

Original Article

Seroprevalence of Hepatitis B Virus Infection and Associated Factors among Cancer Patients at Hawassa University Comprehensive Specialized Hospital, Ethiopia

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Abstract

Introduction: Hepatitis B virus infection is a global public health concern and has a high degree of associated morbidity and mortality. In Ethiopia, Hepatitis B virus infection has a variable seroprevalence among different regions with an estimated overall prevalence of around 6%. However, there is a scarcity of data specific to cancer patients.

Methodology: A hospital-based cross-sectional study was conducted among 384 cancer patients who came for follow-up at the oncology unit of Hawassa University Comprehensive Specialized Hospital from January 1/2020 to October 11/2021. A systematic sampling technique was employed to select the participants. Data was collected using structured and interviewer-administered questionnaires and blood samples were drawn from the patients to test hepatitis B virus sero-status. Data was entered to Epi-Data version 4.6 then exported and analysis was done using SPSS version 25. Descriptive statistics were used to describe the study participants. Finally, bivariable and multivariable binary logistic regression was used to identify significantly associated factors.

Results: The seroprevalence of hepatitis B virus infection among cancer patients was 7.6% [95% CI: (4.54 - 9.79)]. Having multiple sexual partners (AOR = 6.24, 95% CI (3.35-16.80)), a history of dental procedures (AOR = 3.34; 95% CI (1.007-7.66)), and being a hepatocellular carcinoma patient (AOR = 6.13; 95% CI (3.66-18.77)) were factors associated with seropositive status for Hepatitis B virus.

Conclusions: The seroprevalence of Hepatitis B virus infection among cancer patients was high. It is better to consider HBV screening in cancer patients and doing cancer surveillance in HBV-infected patients.

Key words: Hepatitis B virus; seroprevalence; cancer patients.

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Introduction

Hepatitis B virus (HBV) infection is one of the most serious and common health conditions, affecting more than 2 billion people worldwide [1]. Hepatitis B virus has been implicated in the cause of up to 80% of cases of hepatocellular carcinoma (HCC) [2]. HBV infection is also associated with the risk of non-hepatic cancer, such as non-Hodgkin lymphoma (NHL), pancreatic cancer, and gastric cancer [3-6].

Hepatitis B virus is highly contagious, 50–100 times more infectious than the human immune deficiency virus (HIV) and 10 times more infectious than the Hepatitis C virus (HCV) [7]. It can be transmitted from mother to child or via contaminated body fluid exposure such as unprotected sex, contaminated medical equipment, and blood donation [8].

Worldwide more than 240 million people are affected by chronic liver disease due to HBV [9]. The burden is high in Asia, Africa, Southern Europe, and Latin America [8]. The prevalence of HBV infection varies widely due to geographical area and predominant routes of transmission [10]. Africa has the second largest number of chronic HBV carriers after Asia and is considered a region of high endemicity [11]. In sub-Saharan Africa, the prevalence of HBV infection ranges from 10 to 20% [12]. The Prevalence in Ethiopia ranges from 1% in the Amhara region to 36% in Addis Ababa city with an overall pooled prevalence of 6% [13].

Hepatitis B virus causes a life-threatening infection that causes acute and chronic disease [14]. It is also a risk factor for cancer development [10]. The occurrence of cancer can be seen as a failure of the immune system to control and eradicate the cancerous mass [14].

Immunosuppression induced by chemotherapeutic agents increases the risk of HBV reactivation (HBVR), but it depends on the chemotherapeutic agent used and the cancer type [15]. Immunosuppression-induced malignancy is also experienced in Merkel cell polyomavirus infection, which substantially increases the risk for carcinoma [16]. Hence, cancer patients could be more likely to contract the virus and develop the disease [17]. This hypothesis leads us to determine the seroprevalence of HBV infection and its associated factors specifically among cancer patients. In addition, in Ethiopia, we do not have enough information about the HBV burden, specifically in cancer patients. This study aimed to assess the seroprevalence of HBV infection and associated factors among cancer patients at Hawassa University Comprehensive Specialized Hospital (HUCSH).

