The Epidemiology of Cancer and Benign Brain Tumors among Massachusetts (MA) Residents with Hepatitis B or Hepatitis C from 2002-2012

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OBJECTIVE: To evaluate the incidence of cancer and benign brain tumors cases with hepatitis B or C infection in Massachusetts from 2002-2012

BACKGROUND:

Hepatitis B (HBV) is a liver infection caused by the hepatitis B virus. Of those infected, 10% progress to a chronic infection and can pass the virus to others via sexual contact and contact with infected blood, including needle sharing to inject drugs. Pregnant women can also pass the infection to their babies at birth (maternal transmission).[1]

Hepatitis C (HCV) is a liver infection caused by the hepatitis C virus. As opposed to hepatitis B, most people who get infected progress to a chronic infection. Risk factors for transmission include receiving infected blood products before widespread screening in 1992, needle sharing to inject drugs, and maternal transmission. Sexual transmission is possible, but rare.[1]

Nearly 100,000 HCV and 30,000 HBV infected people were reported to the MA Department of Public Health (MDPH) from 2002 to 2012.

Hepatitis B and C and Cancer:

- **The liver inflammation from chronic HBV or HCV infection can cause scarring of the liver which can lead to cirrhosis of the liver and cancer.**
- **The association of liver cancer and HBV was first proposed in 1972, shortly after the discovery of HBV. [2]**
- **The association of liver cancer and HCV was established soon after the discovery of HCV in 1989. [3]**
- **Recent studies have shown an increased risk of liver cancer among HCV infected people ranging from 23 to 35-fold. [3]**
- **Other studies have shown associations between HBV or HCV infection and non Hodgkin lymphoma (NHL) and lung cancer. [3,4]**

Linking HBV and HCV with Cancer:

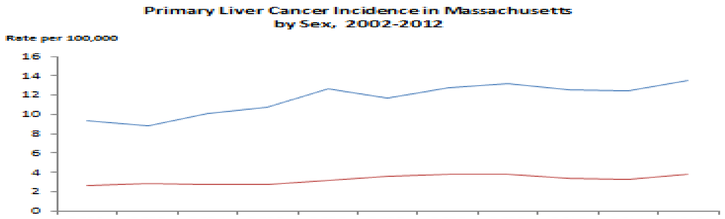
- **Hepatitis B vaccination can prevent maternal, blood, and sexual transmission of the virus. There is currently no hepatitis C vaccine, but the virus can be eliminated with novel therapies.**
- **Effective treatments exist for those infected with HBV or HCV to prevent progression to liver cancer.**
- **This match gives us the opportunity to explore the association of HBV and HCV with liver cancer and examine trends in liver cancer from 2002 to 2012 as well as assess associations with other cancers.**

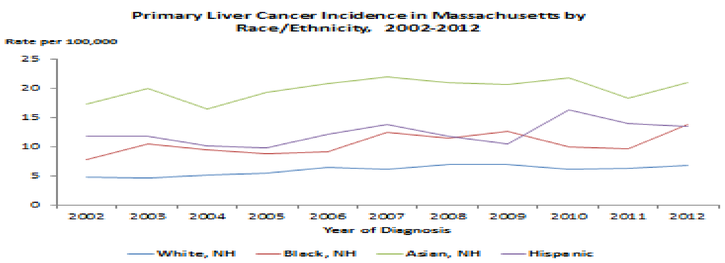
METHODS

- **HCV and HBV data are collected using a web based system, the MA Virtual Epidemiologic Network (MAVEN). MAVEN is maintained by the MDPH. Demographics, clinical characteristics, risk history, and viral hepatitis laboratory results are collected when available.**
- **The Massachusetts Cancer Registry (MCR) collects information on all newly diagnosed cases of *in situ* and invasive cancers and benign brain tumors among MA residents from health care facilities and 40 states and territories**
- **HBV and HCV and MCR data were matched on name and date of birth using Link Plus software, developed by the CDC's National Program of Cancer Registries.**
- **Percentages of individual cancers among HBV or HCV infected MCR cases were compared with percentages among all MCR cases. The population proportions were compared using a z test to determine statistical significance at the p=.05 level.**

RESULTS – Liver Cancer Incidence:

