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MALARIA AND HEPATITIS B CO-INFECTION IN PATIENTS WITH FEBRILE ILLNESSES ATTENDING GENERAL OUTPATIENT UNIT OF THE MURTALA MUHAMMED SPECIALIST HOSPITAL, KANO, NORTHWEST NIGERIA

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ABSTRACT
Malaria and Hepatitis B Virus (HBV) infections are co-endemic throughout much of the tropical and sub-Saharan Africa and both present major threat to public health. A study on the prevalence of HBV and Malaria co-infection was carried out on 200 patients presenting with fever at the General Outpatient Department (GOPD) of the Murtala Muhammed Specialist Hospital (MMSH), Kano using Gold Standard microscopy and rapid diagnostic test (RDT). The effect of mono and co-infection on hematological parameters was also investigated. Fifty one (25.5%) out of the 200 patients studied were Malaria positive. Females had higher prevalence rate(18%) of Malaria infection than males with 7.5%. Age group 15-24 had the highest Malaria prevalence (11%) followed by age group 25-34 with 6.5%. Higher mean parasite density (1,200/µl) was recorded among subjects with mono-infection of Malaria than mean parasite density (518/µl) obtained among the co-infected. Mean parasite density was higher in female than male subjects. Thirteen (6.5%) subjects were HBV positive. Males had higher rate of infection with 4.5% prevalence than females with 2.0%. Nine individuals representing 4.5% of the total population had co-infection with higher prevalence (3%) among the males. Age groups 25-34 were observed to have high co-infection rate of 1.5% and the least prevalence was observed among the age group 15-24 with 0.5% prevalence for both males and females. Hematological evaluation carried out on all the categories of subjects shows significant difference in mean values of PCV (P=0.041), Hb (P=0.018) between the co-infection group and those with malaria infection and control groups. However, no significant difference (P>0.05) was observed in the values of WBC, PLT and Red cell indices among the co-infected and other test group. It was concluded that co-infection with the two ailments had no profound effect on hematologic parameters.
Keywords: Co-Infection, Hepatitis B, Kano, Malaria, MMSH, Prevalence

INTRODUCTION

Malaria has been described as entirely preventable and treatable blood-borne mosquitoes transmittable disease. However, despite continuous global efforts at all levels of health care to achieve global control, it still remains endemic in tropical and subtropical region, though with decreasing trend (WHO, 2012; 2013). Malaria remains a wide spread health threat to humanity, affecting more than halve of the entire humanity, and it was estimated that more than 50% of the population in endemic African region experience at least one episode of malaria yearly (Ikekpeazu, 2010).

Hepatitis B virus (HBV) infection is also a preventable viral infection that affects the liver and can cause both acute and chronic liver disease (WHO, 2013). It is endemic in region of the world including sub-Saharan Africa (WHO, 2013; Gambo, 2012,). The importance of the disease is stressed by the ample reservoir of carriers seen in human population globally which are estimated to be 320-350 million (Paulyn, 2010; Gambo, 2011)

Malaria and HBV infections are co-endemic throughout much of the tropical and sub-Saharan Africa, and they both present major threat to public health (Mazie, 2002; Paulyn, 2010; Jeya ,2010). Co-infection of Malaria and HBV may occur in areas where both infections are endemic and because of their geographical coincidence (Friemanis, 2012; Andrade, 2011). These two infections share some of their developmental stages within the liver which may cause impaired clearance of the liver stages of Malaria parasite due to hepatocytes damage in HBV infection (Thurz, 1995; Paulyn, 2010,). Therefore, co-infection with Plasmodium parasite and HBV virus in an individual may possibly influence further pathogenic progression of both agents resulting in severe morbidity, complications and increased mortality.

MATERIALS AND METHODS

Study Area/Study Population

Before commencement of the study, ethical clearance was obtained from the Ethical Committee of the Kano State Hospital Management Board. The study was conducted between July and December 2013, in General Outpatient Department (GOPD) of the Murtala Muhammed Specialist Hospital (MMSH) in Kano. The study was carried out among patients presented with febrile illnesses. Two hundred informed and consented patients within the age group of 15-64 were recruited for the study. Subjects with an established clinical condition other than malaria and/or HBV infection such as obstructive jaundice, cirrhosis, renal diseases, hypertension, diabetes mellitus, sickle cell disease, pregnancy, cancer and patients already on course of chemotherapy or who had it in the last two weeks for treatment of an earlier diagnosed illnesses were excluded from the study.

