

Hepatitis B&C virus infection in cases of Non-Hodgkin's lymphoma in Saudi Arabia

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Received: May 12, 2006 • **Accepted:** Oct 06, 2006

ABSTRACT

We followed 565 male patients with non-Hodgkin's lymphoma (NHL) in two hospitals of Saudi Arabia. We investigated these cases for presence of hepatitis B virus (HBV) and hepatitis C virus (HCV) by determining the HBsAg and anti-HCV. Anti-HCV positive cases were confirmed by PCR. The NHL cases were classified on the basis of working formulation. The results of HBV and HCV in cases of NHL were compared with the prevalence of these viruses in healthy male blood donors. We found 11.2% of cases of NHL were positive for HBV and 16.1% for HCV, compared to 3.4% HBV and 2.9% HCV among blood donors. The highest numbers of cases (48.4% of HBV and 56% of HCV) were seen in the intermediate and low grade of NHL, respectively. Follicular small cleaved was the predominant type in both types of infection. The variation in prevalence of HBV and HCV in NHL from that of the general population was statistically significant ($p < 0.001$). We observed that the background prevalence of HBV definitely affects the rate of infection in NHL, while infection of HCV in cases of NHL is independent of its background prevalence.

Key Words: Prevalence, hepatitis B virus, hepatitis C virus, Non-Hodgkin's lymphoma

INTRODUCTION

Hepatitis B and C are mainly hepatotropic viruses leading to hepatocellular carcinoma^[1,2]. The role of hepatitis C virus (HCV) in the development of lymphoproliferative disorders has been studied widely, but the studies on the association of hepatitis B virus (HBV) and B cell non-Hodgkin's lymphoma (NHL) are limited^[3,4]. The recent studies have shown that these viruses invade the peripheral mononuclear cells and probably play a role in the causation of NHL^[5-13]. It has been observed that somehow the prevalence of HBV and HCV in a particular region corresponds to the prevalence of lymphoproliferative disorders. The reports show that the association of HCV and NHL varies in different areas depending on the prevalence of hepatitis C in that region, e.g. 0% in the United Kingdom^[14], 9-22% in Japan^[15,16], 9-30% in Italy^[17,18] and 29.5% from Romania^[19]. Prevalence of HBV in cases of NHL has been reported as 30.8% from Romania^[19] and 6.9% from Japan^[20]. The prevalence of HBV and HCV in the general population as seen in the blood donors of Saudi Arabia, where this study was carried out, falls in the moderate prevalence zone for hepatitis B and C. The prevalence of HBV and HCV in the general population is reflected in healthy blood donors. Saudi Arabia has shown a declining trend in the prevalence of HBV and HCV among healthy blood donors in the last five years. Prevalence of HBsAg among healthy blood donors from different regions of Saudi Arabia is reported from 4% to 1.5% and of anti-HCV from 2.9% to 0.55%^[21-24].

We tried to determine the possible role of HBV and HCV in the development of NHL in 565 male patients with NHL.

MATERIALS and METHODS

Five hundred and sixty-five male patients with NHL were investigated at two different hospitals in the central region of Saudi Arabia from February 1996 to December 2004. Female patients were not included in this study, as the data available for the corresponding control group of female blood donors was insignificant. The cases were first diagnosed as NHL on the basis of clinical history and examination, lymph node biopsy (fine needle aspiration cytology-FNAC and histopathology) and tumor markers. NHL was classified on the basis of "working formulation".

The serum samples of the NHL patients were screened for HBSAg and anti-HCV by third generation ELISA kits (Abbott Laboratories) specific

for the tests. The cases positive for anti-HCV were further confirmed for presence of HCV by polymerase chain reaction (PCR). Liver enzymes were estimated on Beckman's analyzer. The persons carrying HBV or HCV infection but normal liver function tests were labeled "healthy carrier". Liver biopsy was done on all HBV- and HCV-positive patients with high alanine aminotransferase (ALT) enzyme levels. Three patients had liver cirrhosis and two hepatocellular carcinoma. The prevalences of HBV and HCV among healthy male blood donors in this region as reported by Mehdi *et al.*, 2000 (considered to be the prevalence in the general population) were compared with our results in NHL.

The results are given in numbers and the percentage in brackets. The chi-square test was used to assess the significance. Comparisons were made by using Welch's t test.

RESULTS

We found that 66 (11.2 %) patients with NHL tested positive for HBSAg compared to only 3.4% of blood donors, while 91 (16.1%) patients with NHL and 2.9% of blood donors were positive for anti-HCV. Distribution of subjects according to age group is given in Table 1. We compared the results of prevalence of HBV and HCV in the NHL patients with the same age groups in the control group of blood donors. HCV was more prevalent in the 5th (41-50) and 6th (51-60) decades, while HBV was detected in the patients in their 3rd (21-30) and 4th (31-40) decades of life.

