RESEARCH

Characteristics of incident liver cancer cases in the District of Columbia metropolitan area

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ABSTRACT

The District of Columbia (D.C.) has the highest liver cancer incidence in the United States (U.S.), but the reasons for this are not fully known. We examined socio-demographic, clinical and behavioral characteristics of incident liver cancer cases in D.C., Maryland (MD) and Virginia (VA) to identify potential risk factors. We obtained data from D.C., MD and VA cancer registries for individuals diagnosed with hepatocellular carcinoma (HCC) or intrahepatic cholangiocarcinoma (ICC) between 2013 and 2016. We estimated age-adjusted incidence rates and conducted descriptive analyses stratified by state/territory, sex, stage at diagnosis, and race/ethnicity. 5,928 incident HCC/ICC cases occurred between 2013-2016. Age-adjusted incidence rates (per 100,000) for HCC/ICC were highest in D.C. (12.2, 95% CI=10.9, 13.5), for males (12.6, 95% CI=12.2, 12.9), and non-Hispanic Blacks (11.3, 95% CI=10.8, 11.8) and Asian/Pacific Islanders (APIs) (10.8, 95% CI=9.7, 11.9). Racial disparities in HCC/ICC incidence were widest in D.C. A substantial proportion of cases were missing data on country of birth and behavioral risk factors. Mean age at diagnosis, marital status, country of birth, insurance status, and alcohol and tobacco use history varied across analytic sub-groups. Non-Hispanic Blacks, APIs and males experience a high burden of liver cancer in the D.C. metropolitan area. There are several socio-demographic disparities by state/territory, sex, and race/ethnicity. More data on country of birth, behavioral risk factors, and comorbidities are urgently needed to understand their contribution to the burden of liver cancer in the D.C. metropolitan area.

KEYWORDS: Hepatocellular carcinoma, intrahepatic cholangiocarcinoma, epidemiology, disparities.

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INTRODUCTION

Liver cancer incidence has been increasing in the United States (U.S.) (Siegel et al., 2020). In 2020, it accounted for 30,160 deaths and was the fifth leading cause of cancer deaths for men and the seventh leading cause of cancer deaths for women (Siegel et al., 2020). Liver and intrahepatic bile duct cancers are projected to become the third leading cause of cancer deaths in the U.S. by 2040 (Rahib et al., 2021). Between 2014 and 2018, the District of Columbia (D.C.) had the highest age-adjusted liver cancer incidence rate (per 100,000) in the U.S. (12.4 (overall), 19.5 (males), 6.6 (females)) (USCS, 2021). In contrast, the surrounding states of Maryland (MD) and Virginia (VA) had relatively lower incidence rates (MD: 8.8 (overall), 13.5 (males), 4.8 (females); VA: 7.5 (overall), 11.6 (males), 4.1 (females)) (USCS, 2021). While there are several hypotheses for the high incidence of liver cancer in D.C., little is definitively known about the populations experiencing the burden of liver cancer, as well as factors that could account for these differences in liver cancer incidence rates between D.C. and its neighboring states, and the clinical and behavioral risk factors driving liver cancer incidence in the D.C. metropolitan area.

Current data indicates that there are racial and ethnic disparities in liver cancer incidence in D.C. Non-Hispanic Blacks (17.0/100,000, 95% CI=15.2, 18.9) have an age-adjusted incidence rate three times higher than non-Hispanic Whites (5.3/100,000, 95% CI=4.1, 6.8) (USCS, 2021). Hepatitis B virus (HBV) and hepatitis C virus (HCV) are prominent clinical risk factors for hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC) (de Martel et al., 2015; Massarweh & El-Serag, 2017), the two most common types of liver cancer. HBV and HCV are endemic in several countries in Africa and Asia (World Health Organization, 2021a, 2021b). Approximately 15% of the D.C. population is estimated to be foreign born (Tatian et al., 2018; The Metropolitan Washington Council of Governments, 2017), and migration of individuals from HBV and HCV endemic countries to D.C. could be contributing to the high incidence of liver cancer. Behavioral risk factors may also play a role. Tobacco use and heavy alcohol use are recognized risk factors for HCC and ICC (Petrick et al., 2018), and there is also evidence that links obesity to a higher liver cancer risk (Campbell et al., 2016). D.C. has one of the highest rates of binge drinking in the U.S. (Centers for Disease Control and Prevention, 2020). Additionally, almost a quarter of adults in D.C. are obese, with a particularly high prevalence among non-Hispanic Blacks (38%) (Centers for Disease Control and Prevention, 2021).