Collection of Blood Samples

Five milliliters of blood were obtained via venepuncture from the subjects using vercoutainer needle (Cheesbrough, 2005). Two milliliters of these were placed in ethylenediethyltetra acetic acid (EDTA) bottles for parasitological and hematological analysis. The remaining 3 mls were taken into universal bottle and centrifuged at 3000rpm for 5 minutes to obtain the serum for serological detection of the HBsAg.

Parasitological examination

Malarial parasites were examined using the gold standard microscopic procedure using Giemsa staining technique on thick and thin film smear for specie determination and the level of parasiteamia. Level of parasiteamia was expressed as number of parasite/µl of blood. (Alperex ,1932; WHO, 1991; Cheesbrough, 2005)

Hepatitis B serology

HBsAg were detected from the serum samples using Micropoint ELISA (Micropoint, USA) commercial Kits technique following the manufacturer's instructions.

Hematological evaluation

This was achieved using the Sysmex KX-21N hematology auto analyser (Sysmex, Japan) following the Manufacturer's instructions and MMSH, Kano standard operation procedure (SOP).

Statistical analysis

Results obtained were analyzed using SPSS software, version 20 (IBM, USA) for both the descriptive and inferential analysis. Results were expressed as mean and standard deviation. One way analysis of variance (ANOVA) was used to determine the level of significance between the parameters. Level of significance was set at $P<0.05$.

RESULTS

The subjects studied were 200 in number (table 1) out of which 90 (45.0%) were males and 110 (55.0%) were females.

Table 1: Distribution of patients based on gender and age group

	Number examined (n,%)		
	GENDER		
Age (years)	Male	Female	Total
15-24	28 (14.0)	39 (19.5)	67 (28.5)
25-34	38 (19.0)	37 (18.5)	75 (37.5)
35-44	20 (10.0)	17 (8.5)	37 (18.5)
45-54	01 (0.5)	11 (5.5)	12 (6.0)
55-64	03 (1.5)	06 (3.0)	09 (4.5)
Total	90 (45.0)	110 (55.0)	200 (100.0)

Malaria assessment

Fifty one (25.5%) out of these 200 subjects studied were positive for malaria parasite. This comprises of 15 (7.5%) males and 36 (18.0%) females. Though statistical analysis showed no significant difference ($P>0.05$) in infection rates between males and females, it was observed that the female population has the higher rate of infection. Among the male population positive for malaria parasite (table 2), those that have the higher rate of infection fall within the age group 25-34 with 7 (3.5%) followed by 6 (3.0%) observed among the age group 15-24. More so, female patients positive for malaria parasites within the age group 15-24 were observed to have the highest rate of infection 18 (9.0%).

This is followed by age groups 25-34 and 45-54 each having 6 (3.0%) of the total population studied. Female patients within the age group 35-44 have 4 (2.0%) infection rates. The least malaria positivity was observed among the age groups 35-44 and 55-64 each with 2 (1.0%) in both gender respectively.

Table 2: Distribution of patients based on malaria positivity according to sex and age

	Malaria positive (n, %)		
	GENDER		
Age (years)	Male	Female	Total
15-24	6 (3.0)	18 (9.0)	24 (11.0)
25-34	7 (3.5)	6 (3.0)	13 (6.5)
35-44	2 (1.0)	4 (2.0)	06 (3.0)
45-54	0 (0.0)	6 (3.0)	06 (3.0)
55-64	0 (0.0)	2 (1.0)	02 (1.0)
Total	15 (7.5)	36 (18.0)	51 (25.5)

Malaria parasite density is presented in Table 5. It shows that coinfection group presented with low mean parasite density than those with only malaria infection.

