Hepatitis C Screening Among Baby Boomers at Risk for Hepatitis B


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Background and Aims:
The Centers for Disease Control (CDC) recommends that baby boomers (adults born between 1945-1965) be screened for hepatitis C (HCV). Patients with HCV are at increased risk of co-infection with hepatitis B (HBV). We investigated HCV screening rates in a baby boomer cohort with chronic HBV or at high-risk for HBV infection from a large healthcare system.
Methods:
We conducted a retrospective cohort analysis of 792 baby boomers, evaluated at New York Langone (NYU) from 2012-2017 with chronic HBV or at high-risk for HBV infection. CDC guidelines were used to assess whether a patient was considered at high-risk for HBV infection. Medical history including hepatitis serology was extracted from electronic health records. Multiple logistic regression was used to identify clinical risk factors independently associated with HCV screening.
Results:
Among 792 patients, 419 (52.9%) were screened. Multivariate regression of factors significant (P<.05) on univariate analysis revealed that health insurance, end-stage renal disease (ESRD), chronic liver disease (CLD), diabetes mellitus (DM) and current alcohol use were each independently associated with HCV screening. The strongest predictors of HCV screening were ESRD (OR: 3.346; 95% CI: 1.688-6.634) and CLD (OR: 3.027; 95% CI: 2.102-4.359), while DM (OR: 0.680; 95% CI: 0.497-0.930) was associated with a decreased likelihood of prior screening.
Conclusion:
In a retrospective study of patients at NYU, the baby boomer cohort with chronic HBV or at high-risk for HBV infection are not being adequately screened for HCV. Improvement in HCV screening should be strongly encouraged by all healthcare systems.

INTRODUCTION

Hepatitis C virus (HCV) is a major public health issue in the United States and worldwide. It is one of the leading causes of cirrhosis and hepatocellular carcinoma (HCC) and the most common indication for liver transplantation in the United States.[1] From 2003 to 2010 an estimated 2.2-3.2 million Americans were chronically infected with HCV, with a high proportion of people unaware of their infection (estimates range from 45-85%).[2,3] Studies show that 76% of people diagnosed with HCV infection in the United

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States are in the "baby boomer" cohort (those born between 1945 and 1965).

Given the strong incidence of HCV within this birth cohort, in 2012 the Centers for Disease Control and Prevention (CDC) recommended one-time testing for HCV in baby boomers without specific HCV risk factors.[3,4] Application of current guidelines for risk-based screening would result in an estimated 25% of the US adult population being tested. [5] Initial evaluation should include a standard anti-HCV antibody serologic test, with a reactive result followed by a confirmatory nucleic acid test or polymerase chain reaction for HCV ribonucleic acid. One-time testing of baby boomers has been estimated to identify 800,000 infections, with subsequent treatment and management potentially avoiding up to 120,000 HCV-related deaths.[6]

Screening rates in this birth cohort in patients with chronic hepatitis B virus (HBV) or in those at high-risk for HBV infections have not been well documented. HCV and HBV patients share common risk factors (intravenous drug use, hemodialysis treatment and human immunodeficiency virus infection). About 2-10% of HCV-positive patients are found to be positive for HBV surface antigen, and 5-20% of patients with HBV are found to be anti-HCV positive.[7-11] Per CDC criteria, all individuals in the birth cohort should be screened for HCV regardless of specific risk factors, yet a better understanding of screening rates in patients with chronic HBV or at high-risk for HBV infection is needed (Table 1). A greater awareness of HCV screening failures could potentially lead to improved screening rates, better HCV and HBV management practices and patient care.

In this study, we report HCV screening rates and independent clinical factors associated with screening adherence in a diverse birth cohort patient population with chronic HBV or at high-risk for HBV infection.

MATERIALS AND METHODS

A retrospective analysis was performed using electronic medical records (EMR) of patients presenting at New York Langone Health between 2012 and 2017 with chronic HBV or at high-risk for contracting HBV infection. Patients were considered at high-risk for contracting HBV infection if they had a medical comorbidity or activity that was classified as high-risk by CDC criteria (Table 1).[4] Medical conditions were identified using ICD-10 classification and patients were randomly selected to be included in the study. Patients were excluded from the study if they were not born between 1945 and 1965 and did not have one of the documented risk factors for HBV infection or a history of chronic HBV infection.

