Original Contribution

Low Rates of Hepatitis B Virus Screening at the Onset of Chemotherapy

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Abstract

Purpose: Patients with hepatitis B virus (HBV) infection are at risk for reactivation after chemotherapy. Effective prophylaxis is available but depends on detection of prior infection. Previous studies have shown low screening rates, but no large-scale US studies have been conducted. We sought to determine predictors of screening and positive HBV test results in patients receiving chemotherapy.

Methods: We conducted a retrospective cohort study of patients with newly diagnosed cancer who received chemotherapy between January 2004 and September 2007 at a comprehensive cancer center. We determined rates and predictors of screening for HBV infection with HB surface antigen (HBsAg) and antibody to hepatitis B core antigen (anti-HBc) tests as well as the prevalence and predictors of positive results. We explored rates of acutely elevated liver function tests and liver decompensation after chemotherapy.

Results: Of 10,729 new patients who received chemotherapy, 1,787 (16.7%) underwent HBsAg or anti-HBc screening. Less than 20% of patients with HBV risk factors were screened, even though their odds of HBV infection were increased four-fold compared with those without risk factors. The prevalence of chronic HBV infection was 1.5%. whereas 7.4% had positive anti-HBc only. The strongest predictors of HBV screening were having a history of HBV infection, hematologic malignancy, and rituximab treatment ($P < .001$). Asian ethnicity was not a significant predictor of screening, despite being a strong and highly significant predictor of positive test results ($P < .001$).

Conclusion: HBV screening among patients with cancer is low, especially among those known to be at high risk for HBV infection. Future research directed toward identifying best screening methods and HBV risk tools will be necessary to reduce the risk of reactivation of HBV infection after chemotherapy.

Introduction

Patients with chronic hepatitis B virus (HBV) infection are at risk for reactivation after chemotherapy.[1,2] Patients who have recovered from previous HBV infection and patients with occult chronic HBV infection are also at risk for reactivation.[3] Reactivation may cause interruptions in chemotherapy and, in severe cases, lead to liver failure and death.[4-6] Administration of oral anti-HBV medications before chemotherapy can reduce the risk of reactivation by more than 79% in patients with chronic HBV infection[7]; however, prophylaxis can only be initiated after HBV infection has been identified.

In the United States, the prevalence of chronic HBV infection as manifested by positive results on both hepatitis B surface antigen (HBsAg) and immunoglobulin G antibody to hepatitis B core antigen (anti-HBc) testing is less than 1% overall[8] but may be as high as 3% to 9% among high-risk groups.[8,9] The US prevalence of convalescent or occult chronic HBV infection as manifested by a negative HBsAg test result but a positive anti-HBc test result has been reported to be 5% to 8% overall[10-12] and up to 15% to 46% in some high-risk groups.[13,14]

There is general agreement about the importance of HBV screening among patients with cancer; however, there are differing opinions about the best screening approach. The Centers for Disease Control and Prevention (CDC) has recommended that all patients be screened for HBV infection before administration of any immunosuppression,[8] a recommendation endorsed by the Institute of Medicine.[15] The National Comprehensive Cancer Network has recommended that patients undergoing intensive immunosuppressive therapies be screened for prior HBV infection.[16] The American Association for the Study of Liver Diseases has recommended that all persons at high risk for HBV be screened for prior HBV infection before chemotherapy.[17] And the American Society of Clinical Oncology (ASCO) has recommended that only certain patients—those at high risk for HBV infection or those who will be receiving highly immunosuppressive therapies such as stem-cell transplantation or rituximab—be screened for HBV infection before chemotherapy.[18] Despite differences about which patients should be screened, all guidelines indicate that some form of systematic screening is needed to identify patients at risk for reactivation so that prophylaxis may be initiated. We hypothesized that patients with cancer with risk factors for HBV infection are not being systematically screened for HBV at the onset of chemotherapy. We tested our hypothesis by retrospectively studying determinants of HBV screening and test results in a cohort of patients with newly diagnosed cancer who received chemotherapy at The University of Texas MD Anderson Cancer Center (Houston, TX).

Methods

Patient Identification

In this retrospective cohort study, we used the MD Anderson Tumor Registry, Pharmacy, Laboratory Results, and Patient Account databases. This study was approved by our institutional review board, which waived informed consent requirement. We reviewed the tumor registry to identify a cohort of patients with newly diagnosed cancer registered between January 1, 2004, and September 30, 2007. We included patients age ≥ 18 years who had a new diagnosis of cancer and were anticipating first administration of chemotherapy at MD Anderson.

