.52, 0.92)	0.01	0.40 (0.26, 0.60)	<0.001
Smoking	Never	213 (47.87%)	71 (19.14%)	306 (35.66%)	390 (31.33%)	Reference	Reference	Reference	Reference

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	Yes, but quit	155 (34.83%)	158 (42.59%)	349 (40.68%)	505 (40.56%)	0.78 (0.57, 1.08)	0.14	0.83 (0.50, 1.40)	0.49
	Yes, currently	64 (14.38%)	133 (35.85%)	179 (20.86%)	315 (25.3%)	0.59 (0.39, 0.88)	0.01	0.50 (0.28, 0.87)	0.02
Alcohol drinking	Never/Rarely	141 (31.69%)	64 (17.25%)	260 (30.30%)	335 (26.91%)	Reference	Reference	Reference	Reference
	Past	247 (55.51%)	212 (57.14%)	460 (53.61%)	675 (54.22%)	1.34 (0.94, 1.90)	0.10	1.17 (0.70, 1.95)	0.54
	Current	42 (9.44%)	72 (19.41%)	105 (12.24%)	179 (14.38%)	1.09 (0.65, 1.81)	0.75	0.80 (0.40, 1.6)	0.53

BMI: body mass index, HCV: hepatitis C virus, HBV: hepatitis B virus, NAFLD: non-alcoholic fatty liver disease.