The number of NHL patients positive for HBV and HCV and classified on the basis of working formulation is shown in Table 2. Two hundred and ten cases were classified as low grade, 295 as intermediate grade and 60 as high grade. The highest number [32 (48.4%)] of HBV-positive cases were seen in the intermediate grade, while the maximum number [51 (56%)] of HCV was detected in low grades of NHL. The predominant histological type was follicular small cleaved in both types of hepatitis, but HBV was equally prevalent in diffuse mixed cell type. There was no significant difference in the high grade subset between HBV- and HCV-positive cases. The only case of Burkitt's was positive for HBV. Two percent of the patients had some underlying chronic liver disease.

Table 1. Prevalence of HBV and HCV in NHL cases and healthy blood donors in different age groups

Age groups	No.	NHL		Blood Donors	
		HBV (%)	HCV (%)	HBV (%)	HCV (%)
21 - 30	21	3 (14.2%)	0	(3.5%)	(2.5%)
31- 40	98	15 (15.3%)	9 (9.4%)	(4%)	(5%)
41- 50	141	17 (12.05%)	26 (18.6%)	(5%)	(4.5%)
51-60	170	20 (11.7%)	34 (20.1%)	(5%)	(5%)
61-70	135	11 (8.1%)	22 (16.5%)	NA	NA
Total	565	66 (11.2%)	91 (16.1%)	378 (3.4%)	320 (2.9%)

Table 2. Prevalence of HBV and HCV in different histological types based on working formulation

Working Formulation Classification	HBV (n=66)	HCV (n=91)
Low grade – 210 (37.1%)	25 (37.8%)	51 (56%)
Follicular small cleaved cell	15 (22.7%)	36 (39.5%)
Follicular mixed cell	10 (15.1%)	15 (16.4%)
Intermediate grade – 295 (52.2%)	32 (48.4%)	29 (31.8%)
Diffuse small cell	9 (13.6%)	8 (8.7%)
Diffuse large cell	8 (12.1%)	13 (14.2%)
Diffuse mixed cell	15 (22.7%)	8 (8.7%)
High grade -60 (10.6%)	9 (13.6%)	11 (12%)
Immunoblastic	4 (6%)	5 (5.4%)
Lymphoblastic	4 (6%)	6 (6.5%)
Burkitt's type	1 (1.5%)	–

DISCUSSION

There are certain viruses besides hepatitis B and C, like Epstein-Barr, human T-lymphotropic virus (HTLV1) and HIV, which are implicated in lymphomagenesis. The B lymphocytes are invaded by hepatitis B and C viruses^[19]. The high prevalence of HBV and HCV in NHL has been reported by several authors. We are reporting the prevalence of HBV and HCV in NHL as 11.2% and 16.1%, respectively, which is much lower compared to the findings of Ferri *et al.*^[1]; Mazzaro *et al.*^[6], (Italy); Izumi *et al.*^[15], (Japan); and Cucuianu *et al.*^[19], (Romania). An earlier study carried out in Saudi Arabia by Harakati *et al.*^[25] reported a higher prevalence of 21% of HCV in cases of NHL. Kuniyoshi *et al.*^[20] reported lower prevalences of HBV and HCV. The background prevalence of HBV and HCV in the general population is reflected in the prevalence of these viruses in NHL^[26,4]. Geographical pattern shows that regions like the United Kingdom, with a very low prevalence of HCV, hardly show presence of the virus in cases of NHL, while high prevalence

zones for HBV and HCV, like Romania, report equally high prevalence of these viruses in NHL. The higher rate of HCV infection in NHL compared to HBV, in spite of higher prevalence of HBV in the general population in our study, is in accordance with the findings of Kuniyoshi *et al.*^[20] and many other investigators, but in contrast to our findings, Cucuianu *et al.*^[19] found a higher prevalence of HBV than HCV in NHL as seen in the general population of Romania.

The prevalence of HBV was much higher in younger age groups of 21-30 and 31-40, while HCV was more prevalent in older patients. These findings correspond well with the results of Kuniyoshi *et al.*^[20].

In variation with some of the previous studies, we found a high prevalence of HBV in the intermediate grade but a high HCV prevalence in the low grade NHL^[19]. Some of the authors have reported high prevalence of both HBV and HCV, either in low grade or intermediate grade NHL^[20].

The role of HCV in lymphomagenesis is almost certain as reported by several authors, but how HBV leads to the development of NHL has been widely debated^[3,4].

We conclude that the prevalence of HBV and HCV in patients with NHL is much higher compared to the prevalence in the general population. The variation is very significant ($p < 0.001$).

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