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Some Haematological Parameters and CD4 Count in HIV and HBV Co-infected Patients in South Western Nigeria

Anslem O. Ajugwo[1*], Kevin E. Aghatise[2], Richard Eze[1], Ivie Osula[2], Tosan A. Erhabor[3] and Beatrice E. Adesina[2]

[1]Department of Medical Laboratory Science, Madonna University, Nigeria.
[2]Department of Medical Laboratory Science, Igbinedion University, Okada, Edo State, Nigeria.
[3]Medical Laboratory Science Council of Nigeria (MLSCN), Abuja, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

This study aims at determining the prevalence of HBV, as well as its effect on immunological and haemtotological profile of HIV infected patients attending government owned health facilities in Osun state, Nigeria. Venous blood was collected from a total of 121 HIV HAART naïve patients and 200 HIV negative subjects as controls. Blood samples were analyzed for antibodies to HIV and HBV using immunochromatographic methods. CD4+ count was done using flow cytometry, Haemoglobin and platelet count of all hiv infected patients were also determined using Sysmex auto-analyzer. A questionnaire was used to obtain demographic data from all consenting patients. HIV status was identified as a risk factor for acquisition of HBV infection in this study (HIV positive vs. HIV negative: 16.5% v 3.5%; OR=5.460, 95% CI=2.233, 13.348, P=0.00). Age and gender of patients did not significantly affect the prevalence of HBV infection among HIV infected patients (P>0.05). The mean haemoglobin concentration, CD4 count and platelet count among HIV/HBV co-infected patients did not differ significantly from values obtained in HIV mono - infected group of

**Corresponding author: E-mail: slemjugwo@yahoo.com;*

patients (P>0.05). Among the HIV/HBV co-infected patients, the mean CD4 count was significantly higher in females than males (male v female 327.6 ± 8 .33 vs. 408.4 ± 331.28, P = 0.008). The mean hemoglobin concentration and platelet count among HIV\HBV co-infected patients did not define significantly with respect with gender (hemoglobin: male v female: 12.58 + 2.75 vs 9.81 + 2.12, P = 0.226). In the HIV/HBV co-infected cohort, age was observed to significantly affect the mean platelet count (P = 0.044) but not mean CD4 count (P = 0.426) and mean haemoglobin concentration (p = 0.122). The prevalence of HBV among HIV infected patients was high. HIV was identified as a risk factor for acquisition of HBV infection. The mean haemoglobin concentration, CD4 and platelet count of HIV/HBV co-infected patients did not differ significantly from values obtained in HIV mono-infected group of patients. Among HIV/HBV co-infected group of patients, gender and age were observed to significantly affect mean CD4 and platelet counts respectively. Routine screening of HBV among HIV infected patients is advocated.

Keywords: Platelet counts; immunology; hematology; HIV; cytometry.

1. INTRODUCTION

The human immunodeficiency virus (HIV) infection is associated with increased mortality and morbidity worldwide, with prevalence rate that varies from region to region. It is known to affect people of all ethnicity, gender, age and sexual orientation [1]. Sub –Saharan African remain by far the most affected region with 24.5 million people living with HIV, representing a little below two third of all people living with HIV in the world [2]. HIV infection is a major health concern in Nigeria, where it is estimated that about 2.9 million people is living with the virus [3]. Global estimates of HIV/AIDS put Nigeria only behind South Africa in the list of HIV/AIDS most endemic counties of the world [4].

Hepatitis B virus (HBV) is a major cause of liver disease morbidity and mortality worldwide, accounting for over 360 million cases of chronic hepatitis and 620,000 deaths per year [5]. It is hyper endemic (i.e. > 8% of the population infected) in sub-Sahara Africa (SSA) and a major cause of chronic liver disease [6]. It has been estimated that 44% of cirrhotic liver disease and 47% of hepatocellular carcinoma cases in SSA are attributed to HBV [7]. Researchers have reported varying national and risk group/specific estimate in Nigeria. Prior reports suggest a prevalence of 10 – 15% in the average risk Nigerian population [8]. In Nigeria, investigators have found varying HBV prevalence rates among different groups. 16.3% was recorded among infants and 5.6% was documented among pregnant women [9,10].