Demographics

Through the tumor registry, we obtained information on age, sex, race/ethnicity, and date of birth. We reported age as a continuous variable and ethnicity as white, black, Hispanic, Asian, or other. For patients with ethnicity classified as other, we used the patient birthplace to assist in classification of Asian race, a practice that has been used in other studies, especially in situations where multiple Asian groups have been studied.[19,20] Second, we used Asian surnames to find Asian patients who might have been incorrectly classified as other. This method has been successfully used in previous studies on cancer control issues to identify Asian Americans in large administrative databases.[19-21]

Types of Cancer and Chemotherapy

Using the tumor registry, we classified malignancies as solid tumors or hematologic malignancies (acute leukemia, chronic leukemia, Hodgkin's lymphoma, non-Hodgkin's lymphoma, other hematologic system cancer, multiple myeloma, and leukemia–not otherwise specified). Liver and bile duct cancers were grouped together as primary liver cancers. In subgroup analyses, we excluded these patients because of the etiologic relationship between HBV infection and primary liver cancers. We classified solid tumors into three stage categories: local or locally advanced disease, distant metastases, and unstaged disease. Because stem-cell transplantation is not routinely captured in our patient account database, we did not include it in this analysis.

We classified chemotherapy agents according to the American Cancer Society classification[22] (Appendix Table A1, online only). Using the pharmacy database, we included chemotherapy delivered by intravenous, intramuscular, subcutaneous, intraperitoneal, or intra-arterial routes but not by enteral tube or unknown routes. We excluded oral chemotherapy because we were not able to monitor adherence. We excluded patients who received investigational chemotherapy as part of a clinical trial because screening might be required by protocol and not represent usual physician practices.

We identified the first time that a patient received chemotherapy at our institution (first administration) and then searched for another administration at least 4 but fewer than 8 weeks after the first administration (second administration). Any chemotherapy drug administered within the first 7 days after first or second chemotherapy administration was included.

HBV Risk Factors and History

Through the medical informatics database, patients with at least one International Classification of Diseases, version 9 (ICD-9), diagnosis code related to nonspecific hepatitis, other liver conditions, hepatitis C virus (HCV), or human immunodeficiency virus infection anytime before HBV screening test or second chemotherapy were considered to have a risk factor for HBV infection. Patients who had an ICD-9 code for HBV entered before the first HBV screening test were considered to have a history of HBV infection. The ICD-9 codes are detailed in Table 1.

Outcome Measures

We searched the laboratory results database for evidence of HBsAg or anti-HBc testing (Ortho-Clinical Diagnostics, Rochester, NY). To comprehensively capture screening efforts, we defined screening as an HBsAg or anti-HBc test ordered in the period from 2 months before the first chemotherapy administration to receipt of the second administration. We defined a positive HBV test result as a positive result on HBsAg or anti-HBc testing or both tests. We did not include antibody to hepatitis B surface antigen (anti-HBs) because it was not routinely tested during the study period. We considered patients with positive HBsAg and anti-HBc to have chronic HBV infection. At the physician's discretion, HBV DNA testing was performed in patients who tested positive for HBsAg or anti-HBc. At our institution, although there is no official policy on HBV screening, several clinics order screening tests in the routine care of patients with hematologic malignancies; however, physicians must order these tests themselves.

Not all patients with HBV infection had HBV DNA level at baseline or during chemotherapy available, and thus we were not able to fully characterize reactivation. Instead, we described clinical outcomes of acute abnormalities of liver tests and liver decompensation, although these outcomes do not substitute for reactivation. Patients with ALT ≥ 100 IU/L and total bilirubin ≥ 2.5 mg/dL anytime after chemotherapy (until death or end of data period [April 2011]) were categorized as having abnormalities of liver tests. Patients with ALT ≥ 100 IU/L plus international normalized ratio ≥ 1.5, ascites, or encephalopathy were categorized as having liver decompensation.