While state level liver cancer incidence data is publicly available from USCS, several gaps exist in the information provided by current data. One limitation is that USCS estimates aggregate HCC and ICC. Although these two types of liver cancers share several risk factors, they also have unique risk factors and etiologies (Massarweh & El-Serag, 2017). Thus, there is a need to independently monitor HCC and ICC trends to better inform prevention and control efforts. USCS enables comparisons of liver cancer incidence and mortality only across select socio-demographic characteristics, such as sex and race/ethnicity. More research that examines a wider range of factors is needed to characterize the liver cancer population in the D.C. area and identify prevailing risk factors to inform the development of targeted interventions. Additionally, owing to the proximity of D.C. to MD and VA, and fluid population movement between D.C. and these neighboring states (Maciag, 2018; Rabinowitz, 2017), understanding the profile of liver cancer cases in MD and VA can provide a more comprehensive picture of risk factors for liver cancer in the D.C.

metropolitan area. Therefore, the objective of this study was to identify socio-demographic, clinical, and behavioral characteristics of incident liver cancer cases in D.C., MD and VA over a four-year period (2013-2016). Additionally, we aimed to examine characteristics of incident liver cancer cases stratified by sex, stage at diagnosis, and race/ethnicity.

METHODS

Data and sample

Data were requested and obtained from the DC, MD, and VA cancer registries. The inclusion criteria for this analysis were a diagnosis: (i) of HCC (ICD-10-CM code: C22.0) or ICC (ICD-10-CM code: C22.1), (ii) in D.C., MD or VA, (iii) between 2013 and 2016. A total of 5,928 incident HCC/ICC cases were identified during this period and included in the analysis.

Measures

For each incident HCC/ICC case, the following variables were requested from the respective cancer registry:

Socio-demographic characteristics: age at diagnosis, sex, race, ethnicity, marital status, country of birth, and health insurance based on primary payer at diagnosis.

Clinical characteristics: primary cancer site, stage at diagnosis based on SEER summary stage 2000, family history, and comorbid complications, obtained as ICD-9-CM codes.

Behavioral risk factors: alcohol and tobacco use history

Analysis

Data cleaning included recoding and creating calculated variables. The following variables were collapsed and/or recoded as follows: combined race and ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Asian/Pacific Islander (API), and other); marital status (single (including unmarried and domestic partner), married (including common law), and separated, divorced or widowed); U.S. born (yes/no); health insurance (not insured, private insurance, Medicaid, Medicare, uniformed services (including TRICARE, Military and VA), and other); stage at diagnosis (localized, regional, and distant); family history of cancer (no history, history of liver cancer (including liver cancer only or liver and other cancer), and history of other cancer only (including type of cancer not specified)); alcohol history (never use, current use, and past use); tobacco history (never use, current use (including combustible only, smokeless only, and combination tobacco product use), and past use). As a different number of comorbidity fields were provided by each registry, this variable was not included in the analysis and instead summarized based on the primary comorbidity recorded. For all variables, unknown or missing was treated as an independent category, except for race/ethnicity and health insurance, where it was combined with "other".

Age-adjusted incidence rates for 2013-2016 were calculated for all sites (HCC and ICC) combined and by primary site (HCC or ICC) across state/territory, sex, and race/ethnicity. Additionally age-adjusted incidence rates were calculated by sex and race/ethnicity within each state/territory. Incidence rates were age-adjusted to the 2000 U.S. standard population using 19 age groups, and confidence intervals (CIs) for incidence rates were estimated using the method proposed by Keyfitz (1966). Rates were suppressed for sub-groups with 1-15 cases due to low reliability, and counts for variables by state/territory were suppressed for cells with <10 cases for confidentiality.

Descriptive analyses, stratified by state/territory, sex, stage at diagnosis, and race/ethnicity were conducted. Tests for statistically significant differences between groups were conducted using chi-square tests for categorical variables and t-tests or ANOVA for continuous variables. All analyses were conducted using Stata version 14. A p-value of 0.05 was considered statistically significant.

Ethical approval

This research was approved by the George Washington Cancer Center Protocol Review and Monitoring Committee, and the Institutional Review Boards of the George Washington University, and the D.C., MD and VA Departments of Health

RESULTS

A summary of sample characteristics is provided in Table 1. Several variables had missing data. Family history, alcohol history, and tobacco history data were not available for MD and were missing for a large proportion of cases in D.C. and VA (>34%). Country of birth was missing for almost half the overall sample (48.5%), and for a majority of cases from VA (70.8%). A sizable proportion of cases were also missing data for stage at diagnosis (31.1%).

Table 1. Characteristics of incident liver cancer cases in D.C., Maryland and Virginia by state/territory and sex (2013-2016).

