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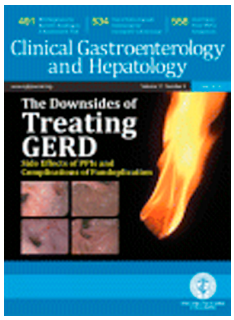

Lifestyle and clinical correlates of hepatocellular carcinoma in South Texas: a matched case-control study

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Title (max 120 char) -- **Lifestyle and clinical correlates of hepatocellular carcinoma in South Texas: a matched case-control study**

Short title (max 45 char) -- **Liver cancer in Texas: a case-control study**

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The incidence of hepatocellular carcinoma (HCC) in the United States is rising even as overall cancer rates are declining, and Latinos are disproportionately affected, especially in Texas. Our case-control study sought to determine relative etiologic contributions of lifestyle-related risk factors in South Texas.

Methods

Between October 2012 and July 2014, we identified, consented and interviewed in person 51 HCC adult cases (diagnosed within the past 12 months and residing in Bexar or any of the 7 surrounding counties) from clinics at University Hospital and the Cancer Therapy and Research Center at UT Health San Antonio; and 104 adult controls, 32 from a related study[1,2] and 72 randomly selected residents in the study counties. From these 51 cases and 104 controls, we created 42 matched pairs, with exact matching on sex, ethnicity (Hispanic, Non-Hispanic), and age category (18–57 years, >57 years). Urine samples (10 mL each) and serum samples (150 μL each) were assessed for biomarkers of previous aflatoxin exposure using procedures previously described.[3] The primary aflatoxin exposure serum biomarker was an aflatoxin B_1 (AFB_1)-lysine DNA adduct. We also assessed urinary aflatoxin M_1. We used matched logistic regression to estimate odds ratios (OR) and 95% confidence intervals. The protocol was approved by a local Institutional Review Board.

Results

Most matched cases and controls were Latino (67%). Compared to controls, HCC cases were more likely to report Medicare or Medicaid, lower income, less education, more lifetime alcohol use, and more smoking (Figure 1). Cases were less likely to report hypercholesterolemia [0.11

(0.02–0.51)], more likely to report hepatitis C [183.74 (27.37–∞), cirrhosis 2.17 (33.3–∞), and transfusions [4.35 (1.60–11.84)], and less likely to be taking aspirin [0.31 (0.11–0.85)], statins [0.03 (0–0.20)], and omega-3/fish oil [0.10 (0.01–0.78)]. Cases did not differ significantly from controls with regard to reported consumption of products made from corn (data not shown). Relative to controls, cases were more likely to have HCV antibodies [174.3 (26.2–∞)] and have detectable aflatoxin levels in blood [6.09 (1.10–33.71)] and urine [3.42 (1.07–10.91)].

Discussion

To our knowledge, this is the first epidemiologic study relating HCC and aflatoxin exposure in a U.S. population, particularly a Latino-majority study population. A recent review of non-U.S. studies[4] reported that aflatoxin may play a causative role in 4.6% to 28.2% of all global HCC cases, and that the combined effect of AFB_1 exposure and HBV infection appears additive rather than multiplicative. In the current study, serum (AFB_1) and urine (AFM1) aflatoxin levels and HCV infection were significantly higher in cases than controls. Our results also support the observations of others that HCV infection is a major risk factor for HCC incidence in the U.S. Although HCV infection is a strong risk factor for development of HCC, rising trends in HCC incidence among Latinos cannot be attributed solely to HCV infection. Our data on a majority-Latino cohort suggest that HCC cases are poor and controls were more affluent, and smoked more with a higher prevalence of cirrhosis than controls. The lack of case-control differences for corn-based foods, a suspected risk factor for HCC, may be due to information bias from use of a 12-month dietary recall assessment. We hypothesized that contaminated corn products contributed to the increased risk of HCC and expected to observe increased consumption of corn-based foods in cases relative to controls; a possible reason we did not may be that cases and