- **The incidence rates for both males and females in Massachusetts increased significantly from 2002-2012 (APC=3.9 and APC=3.6, respectively).**
- **There were significant increases in trends for white, non-Hispanics (NHs) (APC=6.5) and black, NHs (APC=3.3).**





RESULTS FROM HBV/HCV/MCR Linkage:

HCV cases reported 2002-2012 (n=94,701)

MCR cases diagnosed from 2002-2012 (n=463,700)

HBV cases reported 2002-2012 (n=28,070)

5.2% of HBV (n=1,471) and 5.8% of HCV (n=5,499) cases had a benign brain tumor or cancer diagnosis from 2002 to 2012.
1.5% (n=6,970) of MCR cases had an HBV or HCV infection reported from 2002 to 2012

Cancers with HBV or HCV with Significantly Higher Proportional Comparisons* to all Cancer Cases, 2002-2012:	
MALES:	**FEMALES:**
(% of HBV or HCV cancers vs.% of all cancers)	**(% of HBV or HCV cancers vs.% of all cancers)**
Liver Cancer – 28% versus 2% in MCR	**Liver Cancer – 10% versus 1% in MCR**
Non Hodgkin Lymphoma (NHL)-6% versus 4% in MCR	**NHL – 5% versus 3% in MCR**
	Lung Cancer – 13% versus 12% in MCR

* - indicates percentage was significantly elevated (p<.05) compared to percentage of all cancer cases.

RESULTS - Cancer and HBV or HCV Infection:

- **33% and 16% of liver cancer cases diagnosed among males and females, respectively, from 2002-2012 were infected with HBV or HCV.**
- **Liver cancer was the most common cancer among male and third most common among female cancer cases infected with HBV or HCV.**
- **Liver cancer and NHL among males and females and lung cancer among females were disproportionately represented among cancer cases infected with HBV or HCV compared to their proportional representation among all MCR cases .**
- **A significantly higher percentage of cancers among HBV or HCV infected Asian, NH males were liver (47%) compared to 27% of white, NH, 25% of black, NH, and 37%Hispanic males .**
- **A significantly higher percentage of cancer among HBV or HCV infected Asian, non-Hispanic (NH) females were liver (23%) compared to 9% of white, NH, 12% of black, NH, and 15% of Hispanic females .**

CONCLUSIONS

- **Among MCR cases infected with HBV or HCV, liver cancer and NHL were disproportionately represented among males and females while lung cancer was disproportionately represented among female cases.**
- **HBV and HCV have strong lymphotropic properties (stimulating or acting on lymphatic system) and data have shown a causal association with NHL.[4]**
- **A cohort study of inpatient Danish patients found HCV to be associated with lung cancer not controlling for smoking.[3]**
- **The incidence of liver cancer has increased significantly from 2002 to 2012. The extent of the role of HBV and HCV in this increase warrants further investigation.**
- **The BIDLS and the MCR will continue to analyze associations between HBV or HCV infection and cancer and expand to 2013 data.**

LIMITATIONS:

- **Data were not collected on MCR cases without an HBV or HCV infection so comparisons were limited to the HBV or HCV infected MCR cases versus all MCR cases.**
- **Due to manual laboratory reporting prior to the use of electronic laboratory reporting and MAVEN in 2006, it is expected that data prior to that time is incomplete, resulting in fewer records available for the match and the potential for an underestimation of the association with cancer.**
- **HBV and HCV diagnosis date reflects the date of symptom onset, specimen collection date for the first lab result, or MDPH notification date, whichever is the earliest, resulting in a possible misclassification of year of hepatitis infection.**
- **Likewise, MCR diagnosis date reflects the data the tumor was first diagnosed and not when the tumor first became malignant.**

References:

[1]MDPH Fact Sheets on Hepatitis B and Hepatitis C.
[2] Block, T et al., A historic perspective on the discovery and elucidation of the hepatitis B virus, Antiviral Research, 131 (2016) 109-123.
[3]Omland, L et al., Hepatitis C virus infection and risk of cancer: a population-based cohort study. Clinical Epidemiology 2010:2:179-186.
[4]Datta, S et al. Hepatitis viruses and non-Hodgkin's lymphoma: A review,. World Journal of Virology, 2012:1(6):162-163, 2012.

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