Variable	State/territory				Sex	
	Total (N=5,928)	D.C. (N=343)	Maryland (N=2,559)	Virginia (N=3,026)	Male (N=4,209)	Female (N=1,719)
Incidence rate/100,000 (95% CI)[a] (HCC and ICC)	8.2 (8.0, 8.4)	12.2 (10.9, 13.5)	8.8 (8.5, 9.2)	7.6 (7.3, 7.8)	12.6 (12.2, 12.9)	4.5 (4.3 – 4.7)
Incidence rate/100,000 (95% CI)[a] (HCC only)	7.0 (6.8, 7.2)	10.7 (9.5, 11.9)	7.5 (7.2, 7.8)	6.4 (6.1, 6.6)	11.2 (10.8, 11.5)	3.4 (3.2 – 3.6)
Incidence rate/100,000 (95% CI)[a] (ICC only)	1.2 (1.1, 1.3)	1.5 (1.0, 1.9)	1.3 (1.2, 1.4)	1.2 (1.1 – 1.3)	1.4 (1.2 – 1.5)	1.1 (1.0 – 1.2)
Socio-demographics						
Age at diagnosis, mean (SD)	64.6 (11.7)	62.7 (11.8)	64.7 (11.8)	64.7 (11.7)[*]	63.8 (10.9)	66.7 (13.3)[**b]
Male, n (%)	4,209 (71.0)	245 (71.4)	1,809 (70.7)	2,155 (71.2)	--	--
Race/ethnicity, n (%)						
Non-Hispanic White	3,312 (55.9)	35 (10.2)	1,359 (53.1)	1,918 (63.4)[**]	2,339 (55.6)	973 (56.6)[**]
Non-Hispanic Black	1,928 (32.5)	286 (83.4)	932 (36.4)	710 (23.5)	1,418 (33.7)	510 (29.7)
Hispanic	181 (3.1)	10 (2.9)	89 (3.5)	82 (2.7)	107 (2.5)	74 (4.3)
API	367 (6.2)	<10	s	207 (6.8)	251 (6.0)	116 (6.8)
Other/Unknown/Missing	140 (2.4)	<10	s	109 (3.6)	94 (2.2)	46 (2.7)
Marital status, n (%)						
Single	1,275 (21.5)	160 (46.7)	579 (22.6)	536 (17.7)[**]	966 (23.0)	309 (18.0)[**]
Married	2,462 (41.5)	85 (24.8)	1,030 (40.3)	1,347 (44.5)	1,875 (44.6)	587 (34.2)

Separated/Divorced/	1,241 (20.9)	82 (23.9)	458 (17.9)	701 (23.2)	745 (17.7)	496 (28.9)
Widowed	950 (16.0)	16 (4.7)	492 (19.2)	442 (14.6)	623 (14.8)	327 (19.0)
Unknown/Missing						
U.S. born, n (%)						
No	353 (6.0)	38 (11.1)	146 (5.7)	169 (5.6)**	222 (5.3)	131 (7.6)**
Yes	2,699 (45.5)	182 (53.1)	1,801 (70.4)	716 (23.7)	1,981 (47.1)	718 (41.8)
Unknown/Missing	2,876 (48.5)	123 (35.9)	612 (23.9)	2,141 (70.8)	2,006 (47.7)	870 (50.6)
Health insurance, n (%)						
Not insured	258 (4.4)	<10	s	192 (6.4)**	206 (4.9)	52 (3.0)**
Private Insurance	1,420 (24.0)	66 (19.2)	636 (24.9)	718 (23.7)	1,026 (24.4)	394 (22.9)
Medicaid	529 (8.9)	91 (26.5)	258 (10.1)	180 (6.0)	401 (9.5)	128 (7.5)
Medicare	2,377 (40.1)	104 (30.3)	1,059 (41.4)	1,214 (40.1)	1,611 (38.3)	766 (44.6)
Uniformed services	235 (4.0)	<10	s	166 (5.5)	219 (5.2)	16 (1.0)
Other/Unknown/Missing	1,109 (18.7)	70 (20.4)	483 (18.9)	556 (18.4)	746 (17.7)	363 (21.1)
Clinical						
HCC, n (%)	5,082 (85.7)	304 (88.6)	2,196 (85.8)	2,582 (85.3)	3,788 (90.0)	1,294 (75.3)**
Stage at diagnosis, n (%)						
Localized	2,043 (34.5)	127 (37.0)	926 (36.2)	990 (32.7)**	1,495 (35.5)	548 (31.9)**
Regional	1,187 (20.0)	58 (16.9)	546 (21.3)	583 (19.3)	880 (20.9)	307 (17.9)
Distant	854 (14.4)	48 (14.0)	380 (14.9)	426 (14.1)	592 (14.1)	262 (15.2)
Unknown/Missing	1,844 (31.1)	110 (32.1)	707 (27.6)	1,027 (33.9)	1,242 (29.5)	602 (35.0)
Family history, n (%)						
No history	(N=3,369)	78 (22.7)		786 (26.0)**	652 (27.2)	212 (21.9)**
Liver cancer[c]	864 (25.7)	0 (0.0)		65 (2.2)	49 (2.0)	16 (1.7)
Other cancer only/not	65 (1.9)	69 (20.1)		776 (25.6)	550 (22.9)	295 (30.4)
specified	845 (25.1)	196 (57.1)		1,399 (46.2)	1,149 (47.9)	446 (46.0)
Unknown/Missing	1,595 (47.3)					
Behavioral						
Alcohol history, n (%)	(N=3,369)					
Never use	879 (26.1)	50 (14.6)		829 (27.4)**	502 (20.9)	377 (38.9)**
Current use	1,200 (35.6)	s		s	979 (40.8)	221 (22.8)
Past use	57 (1.7)	s		<10	46 (1.9)	11 (1.1)
Unknown/Missing	1,233 (36.6)	169 (49.3)		1,064 (35.2)	873 (36.4)	360 (37.2)
Tobacco history, n (%)	(N=3,369)					
Never user	670 (19.9)	50 (14.6)		620 (20.5)**	349 (14.5)	321 (33.1)**
Current user	709 (21.0)	63 (18.4)		646 (21.4)	581 (24.2)	128 (13.2)
Past user	823 (24.4)	63 (18.4)		760 (25.1)	637 (26.5)	186 (19.2)
Unknown/Missing	1,167 (34.6)	167 (48.7)		1,000 (33.1)	833 (34.7)	334 (34.5)

