

Hepatitis B Virus Screening Prior to Chemotherapy in Patients with Solid Organ Malignancy at the Brazzaville University Hospital

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Abstract

Introduction: Viral hepatitis B is a major public health problem in Africa. In patients receiving chemotherapy, its reactivation can be life-threatening. Systematic screening prior to chemotherapy can prevent this complication. **Aim:** To evaluate the practice of HBV screening before the onset of anti-cancer chemotherapy at the Brazzaville University Hospital (CHUB). **Method:** This was a retrospective study including patients aged 18 years and over who received chemotherapy in the CHUB oncology department from January 2021 to December 2023. Socio-demographic characteristics and frequencies of HBsAg, HBcAb and HBsAb testing prior to chemotherapy were determined. Factors associated with HBV screening were investigated using multivariate analysis. P value < 0.05 was considered significant. **Results:** There were 312 patients, 69.6% of whom were women. Mean age was 54.9 ± 13.1 years. Breast and cervix cancers were found in 45.2% and 15.7% of patients, respectively. HBsAg testing was performed in 66.7% of patients. No patient was tested for HBcAb or HBsAb. Age greater than or equal to 60 years was associated with HBV screening (60 to 69 years: OR = 4.17, P = 0.002). **Conclusion:** The rate of HBV screening was inadequate. Compulsory screening of all patients eligible for chemotherapy and systematic testing for HBsAg, HBcAb and HBsAb should be made more widely available.

Keywords

HBV, Screening, Chemotherapy, CHUB

1. Introduction

Hepatitis B virus (HBV) infection is a major public health problem worldwide. According to the 2023 report on hepatitis B by the French National Authority for Health, approximately two billion people (a third of the world's population) are estimated to be infected with HBV, more than 316 million are estimated to be chronic HBV carriers worldwide, and more than 887,000 die each year [1]. Beyond its spread, HBV infection is also characterized by its uneven distribution.

In its 2021 World Hepatitis Report, the World Health Organization (WHO) points out that in 2019, sub-Saharan Africa was the region with the highest estimated prevalence rate at 7.5%, and recorded the highest number of new HBV infections, with 990,000 new cases. In this region, over 82 million people are thought to be infected, only 2% of whom know their status, while less than 1% receive treatment [2].

HBV-infected patients are at risk of reactivation when receiving chemotherapy or immunosuppressive therapy. HBV reactivation could not only delay the timing of cancer treatment, but also lead to severe hepatitis and even death.

In the Republic of Congo, the prevalence of HBV carriage is 9.9%, with uneven distribution throughout the country [3].

In order to prevent the risk of reactivation, all Congolese patients eligible for chemotherapy should be screened prior to chemotherapy initiation.

For these reasons, we set out to assess the quality of hepatitis B screening practices prior to the start of chemotherapy in cancer patients at the Brazzaville University Hospital (CHUB).

The specific objectives of our study were to describe the patients' socio-demographic characteristics, determine the respective frequencies of HBs antigen, anti-HBc antibody and anti-HBs antibody screening prior to chemotherapy and identify factors associated with HBV screening prior to chemotherapy initiation.

2. Method

The study was conducted at Brazzaville University Hospital (CHUB) in the oncology department. The main mission of the Oncology Department is to care for patients with solid cancer requiring chemotherapy.

This is a cross-sectional, analytical study, with retrospective data collection from the medical records of patients hospitalized and followed in the oncology department, between January 1, 2021 and December 31, 2023, *i.e.*, three years.

The study population consisted of patients aged over 18 who had received or were receiving chemotherapy in the CHUB oncology department during the study period. Records lacking sufficient information on patient demographics, cancer type, cancer stage and pre-chemotherapy biology were excluded from the study. Records of patients with hepatocellular carcinoma were also excluded, as these patients were also followed by gastroenterologists, who systematically screened them for hepatitis B before referring them, if necessary, to an oncologist.

Data were collected in two stages: analysis and selection of the medical files to be analyzed, followed by completion of the pre-established survey forms.

The variables studied were:

- Epidemiological variables: age (in years), gender, occupation.
- Clinical variables: site of primary cancer, stage of cancer.
- Biological variables: ALT value before initiation of chemotherapy, HBV serological markers: HBsAg, total HBcAb, IgG HBcAb, HBsAb.

Data Analysis

Data analysis was performed using R software version 4.4.0, and results were written up using Microsoft Office 2010.

We determined the frequencies of viral marker testing in patients prior to initiation of chemotherapy.

We calculated the frequencies of HBs antigen and HBc antibody testing in all patients. For all HBs antigen-negative patients, we also determined the frequency of those who had tested for the anti-HBs antibody.