Table 3: Malaria parasite density among infected patients in relation to infection

Infection	Mean parasite density/µl
Malaria (n=51)	1,200±2,270
Co-infection (n=9)	518.3±263.2

HBsAg serology

Thirteen persons out of 200 (13/200) subjects studied were positive for HBsAg as shown in Table 3. Higher infection was observed among male population with 9 (4.5%) infection rate than female patients with 4(2.0%). Higher infection rate was observed within 25-34 and 35-44 age groups each with 3(1.5%) among the male population. This is followed by 2 (1.0%) observed within 15-24 age group for both male and female population. Least infection rate 1(0.5%) was seen within the age group 55-64 among male population and within 25-34 and 35-44 age groups among female population.

Table 4: Distribution of patients based on HBsAg positivity according to sex and age

	HBsAg positive (n, %)		
	GENDER		
Age (years)	Male	Female	Total
15-24	2 (1.0)	2 (1.0)	4 (2.0)
25-34	3 (1.5)	1 (0.5)	4 (2.0)
35-44	3 (1.5)	1 (0.5)	4 (2.0)
45-54	0 (0.0)	0 (0.0)	0 (0.0)
55-64	1 (0.5)	0 (0.0)	1 (0.5)
Total	9 (4.5)	4 (2.0)	13 (6.5)

Nine individuals (4.5%) were observed to have co-infection of malaria and Hepatitis B. Again, male population had higher co-infection rate 6 (3.0%) than their female counterparts 3 (1.5%). Male patients within the age group 25-34 were observed to have higher co-infection rate 3(1.5%). This is followed by 2(1.0%) each for both female and male patients within the age groups 35-44 and 25-34 respectively. The least co-infection rate was observed among age group 15-24 1(0.5%) for both male and female population.

Table 5: Distribution of patients based on Malaria/Hepatitis B co-infection according to sex and age

	CO-INFECTION (n, %)		
	GENDER		
Age (years)	Male	Female	Total
15-24	1 (0.5)	1 (0.5)	2 (1.0)
25-34	3 (1.5)	2 (1.0)	5 (2.5)
35-44	2 (1.0)	0 (0.0)	2 (1.0)
45-54	0 (0.0)	0 (0.0)	0 (0.0)
55-64	0 (0.0)	0 (0.0)	0 (0.0)
Total	6 (3.0)	3 (1.5)	9 (4.5)

Hematological analysis

Hematological parameters for the control and test groups are shown in Table 6. It was observed that hemoglobin level in those that have only malaria infection (12.1±2.3) and the control group (12.7±1.8) is low as compared to those that have HBV infection (13.2±1.9) only and co-infection group (13.8±1.4). There is a statistical significant difference between the mean hemoglobin of the co-infection group and those with malaria only (p=0.018). Packed cell volume was also noticed to be more depleted (36.2±7.1) among malaria positives alone patients as compared with the co-infected subjects (41.5±3.7) and also lower than the value obtained among the control group (38.1±5.1) and those with HBV infection only (*39.9±5.7*). Statistical analysis also shows significant difference between the co-infection and malaria alone (p=0.000). There is also a significant difference between co-infection ad control (p=0.041) and between those with malaria alone and HBV only (p=0.000). White blood cells seem to be relatively the same among the control group (7.9 ±2.6) and malaria positive (7.9 ±2.8) as compared with the co-infected group (8.0±1.9) and it is low among those with HBV infection only (6.5±2.5). However, there is no significant difference in the values of total white cell between the groups P>0.05. Reduced platelet level was observed to be more depleted among those with HBV infection *(*275.9±124.5*)* and also among malaria positive only (281.9±106.3) as compared with control groups (301.4±102.4) and co-infected groups (312.7±88.2) with no statistically significant difference P>0.05. Reduced neutrophil (42.6±12.4*)* count was observed among the co-infected group as compared to those with malaria only *(*46.8±12.6*)* and the control *(*48.9±12.9*)* while those with only HBV infection have *(*50.7±18.7*)* high level of neutrophils. However there is no significant difference between the groups P>0.05. Lymphocyte is observed among the co-infected group *(*44.3±10.7*)* to be high when compared with malaria positive (41.8±10.7*)* and the control *(*40.4±10.7*)* while those with HBV infection have lower level of lymphocytes *(*37.9±15.3) and there is no statistically significant difference between the groups P>0.05.