Notes. % = column totals; blank cells = data not available; <10 = case counts of 1-9 are suppressed for confidentiality; s = case counts are suppressed to prevent back calculation of counts in other cell(s); SD=standard deviation; $^{*}p<0.05$, $^{**}p<0.0001$

[a]Incidence rate age-adjusted to the 2000 U.S. standard population; [b]One-way ANOVA with post-hoc Bonferroni adjustment indicated that mean age in DC was significantly different from MD and VA; [c]Includes liver cancer only or liver and other cancer

The overall age-adjusted incidence rate of HCC/ICC for D.C., MD and VA between 2013-2016 was 8.2/100,000 (95% CI=8.0, 8.4), with a higher incidence rate for HCCs (7.0/100,000, 95% CI=6.8, 7.2) than for ICCs (1.2/100,000, 95% CI=1.1, 1.3). The mean age at diagnosis was 64.6 years (standard deviation (SD)=11.7). The majority of cases were male (71%) and non-Hispanic White (55.9%). Almost half the sample was U.S. born (45.5%). A large proportion of cases were married at the time of diagnosis (41.5%), and a sizable proportion of cases had Medicare insurance (40.1%). In terms of clinical characteristics, a majority of cases were HCCs (85.7%) and commonly diagnosed at the localized stage (34.5%). The most commonly recorded primary comorbidities were hypertension (6.3%), HCV (4%), alcoholic liver cirrhosis (3.3%), and diabetes (3%). A larger proportion of individuals currently used alcohol (35.6%) compared to tobacco (21%).

Differences in characteristics between incident HCC/ICC cases in D.C., MD and VA are also provided in Table 1. Of the 5,928 HCC/ICC cases, 343 occurred in D.C., 2,559 occurred in MD, and 3,026 occurred in VA. The HCC/ICC incidence rate was highest in D.C. (12.2/100,000, 95% CI=10.9, 13.5) and lowest in VA (7.6/100,000, 95% CI=7.3, 7.8). Similar trends in HCC and ICC incidence rates were observed when evaluated separately, although differences in ICC incidence rates across D.C., MD, and VA were not statistically significant. Incidence rates in D.C., MD and VA did differ by sex and race/ethnicity. Incidence rates were higher for males in all 3 states/territories, and incidence rates for males (18.9/100,000, 95% CI=16.5, 21.3) and females (6.6/100,000, 95% CI=5.3, 7.9) were highest in D.C. (Figure 1). Racial disparities were wider in D.C. compared to MD and VA (Figure 2). Socio-demographic characteristics of liver cancer cases in D.C. were also significantly different from MD and VA with regard to mean age of diagnosis, which was lower (62.7 years (D.C.) vs 64.7 years (MD, VA)). D.C. had a higher proportion of individuals who were single or unmarried (46.7% (D.C.) vs 22.6% (MD), 17.7% (VA)), non-U.S. born (11.1 (D.C.) vs 5.7% (MD), 5.6% (VA)), and covered by Medicaid (26.5% (D.C.) vs 10.1% (MD), 6% (VA)).

Figure 1. Age-adjusted incidence rate of liver cancer (2013-2016) in D.C., Maryland and Virginia by sex

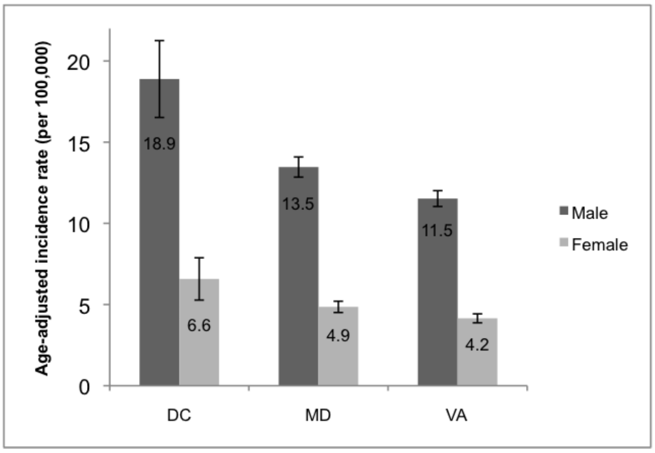
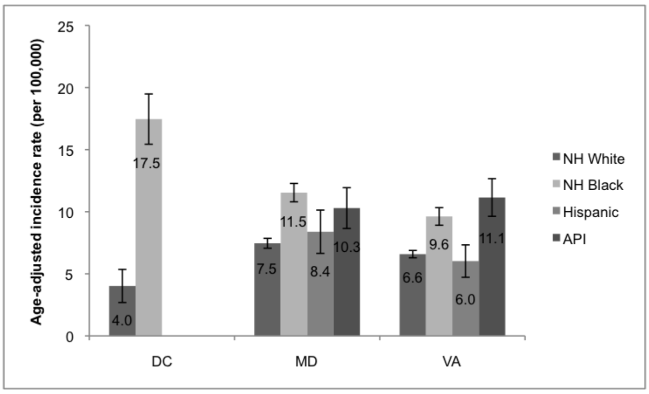