Methodology

Study Area and Designs

The study was conducted at HUCSH oncology unit. It is the biggest and the only tertiary hospital located in the Sidama region. The hospital serves more than 18 million populations from Southern Nations Nationalities & Peoples (SNNP) & neighboring Oromiya region. The hospital provides services in major departments (Internal medicine, Surgery, Pediatrics, Gynecology & Obstetrics), Oncology, Ophthalmology, dermatology, ENT (Ear, Nose, and Throat), Radiology, Laboratory & pharmacy. The oncology clinic provides a follow-up service for cancer patients.

Study Period

The study was conducted between 1st January 2020 and 11th October 2021.

Study Design and Population

An institutional-based cross-sectional study was conducted.

All cancer patients who have followed up at the oncology clinic in HUCSH were our Source populations and all cancer patients who have followed up at the oncology clinic in HUCSH during our data collection period were our Study populations.

Inclusion and Exclusion Criteria

Inclusion Criteria

Cancer patients who attend the hospital outpatient department at the time of data collection

Exclusion Criteria

Cancer patients who were seriously ill (comatose and unable to make interview)

Study Variables

Dependent variables

- Seroprevalence of HBV infection

Independent variables

- Socio-demographic variables
- Risk factors for HBV (multiple sexual partners, sharing of sharps, family history of HBV)
- Immunization history for HBV
- Type & stage of cancer
- Type of chemotherapy
- HIV sero status.

Sample Size Determination

The single population proportion formula was used to determine the sample size:

$$n = (Z_{\alpha/2})^2 \times P \times (1 - P) / d^2$$

Where: n = the minimum sample required; P = proportion; d = margin of error; and Z = 1.96 (i.e., for a 95% CI).

Since there is no similar study in the study area the researcher decided to take a *p* value of 0.5.

$$n = (1.96)^2 \times 0.5 \times (1 - 0.5) / (0.05)^2$$

$$n = 384$$

Our final sample size was 384.

Sampling Method

Cancer patients who attended the oncologic were selected by systematic random sampling techniques with a skipping interval of K = 2.

Data Collection Instrument and Method

Data was collected through closed-ended questionnaires, interviews, and chart review, and 1mL of venous blood sample was collected from each study participant by the laboratory technician HBV diagnosis was accomplished by testing for a series of serological markers of HBV (HBsAg marker and total antibody to hepatitis B core protein) using the standard Strip Test. The sensitivity and specificity of the test kit were 97%. The data collection was done by trained general practitioners and residents working at an oncology clinic supervised by an investigator.

Data Quality Management

The data collection process was supervised by the principal investigator and the data were checked for completeness and accuracy on a daily base. A pretest

was conducted before actual data was and any ambiguity in the questionnaires was corrected before final data collection.

Method of Data Analysis

All responses to the questionnaires were cleaned and coded. The coded data was then entered into Epi-Data Version 4.6 and the data was exported to SPSS version 25 for analysis. Descriptive and analytical statistics were employed. Descriptive analysis including percentages, frequencies, and charts was used to describe the major characteristics of the respondents. In bivariable regression, a variable with $p < 0.25$ was entered into multivariable binary logistic regression analysis to identify factors associated with seroprevalence of HBV infection. A p value of 0.05 was used as the cut-off to declare statistical significance in multivariable analysis. The strength of the association was also measured by odds ratio with a corresponding

95% confidence interval (CI). Finally, results were compiled and presented using tables and texts.

Ethical Consideration

Before data collection, appropriate ethical clearance letter was obtained from Hawassa University College of Medicine and Health Sciences Institutional Review Board (IRB) with reference number IRB 255/13. Written permission was obtained from the hospital manager. After the introduction of the data collector, participants were informed about the objectives and benefits of the research and its findings, preceding the data collection. They were informed about the confidentiality of the information they give and written consent was obtained from each participant.

Results

Socio-demographic characteristics of study participants

A total of 384 cancer patients were enrolled in this study with a 100% response rate. Of these, 58.3% (224/384) were females. The mean age of the respondents was 47.13 ± 15.26 years. Of the total respondents, 79.9% (307/384) of the participants were married. Most of the patients (230, 59.9%) were rural residents. Regarding the occupation of patients, 36.2% (139/384) were housewives (Table 1).