To compare the characteristics of patients who were screened with those who were not, t-test was used for continuous values and chi-squared test for categorical variables.

Multivariate analysis was used to determine whether or not age, gender, ALT value and cancer stage were associated with completion of hepatitis B screening. The significance threshold was $P < 0.05$.

3. Results

3.1. Characteristics of the Population

A total of 312 cancer patients who received systemic anticancer chemotherapy between January 1, 2021 and December 31, 2023 in the medical oncology department of Brazzaville university hospital were included in our study. The mean age of these patients at the time of chemotherapy initiation was 54.9 ± 13.1 years, and 217 (69.6%) of them were female.

Breast cancer (141 patients; 45.2%), cervix cancer (49 patients; 15.7%) and prostate cancer (37 patients; 11.9%) were the most frequent primary cancers.

The mean ALT value was 21.7 ± 14.6 IU/mL, and 284 (91%) patients had normal ALT levels.

The basic characteristics of the study population are summarized in **Table 1**.

3.2. HBV Screening Rate

The overall rate of HBV screening before the start of chemotherapy was 66.7% ($n = 208$). Only HBsAg was performed for hepatitis B screening (see **Table 2**).

The characteristics of patients who had been screened and those who had not are reported in **Table 3**. Of the patients screened for HBsAg, 17 (8.2%) were positive. All patients with positive screening test were prescribed Tenofovir, an anti-viral treatment.

Table 1. Baseline characteristics of the study population.

Characteristics	Number	Percentage (%)
Gender		
Male	95	30.5
Female	217	69.6
Age (years)		
30 - 39	45	14.4
40 - 49	60	19.2
50 - 59	86	27.6
60 - 69	75	24.0
≥70	46	14.7
Occupation		
Students	6	1.9
Employed	160	51.3
Retiree	56	17.9
Jobless	90	28.8
Stage of cancer		
I	4	1.3
II	17	5.5
III	103	33.0
IV	188	60.3
ALT		
<1 ULN*	284	91.0
1 ULN - 2 ULN	22	7.1
2 ULN - 3 ULN	6	1.9
Primitive cancer sites		
Breasts	141	45.2
Colon and/or Rectum	33	10.6
Prostate	37	11.8
Stomach	17	5.4
Uterus	49	15.7
Other	35	11.2

*ULN: upper limit of the normal.

Table 2. Practice patterns of HBV screening in whole patients.

HBV testing	Number	Percentage (%)
HBsAg		
Yes	208	66.7
No	104	33.3

Continued

HBcAb-IgG		
Yes	-	-
No	312	100
HBsAg + HBcAb		
Yes	-	-
No	312	100
HBsAb		
Yes	-	-
No	191**	100

**Of the 208 patients tested for HBsAg, 191 were negative. Among these 191 patients, we looked for those who had been tested for HBsAb.

Table 3. Patients characteristics between HBV screened and unscreened groups.

	Screened group	Unscreened group	P value
	N (%)	N (%)	
	208 (66.7)	104 (33.3)	
Gender			0.007
Male	53 (55.8)	42 (44.2)	
Female	155 (71.4)	62 (28.6)	
Age (years)			0.001
30 - 39	32 (71.1)	18 (28.9)	
40 - 49	41 (68.3)	19 (31.7)	
50 - 59	70 (81.4)	16 (18.6)	
60 - 69	42 (56.0)	33 (44.0)	
≥70	23 (50.0)	23 (50.0)	
Occupation			0.004
Student	2 (33.3)	4 (66.7)	
Employed	117 (73.1)	43 (26.9)	
Retiree	28 (50.0)	28 (50)	
Jobless	61 (67.8)	29 (32.2)	
Stage of cancer			0.2
I	3 (75.0)	1 (25.0)	
II	15 (88.2)	2 (11.8)	
III	70 (68.0)	33 (32.0)	
IV	120 (63.8)	68 (36.2)	
ALT			0.2
<1 ULN	190 (66.9)	94 (33.1)	
1 ULN - 2 ULN	16 (72.7)	6 (27.3)	
2 ULN - 3 ULN	2 (33.3)	4 (66.7)	

Continued

Primitive cancers		<0.001	
Breast	106 (75.2)	35 (24.8)	
Colon and rectum	20 (60.6)	13 (39.4)	
Prostate	13 (35.1)	24 (64.9)	
Stomach	12 (70.6)	5 (29.4)	
Uterus	34 (69.4)	15 (30.6)	
Other	23 (65.7)	12 (34.3)	

3.3. Predictors of HBV Screening

In multivariate analysis, age over 60 was significantly associated with HBV screening. No association was found for gender, ALAT value or cancer stage (see **Table 4**).