Statistical Analyses

Primary outcomes were prevalence of HBV screening and positive HBV test results during the screening period. We used χ^2 tests to examine characteristics of patients who were screened compared with those who were not. We used SAS software, version 9.13 (SAS Institute, Cary, NC), for statistical analyses. An exploratory two-stage method was used to identify factors predictive of outcomes. First, through univariate analysis, we assessed the associations of these outcomes with age, sex, ethnicity, US residence, risk factors for HBV infection, history of HBV infection, cancer type, and chemotherapy type to identify clinically relevant predictors. Second, potential predictors with $P \leq .20$ were entered into multivariable logistic regression models to ascertain

Table 1. Characteristics of the Study Population by HBV Screening Status

Characteristic	Total (N = 10,729)		HBV Screening: Yes (n = 1,787)		HBV Screening: No (n = 8,942)	
	No.	%	No.	%	No.	%
Age, years						
Mean	54.9		51.5		55.5	
SD	13.8					
Sex						
Male	4,866	45.4	1,060	21.8	3,806	78.2
Female	5,863	55.6	727	12.4	5,136	87.6
Ethnicity						
White	7,810	72.8	1,310	16.8	6,500	83.2
Hispanic	1,279	11.9	230	18.0	1,049	82.0
Black	1,138	10.6	139	12.2	999	87.8
Asian	266	2.5	45	16.9	221	83.1
Other	236	2.2	63	26.7	173	73.3
US residence	10,428	97.2	1,716	16.5	8,712	83.5
History of HBV infection*	95	0.9	65	68.4	30	31.6
HBV risk factors†	2,612	24.3	513	19.6	2,099	80.4
Cancer type						
Solid tumor	9,009	84.0	555	6.2	8,454	93.8
Hematologic malignancy	1,720	16.0	1,232	71.6	488	28.4
Chemotherapy type						
Chemotherapy/ nonimmunotherapy	8,315	77.5	887	10.7	7,428	89.3
Immunotherapy, excluding rituximab	1,293	12.1	100	7.7	1,193	92.3
Rituximab	1,121	10.4	800	71.4	321	28.6

NOTE. HBV screening refers to either HBsAg or anti-HBc screening test ordered; all comparisons between screened and unscreened patients are statistically significant using χ^2 test ($P < .001$).

Abbreviations: anti-HBc, antibody to hepatitis B core antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; ICD-9, International Classification of Diseases, version 9; SD, standard deviation.

* Patients who had an ICD-9 code for hepatitis B (070.2, 070.3, 070.20, 070.21, 070.22, 070.23, 070.310, 070.31, 070.32, 070.33, or v02.61) entered before HBV screening were considered to have a history of HBV infection.

† Patients with at least one of the following ICD-9 diagnoses codes entered into the database anytime before HBV screening were considered to have a risk factor for HBV infection: (A) hepatitis, not specific (codes 070, 070.4, 070.49, 070.5, 070.59, 070.6, 070.9, 571.4, 571.40, 571.41, 571.42, 571.49, 573.1, 573.2, 573.3, v02.6, v02.60, and v02.69); (B) other liver conditions (codes 571, 571.0, 571.0, 571.2, 571.3, 571.5, 571.6, 571.8, 571.9, 572, 572.0, 572.8, 573, 573.8, 573.9, 782.4, 789.1, and 794.8); (C) hepatitis C (codes 070.41, 070.44, 070.51, 070.54, 070.7, 070.70, 070.71, and v02.62); and (D) human immunodeficiency disease (codes 042, 042.0, 042.1, 042.2, 043, 043.0, 043.1, 043.2, 043.3, 044.0, 044.9, 079.53, 795.71, 795.8, v08, and v65.44).

their independent predictive ability. We created two different multivariable logistic regression models to determine factors related to HBV screening and HBV test results (positive results for both HBsAg and anti-HBc testing *v* negative results on both tests). Because of the small number of patients without a history of HBV infection who had positive HBsAg and anti-HBc test results, we ran the last model without the variable HBV history. Final models were identified using a stepwise method, which ensured the independent predictability of included model variables. The Hosmer and Lemeshow goodness-of-fit tests were used to evaluate the fit of the logistic regression models to our data. We examined rate of abnormalities of liver tests and liver decompensation among patients with HBV infection.