Figure 2. Age-adjusted incidence rate of liver cancer in D.C., Maryland and Virginia by race/ethnicity



Note. Rates for Hispanics and APIs in D.C. were suppressed for reliability as the number of cases was below 15.

Sex-stratified analyses are also presented in Table 1. The incidence rate for males (12.6/100,000, 95% CI=12.2, 12.9) was almost three times the rate for females (4.5/100,000, 95% CI=4.3, 4.7). This trend held for HCCs, but the ICC incidence rate was only marginally higher for males (1.4/100,000, 95% CI=1.2, 1.5) compared to females (1.1/100,000, 95% CI=1.0, 1.2). Males differed from females with respect to younger age at diagnosis (63.8 years vs 66.7 years). Males were more likely to be non-Hispanic Black compared to females (33.7% vs 29.7%), while females were more likely to be Hispanic than males (4.3% vs 2.5%). A higher proportion of males were married (44.6% vs 34.2%), whereas a higher proportion of females were separated, divorced or widowed (28.9% vs 17.7%). ICCs made up a larger share of liver cancers for females compared to males (24.7% vs 10%). Females were more likely than males to have Medicare insurance (44.6% vs 38.3%), and report never use of alcohol (38.9% vs 20.9%) and tobacco (33.1% vs 14.5%).

Characteristics of cases by stage at diagnosis are presented in Table 2. A slightly higher proportion of uninsured individuals were diagnosed at the regional and distant (5.9%) stages vs localized stage (3.3%). ICCs were more likely to be diagnosed at the distant stage (30.7%) than the localized (7.7%) and regional (15.7%) stages.

Table 2: Characteristics of incident liver cancer cases in D.C., Maryland and Virginia (2013-2016) by stage at diagnosis

Variable	Total (N=4,084†)	Localized (N=2,043)	Regional (N=1,187)	Distant (N=854)
Socio-demographics				
Age at diagnosis, mean (SD)	63.8 (11.4)	64.0 (10.7)	63.3 (11.7)	64.1 (12.5)
Race/ethnicity, n (%)				
Non-Hispanic White	2,301 (56.3)	1,122 (54.9)	683 (57.5)	496 (58.1)*
Non-Hispanic Black	1,296 (31.7)	671 (32.8)	356 (30.0)	269 (31.5)
Hispanic	133 (3.3)	71 (3.5)	30 (2.5)	32 (3.8)
API	267 (6.5)	131 (6.4)	96 (8.1)	40 (4.7)
Other/Unknown/Missing	87 (2.1)	48 (2.4)	22 (1.9)	17 (2.0)
Marital status, n (%)				
Single	980 (24.0)	514 (25.2)	279 (23.5)	187 (21.9)
Married	1,964 (48.1)	950 (46.5)	591 (49.8)	423 (49.5)
Separated/Divorced/Widowed	930 (22.8)	481 (23.5)	258 (21.7)	191(22.4)