Patient information was obtained from the EMR by individual chart review and entered into a password-protected, HIPPA-compliant and de-identified REDCap repository (Vanderbilt University, Nashville, TN). Patient demographics and clinical history were compared between a cohort of patients who were screened for HCV versus a cohort of patients who were not screened for HCV. Screening was considered to have been performed if HCV serology was listed in the EMR

Table 1. Center for Disease Controls indications to be considered high-risk for contracting HBV infection

You have sex with more than one partner or are sexually active and not in a long-term monogamous relationship (High risk sexual behavior)
You seek care in a clinic for sexually transmitted diseases, HIV testing or treatment, or drug treatment
Men who have sexual contact with other men
You share needles, syringes, other drug-injection equipment or inject drugs
You are a hemodialysis patient or have end-stage renal disease
You have HIV infection
You have chronic kidney disease
You have chronic liver disease
You have diabetes

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(either positive or negative for HCV antibody). Results are presented as frequencies or percentages, with categorical variables compared using chi-square and continuous variables compared using two-sided Student's t-test or Mann–Whitney U test, as appropriate. Covariates found significant on univariate analysis were inputted into a multiple logistic regression with HCV serology listed as the binary dependent variable. The Hosmer-Lemeshow statistic was used to assess model calibration. Statistical analysis was performed using SigmaPlot v10.2 (Systat Software, San Jose, CA). The Institutional Review Board of New York University Langone Health approved this study.

RESULTS

A total of 1,100 high-risk patients were evaluated in the initial data set, of which 792 were born between 1945 and 1965 and included in the final study (Figure 1). Patient demographics for the entire study cohort are listed in Table 2, showing that most patients were older (mean age: 61.7 years), male (63.9%) and overweight (median BMI: 27.4 kg/m2). The study population was socio-economically diverse with 51.9% of respondents reporting non-white ethnicity and 43.6% lacking private health insurance.

High-risk medical conditions for the study population are listed in Table 3. Diabetes mellitus (DM) (46.3%; median hemoglobin A1c: 6.4%; 25-75th quartiles: 5.6-7.7%), chronic kidney disease (CKD) (43.7%) and high-risk sexual behavior (27.2%) were the most commonly reported comorbidities. End-stage liver disease (ESLD) was present in 12.9% of patients with 9.2% listed for liver transplant with median Model for End-Stage Liver Disease (MELD) score of 13 (25-75th quartiles: 9-21). A total of 37 (4.7%) patients died during the data collection period, including 13 (1.6%) from liver-related etiologies. Most patients (75.8%) had two or more high-risk conditions, while 39.6% had 3 or more conditions. Importantly, a history of intravenous drug use (2.8%) or alcoholic hepatitis (3.2%) was reported in only small subset of these patients. Other medical comorbidities are

Table 2. Patient demographics of entire study cohort – Comparison between those screened for Hepatitis C and those that were not

Demographic	Entire cohort	Screened for Hepatitis C	Not screened for Hepatitis C	P-value
Mean age (SD)	61.7 (5.9)	61.5 (5.6)	61.9 (6.1)	0.314
Male	63.9%	65.4%	62.2%	0.390
Body Mass Index				0.144
<25	31.7%	35.4%	27.5%	
25-30	33.9%	32.7%	35.2%	
30.1-35	20.5%	19.5%	21.7%	
>35	13.9%	12.4%	15.6%	
Race				0.117
White	48.1%	45.1%	51.5%	
Black	18.4%	18.4%	18.5%	
Hispanic	12.0%	14.3%	9.4%	
Other	21.5%	22.2%	20.6%	
Insurance				0.004
Private	56.4%	58.0%	54.7%	
Medicare	32.6%	34.4%	30.6%	
Medicaid	7.3%	6.0%	8.8%	
Uninsured	3.7%	5.9%	5.6%	

listed in Table 4. Cardiovascular risk factors such as hypertension (58.0%), hyperlipidemia (42.9%) and a history of tobacco use (40.2%) were highly prevalent in our patient population. Primary care physicians evaluated a total of 29.4% of patients at least annually, while a gastroenterologist evaluated 26.4% of patients at least yearly.