Table 6: Mean and Standard deviation values of hematological parameters for all test subjects and control

Parameters	Malaria positive (n=51)	HBsAg reactive (n=13)	Co-infection (n=9)	Control (n=127)
Hb(g/dl)	12.1±2.3[b]	13.2±1.9[a]	13.8±1.4[a]	12.7±1.8[a]
PCV (%)	36.2±7.1[b,c]	39.9±5.7[d]	41.5±3.7[a]	38.1±5.9
WBC(x10^6/l)	7.9±2.6	6.5±2.5	8.0±1.9	7.9±2.8
PLT(x10^6/l)	281.9±106.3	275.9±124.5	312.7±88.2	301.4±102.4
NEU (%)	46.8±12.6	50.7±18.7	42.6±12.4	48.9±12.9
LYM (%)	41.8±10.7	37.9±15.3	44.3±10.7	40.4±10.7
MON (%)	8.8±5.1	7.7±4.6	7.9±3.6	7.5±4.7
EOS (%)	3.4±2.5	3.0±2.9	4.3±2.2	2.8±2.6
BAS (%)	0.4±0.8	0.5±0.9	0.7±1.3	0.4±0.6

Hb: hemoglobin, PCV: pack cell volume, WBC: white blood cells, PLT: platelet, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, MCV: mean corpuscular volume, NEU: neutrophil, LYM: lymphocyte, MON: monocyte, EOS: eosinophil , BAS: basophils.

Values with different superscript differ significantly at p<0.05

DISCUSSION

Malaria and HBV infection are both endemic and life threatening diseases in this part of the world. This study presents 25.5% of malaria parasiteamia among the study population which is less than 30.59% reported by Gobir (2014) from Kano metropolis and 77.6% reported by Igwe (2014) from Enugu, South-East Nigeria. The reduction in trend as observed in this study may be due to adequate measures taken in malaria prevention and prompt diagnostic measures. Female population in this study is more affected with 18.0% prevalence. This may point to high vulnerability of women especially when they are pregnant. This finding is consistent with the findings by Gobir (2014) which showed 61.54% of the female population were malaria parasite positive than their male counterparts at 38.46% more than 7.5% reported for males in this study. These results showed continuous decline in malaria prevalence as stated by World Health Organization (2013). Age group affected in both female and male population was within 15-24 and 25-34.

This study presents prevalence of HBsAg at 6.5% which differs from the results obtained from other studies within the same state and from other geopolitical zones of Nigeria. Prevalence rates obtained in the last one decade showed a fluctuating trend, 14.6% in 2004, and 10.1% in 2005 and in 2006 it was 10.7% (Nwokedi, 2010). Recent report on the prevalence of Hepatitis B infection on adolescent in Kano puts the rate at 12.5% (Yunusa, 2014). The figure is also lower than 11% (Sule, 2010) reported from studies in Anyingba, Kogi state, 11.5% (David, 2012) from Ekiti State and 10.6% (Esumeh, 2003) from South-South region.

It is also lower than 12.3%, (Hamza, 2013) and 18.2% (Luka, 2008) obtained among HIV infected population in Aminu Kano Teaching Hospital and among pregnant women in Zaria, respectively. It is also lower than 47.2% and 20% reported from Benue State among blood donors and Borno State among primary school pupils respectively. Nneka (2007) also reported 17.1% from Nassarawa State among sex workers which is also higher than the present figure. Several Studies also reported values similar or less than this. For instance Dawaki and Kawo (2006) reported 7.3% prevalence among pregnant women in Kano, 6.8% by Ndako (2011) among secondary school students in north central Nigeria, 4.2% by Mukhtar (2005) in Zaria, 4.1 % by Ugwuja (2010) and Okonko (2010) from southeastern and southwestern Nigeria respectively.

Age specific prevalence rate was found to be 1.5% which is higher among 25-34 and 35-44 age groups followed by 1.0% each among 15-24 age groups. Least infection rate was observed among 55-64 age group at 0.5%. These findings agree with that reported by Gambo (2012) and Okonko (2010) indicating the high rate of hepatitis B infection among age groups 25-34 and 35-44. This is because they constitute the sexually active population among the study group and they are at high risk of engaging in several ways through which one can contract the infection. The study figured out no significant difference ($p=0.94$) in HBV among the two sex groups with male patients having 4.5% while females recorded 2.0% prevalence rate. This finding is in agreement with 12.1% and 32% prevalence among male population reported from Kano, North west and North east by Nwokedi (2010) and Gambo (2012) respectively. This can probably be explained by unequal exposure to risk factors of contracting the infection. Male population in this part of the country are more engaged in one form of risk behavior or the other while the female population are always under close monitoring by parents. In this area, the ratio of men to women that are engaged in business occupation, civil service, schools and other outdoor activities is significant going by their tradition, culture and religion.