Results

Patient Characteristics

Of 70,737 patients with newly diagnosed cancer seen at MD Anderson during the study period, 10,729 (15.2%) received at least two administrations of chemotherapy according to our criteria (Table 1). Most patients had solid tumors, and of these, 56.3% had local or locally advanced disease, 34.1% had distant metastases, and 9.6% had unstaged disease; 65 patients had primary liver cancers. Among the patients with hematologic malignancies, most had lymphoma (62.4%), leukemia (25.4%), or multiple myeloma (6.4%). Over 52% of the patients with hematologic malignancies received rituximab. Most patients were from the United States, and approximately half (n = 4,637; 44.5%) were from Houston, Texas. In our cohort, 21.5% of the patients (n = 2,308) were tested for anti-HCV, and 4.5% (n = 105) had a positive result. Of these, none had a positive HBsAg test, but 26 patients (24.8%) had an isolated positive anti-HBc test. In the group who tested negative for anti-HCV (n = 2,203), 24 patients (1%) had a positive HBsAg test, and 92 patients (4.2%) had an isolated positive anti-HBc test.

Predictors of HBV Screening

Among 10,729 new patients who received chemotherapy, 1,787 (16.7%) were screened for HBV infection before chemotherapy. We compared characteristics of these patients with those of patients who were not screened (n = 8,942).

We found a similar ethnic distribution in the screened and unscreened populations. The proportion of patients with an HBV risk factor was higher in the screened population (513 of 1,787; 28.7%) than in the unscreened population (2,099 of 8,942; 23.5%; $P < .001$). The screened population also had significantly higher proportions of patients with hematologic malignancies (1,232 of 1,787; 68.9% *v* 288 of 8,942; 5.5%) and patients treated with rituximab-containing regimens (800 of 1,787; 44.8% *v* 321 of 8,942; 3.6%).

Among Asian patients, 16.9% underwent HBV screening, and among patients with risk factors, 19.6% were screened (Table 1). The prevalence of screening was 5.9% (530 of 8,944) among patients with solid tumors excluding primary liver cancers, 38.5% (25 of 65) among patients with primary liver cancers, and 71.6% (1,232 of 1,720) among patients with hematologic malignancies.

On univariate analysis, the following factors were associated with screening: age, sex, ethnicity, US residence, history of HBV infection, HBV risk factors, cancer type, and chemotherapy type. In the multivariable logistic regression model of screening (Table 2), younger age, male sex, history of HBV infection, and HBV risk factors predicted HBV testing. The odds of undergoing HBV

Table 2. Predictors of HBV Screening* in Multivariable Logistic Regression Analysis

	Screened for HBV†	
Predictor	**OR**	**95% CI**
Age	0.98	0.98 to 0.99‡
Sex		
Male	1.5	1.3 to 1.7‡
Female	Reference	
Ethnicity		
Hispanic	0.9	0.7 to 1.1
Black	0.7	0.6 to 0.9§
Asian	1.3	0.8 to 2.0
Other	1.4	0.9 to 2.2
White	Reference	
History of HBV infection		
Yes	10.2	5.9 to 17.6‡
No	Reference	
HBV risk factors		
Yes	1.6	1.3 to 1.9‡
No	Reference	
Cancer type		
Hematologic malignancy	21.5	18.3 to 25.2‡
Primary liver cancer	7.0	3.9 to 11.8‡
Solid tumor, excluding primary liver cancer	Reference	
Chemotherapy type		
Rituximab	4.2	3.4 to 5.1‡
Immunotherapy, excluding rituximab	1.0	0.8 to 1.2
Chemotherapy/nonimmunotherapy	Reference	

Abbreviations: anti-HBc, antibody to hepatitis B core antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; OR, odds ratio.
* Either HBsAg or anti-HBc test.
† Total of 1,752 patients had HBsAg screening test; 1,700 had anti-HBc screening test; 1,665 had both HBsAg and anti-HBc screening tests.
‡ $P < .001$.
§ $P < .01$.

screening were 30% less for blacks than whites. The odds of screening were 22 times greater for patients with hematologic malignancies than for patients with solid tumors. The odds of screening were four times greater for patients who were anticipated to initiate rituximab therapy than for patients who did not receive immunotherapy. We also modeled HBsAg and anti-HBc testing separately and found similar results.