Hepatitis B Virus risk factor assessment

The most common risk factor found in our study was multiple sexual partners 18.5% (71/384), a history of dental procedures 11.7% (45/384), and a history of

Table 1. Socio-demographic characteristics of study participants at Hawassa University Comprehensive Specialized Hospital, Hawassa, Ethiopia, 2022 (n = 384).

Variable	Frequency	Percent
Age in year		
15-29	51	13.3
30-45	152	39.6
46-85	181	47.1
Sex		
Male	160	41.7
Female	224	58.3
Marital status		
Married	307	79.9
Single	35	9.1
Divorced	13	3.4
Widowed	20	5.2
Separated	9	2.3
Educational level		
Not attended formal school	191	49.7
Read and write	50	13.0
Primary	55	14.3
Secondary	58	15.1
Post- secondary	30	7.8
Religion		
Orthodox	118	30.7
Protestant	150	39.1
Catholic	13	3.4
Muslim	103	26.8
Ethnicity		
Oromia	158	41.1
Sidama	160	41.7
SPNN	64	16.7
Somale	2	.5
Residence		
Rural	230	59.9
Urban	154	40.1
Occupation		
Farmer	106	27.6
Governmental employee	72	18.8
Merchant	48	12.5
Housewife	139	36.2
Student	19	5

Table 2. Assessed risk factors among cancer patients at Hawassa University Comprehensive Specialized Hospital, Ethiopia, 2022 (n = 384).

Risk factors	Frequency	Percent
Multiple sexual partner		
Yes	71	18.48
No	313	81.52
Sharing of sharps		
Yes	38	9.89
No	346	90.11
History of dental procedure		
Yes	45	11.71
No	339	88.28
History of surgical procedure		
Yes	20	5.2
No	364	94.8
History of tattooing		
Yes	30	7.8
No	354	92.2
History of blood Transfusion		
Yes	30	7.8
No	354	92.2
Immunization against HBV		
Yes	0	0
No	384	100
HIV-AIDS sero-status		
Reactive	13	3.4
Nonreactive	371	96.6

surgical procedures 5.2% (20/384). All of our patients were not immunized against HBV and 3.4 % (13/384) of our participants' HIV-AIDS sero status were positive (Table 2).

Seroprevalence of hepatitis B virus infection

Of the total 384 cancer patients who participated in the study, 7.6% (29/384) were seropositive to hepatitis B virus infection (Figure 1).

Types of the Tumor

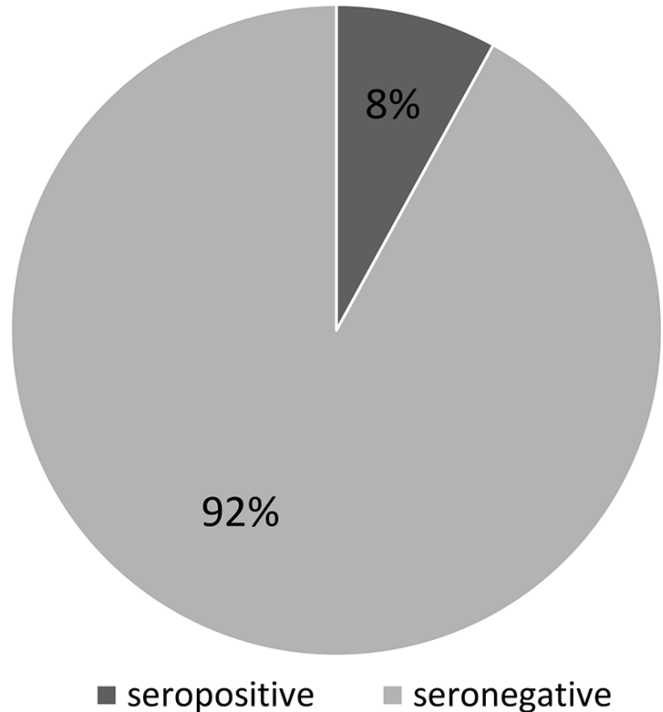
Among the study participants 22.7% (87/384) have been diagnosed with breast cancer followed by colorectal cancer 12.2% (47/384) and non-Hodgkin's lymphoma 10.2% (39/384) (Table 3). Only 84/384 (21.9%) were started on chemotherapy. From this, 44/84 (52.4%) were on palliative and 36/84 (42.8%) were on radical type of chemotherapy (Table 4).