Unknown/Missing	210 (5.1)	98 (4.8)	59 (5.0)	53 (6.2)
U.S. born, n (%)				
No	261 (6.4)	120 (5.9)	92 (7.8)	49 (5.7)**
Yes	1,807 (44.3)	847 (41.5)	547 (46.1)	413 (48.4)
Unknown/Missing	2,016 (49.4)	1,076 (52.7)	548 (46.2)	392 (45.9)
Health insurance, n (%)				
Not insured	187 (4.6)	67 (3.3)	70 (5.9)	50 (5.9)**
Private Insurance	1,126 (27.6)	506 (24.8)	379 (31.9)	241 (28.2)
Medicaid	415 (10.2)	197 (9.6)	129 (10.9)	89 (10.4)
Medicare	1,840 (45.1)	970 (47.5)	493 (41.5)	377 (44.2)
Uniformed services	200 (4.9)	133 (6.5)	44 (3.7)	23 (2.7)
Other/Unknown/Missing	316 (7.7)	170 (8.3)	72 (6.1)	74 (8.7)
Clinical				
HCC, n (%)	3,478 (85.2)	1,885 (92.3)	1,001 (84.3)	592 (69.3)**
Family history, n (%)	(N=2,232)			
No history	666 (29.8)	337 (30.2)	182 (28.4)	147 (31.0)*
Liver cancer[a]	43 (1.9)	20 (1.8)	13 (2.0)	10 (2.1)
Other cancer/ not specified	651 (29.2)	285 (25.5)	203 (31.7)	163 (34.4)
Unknown/Missing	872 (39.1)	475 (42.5)	243 (37.9)	154 (32.5)
Behavioral				
Alcohol history, n (%)	(N=2,232)			
Never use	629 (28.2)	294 (26.3)	180 (28.1)	155 (32.7)*
Current use	877 (39.3)	418 (37.4)	270 (42.1)	189 (39.9)
Past use	42 (1.9)	22 (2.0)	12 (1.9)	8 (1.7)
Unknown/Missing	684 (30.7)	383 (34.3)	179 (27.9)	122 (25.7)
Tobacco history, n (%)	(N=2,232)			
Never user	488 (21.9)	224 (20.1)	141 (22.0)	123 (26.0)*
Current user	505 (22.6)	244 (21.8)	150 (23.4)	111 (23.4)
Past user	606 (27.2)	288 (25.8)	185 (28.9)	133 (28.1)
Unknown/Missing	633 (28.4)	361 (32.3)	165 (25.7)	107 (22.6)

Notes. †Stage unknown or missing for n=1,844; % = column totals; SD=standard deviation; *p<0.05, **p<0.0001; [a] Includes liver cancer only or liver and other cancer.

Analyses of characteristics stratified by race/ethnicity are presented in Table 3. Across D.C., MD and VA, incidence rates for HCC/ICC and HCCs only were highest among non-Hispanic Blacks (HCC/ICC: 11.3/100,000, 95% CI=10.8, 11.8; HCC: 10.1/100,000, 95% CI=9.6, 10.6), followed by APIs (HCC/ICC: 10.8/100,000, 95% CI=9.7, 11.9; HCC: 9.4/100,000, 95% CI=8.3, 10.4). ICC incidence rates were highest for APIs (1.5/100,000, 95% CI=1.1, 1.9), although differences were not statistically significant. Hispanics (62.1 years) and non-Hispanic Blacks (62.4 years) had the youngest average age at diagnosis. Non-Hispanic Blacks were most likely to be single or unmarried (34.1%), while APIs were most likely to be married (65.1%). Hispanics were most likely to be uninsured (14.4%). Non-Hispanic Blacks were least likely to report never use of alcohol (18.4%) or tobacco (15.4%), and Hispanics

(40.2%) and APIs (40.7%) were more likely to report never use of alcohol. Hispanics were also most likely to report never use of tobacco (41.3%).

Table 3: Characteristics of incident liver cancer cases in D.C., Maryland and Virginia (2013-2016) by race/ethnicity.

Variable	Total (N=5,788[†])	NH White (N=3,312)	NH Black (N=1,928)	Hispanic (N=181)	API (N=367)
Incidence rate/100,000 (95% CI)[a] (HCC and ICC)		6.9 (6.6, 7.1)	11.3 (10.8, 11.8)	7.0 (6.0, 8.0)	10.8 (9.7, 11.9)
Incidence rate/100,000 (95% CI)[a] (HCC only)		5.6 (5.4, 5.9)	10.1 (9.6, 10.6)	5.8 (4.9, 6.7)	9.4 (8.3, 10.4)
Incidence rate/100,000 (95% CI)[a] (ICC only)		1.2 (1.1, 1.3)	1.2 (1.0, 1.3)	1.2 (0.8, 1.6)	1.5 (1.1, 1.9)
Socio-demographics					
Age at diagnosis, mean (SD)	64.6 (11.8)	65.9 (12.0)	62.4 (10.2)	62.1 (15.4)	65.6 (13.0)[**b]
Marital status, n (%)					
Single	1,247 (21.5)	522 (15.8)	657 (34.1)	41 (22.7)	27 (7.4)[**]
Married	2,401 (41.5)	1,535 (46.4)	551 (28.6)	76 (42.0)	239 (65.1)
Separated/Divorced/Widowed	1,219 (21.1)	738 (22.3)	402 (20.9)	34 (18.8)	45 (12.3)
Unknown/Missing	921 (15.9)	517 (15.6)	318 (16.5)	30 (16.6)	56 (15.3)
Health insurance, n (%)					
Not insured	247 (4.3)	95 (2.9)	101 (5.2)	26 (14.4)	25 (6.8)[**]
Private Insurance	1,390 (24.0)	799 (24.1)	450 (23.3)	36 (19.9)	105 (28.6)
Medicaid	521 (9.0)	193 (5.8)	279 (14.5)	25 (13.8)	24 (6.5)
Medicare	2,322 (40.1)	1,518 (45.8)	616 (32.0)	50 (27.6)	138 (37.6)
Uniformed services	227 (3.9)	109 (3.3)	106 (5.5)	5 (2.8)	7 (1.9)
Other/Unknown/Missing	1,081 (18.7)	598 (18.1)	376 (19.5)	39 (21.6)	68 (18.5)
Clinical					
HCC, n (%)	4,959 (85.7)	2,740 (82.7)	1,751 (90.8)	149 (82.3)	319 (86.9)[**]
Family history, n (%)	(N=3,257)				
No history	841 (25.8)	491 (25.1)	251 (25.2)	30 (32.6)	69 (31.9)[**]
Liver cancer[c]	63 (1.9)	38 (2.0)	17 (1.7)	1 (1.1)	7 (3.2)
Other cancer/not specified	827 (25.4)	561 (28.7)	224 (22.5)	14 (15.2)	28 (13.0)
Unknown/Missing	1,526 (46.9)	863 (44.2)	504 (50.6)	47 (51.1)	112 (51.9)
Behavioral					
Alcohol history, n (%)	(N=3,257)				
Never use	846 (26.0)	538 (27.6)	183 (18.4)	37 (40.2)	88 (40.7)[**]
Current use	1,177 (36.1)	756 (38.7)	361 (36.2)	19 (20.7)	41 (19.0)
Past use	56 (1.7)	6 (0.3)	48 (4.8)	2 (2.2)	0 (0.0)
Unknown/Missing	1,178 (36.2)	653 (33.4)	404 (40.6)	34 (37.0)	87 (40.3)
Tobacco history, n (%)	(N=3,257)				