Both human immunodeficiency virus-1 (HIV) and hepatitis B virus (HBV) are transmitted through similar routes, thus, coinfection with both viruses is common [11]. Worldwide, it is estimated that 10% of the 40 million HIV-infected individuals have chronic hepatitis B. Since the introduction of highly active antiretroviral therapy (HAART) in the United States and other industrialized countries, death from AIDS-related causes have declined, but liver disease has emerged as one of the leading causes of morbidity and mortality [7]. As HAART is introduced into areas of the world with high HBV endemicity, hepatitis B-related liver disease has increased in the HIV-infected population [11]. It is therefore important to understand the interaction of these two chronic viral infections. Concomitant HIV-HBV infections have been reported to increase the infectivity of HBV, the rate of HBV reactivation and the risk of cirrhosis [12]. Conflicting reports exist on the role of HBV in HIV disease progression. While some studies have reported no significant effect of HBV on HIV disease progression [12,13], others report otherwise [14,15]. Again, infection with HBV has been reported to cause aplastic anaemia, an uncommon but distinct variant of aplastic anaemia in which pancytopenia appears two to three months after an acute attack of hepatitis [16]. Previous studies have recorded varying CD4 counts in HIV/HBV co-infection. Data on prevalence on HBV among HIV infected patients and its effects on HIV disease progression and other haematological parameters is missing in Osun State, South Western Nigeria. Against this background, this study aimed at determining the prevalence and effect of HBV on mean CD4 count and some hematological parameters among HIV infected patients attending government owned hospitals in Osun State, Nigeria.

2. MATERIALS AND METHODS

2.1 Subjects

This study was conducted among 121 HAART naïve HIV-infected subjects attending State Specialist Hospital Osogbo and State Hospital

Iwo both in Osun State, South Western Nigeria. 200 HIV negative subjects was recruited and served as control. A structured questionnaire was used to obtain demographic information from consenting subjects and verbal informed consent was obtained from all subjects.

2.2 Sample Collection

Ten milliliters of blood was collected from each participant and 5 ml was dispensed into EDTA container while the remaining 5 ml was dispensed into plain container and allowed to clot. The sera obtained were used for serological diagnosis of HIV and HBV using previously described methods [2,9]. The anti-coagulated blood was used for the determination of CD4 count, haemoglobin concentration and Platelet count.

2.3 Sample Analysis

HIV Serodiagnosis: HIV serology was carried out using the current National algorithm for HIV sero-diagnosis. This involved the use of three rapid diagnostic kits, following their manufacturer's instruction. Briefly, each patient's serum was screened for the presence of HIV antibodies using Determine (Abbott Laboratories, Tokyo Japan) and Unigold HIV (Trinity Biotech Plc Bray, Co. Wicklow Ireland). When both kits showed positivity, the sample was regarded as positive for HIV infection and vice versa. However, when test results were discordant, a third kit (tie breaker) HIV ½ Stat Pak (Chembio Diagnostic Systems, New York, NY USA) was used. The result is taken as the result of either of the first two kits that agree with that of the third kit.

Hepatitis B Virus (HBsAg) Detection: This was performed using Immunochromatographic methods (Clinotech Diagnostics, Richmond, Canada) according to manufacturer's instruction.

CD4+ Cells, Haemoglobin and Platelets count: CD4+ count was determined for all HIV infected subjects. Blood sample was analyzed for CD4+ lymphocyte cell count using flow cytometry (Partec GmbH, Germany). Briefly, 20 µl of CD4 PE antibody was placed into a Partec test tube and 20 µl of well-mixed whole EDTA blood was added, mixed gently and incubated in the dark for 15 min at room temperature. The mixture was agitated during incubation every 5 minutes. Eight hundred microliters of CD4 buffer was added to the mixture of antibody and sample and mixed gently. This was then plugged to the counter for counting.

Haemoglobin concentration and platelet counts were determined using an auto-analyzer, Sysmex KX-21 (Sysmex Corporation, Kobe Japan).

3. RESULTS

In both male and female groups, the highest frequency of HBV was seen in age group 25 – 31 years (Table 2). In HIV mono-infected, the lowest value for CD4 count of 196.35+155.42 was noted in 46 – 52 years group while for HIV/HBV co-infected group the lowest CD4 count of 285.5+106.77 was noted in 39 – 45 years group (Table 4).

4. DISCUSSION

With so much emphasis given to the study of HIV/AIDS in Nigeria in recent years, little attention has been drawn to hepatitis B Viral infection which have been shown to have similar route of transmission as human immunodeficiency Virus [9] and responsible for increased morbidity and mortality among HIV infected patients. The prevalence of HIV/HBV co-infection is known to vary from place to place and even within the same place over a period of time.

