

## Seroprevalence of HIV, Hepatitis B and C Viruses in Patients with Haematological Malignancies in Lagos

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### Abstract

**Background:** Haematological malignancies are often associated with immunosuppression as a result of the disease and/or chemotherapy. This increases the risk of infections by pathogens as well as the reactivation of latent infections which may be associated with adverse prognosis. Hepatotrophic viruses may be reactivated in subjects with haematological malignancies.

**Objectives:** To determine the seroprevalence of hepatitis B and C in patients with haematological malignancies.

**Methods:** This is a hospital based case control study. Consecutive subjects with haematological malignancies were recruited into the study through the haematology clinics/wards while blood donors were recruited as controls from the donor clinic. Samples of study participants were screened Hepatitis B surface Antigen (HBsAg), Hepatitis B core antibody (HBcAb), Hepatitis B envelope Antigen (HBeAg) and Antibodies to Hepatitis C virus using ELISA based assay. Results were analyzed using SPSS version 11. Chi square, Fishers Exact test and student's T-test were used where appropriate to compare results between groups. P value < 0.05 was considered significant. **RESULTS:** Eighty-eight subjects were recruited into the study comprising 42 patients with haematological malignancies and 46 apparently healthy blood donors. Frequency of HBsAg for the patients group (14.3%) was not significantly different from 21.3% for the control group  $P > 0.05$ . Two of the study subjects were positive for HBeAg. There was no significant difference in the seroprevalence of HBcAb between both groups ( $P = 0.68$ ). **CONCLUSIONS:** This study suggest that there is no significant difference in the seroprevalence of HbsAg, HBcAb and anti-HCV antibodies in both study groups however patients with haematological malignancies are at increased risk of reactivation or developing active disease

**Keywords:** HBV, HBC, Haematologic malignancy, Calabar, Nigeria

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### I. Introduction

Viral infections are implicated in the aetiopathogenesis of cancers including haematological malignancies. 1, 2 Hepatitis B and C viruses though hepatotropic, can replicate in lymphoid cells. 3, 4 Chronic infection by hepatotropic viruses especially hepatitis B and C viruses are implicated in the pathogenesis of haematological malignancies especially lymphoid neoplasm. An association between HCV and/or HBV infection with B-cell non Hodgkin's lymphoma as well as other haematological malignancies has been reported in several studies. 5 – 11 Viral infections are also associated with significant morbidity and mortality in patients with cancers especially those with haematological malignancies. The impaired immunity associated with the underlying malignancy and/or the therapy induced immunosuppression due to therapeutic intervention predisposes them to the development of new infections, reactivation of latent viruses and flaring up of ongoing acute or chronic HBV and HCV infections. 12, 13 This is associated with increased morbidity and mortality. Hepatitis B virus (HBV) is a 42nm DNA virus, member of the Hepadnaviridae family. HBV is characterized by a genome consisting of 4 overlapping open-reading frames: the S gene, encoding envelope proteins; the core gene, encoding the core and "e" proteins; the P gene, encoding DNA polymerase; and the X gene, encoding a transcriptional transactivator. Antigens and antibodies associated with HBV infection include HBsAg, HBcAg, HBeAg, anti-HBs, anti-HBc, and anti-HBe. The elaboration of HBV DNA and HBeAg is suggestive of active replication with potentials of transmission to contacts. Hepatitis C virus (HCV) is a positive, single-stranded RNA virus, member of the Flaviviridae family. The HCV genome produces a single polypeptide that is proteolytically processed by viral and cellular proteases to produce structural and nonstructural proteins.

HCV infection is associated with the production of anti-HCV. Both viruses are transmitted parenterally through blood contacts, sexual intercourse, sharing of sharp objects and vertically from mother to fetus through the placenta among others. Although the risks of acquisition of HBV and HCV reactivation of latent HBV and HCV infections are known in patients with haematologic malignancies undergoing cytotoxic or immunosuppressive therapy. 14 – 21 the frequency of such has not been documented in our locality hence this study seeks to establish the prevalence of markers of HBV, HCV infection in patients with newly diagnosed haematologic malignancies in some major hospitals in Lagos state. The introduction of the paper should explain the nature of the problem, previous work, purpose, and the contribution of the paper. The contents of each section may be provided to understand easily about the paper.

