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Seroprevalence of HBV, HCV and HIV infection in Patients with Haematological Malignancies seen at the University of Benin Teaching Hospital, Benin City, Nigeria

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Abstract:
Introduction: *Viruses are implicated in the etiopathogenesis of malignancies. There is a high risk of reactivation of latent viral infections in persons with HMs. The sero-prevalence of some of these virus has not been reported in our environment.*
Objective: *To determine the seroprevalence of HIV, HBV and HCV in subjects with HMs; to establish if any its association with specific HMs and blood transfusion history.*
Method: *This is an ambispective study conducted at the University of Benin Teaching Hospital, Benin City. Fifty one patients with HMs were recruited for this study. Data on demographics, daignosis of HMs and transfusion history was obtained with an interviewer administered questionnaire. Sample was collected and analyzed for HBV, HCV and HIV status using rapid kit tests. Results were analyzed with SPSS version 16.*
Result: *The subjects included 30 (58.8%) males and 21 (41.2%) females. The median age of the participants was 48 years. Non Hodgkins lymphoma and CLL are the commonest HMs in this centre. The seroprevalence of HBV, HCV and HIV were 9.8%, 2% and 2% respectively. HBV seropositivity was associated with NHL (p value =0.013). The odd of HBV seropositivity with blood transfusion prior to diagnosis is high (5.5).*
Conclusion: *The seroprevalence of HBV, HCV and HIV in subjects with HMs seen in UBTH, Benin City were 9.8%, 2% and 2% respectively. HBV seropositivity was significantly associated with NHL.*
Keywords: *Benin City, Haematologic malignancies, HBV, HCV, HIV, Seroprevalence.*

I. Introduction

Haematological malignancies (HMs) are neoplastic proliferations originating primarily from lympho-haematopoietic tissues. Traditionally, HMs are categorized as non-hodgkin's lymphoma (NHL), Hodgkin's lymphoma (HL), leukaemias (acute and chronic, lymphoid and myeloid) and plasma cell dyscrasia. Recent authoritative consensus classification (WHO) favours two major divisions including myeloid and lymphoid neoplasms. [1, 2]

HMs constitute 6 – 9% of all cancers and are the fourth commonest in men (after prostate, lung and colo-rectal cancers) and in females (after breast, lung and colo-rectal cancers).[3, 5] In a recent UK estimate, HMs were more frequent in male; the incidence of lymphoid neoplasms was more than two-fold compared to myeloid neoplasms.[6] Non-hodgkin's lymphomas are the commonest, followed by chronic lymphocytic leukaemia and plasma cell neoplasm.[6] Local report suggest that HMs constitute about 17.4% of all cancers seen at the University of Benin Teaching Hospital, Benin City, Nigeria.[7] Local studies also show that malignant lymphomas (mostly non-Hodgkin's lymphoma) are the most prevalent form of HM in Nigeria.[7, 8]

Microbiologic agents such as certain viruses, bacteria and parasites have been implicated in the etiopathogenesis of HMs.[9] The oncogenic potentials of Human T Lymphotropic Virus - 1 (HTLV-1), Human Herpes Virus-8 (HHV-8) and Ebstein Barr Virus (EBV) in lymphomagenesis are well documented[9, 10]

Apart from the oncogenic potential of some viruses, reactivation of viruses capable of causing latent infections (HBV, HCV and HIV among others) may occur in persons with HM due to the severe immunosuppression caused by the underlying HM or due to the effects of therapy.[11] This may impact adversely on the prognosis of the disease.

HBV and HCV are hepatotrophic viruses belonging to Hepadnaviridae family (DNA) and Flaviviridae (RNA) families respectively. They can cause acute and chronic hepatitis as well as latent hepatic infection. The etiologic associations of Hepatitis B virus (HBV) and hepatitis C virus (HCV) with HMs especially NHL has also been documented.[13] HIV is a non-transforming RNA virus of the lentivirinae family; it causes marked immunosuppression which may predispose to opportunistic viral infections such as HTLV, EBV, HHV-8 and Human Papilloma Virus (HPV) which are associated with oncogenicity.[14] HBV, HCV and HIV are transmitted parenterally (including through blood tansfusion), sexually and vertically from mother to child.