Factors associated with hepatitis B Virus infection

Based on the findings of bivariable logistic regression analysis; the educational status of the patient, hepatocellular carcinoma, cervical cancer, multiple sexual partners, sharing of sharps, history of dental procedure, and history of surgical procedure were the competent variables for multivariable logistic regression at *p* values of less than 0.25.

After controlling the effects of confounder in the final multivariable binary logistic regression model having multiple sexual partners, a history of dental

Figure 1. The proportion of HBV infection among cancer patients at Hawassa University Comprehensive Specialized Hospital, 2022 (n = 384).



procedure, and hepatocellular carcinoma had a statistically significant association with HBV infection.

Patients who had multiple sexual partners were 6.24 more likely to have HBV seropositive status than patients who had multiple sexual partners (AOR = 6.24; 95% CI (3.35-16.80)). Cancer patients who had dental

Table 3. Types of cancer among the study participants at Hawassa University Comprehensive Specialized Hospital, Ethiopia, 2022 (n = 384).

Type of cancer	Frequency	Percent
Breast cancer	87	22.7
Colorectal cancer	47	12.2
Non-Hodgkin's lymphoma	39	10.2
Lung cancer	28	7.3
Head and neck cancer	27	7.0
Gastric cancer	24	6.3
Esophageal cancer	22	5.7
Hodgkins Lymphoma	16	4.2
Ovarian cancer	15	3.9
Hepatocellular carcinoma	14	3.6
Cervical cancer	12	3.1
Bladder cancer	11	2.9
Rabdomyosarcoma	11	2.9
Pancreatic cancer	11	2.9
Prostatic cancer	6	1.6
Endometrial cancer	4	1.0
Melanoma	3	0.8
Kaposi sarcoma	2	0.5
Multiple myeloma	2	0.5
Ewing sarcoma	2	0.5
Renal cell carcinoma	1	0.3
Total	384	100.0

Table 4. Shows the stage, grade, and chemotherapy status of cancer patients at Hawassa University Comprehensive Specialized Hospital, Ethiopia, 2022 (n = 384).

Stage of cancer	Frequency	Percent
Stage-4	287	74.7
Stage-3	86	22.4
Unknown	10	2.6
Stage-2	1	0.3
Total	384	100.0
Grade of cancer		
Unknown grade	378	98.4
High grade	5	1.3
Low grade	1	0.3
Total	384	100.0
Chemotherapy started		
No	300	78.1
Yes	84	21.9
Total	384	100.0
Type of chemotherapy		
Palliative	44	11.5
Radical	36	9.0
Total	81	21.1

procedures were 3 times more likely to have HBV seropositive status (AOR = 3.34; 95% CI (1.007-7.66). Patients having hepatocellular carcinoma were 6.13 times more likely to be HBV seropositive than those having non-hepatocellular carcinoma (AOR = 6.13: 95% CI (3.66-18.77)) (Table 5).

Discussion

In this study, the seroprevalence of HBV among cancer patients was 7.6 % (29/384). This makes the study sites an intermediate risk area for HBV infection according to WHO criteria [18]. As the seroprevalence of HBV infection varies geographically, from high (> 8%), intermediate (2-8 %) to low (< 2%) prevalence [19]. Hepatitis B infection is also moderately endemic in parts of Eastern and Southern Europe, the Middle East, Japan, and part of South America [19]. In moderately endemic areas it is supposed that mixed patterns of transmission exist, including infant, early childhood, and adult transmission [20].

Our result is in agreement with a finding study done in France which was 8.5% [21]. this finding is lower than a finding of a study done among cancer patients in Cameroon which reports a prevalence of 9.84% [22]. However, a lower prevalence was reported in a study done among cancer patients in Turkey, which was determined as 4.2% [23]. This may be due to variations

in risk exposure and differences in socio-demographic characteristics.