## II. Materials And Methods

Patients with haematological malignancies attending clinics in tertiary hospitals (Lagos University Teaching Hospital (LUTH), Lagos State University Teaching Hospital (LASUTH)) and General Hospital, Lagos (GHL) over a 6 month period were recruited for this study. Patients diagnosed by clinical and laboratory methods using peripheral blood and bone marrow cytology, and tissue histology where necessary. Blood donors were recruited from blood donor clinic to serve as controls. Blood sample was collected from each subject and dispensed into a sterile universal bottle and EDTA bottles. Blood in the plain sample bottle was allowed to clot and retract. Serum was separated from each sample within 1 hour of collection and kept frozen at -20°C. The participants' sera were screened with third generation ELISA for: HBsAg, HBcAb, HBeAg and anti-HCV using MONOLISA Ag HBs PLUS by BIO-RAD, ELISA Kit for HBcAb by BioChain Institute Inc. USA, HBeAg ELISA by DIAGNOSTIC AUTOMATION USA and HCV Ab by BIOTEC Laboratories Ltd. All tests were performed in conformity with manufacturer's instructions. The study was approved by the LUTH ethical committee and the management authorities of the various hospitals involved in the study. All study participants consented to participate in the study. Results were analyzed using statistical software SPSS version 11, EPI-INFO version 6 and File-maker 4. Simple proportions were calculated and relationships between different variables established using the chi square or student – T test. Significant levels was set at  $P < 0.05$ .

## III. Results

A total of 88 subjects comprising 42 patients with different types of haematological malignancies and 46 apparently healthy blood donors were studied. The study group includes 24 males and 18 females while the controls include 26 males and 20 females. The mean age of the study group is  $50.3 \pm 14.42$  with a median of 51 years while the control is  $33.8 \pm 8.94$  with a median of 33 years. Among the 42 subjects with haematological malignancies; 31 have chronic lymphoid neoplasia, 3 acute lymphoid neoplasia and 8 have myeloproliferative neoplasia. They include 13 chronic lymphocytic leukemia (CLL), 9 Non Hodgkin's Lymphoma (NHL), 5 Hodgkin's lymphoma (HL), 4 multiple myeloma (MM); 3 acute lymphoblastic leukemia (ALL), 7 chronic myelogenous leukemia (CML) and 1 essential thrombocythaemia (ET).

### 3.1 HBsAg

Six (14.3%) of subjects with HM were positive for HbsAg while 10 (21.74%) of the controls were positive. This was not statistically significant ( $\chi^2 = 0.82$ ,  $P = 0.36$ ) (Table 3). The seroprevalence within the HM group did not differ significantly. The 6 subjects positive for HBsAg, have lymphoid neoplasm giving a seroprevalence rate of 19.3%. the prevalence rate within the NHL population is 22.2% while none of those with myeloid neoplasm was positive.

### 3.2 HBeAg

Only 2 patients were HBeAg positive and both of them have lymphoma while none (0%) of the control was HBeAg positive.  $P = 0.23$  (table 3).

### 3.3 HBcAb-IgG

HBcAb is highly prevalent in both the control and patient population. Twenty (47.6%) HM subjects were positive for HBcAb while 25 (54.3%) controls were positive ( $P = 0.528$ ).

### 3.4 Hcv Antibodies

Only 1 (2.3%) of the subjects with HM was positive for HCV antibodies and this patient have NHL while 6 (13.04%) of the controls was positive. This was not statistical significance ( $P = 0.113$ ).

## IV. List of Tables

4.1 Table 1: Age Distribution of Patients

Age group (yrs)	Haematological malignancies			Controls		
	Males	Females	Total	Males	Females	Total
<20	0	1	1	2	1	3
20 – 29	3	0	3	6	7	13
30 – 39	2	2	4	12	8	20

40 – 49	8	2	10	5	2	7
50 – 59	8	8	16	1	2	3
60 – 69	1	3	4	0	0	0
≥ 70	2	2	4	0	0	0
Total	24	18	42	26	20	46

**4.1. Table 2 Age and sex distribution of patients**

Variables	Haematological Malignancy N = 42	Controls N = 46	P- value
Age (mean ± SD) (median)	50.3 ± 14.4 51.0	33.8 ± 8.9 33.0	
Sex			
Males	24	26	0.85
Females	18	20	
Seroprevalence			
HBsAg	6	10	0.365
HBeAg	2	0	0.225
HBcAb (IgG)	20	25	0.528
HCV Ab	1	6	0.113

**4.2table 3:Hepatitis B and Hepatitis C Serological Markers**

	Ctrls (N = 46)	CLL (N = 13)	NHL (N = 9)	CML (N = 7)	HL (N = 5)	MM (N = 4)	ALL (N = 3)	ET (N = 1)	TOTAL
HBsAg Pos	10	1	2	0	1	2	0	0	6
HBeAg Pos	0	0	0	0	2	0	0	0	2
HBcAb Pos	25	5	5	4	3	3	1	1	22
Anti-HCV Pos	6	0	1	0	0	0	0	0	1