In Nigeria, recent evidence suggests that viral safety of blood components is still largely sub-optimal.[15] The seroprevalence of these viruses in potential blood donors is still unacceptably very high in our populace hence blood transfusion therapy an integral component of Cancer therapy is still a serious hazard capable of transmitting these viruses to potential recipient.

Suffice to say that HBV, HCV or HIV co-infections in HMs constitutes additional disease burden, and may precipitate disease flares in stable/controlled hepatitis infections due to the immune-suppressive nature associated with HMs, narrow down therapeutic options, and invariably worsens survival outcomes in these group of patients.[16]

This study therefore aims to determine the prevalence of HBV, HCV and HIV infections among adult haemato-oncology patients seen at the University of Benin Teaching Hospital. It also seeks to determine if there is any significant association between each of these viruses and the different malignancies.

II. Patients And Method

This is an ambispective study conducted in the department of Haemato-Oncology, University of Benin Teaching Hospital, Benin City, Edo State.

Study population: this include all patients with haematologic malignancies recieving care in the centre during the study period including old and newly diagnosed subjects. HMs were diagnosed by routine procedures including clinical examination, full blood count, bone marrow aspiration and biopsy, lymph node biopsy for histology and occassional immunohistochemical techniques were applied.

Study duration: the study was conducted over a six months period (October, 2014 to April 2015)

Sample Size: A total of 51 subjects participated in this study.

Inclusion Criteria: Subjects aged ≥18 years and evidence of established diagnosis of Haematologic Malignancies

Exclusion Criteria: Subjects <18 years and those with inconclusive diagnosis.

Sources of data: Data was obtained from participants with an interviewer administered questionnaire after obtaining consent. Data include demographic parameters, type of malignancy, age at diagnosis, method of diagnosis, history of transfusion prior to diagnosis and after diagnosis. Blood sample was collected from newly diagnosed subjects for serological diagnosis of HBV, HCV and HIV status while results of previously diagnosed patients currently on therapy was obtained from their case notes.

Sample collection: Two millitres of venous blood was collectd from antecubital veins of consenting subjects under aseptic conditions and dispensed into a plain tube. The blood was allowed to clot and the clotted blood was centrifuged at 1500 rpm for 15 minutes. Serum was harvested using a pippette and dispensed into a plain tube. Samples were analyzed immediately for HBV, HCV and HIV status using enzyme linked immunosorbent assays (ELISA) rapid test kits. Plasma from the subject was tested by dropping a little portion on the specimen pad at one end of the test strip. A waiting time of 15 minutes was observed before the results were read.

Serological Assays: HbsAg and Anti-HCV were tested by applying serum to the rapid kits manufactured by Acumen diagnostic kits (Acumen diagnostics Incorporated), China. HIV assay was done using WHO precribed alternate kit methods. HIV kits used include: Alere Determine™ HIV-1/2 strip manufactured by The Alere Logo, Alere, US and Unigold kits were used for HIV screening.

Statistical Analysis: Data was analyzed using statistical package for social science (SPSS) version 16. Data were expressed as mean, median, standard deviation and percentages as appropriate. Associations between the seroprevalence of HBV, HCV and HIV with sex, haematologic diagnosis and history of transfusionn were tested using chi-square and Fishers Exact test. P value was set at 0.05.

III. Results

Fifty one subjects participated in this study including 30 (58.8%) males and 21(41.2%) females. Their median age was 48 years with a median age at diagnosis of 45 years. Thirty four (66.7%) of the participants reside in Benin City and 12 (23.6%) reside in Delta State. Details of demographic parameters are show in table 1.

The spectrum of haematologic malignancies include non Hodgkin's lymphoma, chronic lymphoid leukaemia (CLL), multiple myeloma (MM), chronic granulocytic leukaemia (CGL), acute leukaemia, Hodgkins lymphoma, myeloproliferative neoplasm (MPN) and myelodysplastic syndrome (MDS) in 16 (31.4%), 10 (19.6), 6 (11.8), 6 (11.8), 5 (9.8), 4 (7.8), 3 (5.9) and 1 (2.0) subjects respectively.

Three (5.9%) of the subjects had been transfused prior to diagnosis while 30 (58.8%) were transfused after diagnosis.