The prevalence of HBV infection among HIV infected patients in this study was 16.5%. This is lower than 28.7% and 20.6% reported in some Nigerian studies [17,18]. It is however higher than 2.2%, 0.4% and 12.3% recorded in other studies [19,20,21]. The observed variation in prevalence of HBV infection may be due to differences in geographical location as these studies were conducted in South Eastern Nigeria [19], North Central Nigeria [20] and North Central Nigeria [21] respectively, in contrast to our study which was conducted in South Western Nigeria.

Table 1. Prevalence of Hepatitis B virus infection among study participants

Variables	N	No HbsAg pos (%)	OR	95%CI	P value
HIV Status					
Positive	121	20 (16.5)	5.460	2.233,13.348	0.001
Negative	200	7 (16.5)			
	321	27 (8.4)			

Table 2. Age and sex distribution of HBV sero-prevalence among HIV infected patients

Variable	N	No HbsAgPos(%)	OR	95%CI	X^2	P value
Male					2.200	0.138
4-10	2	0 (0.0)				
11-17	1	0 (0.0)				
18-24	3	2 (66.0)				
25-31	5	1 (20.0)				
32-38	2	1 (50.0)				
39-453	1	1 (33.3)				
46-52	1	1 (100.0)				
Female						
4-10	4	0 (0.0)			0.210	0.646
11-17	3	0 (0.0)				
18-24	9	2 (22.2)				
25-31	34	5 (14.7)				
32-38	33	5 (15.1)				
39-45	13	3 (23.1)				
46-52	8	0 (0.0)				
Gender						
Male	17	5 (29.4)	2.472	0.761	8.032	0.156
Female	104	15 (14.4)				

N - Number examined OR-odd ratio, confidence interval

Table 3. Effect of Hepatitis B virus on haemoglobin concentration of HIV infected patients

Variables	HIV/HBV Co-infected		HIV mono-infected		P Value
	N	Mean Hb Conc (±SD)	N	Mean Hb Conc(±SD)	
Age (years)					
4-10	-	-	5	8.95±1.590	ND
11-17	-	-	4	10.42±1.70	ND
18-24	4	8.87±2.08	9	10.58±1.24	0.107
25-31	6	9.31±1.17	33	9.94±1.72	0.291
32-38	6	10.78±2.61	29	9.85±1.97	0.157
39-45	2	14.55±0.49	14	10.18±2.28	0.167
46-52	2	12.4±3.11	7	9.25±2.24	0.214
Gender					
Male	5	12.58±2.75	13	11.6±2.67	0.415
Female	15	9.81±2.12	88	10.01±2.03	0.374
HIV-HBV co-infected patients			**HIV mono–infected patients**		
P value (age) = 0.122			P value (age) = 0.321		
P value (gender) = 0.211			P value (gender) = 0.074		

Of all 200 HIV negative control patients screened in this study only 7(3.5%) was infected with HBV. The prevalence of HBV infection among HIV infected patients were observed to be significantly higher than value recorded among HIV negative cohort in this study (p = 0.001). Indeed, the HIV infected patients had a 1 -6 fold increased risk of being infected with HBV than HIV negative subjects. Reports indicate that clearance of HBV in HIV infected patients is slower than in HIV negative ones [22]. Thus the observed significantly higher prevalence of HBV infection among HIV/HBV co-infected patients in comparison with HIV-negative group may be due to difference in HBV clearance rate among them. In addition, HIV infected individuals are more likely to loose previously developed protective anti – HBs antibody and develop acute hepatitis B infection [23]. This may also explain the higher prevalence of HBV infection among the HIV infected cohort of this study.

Table 4. Effect of Hepatitis B virus on haemoglobin concentration of HIV infected patients

Variables	HIV/HBV Co-infected		HIV mono-infected		P Value
	N	Mean CD4 count (+SD)	N	Mean CD4 count (SD)	
Age (years)					
4-10	-	-	5	584.2+452.4	ND
11-17	-	-	4	472.25+283.49	ND
18-24	4	644.75289.10	9	411.0+189.59	0.161
25-31	6	349.5+288.66	33	397.5+288.79	0.579
32-38	6	294.17+394.76	29	348.75+263.53	0.154
39-45	2	285.5+106.77	14	289.71+195.90	0.405
46-52	2	326+62.25	7	196.35+155.42	0.299
Gender					
Male	5	327.6+81.33	13	274.5+200.64	0.448
Female	15	408.4+331.28	88	1391.96++282.84	0.184
HIV-HBV co-infected patients			**HIV Mono–infected patients**		
P value (age) = 0.426			P value (age) = 0.508		
P value (gender) = 0.008			P value (gender) = 0.093		