## V. Discussion

This study has found a seroprevalence rate of 14.3% for HBsAg in patients with haematological malignancy. All the positive subjects were patients with lymphoid neoplasia; this affirms the findings of other researchers who have found an association between HBV infection and lymphoid neoplasm. The control group recorded a relatively higher rate of 21.7% but it was not statistically significant. This suggest a high seroprevalence rate of HBV in Lagos. The prevalence rate within the subgroup of patients with NHL is however higher than the controls. The prevalence rate of HBV differ from one geographical location to another and from one study group to another. Otegbayo et al<sup>22</sup> in UCH Ibadan southwest Nigeria reported a rate of 21.7% in blood donors; Alao et al<sup>23</sup> in Benue state northeast Nigeria report rate of 20% in blood donors. Lower rates of 1.57% and 5.4% were reported by Ejele et al<sup>24</sup> and Halim et al<sup>25</sup> in Port Harcourt and Benin City south south Nigeria respectively. These results further confirm that some regions of Nigeria are endemic for hepatitis B virus infection. The high prevalence of HBsAg among donors in this study and some other studies may not be a true representative of the seroprevalence of the general populace as the donor populace are mainly family replacement and remunerated donors. There are few published work on the seroprevalence of HBsAg in patients with haematological malignancy in Nigeria. The prevalence of HBV in patients with haematological malignancy may depend on its prevalence in the general populace however some studies have shown significantly higher prevalence in patients with HM, while few others did not. Nashwa et al<sup>6</sup> in a case control study found an association between the prevalence of HBV infection and B cell-NHL. Similarly, Olatunji et al<sup>7</sup> reported a seroprevalence rates of HBsAg of 35.6% and 7.7% in patients with malignant lymphoproliferative disorder and normal controls respectively. The latter study showed a significant association between HBV and lymphoproliferative disorders.

Takai et al<sup>7</sup> reported HBsAg prevalence rate of 7.3% in Japanese patients with haematological malignancies. There is lower prevalence in that country (1.7%) and 1.2% among blood donors. Similar low prevalence (5.4%) was reported by Alexopoulos and fellow workers in Greece among patients with haematological malignancies.<sup>8</sup>

Anderson et al<sup>26</sup> selected from the U.S. Surveillance, Epidemiology, and End Results- Medicare database 61,464 cases with hematopoietic malignancies and 122,531 population-based, matched controls. HBV was not associated with any hematopoietic malignancy. The prevalence of HBV infection in the control population, however, was very low (0.2%). Similarly, a case-control study in eight European countries, that included 739 incident cases of NHL, 238 of multiple myeloma (MM), 46 of Hodgkin's lymphoma (HL), and 2,028 matched controls did not show a significant association between HBsAg-positivity and each of NHL, MM, and HL.<sup>27</sup> However a significant association, was observed between HBsAg-positivity and the combination of NHL, MM, and HL (OR, 2.21; CI, 1.12-4.33). Though the index study did not show a significant association

between HBsAg and HM, we found an increased seroprevalence in the NHL subgroup. HBeAg is one of the markers of active disease. Two (4.7%) of the subjects with haematological malignancy were positive for HBeAg. The affected subjects have lymphoma. HbcAb is a marker of prior infection. Subjects who have been exposed and are HbcAb positive are at increased risk of reactivation. This study found a high seroprevalence of HbcAb in subjects with HM. This is lower than that of the control population and is further suggestive of the endemicity of HBV in the study populace. Marcucci et al<sup>28</sup> detected a significantly higher number of HBcAb-positive, HBsAb-negative patients, among NHL patients. The reactivation of HBV infection has been reported in different haematological malignancies including myeloid, lymphoid and plasma cell neoplasia.<sup>21</sup> Reactivation is common following commencement of steroid based regimen.<sup>21</sup> Rituximab, anthracyclines and Fludarabine based regimen are also associated with increased risk of reactivation.<sup>14-21</sup> Reactivation may result in hepatitis flare, hepatic failure and even death.<sup>21</sup> In the light of the above, all patients with malignancies especially haematological malignancies should as a routine be screened for HBV infection prior to therapy. It is imperative that continuous surveillance of the HBV activity in persons with prior infection to detect reactivation so that appropriate intervention is instituted. The management approach could be prophylactic or preemptive. This study found low seroprevalence of HCV antibodies in subjects with HM compared to controls. The relatively high seroprevalence rate in the control may be attributed to the increased number of remunerated donors posing as voluntary and family replacement donors. There was no association between HCV antibody and HM in our study. Nashwe et al<sup>5</sup> did not also find any association between HCV and B-cell NHL. However some studies have established a significant association between HCV and HM especially B-cell lymphoproliferative disorders.<sup>9-11</sup>

## VI. Conclusion

In conclusion, this study has found an increased seroprevalence in control populace which is not significantly different from those of subjects with haematological malignancies. However subjects with NHL, have a higher seroprevalence for HbsAg. In view of the increased risk of reactivation in patients with haematological malignancies especially following commencement of chemotherapy; there is need for assessment of HBV and HCV status prior to commencement of therapy and continuous surveillance during and after therapy to prevent the morbidity and mortality associated with reactivation.

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