Table 4. Predictors of HBV screening test.

	OR	95% CI	P-value
Gender			
Female (Ref)	-	-	
Male	0.63	0.23 - 1.68	0.4
Age (years)			
50 - 59 (Ref)	-	-	
30 - 39	1.37	0.48 - 3.79	0.5
40 - 49	1.71	0.74 - 3.99	0.2
60 - 69	4.17	1.33 - 10.4	0.002
≥70	4.56	1.40 - 15.2	0.012
Occupation			
Employed (Ref)	-	-	
Student	5.02	0.72 - 45.2	0.11
Retiree	1	0.38 - 2.54	>0.9
Jobless	1.2	0.61 - 2.32	0.6
Stage of cancer			
IV (Ref)	-	-	
I	0.28	0.01 - 2.84	0.3
II	0.23	0.03 - 1.03	0.085
III	1.43	0.77 - 2.68	0.3
ALT			
<1 ULN (Ref)	-	-	
1 ULN - 2 ULN	1.22	0.38 - 3.52	0.7
2 ULN - 3 ULN	6.37	0.94 - 58.2	0.067

4. Discussion

To the best of our knowledge, the present study is the first to examine the practice of HBV screening prior to the initiation of chemotherapy in solid cancer patients at Brazzaville University Hospital. Its aim was to contribute to the prevention of HBV reactivation through good screening practice.

4.1. Socio-Demographic Characteristics of the Study Population

The mean age of patients in our study was 54.9 ± 13.1 years.

An average age in the fifties at the time of chemotherapy has been reported by other authors. In a study carried out in Türkiye, for example, the mean age of patients was 58 years [4]. Similarly, mean ages of 55 and 58.4 years were reported in studies conducted in Thailand and the Taiwan region, respectively [5] [6].

Our patients were predominantly female (69.6%). In contrast to our work, a male predominance has been found in several studies [4]-[6].

The female predominance in our work could be explained by the high awareness of female cancers compared with male cancers in our country. This could result in the diagnosis of a greater number of cancers in women than in men [7]. It has also been reported that women's specific health events (pregnancy, menstrual problems) make them more likely than men to consult a doctor and be screened for cancer [8].

4.2. Primary Cancer Sites

Breast cancer was most frequent in our series (45.2%), followed by cancer of the cervix (15.7%). Like us, an author in Lebanon found a predominance of breast cancer in 34.2% of patients [9]. In a Thai and a Turkish study, the most frequent cancers were head and neck cancers and gastrointestinal cancers, respectively [4] [5].

Regional differences in exposure to environmental risk factors, and the predominance of genetic factors for cancer in certain populations may be one explanation for these differences.

4.3. HBV Screening Prior to Initiation of Chemotherapy

The frequency of patients screened was 66.7%.

HBs antigen was the only HBV serological marker prescribed for screening patients in our series.

The reasons why only HBs antigen was used for hepatitis B screening are not known, and further work would be required to determine them. We believe, however, that insufficient awareness of hepatitis B reactivation among those involved in prescribing chemotherapy and the lack of national or hospital guidelines on hepatitis B screening in patients eligible for cancer chemotherapy are possible explanations.

Indeed, according to Mongo's work with physicians from 11 French-speaking African countries attending the 7th Euro-African Congress of Oncology in 2016,

more than half of them (56.6%) were unaware of the risk of HBV reactivation during chemotherapy. Eighty-three people had taken part in the survey, including 68 oncologists (81.9%), and only 66.6% of those surveyed had claimed to prescribe HBV testing for patients receiving chemotherapy [10].

Similarly, low rates of HBV screening by oncologists were reported in two studies, in the Netherlands and India. Of 110 oncologists surveyed in the Netherlands, only 12% screened all their patients for HBV, and 18% did not screen any of their patients [11]. In the Indian study, out of 161 oncologists, 19% did not prescribe any HBV screening to their patients [12].

In studies of cancer patients, rates of hepatitis B screening prior to initiation of chemotherapy varied widely from country to country. In Japan, YAZAKI reported an overall screening rate of 70.6% [13]. Of the patients screened in his series, 48.8% were screened for HBs antigen only, and 41.3% were screened for both HBs antigen and HBc antibody. In Thailand, the rate of HBs antigen testing prior to chemotherapy was 27.7%, and the rate of HBc antibody testing was 4.6% [5].

In the Taiwan region, the frequencies of different HBV serologies were 64.6% for HBsAg alone, 22.1% for HBsAg and HBcAb, and 0.7% for HBsAg, HBcAb and HBsAb [6].