Never user	650 (20.0)	393 (20.1)	153 (15.4)	38 (41.3)	66 (30.6)**
Current user	694 (21.3)	421 (21.6)	250 (25.1)	4 (4.4)	19 (8.8)
Past user	796 (24.4)	524 (26.8)	210 (21.1)	16 (17.4)	46 (21.3)
Unknown/Missing	1,117 (34.3)	615 (31.5)	383 (38.5)	34 (37.0)	85 (39.4)

Notes. †Race and ethnicity unknown or missing for n=140; % = column totals; NH=non-Hispanic; SD=standard deviation; *p<0.05, **p<0.0001; [a]Incidence rate age-adjusted to the 2000 U.S. standard population; [b]One-way ANOVA with post-hoc Bonferroni adjustment indicated that mean age was significantly different for NH White vs NH Black, NH White vs Hispanic, NH Black vs API, and API vs Hispanic; [c]Includes liver cancer only or liver and other cancer.

DISCUSSION

This analysis examined socio-demographic and clinical characteristics, and behavioral risk factors that could potentially explain the high liver cancer incidence in the D.C. metropolitan area. The overall incidence rate of liver cancer between 2013-2016 in the D.C. metropolitan area (8.2/100,000) was similar to the national incidence rate during a similar period (2014-2018) (8.6/100,000) (USCS, 2021). Incidence rates by sex (males: 12.6/100,000, females: 4.5/100,000) also mirrored national rates (males 13.1/100,000, females 4.7/100,000) (USCS, 2021), but patterns in incidence rates by race/ethnicity somewhat differed from national patterns. Like in the U.S., the incidence rate in the D.C. metropolitan area was also high among APIs (10.8/100,000 (D.C. region) vs 12.3/100,000 (U.S.)). However, non-Hispanic Blacks had the highest incidence rate in the D.C. metropolitan area (11.3/100,000), in contrast to the overall U.S., where Hispanics have the highest incidence rate (13.7/100,000) (USCS, 2021).

Stratified analyses revealed several other notable disparities by state/territory, sex, stage at diagnosis, and race/ethnicity. Racial disparities were far more pronounced in D.C., relative to MD and VA. In D.C., the incidence rate for non-Hispanic Blacks was more than four times the rate for non-Hispanic Whites. These geographic, sex and racial disparities in liver cancer incidence are likely driven by disparities in HCV. A previous study found patterns of HCV prevalence that correspond to our findings on HCC/ICC incidence by state/territory, sex, and race/ethnicity. D.C. had the highest HCV prevalence among males (3.1/100) and females (1.8/100) (Bradley et al., 2020). Furthermore, in D.C., the prevalence ratio of HCV for non-Hispanic Blacks to other racial and ethnic groups was 12.4, compared to a prevalence ratio of 2.2 for non-Hispanic Blacks nationally (all U.S. states and D.C) (Bradley et al., 2020). In our sample, HCV was the second most common primary comorbidity, reported in 4% of cases. Future studies could examine whether disparities in HCV incidence are in fact a key driver of racial disparities in liver cancer incidence.