Results of HBV Tests

Among 1,787 patients who underwent screening, the prevalence of either a positive HBsAg or anti-HBc result was 8.5% (151 of 1,787; Appendix Fig A1, online only). Among 1,665 patients screened using both tests, the prevalence of chronic HBV infection was 1.5%. The prevalence of having a positive anti-HBc result but negative HBsAg test was 7.4%. Among 1,541 patients who had either both tests positive or both tests negative, the prevalence of chronic HBV infection was nearly 40% among Asian patients and 4% among patients with HBV risk factors (Table 3). Among 151 patients with positive HBsAg and/or anti-HBc screening tests, 25 patients (17%) developed abnormalities of liver tests after chemotherapy, and nearly 20% of patients had liver decompensation.

Predictors of Positive Results

We examined factors related to having chronic HBV infection versus negative results on both tests (Table 3). We did not include history of HBV in this model because of the small numbers of patients (n = 5) with positive HBsAg and anti-HBc test results without a history of HBV. On univariate analysis, sex, ethnicity, HBV risk factors, cancer type, and chemotherapy type were associated with positive results on both tests. On multivariable analysis, male sex, Asian ethnicity, black ethnicity, and HBV risk factors predicted positive results on both tests. Not surprisingly, primary liver cancer also predicted positive results on both tests. We also explored factors related to having a positive anti-HBc but negative HBsAg test, and we found similar results.

Discussion

Our study is the first to our knowledge to examine determinants of HBV screening at the onset of chemotherapy in a large population of patients with cancer undergoing chemotherapy in the United States. Our study was conducted before the CDC recommendation, and our results could serve as a baseline against which results of future studies of HBV screening can be compared. We found low rates of HBV screening among patients at high risk for HBV infection and potentially at risk for reactivation after chemotherapy.

Although patients with HBV risk factors had four-fold increased odds of positive HBV screening test results, less than 20% were screened for HBV infection. Previously, Tran et al[23] found that 38% of American Medical Association oncologists reported screening patients with risk factors for HBV infection, and Khokhar et al[24] found that 86% of oncologists reported screening patients with HBV risk factors. These studies show that oncologists may be screening based on HBV risk factors; however, they represent self-reported screening behavior, which may overestimate screening rates.[25,26]

Although certain ethnic groups have higher risks of HBV infection, we found that many of these patients were not screened. Although Asian and black patients had a high likelihood of infection on screening, only 17% Asians and 12% of blacks in our study were screened. The prevalence of past or present HBV infection in the United States has been reported to be 12.2% among blacks[27] and 8.9% to 13.4% among Asian Americans.[9]

Given our finding that the rate of chronic HBV infection before chemotherapy was less than 2% overall but higher among Asian patients and patients with other HBV risk factors, at minimum, patients with risk factors should be screened for HBV infection. However, to optimize selective screening, providers need tools to predict HBV infection and reactivation in different patient subgroups—tools that do not yet exist. At present, many patients with HBV may not know their own risk or that they are infected.[9,28] They might not even have identifiable HBV risk factors. Previous studies of antenatal HBV

Table 3. Odds of Positive Results on Both HBsAg and Anti-HBc Tests Versus Both Tests Negative in Univariate and Multivariable Logistic Regression Analyses

			Both HBsAg and Anti-HBc Positive (n = 25)			
			Univariate Analysis*		Multivariable Analysis	
Predictor	No.	%	OR	95% CI	OR	95% CI
Age, years			1.0	0.97 to 1.01		
Mean		48.8				
SD		11.0				
Sex						
Male	20 of 914	2.2	2.8	1.0 to 7.5†	7.4	2.0 to 27.0‡
Female	5 of 627	0.8	Reference		Reference	
Ethnicity						
Hispanic	3 of 204	1.5	4.3	1.0 to 19.4	4.5	1.0 to 20.7
Black	3 of 98	3.1	9.1	2.0 to 41.3‡	9.7	2.1 to 45.6‡
Asian	12 of 31	38.7	182.3	53.9 to 616.9§	270.8	65.4 to 1,109.0§
Other	3 of 49	6.1	18.8	4.1 to 86.6‡	13.0	2.6 to 64.6‡
White	4 of 1,159	0.4	Reference		Reference	
Residence						
Outside United States	2 of 59	3.4	2.2	0.5 to 9.7		
United States	23 of 1,482	1.6	Reference			
HBV risk factors						
Yes	17 of 414	4.1	6.0	2.6 to 14.0§	3.9	1.4 to 10.5‡
No	8 of 1,127	0.7	Ref.		Reference	
Cancer type						
Hematologic malignancy	11 of 1,097	1.0	0.4	0.2 to 0.9†	0.7	0.3 to 2.1
Primary liver cancer	3 of 21	14.3	6.2	1.6 to 24.3‡	8.3	1.5 to 46.3†
Solid tumor, excluding primary liver cancer	11 of 423	2.6	Reference		Reference	
Chemotherapy type					—	
Rituximab	6 of 709	0.9	0.5	0.2 to 1.8	—	
Immunotherapy, excluding rituximab	5 of 80	6.3	3.5	1.2 to 10.0†	—	
Chemotherapy/nonimmunotherapy	14 of 752	1.9	Reference		—	