N - Number examined, SD standard deviation

Table 5. Effect of Hepatitis B virus on platelet count of HIV infected patients

Variables	HIV/HBV co-infected		HIV mono-infected		P Value
	N	Mean platelet count (+SD)	N	Mean platelet count (SD)	
Age (years)					
4-10	-	-	5	314+94.706	ND
11-17	-	-	4	294.75+85.46	ND
18-24	4	347.25+106.05	9	240.75+141.39	0.294
25-31	6	338.6+119.7	33	273.82+101.98	0.259
32-38	6	161.67+98.43	29	279.79+132.97	0.262
39-45	2	193.0+59.39	14	296.35+121.26	0.367
46-52	2	237.0+46.67	7	243.83+113.04	0.305
Gender					
Male	5	180.2+82.98	13	265.46+109.13	0.537
Female	15	286.7+124.4	88	279.5++114.30	0.316
HIV-HBV co-infected patients			**HIV mono–infected patients**		
P value (age) = 0.044			P value (age) = 0.124		
P value (gender) = 0.226			P value (gender) = 0.461		

HBV infection was observed among young and adolescent (4 – 17 years) HIV infected patients while the highest prevalence was recorded among patients within the age group of 18-24 years. The low prevalence of HBV infection in the young adolescence HIV infected patients in this study is in contrast to finding from another African study, where the highest prevalence of HBV infection was recorded among patients less than 20 years old [24]. The prevalence of HBV infection is reported to vary from country to country and from time to time even within the same region and depends on a complex mix of behavioral, environmental and host factors [25]. In recent past, the Nigerian government and other non-governmental agencies have made great strides in enlightenment of the general public on the dangers of indiscriminate sexual activities and use of unsterilized sharp instruments which are potent vehicles for the transmission of HIV and HBV infections. This awareness may have precipitated the desired behavioral changes on the part of young people with regards to use of unsterilized sharp instrument and thus reflecting in the low prevalence observed among them in our study. Nigeria commenced her universal HBV immunization program in 2004 [10]. Study

participant within the age group 4-17 years are more likely to be beneficiaries of such a young program than older participant, and thus present with lower risk for HBV infection. However, age of HIV infected patients not identified as a risk factor for HBV Sero-posivity (p = 0.631). This agrees with findings from a Nigerian study [26], but disagrees with another research [24].

Several reports have indicated that the rate of HBV clearance is higher in females than males leading to a generally higher prevalence of HBV among male population [27]. This is consistent with finding from this work where a higher prevalence of HBV infection however did not differ significantly with respect to gender (p = 0.156). A similar finding has been reported elsewhere [28].

The association between HIV and anaemia is well documented in literature. It is common knowledge that HIV infection is associated with anaemia, necessitating frequent blood transfusion. Report indicates that most blood used for transfusion in developing countries do not undergo standard screening recommended by WHO [29]. Frequent receipt of such blood by HIV infected persons, places them at higher risk of contracting other blood borne related diseases such as HBV. This may well explain the higher prevalence of HBV in HIV infected persons. Studies have also reported that infection with hepatitis viruses such as HAV, HBV, HCV, HDV and HEV can lead to bone marrow failure and pancytopenia causing anaemia [16]. In this study, though varying mean haemoglobin concentration was recorded between the HIV mono-infected and HIV/HBV co-infected patients in all age groups, hepatitis B virus infection was not found to significantly affect the haemoglobin concentration among them. This is in contrast to findings from another Nigerian study [30]. The variation in findings may be due to differences in the nature of study populations, as [30] were HIV infected patients on HAART, as compared to ours which were HAART naïve HIV infected patients. The difference in mean haemoglobin concentration between HIV mono-infected and HIV/HBV co-infected patients also did not differ significantly among males and females in this study (P>0.05).

Evaluation of mean CD4 concentration of HIV/HBV and HIV mono-infected patients in the same age group category did not show any significant difference between them (P>0.05). This is in contrast with findings from other Nigerian which showed a statistically significant difference in CD4 + count in HIV/HBV infected and HIV mono-infected groups [23,30]. A recent Nigerian study showed that the CD4 count varies significantly among apparently healthy individual with respect to age [31]. Similar findings have been reported elsewhere outside Africa [32,33]. Earlier study [30] did not take into consideration the effect of age on CD4 count between HIV/HBV co-infected patients and HIV mono-infected patients. The mean CD4 count of all HIV/HBV co-infected patients and HIV mono-infected patients irrespective of the differences in age were compared and the deductions made [30]. This does not provide a level ground for the assessment of the effect of HBV on CD4 count of HIV infected patients, and may account for the variation in our findings.