A total of 419 patients (52.9%) were screened for HCV while 373 patients (47.1%) were not screened. Univariate analysis revealed that patients who were screened for HCV more frequently had private health insurance (58.0% vs 54.7%; *P*=0.004; Table 2), history of intravenous drug use (4.1% vs 1.3%; *P*=0.035; Table 3) or were currently using alcohol (35.1% vs 25.0%; Table 4). Patients who were screened were more likely to have a significant liver history including chronic liver disease (CLD) (44.9% vs 22.0%; *P*<0.001; Table 4) or ESLD (18.4% vs 6.7%; *P*<0.001; Table 3). Patients with HCV screening also presented with a higher rate of renal pathology including CKD (50.4% vs 36.2%; *P*<0.001) and end-stage renal disease (ESRD) (44.9% vs 29.2%; *P*<0.001), and less frequently with DM (40.3% vs 53.1%; *P*<0.001; Table 3).

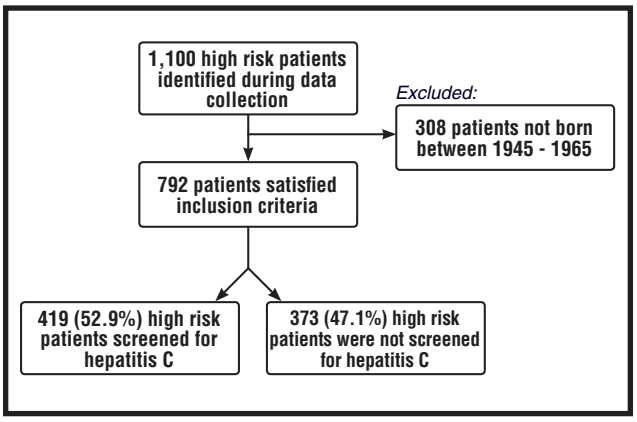

Figure 1. Study design showing patient selection

Multivariate regression of factors significant (*P*<0.05) on univariate analysis revealed that health insurance, ESRD, CLD, ESLD, DM and current alcohol use were each independently associated with HCV screening (Model 1; Table 5). The strongest predictors of HCV screening were ESRD (OR: 3.346; 95% CI: 1.688-6.634) and CLD (OR:

Table 3. High-risk medical conditions of entire study cohort – Comparison between those screened for Hepatitis C and those that were not

High risk condition	Entire cohort	Screened for Hepatitis C	Not screened for Hepatitis C	P-value
Intravenous Drug Use	2.8%	4.1%	1.3%	0.035
Men who have Sex with Men	6.3%	7.6%	4.8%	0.140
End Stage Renal Disease	37.5%	44.9%	29.2%	<0.001
Chronic Kidney Disease	43.7%	50.4%	36.2%	<0.001
Chronic Liver Disease	34.1%	44.9%	22.0%	<0.001
Alcohol Hepatitis	3.2%	4.5%	1.6%	0.032
Primary Sclerosing Cholangitis	0.5%	0.2%	0.8%	0.536
Primary Biliary Cirrhosis	0.9%	0.2%	1.6%	0.094
Cryptogenic Liver	0.8%	1.0%	0.5%	0.789
Hemochromatosis	0.4%	0.2%	0.5%	0.920
Non-Alcoholic Fatty Liver Disease	10.4%	11.9%	8.6%	0.153
Non-Alcoholic Steatohepatitis	1.4%	1.7%	1.1	0.679
Autoimmune hepatitis	0.6%	1.0%	0.3%	0.442
End Stage Liver Disease (Cirrhosis)	12.9%	18.4%	6.7%	<0.001
Human Immunodeficiency Virus	19.4%	17.2%	22.0%	0.107
High risk sexual behavior	27.2%	28.4%	25.7%	0.446
Diabetes Mellitus	46.3%	40.3%	53.1%	<0.001

Table 4. Other medical comorbidities and characteristics of entire study cohort – Comparison between those screened for hepatitis C and those that were not