NOTE. Model includes 1,541 patients who had either both tests positive (n = 25) versus both tests negative (n = 1,516). Age and residence variables were not entered in the multivariable model because their $P > .20$. Empty cells with dashes refer to variables not retained in the final step of the multivariable model because their $P > .05$.
Abbreviations: HBsAg, hepatitis B surface antigen; anti-HBc, antibody to hepatitis B core antigen; OR, odds ratio; SD, standard deviation.
* $P \leq .20$ for the following predictors in the univariate logistic regression model, which were entered into the multivariable model: sex, ethnicity, HBV risk factors, cancer type, and chemotherapy type. History of HBV infection was not entered into the model because of small numbers of patients without a history HBV infection but with positive HBsAg and anti-HBc test results.
† $P < .05$.
‡ $P < .01$.
§ $P < .001$.

screening showed that HBV in nearly 45% to 65% of patients with infection would have been missed if only patients with known risk factors were screened.[29,30] Thus, until risk models are developed and clinically applicable risk tools are incorporated into medical practice, universal screening for HBV before chemotherapy could be considered, paralleling universal antenatal screening.[30-33] Rigorous future studies should examine whether risk-based or universal screening for HBV infection before chemotherapy should be implemented.

ASCO has recommended screening patients known to have HBV risk factors or who are anticipating highly immunosuppressive therapies, such as stem-cell transplantation and rituximab.[18] Our finding of low screening rates among patients with risk factors for HBV infection indicates that physicians were not systematically screening for HBV among select high-risk groups during our study period.

An interesting finding of this study was that substantial numbers of patients had positive anti-HBc but negative HBsAg test results. These patients may be convalescent from previous infection (if anti-HBs positive) or have occult HBV infection (if anti-HBs negative). Covalently closed circular DNA may persist indefinitely in hepatocytes of patients after acute infection who have positive anti-HBc and negative HBsAg.[34,35] Further study about the natural history and role of prophylaxis among these patients is needed because previous studies have shown that patients with positive anti-HBc and negative HBsAg may be at risk of reactivation after chemotherapy.[3,36-41] Screening strategies using anti-HBc as the first test (with reflex testing of

HBsAg, anti-HBs, and HBV DNA) should be explored because anti-HBc is a reliable serologic marker of HBV infection, whether chronic, convalescent, or occult.[42,43]

The main limitations of our study result from its retrospective nature. Because we did not have HBV DNA data at baseline or during chemotherapy, we described outcomes of abnormalities of liver tests and liver decompensation in patients with HBV after chemotherapy; however, these outcomes cannot substitute for reactivation because they could alternatively be explained by drug toxicity, infiltrative malignancy, or other causes of liver injury. We did not explore these outcomes in patients who were without HBV infection, and this is a weakness of our study design because these patients could also have abnormalities of liver tests and liver decompensation after chemotherapy. We were not able to ascertain patients' complete HBV risk factors,[17] and this may have decreased the accuracy of screening rates. Furthermore, screening rates may have reflected providers' investigating unspecified liver disease rather than screening to prevent reactivation of HBV infection. Our single-institution study may have inherent biases; however, our findings are based on a substantial sample of insured and indigent patients whose physicians drive screening. Unfortunately, patients' race was not self-identified, which limits the accuracy of this variable, and the proportion of nonwhite patients is lower at MD Anderson (25%; Tumor Registry Department New Patient Profile, 2010)[44] than in the overall US population (36%),[45] limiting the generalizability of findings.