The seroprevalence of HBV, HCV and HIV in the study subjects were 5 (9.8%), 1 (2.0%) and 1 (2.0) respectively. Four of the seropositive HBV subjects had NHL while one had acute leukaemia. The HIV and HCV sero-positive subjects had NHL and acute leukaemia respectively.

HBV seropositivity was significantly associated with NHL p value = 0.013. There were no significant association between sex, history of transfusion with HBV seropositivity however the odd that females with HM will be HBV seroposive is 2.33 while that of positive history of transfusion prior to diagnosis was 5.5 as shown in table 2.

There is no significant association between HIV and HCV seropositivity each with sex, haematologic malignancies and transfusion as shown in tables 3 and 4 respectively.

IV. Discussion

We found a relatively higher frequency of males with HMs. This affirms the observations of several other authors who reported a relatively higher incidence of HM in males.[7, 8] We also found that NHL and CLL were the leading HMs diagnosed in our environment. This is similar to the observations of Nwannadi et al[7] in a 10 year retrospective study on the epidemiology of HM in Benin City and Mbanya et al in a Camerounian study.[17]

The seroprevalence of HBV, HCV and HIV in patients with HMs to our knowledge has not been reported in our environment. We found a relatively higher seroprevalence of 9.8% for HBV compared to 2% each for HCV and HIV.

The seroprevalence rate of an infective agent in a study sample may reflect or depend on its prevalence in the general population. Nigeria has a high seroprevalence rate for HBV infection which is variable from region to region.[18] We found a relatively higher rate of HBV seropositivity in our study sample compared to the 4.7% reported in blood donors in the same facility by Nwogoh et al.[19] Berberologu et al[20] in a similar study though in younger age group in Turkey a developing country with endemic HBV infection like ours reported a seroprevalve rate of 4%. Omar et al[21] in another related study including patients with leukaemic malignancies reported a significantly higher seroprevalence rate of 32.3%.

Our study also showed a significant association between HBV sero-positivity with NHL similar to the observations of Engels et al[22] among others. Though we can not conclude that this relationship is causal, further research is require to establish this. Engels however in their study followed up a cohort of baseline HbsAg positive population over a period of 4 years and compare the the risk of NHL in them to those of another group with HbsAg seronegativity in South Korea. They concluded that HbsAg seropositive populace have an increased risk of NHL compared to seronegative subjects thereby establishing a strong association between NHL and HBV infection.

The high prevalence of HBV in our study populace portends some challenges in the care of these group of patients to haematologist which should not be overlooked. Patients requiring high doses of chemotherapy, immunotherapy and immunosuppression especially for haemopoietic stem cell transplant (HSCT) harbour a great risk of reactivation and hepatitis flares. Pompili et al[11] documented reactivation in some group of patient with HM 12 months after HSCT.

The seroprevalence of HCV was found to be 2%. This is higher than 0.4% reported in blood donors in Benin City by Nwogoh et al.[19] Omar et al[21] in a case control study in central Iraq reported a higher seroprevalence in patients with HM compared to controls. Berberoglu[21] in Turkey reported a lower rate of 0.9% in a population of young patients with malignancies. The lower rate in the later study may be attributed to the younger age group under study as exposure and infection increase with age. This also affirm by the Omar study.

Our study did not find any assoociation between HCV seropositivity with any HM. Contrary to the observations of Engels,[23] Dogan et al[24] among others that have found an association between HCV infection and NHL. The paucity of seropositive participants may be responsible for this observation. If a cohort of HCV seropositive subjects were followed up over time, it is possible some association may be established.

We found a low seroprevalence of HIV of 2%. This is lower than 4.1%, 5.3% and 7.2% reported as the national, the state and even the rate reported in Blood donors in the same institute respectively.[19, 25] There are paucity of literature on seroprevalence of HIV in HM subjects however the prevalence of HM in HIV patients have been widely researched. Mbanya et al reported a seroprevalence rate of 26.5% in patients with HM in Cameroun.[17]

Blood transfusion is still hazardous and is a serious means of tranmitting the viruses under study. Safety profile of blood products in our environment is relatively low compared to developed nations.[15] Our study though did not establish any association between the seroprevalence of these viruses in subject who were transfused prior to, during and post diagnosis of HM however a high odd ratio (5.5) was found with HBV seropositivity in patient who had previous transfusions prior to the development and diagnosis of HM with this practice. This further strenghten the association between prior HBV infection with HM and highlights also the inherent risk of blood transfusion as a means of transmitting these infections. The lack of a significant odd ratio with post diagnosis transfusion is probably because most of the care including blood transfusion were conduct in the tertiary facility with relatively higher blood transfusion safety profile.