Although a substantial proportion of cases were missing data on country of birth, and any findings pertaining to this variable should be interpreted with caution, it is noteworthy that D.C. had a higher proportion of foreign-born cases (11.1%) compared to MD (5.7%) and VA (5.6%). In immigrant populations, HBV is thought to be a key risk factor for liver cancer and studies conducted in the D.C. area have found a high prevalence of HBV in foreign-born individuals, particularly those born in Asia (Ha et al., 2019; Juon et al., 2019). In addition to hepatitis exposures, dietary exposure to aflatoxin is another known HCC risk factor for people born outside of the U.S. (Hamid et al., 2013; Smith et al., 2017). However, lack of adequate data on comorbidities, country of birth, and dietary exposures did not allow us to examine the associations between these variables. More complete and systematic collection of these variables by state cancer registries and hospital-based registries is needed. Partnering with community-based organizations that serve immigrant populations in the D.C. metropolitan area could help to ascertain the burden of liver cancer in foreign-born individuals. Additionally, this data could inform screening efforts for HBV and other known exposures, such as dietary aflatoxin. Prospective studies that monitor foreign-born individuals for the development of liver cancer or its intermediate markers are needed to determine the contribution of these risk factors to liver cancer incidence in the D.C. metropolitan area.

Consistent with previous studies, we found that males with HCC/ICC were diagnosed at a younger age, and were more likely to have a history of alcohol and tobacco use compared to females with HCC/ICC (Ladenheim et al., 2016; Wu et al., 2018). We also found that Hispanics made up a slightly higher proportion of cases among females compared to males. Two analyses using national data found that the incidence of liver cancer has stabilized in Hispanic men, but continues to increase in Hispanic women (Ryerson et al., 2016; Salvatore et al., 2019). However, the reason for this finding is unclear and more research is needed to identify sex differences in risk factors across racial and ethnic groups.

Other racial disparities identified included a lower mean age at diagnosis for non-Hispanic Blacks and Hispanics than other groups, which correspond with findings on racial and ethnic disparities in mortality (Ryerson et al., 2016). However, a large retrospective cohort study found that, on average, Hispanic patients had an older age at diagnosis compared to non-Hispanic Whites (Pomenti et al., 2020). A few studies among HCC patients have found that compared to other racial and ethnic groups, Hispanics are more likely to have modifiable metabolic risk factors, such as diabetes and hyperlipidemia, and less likely to have HCV or a history of tobacco use (Pomenti et al., 2020; Venepalli et al., 2017). Although we were unable to examine racial and ethnic differences in the distribution of comorbidities, we found that hypertension and diabetes were among the most commonly reported primary comorbidities overall. We also found that Hispanics were less likely to have a history of tobacco use. Thus, it is likely that different risk factors are relevant for different racial and ethnic groups in the D.C. metropolitan region, which has implications for liver cancer prevention approaches. In light of the growing evidence for the association between metabolic (Ren et al., 2019; Welzel et al., 2011) and behavioral risk factors (Petrick et al., 2018) and liver cancer risk, more data is urgently needed to identify their contribution to the increasing burden of liver cancer in the D.C. metropolitan area and inform tailored intervention approaches.

Disparities by stage at diagnosis included cancer site and insurance status. ICCs tended to be diagnosed at a later stage, likely owing to a lack of clear symptoms (Blechacz et al., 2011; Zhang et al., 2016). Consistent with previous research, we found that uninsured individuals more likely to be diagnosed at later stages (Wang et al., 2018). Lack of insurance may contribute to delays in seeking care and reduced utilization of preventative services, such as screening, which could lead to delayed detection of cancer.

Limitations

This analysis had several limitations. Lack of adequate data on several important variables, including country of birth, comorbidities, metabolic factors, and alcohol and tobacco use hindered our ability to examine differences in their distributions by state/territory, sex, stage of diagnosis, and race/ethnicity. As this analysis was cross-sectional and lacked a non-cancer comparison group, no causal conclusions can be made regarding the association between any risk factors and liver cancer incidence.

Strengths of this analysis included a large sample size. Additionally, the inclusion of cases from MD and VA provided a broader snapshot of the burden of liver cancer in the D.C. metropolitan area and highlighted differences in the profile of liver cases between D.C. and neighboring states, which can inform intervention approaches. We also separately estimated incidence rates for HCCs and ICCs. Although we did not identify major differences in ICC incidence rates across socio-demographic groups, other studies have documented sex and racial/ethnic differences in ICC incidence (Mosadeghi et al., 2016), highlighting the need to independently monitor HCC and ICC trends and risk factors.

Conclusions

Males, non-Hispanic Blacks and APIs are priority populations for liver cancer control efforts in the D.C. metropolitan area. Data on country of birth, comorbidities, and alcohol and tobacco use are urgently needed to inform tailored intervention approaches by state/territory, sex, and race/ethnicity. To address limitations in data availability from state cancer registries, hospital-based case control or cohort studies could provide more robust evidence for the association between a wider range of well-established and emerging socio-demographic, clinical and behavioral risk factors and the increasing burden of liver cancer in the D.C. metropolitan area.

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Authors' contributions

Research design, data acquisition, data analysis and writing of the manuscript: Krishnan, N.

Research design and critical revision: Robien, K., Abroms, L.C.

Critical revision: Le, D., Yang, Y.T., Aduli, F.

All authors approved the final version of the manuscript.

Availability of data and materials

Data cannot be shared due to the terms of the data use agreements with the D.C, MD and VA cancer registries

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Conflicts of interest

All authors declared that there are no conflicts of interest

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