In conclusion, the findings of our study, reflecting a period before the 2008 release of the CDC recommendation for widespread HBV screening, indicate that the overall rate of HBV screening was low. Additionally, we found that screening was low among patients with selected risk factors for HBV infection. Data from population-based studies are seriously lacking, and recent studies of screening practices have been limited because of recall bias[46] or have not incorporated risk factors for reactivation.[47] To ascertain appropriate screening strategies for patients with cancer with HBV infection, oncologists need sound evidence to make effective clinical decisions. Future large and prospective studies to identify best screening methods as well as risk models for HBV infection and reactivation will be important to elucidate solutions for this serious complication of chemotherapy.

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Appendix

Table A1. Classification of Chemotherapy Drugs Received by Study Population

Classification	Drugs
Alkylating agents	Busulfan, carboplatin, carmustine, chlorambucil, cisplatin, cyclophosphamide, dacarbazine, ifosfamide, lomustine, mechlorethamine, melphalan, oxaliplatin, procarbazine, streptozocin, temozolomide
Antimetabolites	Azacitidine, capecitabine, cladribine, clofarabine, cytarabine, cytarabine liposome, decitabine, fludarabine, fluorouracil, gemcitabine, hydroxyurea, mercaptopurine, methotrexate, pemetrexed, pentostatin, thioguanine
Mitotic inhibitors	Docetaxel, ixabepilone, vinblastine, vincristine, vinorelbine
Antitumor antibiotics	Bleomycin, dactinomycin, daunorubicin, doxorubicin, epirubicin HCl, idarubicin, mitomycin, mitoxantrone
Immunotherapy	Aldesleukin, alemtuzumab, bevacizumab, cetuximab, gemtuzumab ozogamicin, interferon alfa-2b, rituximab
Hormone therapy	Anastrozole, bicalutamide, estramustine phosphate, exemestane, flutamide, fulvestrant, goserelin, letrozole, leuprolide, megestrol, mitotane, nilutamide, tamoxifen
Targeted therapy	Bortezomib, dasatinib, erlotinib, everolimus, imatinib, lapatinib, sorafenib, sunitinib, temsirolimus, vorinostat
Topoisomerase inhibitors	Etoposide, irinotecan, topotecan
Miscellaneous chemotherapy drugs	Asparaginase, denileukin diftitox, pegaspargase, porfimer
Differentiating agents	Arsenic trioxide, bexarotene, tretinoin

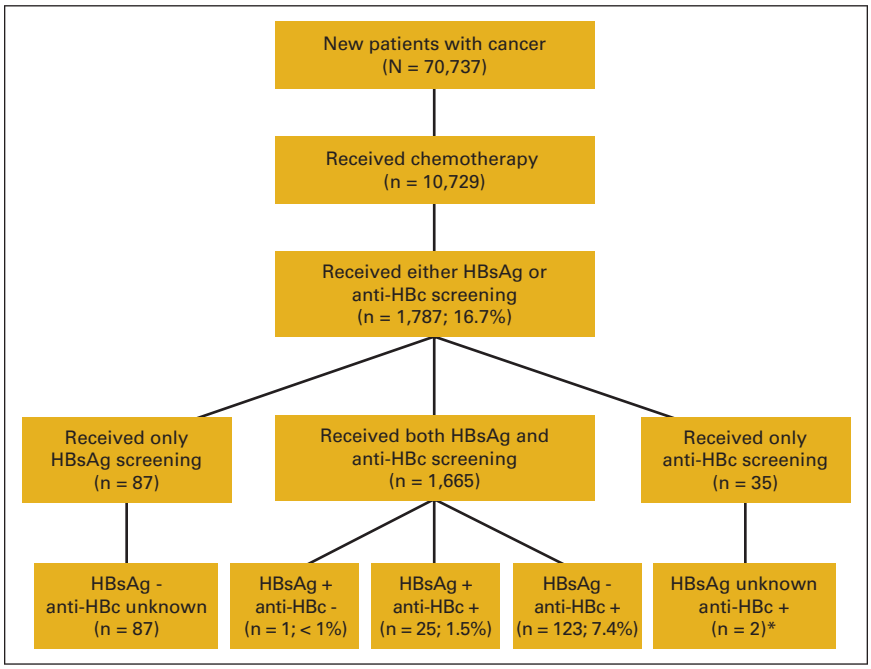

Figure A1. Hepatitis B virus screening and results among new patients with cancer who received chemotherapy at MD Anderson Cancer Center, 2004-2007. Abbreviations: HBsAg, hepatitis B surface antigen; anti-HBc, antibody to hepatitis B core antigen.