Comorbidity	Entire cohort	Screened for Hepatitis C	Not screened for Hepatitis C	P-value
Model For End-Stage Liver Disease[1] (med; 25-75%ile)	13 (9-21)	13 (8-21)	12 (9-21)	0.763
Acute Liver Failure	0.4%	0.5%	0.3%	0.920
Hyperlipidemia	42.9%	42.2%	43.7%	0.733
Hypertension	58.0%	58.0%	57.9%	0.962
Coronary artery disease	18.2%	17.7%	18.8%	0.756
Congestive heart failure	7.7%	6.4%	9.1%	0.203
Chronic obstructive pulmonary disease	5.2%	4.5%	5.9%	0.482
Peripheral artery disease	4.3%	3.6%	5.1%	0.382
Cerebral vascular accident	6.8%	6.9%	6.7%	0.985
Psychiatric disorder	11.5%	12.6%	10.2%	0.331
Low-density lipoprotein (med; 25-75%)	84 (64-110)	85 (66-111)	79 (59-109)	0.230
High-density lipoprotein (med; 25-75%)	48 (38-57)	47 (38-57)	49 (39-56)	0.758
Current tobacco user	8.3%	7.4%	9.4%	0.379
Current or former tobacco user	40.2%	43.0%	37.0%	0.102
Current Alcohol use	30.3%	35.1%	25.0%	0.002
Cancer (any)	17.7%	19.3%	15.8%	0.230

[1]Only available for 12.2% patients

3.027; 95% CI: 2.102-4.359), while DM (OR: 0.680; 95% CI: 0.497-0.930) was associated with a decreased likelihood of prior screening. The Hosmer-Lemeshow statistic was not significant (P=.215), indicating that the regression fit the data. Using more restrictive modeling where only the most significant (P<0.01; Model 2) factors were inputted into the multivariate analysis, there was no appreciable change in the study findings, suggesting that intravenous drug use and alcoholic hepatitis do not change the likelihood of HCV screening.

In addition, patients who were not screened for HCV were less frequently vaccinated against hepatitis A (12.8% vs 76.1%; P<0.001) or HBV (6.3% vs 42.9%; P=0.009). These patients were less likely to utilize health care resources such as annual primary care evaluation (19.8% vs 38.0%; P<0.001), emergency department visits (26.0% vs 39.4%), or a gastroenterology specialist consultation (13.4% vs 38.0%; P<0.001). Listing for liver transplant was also less likely (5.1% vs 12.9%; P<0.001) in patients who were not screened for HCV, despite no difference in MELD score between groups (median: 13 vs 12: P=0.763). All-cause mortality (6.9% vs 2.1%; P=0.003) and liver-related mortality (2.6% vs 0.5%; P=0.042) were significantly increased in patients who were screened for HCV.

DISCUSSION

Despite CDC recommendations concerning practice management guidelines for HCV and HBV, baby boomers with chronic HBV or at high-risk for HBV infection are not being adequately screened for HCV. These patients are also less frequently vaccinated for other conditions such as

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hepatitis A or HBV, less likely to utilize primary care or specialty services and less likely to be listed for liver transplant.

Most individuals are unaware of their HCV and HBV infection status.[12] This study retrospectively evaluated HCV screening patterns in a diverse, birth cohort in the New York area, which revealed a screening non-adherence rate (52.9%) more than twice that reported in a previous study.[13] This study also identified socioeconomic risk factors such as insurance status that were independently associated with reduced HCV screening. These patients were also less likely to utilize health care resources such as primary care or gastroenterology subspecialist services. Patients who were not screened for HCV were also significantly less likely to be listed for liver transplant, despite no differences in MELD score between patient groups. Thus, socioeconomic factors can impair access to appropriate medical care, often resulting in non-adherence with HBV and HCV practice management guidelines and adverse patient outcomes. Larger studies with longer patient follow-up are needed in order to assess whether socioeconomic factors in the at-risk HBV birth cohort results in increased all-cause or liver-related mortality. Due to the 2012 CDC recommendations on HBV screening, the New York State legislation enacted a public health law in 2014 that requires all health care providers to offer HCV screening. Thus, hepatitis screening and virus detection are expected to improve.[14,15]