Among 29 (7.6%) HBsAg-positive cancer patients, 5 (17.24%) were Hepatocellular carcinoma patients, 4 (13.8%), and 2 (6.89%) were Breast cancer patients. Although HBV is mainly thought to be hepatotropic, it has been demonstrated that seropositive HBV status is closely associated with a variety of non-HCC neoplasms such as cervical, uterine, breast, thyroid, and lung cancers [24]. However, our study showed no statistically significant associations between HBV and non-HCC neoplasm. This may be due to our small sample size.

In our study on cancer, patients with multiple sexual partners had higher odds of HBV infection compared to their counterparts. This is also in agreement with a study done among surgical patients at Hawassa University [25] and in Nigeria [26]. The high prevalence rate may be due to the fact that Hepatitis B virus infection is sexually transmitted and the transmission increases with the duration of sexual activity and number of sexual partners.

In this study, patients who had a history of dental procedures had a higher chance of acquiring HBV. This finding was also supported by a study [27]. The higher prevalence in those who practiced might be due to most of the dental practices being done out of health

Table 5. Bivariate and multivariable logistic regression summary on factors associated with Positive HBSAG among cancer patients, Ethiopia, 2022 (n = 384).

Category	Positive HBSAG		COR (95% CI)	AOR (95% CI)
	Yes	No		
Age				
15-29	5	47	1	1
30-45	12	139	0.81 (0.272-2.42)	0.62 (0.31-3.45)
46-85	12	169	0.66 (0.224-1.990)	0.91 (0.29-1.93)
Multiple sexual partner				
Yes	11	59	3.066 (1.3-6.83)	6.24 (3.35-16.80)
No	18	296	1	1
Sharing of sharps				
Yes	5	33	2.033 (0.72-5.68)	2.304 (0.353- 15.033)
No	24	322	1	1
History of dental procedure				
Yes	11	45	5.059 (2.112-12)	3.34 (1.007-7.66)
No	18	310	1	1
History of surgical procedure				
Yes	8	34	3.59 (2.34-18)	1.64 (0.347-7.8)
No	21	321	1	1
Breast cancer				
Yes	4	83	0.52 (0.35-5.5)	1.632 (0.303-8.47)
No	25	272	1	1
Lung cancer				
Yes	2	26	0.94 (0.27-9.21)	1.22 (0.172-8.65)
No	27	329	1	1
Hepatocellular carcinoma				
Yes	5	9	8.00 (2.6-30.8)	6.13 (3.66-18.77)
No	24	346	1	1
Chemotherapy status				
Started	7	77	1.15 (0.36 - 2.11)	1.11 (0.39- 2.78)
Not started	22	278	1	1

institutions with unhygienic conditions and without proper sterilization.

In this study, we found that HBV infection had a higher odd among patients with hepatocellular carcinoma. A study which was conducted in Turkey also found that hepatocellular carcinoma and HBV infection had a significant association [28]. Although the underlying mechanisms have not been identified, several mechanisms of HBV-induced HCC have been proposed. Among these, integration of HBV DNA into the genome of hepatocytes is widely accepted. Although integration at cellular sites that are important for the regulation of hepatocyte proliferation appears to be a rare event [29].

Limitations of the study

The cross-sectional nature of the study and the fact that this study was conducted at only one hospital is one of its key limitations.

Conclusions and Recommendations

The seroprevalence of Hepatitis B virus infection among cancer patients was high. This is attributed to the presence of possible risk factors for HBV transition such as multiple sexual partners, and a history of dental and surgical procedures.

Our findings may offer additional insights into the development of these neoplasms and may suggest the need to consider HBV screening in cancer patients and cancer surveillance in HBV-infected subjects.

Health professionals who would be assigned to manage cancer patients should assess risk factors for hepatitis B transmission for all cancer patients and encourage screening for HBV infection for all patients before chemotherapy starts.

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Authors' contributions

All authors participated in conceptualization, formal analysis, investigation, methodology, supervision, visualization, writing-original draft, writing-review and editing, and approving the final draft. All authors read and approved the manuscript.

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