However, the CD4 count of HIV/HBV co-infected patients was generally observed to decrease steadily with increase in age of study participants. Multiple cohort studies involving untreated HIV-infected persons have established that older persons have a more rapid progression to AIDS and shortened survival when compared with younger persons [34,35,36,37].

Research from animal models and human subjects suggest that with increasing age, there are several important changes in the innate and adaptive immune response, a phenomenon termed “immunosenescence” [38]. This altered immune responses observed with increasing age may be responsible for the pattern of CD4 count observed. The difference in mean CD4 count among HIV/HBV co- infected patients was not found to differ significantly with respect to age (P = 0.426).

Although studies have reported that HBV increases HIV proliferation, a situation that should naturally be associated with reduced CD4 count. In our study, the mean CD4 count among the male HIV positive patient co-infected with HBV was observed to be significantly (P = 0.048) higher than that of HIV mono infected group. The reason for this is not quite clear. Further research may be necessary to elucidate this finding. However, with respect to gender, female in the mono infected and HIV/HBV co-infected groups were observed to have higher mean CD4 count than their male counterparts, albeit the difference did not reach statistical significance. Several studies only in the mono infected group within African [33,39,40], have reported a generally higher CD4 count among females than males.

The reason for the higher CD4 count observed among female population in this study is unclear. Perhaps both environment and genetic factor may play a role in this finding.

Thrombocytopenia is common during or after viral infection and several mechanism have been proposed to contribute to the drop of platelet count, including platelet destruction mediated by platelet – associated immunoglobulin G (IgG) or platelet-leukocyte aggregation, possibly leading to sequestration by macrophages, sequestration of platelet in the enlarged spleen, impaired production of thrombopoiesis and direct effect of viruses on platelets [16] while more platelets are ordinarily expected to be destroyed by a possible combination of action of HIV and HBV in co-infected than HIV mono-infected patients, the pattern of results obtained in our study did not indicate that. Indeed, young people (18-24 years and 25-31 years) that were infected with HIV and HBV were observed to have a higher mean platelet count than HIV mono-infected patients in the same age group category, while the converse was the case in the older study subjects, suggesting that young age may confer some form of protection against the action of HIV and HBV on platelet. However the difference in platelet count HIV/HBV co-infected patients and HIV mono-infected patients did not differ significantly among each age infected patients studied (P>0,05). This is contrast to finding elsewhere where HIV mono-infected patients were observed to have significantly higher platelet count than HIV/HBV co-infected patients [30].

Age was identified to significantly affect the mean platelet count among HIV-HBV co-infected patients with participants in adolescents (18-24 years) having the highest mean platelet count and those within the age group category of 32-38 years have the least. Analyses of small groups of healthy subjects initially suggested that platelet count is higher in youth than in old age [41,42], with larger studies later confirming these findings [43]. However, the reason for the sharp decline in mean platelet count of middle age subjects as compared to much older participants is not entirely clear. Perhaps they may harbor higher viral loads of both viruses than older subjects which may facilitate the destruction of platelets in them. The disparity in mean platelet count could also be due to the genetic disposition of study participants as platelet count has been reported to be influenced by host genetic factors [44]. However, this will need further studies to confirm.

The findings in this study that females in both co-infected and mono-infected groups had higher mean platelets count than their counterparts was not surprising as several studies in the past have reported a generally higher mean platelets count in female than males [43,45].

5. CONCLUSION

In conclusion, the prevalence of HBV among HIV infected patients was high. HIV was identified as a risk factor for acquisition of HBV infection. The mean haemoglobin concentration, CD4 and platelet count of HIV/HBV co-infected patients did not differ significantly from values obtained in HIV mono-effected group of patients. Among HIV/HBV co-infected group of patients, gender and age were observed to significantly affect mean CD4 and platelet counts respectively. Routine screening of HBV among HIV infected patients is advocated. Although, no statistically significant difference was observed in mean haemoglobin, CD4 and platelet count between HIV/HBV co-infected and HIV mono-infected groups of patients regular monitoring of immunological and haematological profile of HIV/HBV co-infected patients is encouraged to stem associated sequalea.

CONSENT

As per international standard, patient's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard, written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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