HBV and HCV co-infection is frequent due to shared risk factors and modes of transmission such as intravenous drug use. Previous studies have demonstrated that HBV/HCV co-infected patients carry a greater risk of advanced liver disease, cirrhosis and hepatocellular carcinoma in comparison to monoinfected patients.[11,16] Early detection and treatment of HBV and HCV could potentially prevent progression of liver disease, decrease the need for liver transplantation and reduce the risk for overall liver disease-related morbidity and mortality.[17,18] With only 52.9% of eligible patients appropriately screened for HCV, our study identifies a substantial potential area of improvement in practice management that could significantly improve patient care. However, increasing patient and clinician awareness of viral liver disease continues to pose challenges, which may be attributed to a number of factors in our diverse study population including lack of physician emphasis and knowledge regarding current screening recommendations, cultural barriers and socioeconomic elements constraining access to appropriate medical care.[19]

Few studies have focused on HBV and HCV screening and vaccination rates in at-risk HBV patients in the baby boomer cohort.

Viral hepatitis serology is frequently completed in order to properly manage chronic HBV infection. Despite the low rate of screening in our high-risk cohort, HCV screening is performed even less frequently in the general birth cohort. One 2004-2008 study of the commercially-insured birth cohort population in New York estimated an HCV

Table 5. Multiple logistic regression showing odds ratio for variables independently associated with Hepatitis C screening

	Model 1 (P<0.05)			Model 2 (P<0.01)		
Variable	**Odds ratio**	**95% CI**	**P-value**	**Odds ratio**	**95% CI**	**P-value**
Health insurance	0.798	0.652-0.977	0.029	0.802	0.656-0.980	0.031
Chronic Kidney Disease	1.122	0.581-2.167	0.732	1.088	0.563-2.103	0.802
End Stage Renal Disease	3.289	1.662-6.511	<0.001	3.346	1.688-6.634	<0.001
Chronic Liver Disease	2.898	2.004-4.192	<0.001	3.027	2.102-4.359	<0.001
End Stage Liver Disease	2.682	1.501-4.791	<0.001	2.554	1.495-4.363	<0.001
Diabetes Mellitus	0.688	0.502-0.942	0.020	0.680	0.497-0.930	0.016
Current alcohol use	2.069	1.457-2.938	<0.001	2.053	1.449-2.907	<0.001
Intravenous Drug Use	2.146	0.741-6.218	0.160	--	--	--
Alcoholic hepatitis	0.841	0.278-2.544	0.759	--	--	--

screening rate of 17.6%.[20] Another study examining hospitalized patients reported that only 35% of eligible patient underwent HCV screening.[15] Certainly, while the presence of chronic HBV or risk factors for HBV infection contribute to the differences in screening, it is important to note that screening rates for both the general and high-risk population remain low.

This study was subject to several limitations. Retrospective reviews of EMR data are limited by the ability to extract relevant data from the patient record. It is possible that patients were screened by outside providers or primary care facilities that were not accessible in the EMR, raising the possibility that true HCV screening rates are underestimated. Another possibility is that appropriate screening was indeed performed, but not accurately listed in the patient EMR. Although the CDC recommends one-time HCV screening in all individuals born between 1945-1965 regardless of risk, clinical judgment and cognitive bias may often direct screening practices. Other potential biases include selection bias and errors in patient sampling. However, these biases are believed to be mitigated by the size of our sample population. Patients also may not know their complete medical history or choose not to divulge their behaviors to the attending physician, resulting in the underestimation of the high-risk patient population. For example, disclosure of past or current intravenous drug use is often not disclosed or under-reported. With recent reports of HCV infections tripling between 2010 and 2015, with highest rates among 20-29 year-old users of illicit substances, it is even more important to thoroughly review and document a patient's medical history.[4] Lastly, during the study one of the academic hospitals in our health system underwent a change in EMR and information on some patients could therefore not be obtained. One subject that remains to be explored is how to improve HCV screening awareness and specific barriers to screening.

CONCLUSION

This study reveals that HCV screening in patients in the birth cohort with chronic HBV or at high-risk for HBV infection remains low despite CDC practice recommendations. Due to the fact that HBV/HCV co-infection is not uncommon and may lead to more rapid progression to advanced liver disease compared to monoinfection, including HCC, it remains imperative to properly screen these individuals to allow for early recognition and management. Greater emphasis should be placed on increasing physician awareness of CDC guidelines advocating for one-time HCV screening of people born between 1945-1965, particularly those with chronic HBV or at high risk for infection. However, challenges remain to identify methods that improve physician adherence with these recommendations. ■

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