controls are consuming corn products differentially contaminated with aflatoxin (e.g., commercial vs. home-grown). Random assays of corn products purchased by cases and controls should be done in a future study to verify this. Study strengths include case-control matching on sex, ethnicity, and age; and in-person interviewing of subjects in their language of choice. A possible weakness is that cases and controls were not randomly selected with the same inclusion criteria; therefore, selection bias may exist. Cases were selected as a convenience sample from local medical facilities, whereas controls were selected from an existing prevention study and randomly from the surrounding county populations. A larger study will be needed to address sources of aflatoxin exposure as a risk factor for HCC.

Figure 1

Association between lifestyle and clinical factors and hepatocellular carcinoma risk in South Texas. Odds ratios (95% CI) derived from matched logistic regression.

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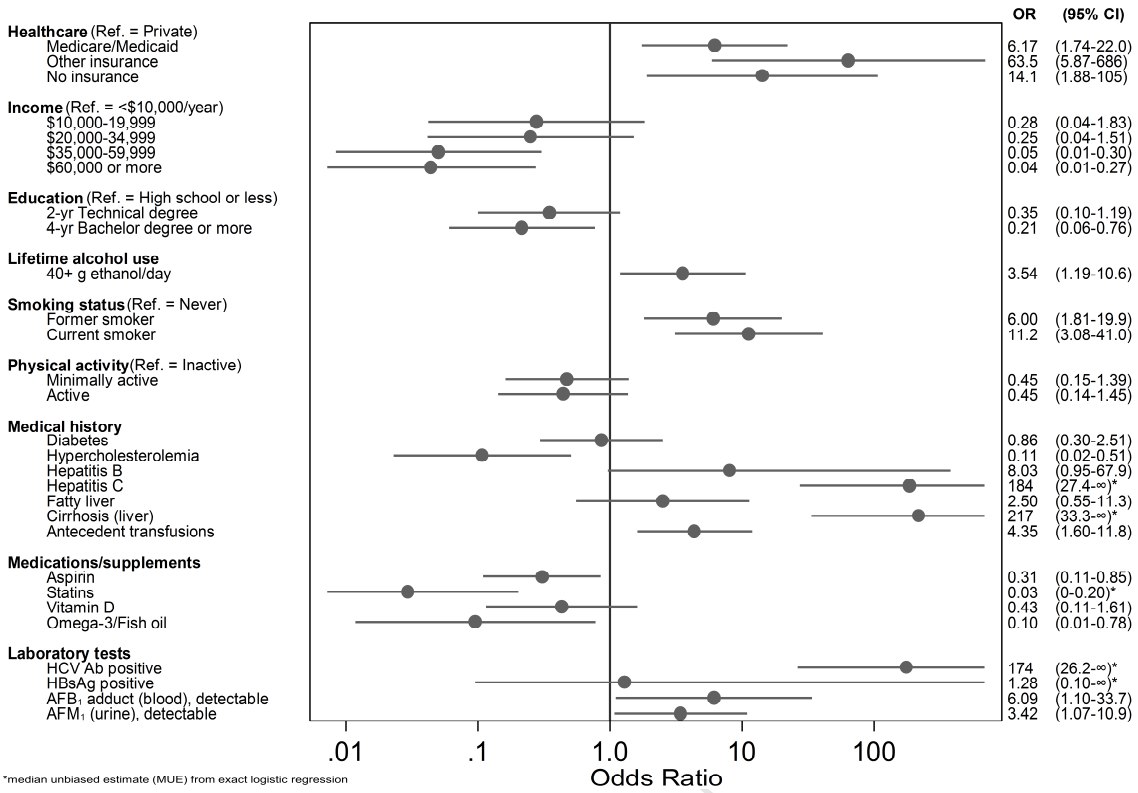

*median unbiased estimate (MUE) from exact logistic regression