In a major US hospital network, including a large university hospital, community teaching hospitals and community oncology clinics, Kwak *et al* found 17.1% of patients who were screened for either HBsAg or HBcAb before chemotherapy [14].

At the MAYO Clinic (USA), a similar screening rate of 16% was reported by Wi *et al.* [15].

In a study of 1347 patients in Montreal, 600 (44.5%) were screened before the start of chemotherapy. Of these patients, 179 had screening request on chemotherapy orders and 421 were screened on demand from medical team [16].

In Türkiye, the rate of HBV screening prior to chemotherapy reported in the SAMI FIDAN study was 63%. HBcAb was tested in only 18.9% of patients [4].

It is possible that screening practices in a country are influenced by the country's level of endemicity. Thus, countries with high endemicity would tend to screen less than countries with low endemicity. However, the low screening rate observed in Thailand, despite its high endemicity, suggests the involvement of other factors.

Differences in the recommendations of learned societies on the criteria defining patients to be screened may also be at the root of the low rates reported in the aforementioned studies.

In the year 2008, the US Centers for Disease Control and Prevention (CDC) recommended viral hepatitis B screening for all patients undergoing chemotherapy, while the 2010 guidelines of the American Society of Clinical Oncology recommended screening only for those at high risk of reactivation [17] [18].

However, in its 2020 update, ASCO recommended, as did the American Association for the Study of Liver Diseases (AASLD), the Asia Pacific Association for

the Study of the Liver (APASL) and the European Association for the Study of the Liver (EASL), that all patients planning systemic anticancer therapy should be tested for HBV [19]-[22].

4.4. Factors Associated with Screening

In our series, after multivariate analysis, the factor associated with the performance of HBV screening was age greater than or equal to 60 years (60 to 69 years: OR = 4.17, P = 0.002; Age \geq 70 years: OR = 4.56, P = 0.012). The higher frequency of comorbidities in subjects over 60 may motivate a more cautious attitude prior to chemotherapy, hence a broader pre-therapeutic workup including HBV screening.

In the United States, Kwak found that the presence of hematological cancer and black race were associated with greater HBV screening [14]. A positive association between the presence of hematological cancer and HBV screening was also found by Yazaki in Japan [13]. In our case, none of the patients had hematological cancer, as only patients with solid organ malignancies are cared for in the oncology department of our center. Those with haematological cancers are cared for in the haematology department.

4.5. Screening Results

HBsAg was the only screening test used in our study. It was positive in 8.2% of patients. A result close to our own was reported by Ratchapong in Thailand, which like Congo is in an area of high HBV endemicity [5].

Lower frequencies of HBs antigen-positive patients have been reported by authors in the USA and Türkiye, respectively, countries of low and medium endemicity. In the USA, the frequency of HBs antigen-positive patients was 0.9%, and in Türkiye, 2.9% [4] [14].

HBs antigen should not be the only test to be carried out for screening prior to the initiation of chemotherapy. Some HBs antigen-negative patients may be carriers of occult hepatitis B, and therefore present a significant risk of reactivation as a result of chemotherapy. That is particularly true for patients living in Africa, where the prevalence of occult hepatitis has been estimated at 14.8% [23].

4.6. Study Limitations

This was a retrospective study based on patients' medical records. Some potentially relevant data not reported in the medical records could not be taken into account. This is the case for patients' socioeconomic status. This could have made it possible to determine whether the absence of HBV screening was due to a lack of prescription by the physician or to the patient's inability to pay for screening.

The notion of HBV vaccination was also not regularly reported, and some patients did not know whether or not they had been vaccinated against HBV. The absence of a record of patients' hepatitis B vaccination status in medical records made it impossible to determine the number of patients who had not been

screened because they were regularly vaccinated.

Finally, our sample was relatively small. As a result, the small number of patients for certain variables could bias the search for the existence of an association between these variables and the performance of the screening test.

5. Conclusion

About two-thirds of our patients were screened for HBV prior to chemotherapy. However, this rate is insufficient, as Congo is located in a zone of high HBV endemicity. What's more, HBcAb was not performed in any of the patients in our series; only the HBs antigen was sought. Consequently, patients at risk of reactivation requiring either prophylactic antiviral treatment or increased surveillance, such as those with occult hepatitis, were not identified. These facts underline the need to make doctors in charge of cancer patients aware of the importance of good HBV screening practice prior to anti-cancer chemotherapy, *i.e.*, systematic and universal screening including HBsAg, HBcAb, and HBsAb. Setting up a training program for oncologists on the management of viral hepatitis in cancer patients will help achieve this objective.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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