The prevalence of co-infection is 4.5% which is lower than 7.81%, 8.7%, and 40.67% obtained by Omalu (2012), Ikekpeazu (2010), and Paulyn (2010) from studies done in South East and North Central Nigeria respectively. Another studies in Vietnam reported a co-infection prevalence rate of 23.77% (Mazie, 2002). This study reports 3.0% prevalence of the co-infection among male population within the more younger age group 25-34 which carries the highest rate of infection at 1.5% followed by 1.0% among 35-44 age group. This finding is consistent with the findings by Paulyn (2010) and Kuolentalaki (2001). The high prevalence observed in this age group probably reflects the high rate of exposure and reckless behavior engaged by this age group which makes them prone to contracting this form of disease. Female population presents with 1.5% co-infection rate out of which 1.0% was observed among age group 25-34. Lower prevalence among female population observed in this study is consistent with study by Paulyn (2010) who reported 2.37% among female population.

Studies previously conducted attempt to address potential interaction between HBV and Plasmodium parasite infection in relation to severity and prognosis of both infections. This study reports low parasite density among patient co-infected with the two pathogens while those with only malaria infection recorded high mean parasite density. This finding is consistent with the findings reported by Andrade (2011) where HBV infected patients presented with low parasiteamia and reduced malaria severity. The study however, linked this effect to increased Interferon gamma (IFN) in HBV infection which is important for Plasmodium clearance leading to reduced parasite load and subsequent reduction in severity of malaria infection. The finding by this study however disagrees with the finding from study conducted by Freimanis (2012) that the two infections do not appear to significantly affect each other. It also disagrees with the reported finding from Vietnam by Mazie (2002) that HBV may worsen the prognosis of malaria infection.

Changes in hematological parameters in malaria infection and HBV infection have been studied by various researchers (Kayode, 2011; George, 2001; Akaninwor, 2013) but there are little or no findings as for the changes in co-infection of Malaria and HBV. These two infections are both endemic in this part of the world and both represent a key threat to humanity.

An alteration in selected hematological parameters was also observed in this study. This was seen among those with only malaria positive, HBV positive on one hand and the concurrent co-infection on the other hand in comparison with control group. Significant changes in the mean values of hemoglobin, pack cell volume and platelets were observed among patients with malaria infection. Hemoglobin and pack cell volume were significantly ($P<0.05$) reduced in both malaria and control as compared to co-infection and HBV infection. Statistically Significant difference between the values of hemoglobin and pack cell volume obtained among those with malaria and the co-infection shows that presence of the co-infection suppressed the effects of Plasmodium parasites on red blood cells. Lower levels of heamoglobin and pack cell obtained in this study are in agreement with several studies (Taha, 2007; Eze, 2009; Etang, 2010; George, 2011; Kayode, 2011; Shamin, 2012; Akanninwor, 2013) on the effect of malaria on hematological parameters. Though there is no significant difference between the groups, the mean white blood cell counts in both Malaria, control and the co-infection are relatively the same higher than what was obtained among those with HBV infection.

This shows no severity of disease among the groups and the low value among those with HBV infection was also observed by Lin (1991) in patients with chronic HBV infection. Despite no statistically significant difference between the groups in the level of platelets, the co-infection group shows higher platelets value which can explain low severity of the plasmodium parasite in settings of co-infection. Findings in platelets level among malaria and HBV infection groups are in agreement with the reported cases of thrombocytopenia in patient with chronic HBV infection and malaria infection by Lin (1991), Eze (2009) and Waseem (2010).

CONCLUSION

From the study, it can be concluded that females had more malaria infection than males but males were more infected with HBV. The study also shows that co-infection had no profound effect on hematologic parameters hence points to possibility of interaction between HBV and Plasmodium parasite that may lead to decrease severity of malaria infection thereby lowering morbidity and mortality.

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