V. Conclusion

The seroprevalence of HBV, HCV and HIV in subjects with HMs seen in UBTH, Benin City were 9.8%, 2% and 2% respectively. HBV seropositivity was significantly associated with NHL. The odd for HBV seropositivity in subjects who had blood transfusion prior to diagnosis is high (5.5).

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List of tables

Table 1: Demographics, Spectrum of Malignancies and Transfusion History

Variables	
Age	
Mean ± SEM	46.6± 2.0 years
Median	48 years
Range	18 – 86 years
Age at diagnosis	
Mean ± SEM	45.6 ± 2.0 years
Median	45 years
Range	18 – 45 years
Sex	**Frequency (%)**
Male	30 (58.8)
Female	21 (41.2)
M:F	1.43:1
Place of Resident	
Benin City	34 (66.7)
Delta	12 (23.6)
Lagos	3 (5.9)
Others	2 (4.0)
Spectrum of HM	
NHL	16 (31.4)
CLL	10 (19.6)
Multiple myeloma	6 (11.8)
CGL	6 (11.8)
Acute leukaemias	5 ((9.8)
Hodgkins lymphoma	4 (7.8)
MPN	3 (5.9)
MDS	1 (2.0)
Transfusion History	
Prediagnosis	3 (5.9)
Post diagnosis	30 (58.8)

Table 2: Association between HBV seropositivity, Sex, Specific HM and Transfusion History

Variables	**HbsAg Positive**	**HbsAg Negative**	**P value**	**Odd ratio**
Sex	**Freq. (%)**	**Freq. (%)**		
Female	3 (5.9)	18 (35.3)		
Male	2 (3.9)	28 (54.9)	0.637	2.33
Diagnosis				
NHL	4 (7.8)	12 (23.5)		
Acute leukaemias	1 (2.0)	4 (7.8)	0.013	
Others	0 (0.0)	30 (58.8)		
Transfusion History				
Prediagnosis				5.5
Yes	1 (2.0)	2 (3.9)	0.271	
No	4 (7.8	44 (86.3)		
Postdiagnosis				
Yes	3 (5.9)	27 (52.9)	1.000	1.06
No	2 (3.9)	19 (37.3)		

Table 3: Association between HIV seropositivity, Sex, Specific HM and Transfusion History

Variables	**HIV Positive**	**HIV Negative**	**P value**
Sex	**Freq. (%)**	**Freq. (%)**	
Female	1 (2.0)	20 (39.2)	
Male	0 (0.0)	30 (58.8)	0.412
Diagnosis			
NHL	1 (2.0)	15 (29.4)	0.314
Other HM	0 (0.0)	35 (68.6)	
Transfusion History			
Prediagnosis			
Yes	1 (2.0)	2 (3.9)	0.059
No	0 (0.0)	48 (94.1)	
Postdiagnosis			
Yes	0 (0.0)	30 (58.8)	0.412
No	1 (2.0)	20 (39.2)	

Table4: Association between HCV seropositivity, Sex, Specific HM and Transfusion History

Variables	Anti-HCV Positive	Anti-HCV Negative	P value
Sex	**Freq. (%)**	**Freq. (%)**	
Male	0 (0.0)	30 (58.8)	0.412
Female	1 (2.0)	20 (39.2)	
Diagnosis			
Acute leukaemias	1 (2.0)	4 (7.8)	0.098
Other HM	0 (0.0)	46 (90.2)	
Transfusion History			
Prediagnosis			
Yes	0 (0.0)	2 (3.9)	1.000
No	1 (2.0)	48 (94.2)	
Postdiagnosis			
Yes	1 (2.0)	29 (56.7)	1.000
No	0 (0.0)	21 (41.2)	