Correlation between Anemia and Malaria Infection Severity in Patients with Type 2 Diabetes Mellitus in Nigeria

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Abstract

Background: Malaria and diabetes mellitus are still a significant global public health problem despite the phenomenal progresses in clinical sciences related to the diseases. Both anemia and malaria parasitemia are common in developing countries. It is therefore important to diagnose and determine the correlation between anemia level and malaria infection severity in diabetic patients for better management.

Methods: Patients with diabetes mellitus (DM) infected with malaria were recruited (n=50) as subjects and non-diabetic patients were used as control in this study, who were further divided into two sub-group: non-DM infected with malaria (n=25) and non-DM without malaria parasitemia (n=25). Blood sample were collected to examine the fasting blood sugar (FBS) level, packed cell volume (PCV), hemoglobin (Hb) level, and malaria parasitemia. Statistical analysis was then performed using ANOVA with a p value of less than or equal to 0.05 considered statistically significant.

Results: The parasite density in DM with malaria was significantly lower ($p<0.05$) than in the non-DM with malaria. Interestingly, there was a higher PCV and hemoglobin level ($p<0.05$) in DM with malaria when compared with non-DM with malaria.

Conclusions: DM patients infected with plasmodium have low parasite density but higher hemoglobin level and PCV compared to the control group. There is no correlation between the severity of anemia and malaria parasitemia in DM patients infected with malaria when compared to non-diabetic subjects infected with malaria. Further studies are needed to explore the correlation between hemoglobin level in DM and plasmodium infection.

Keywords: Anemia, hemoglobin, hyperglycemia, malaria, parasitemia

Introduction

Malaria is the most common vector-borne parasitic disease of the globe and still a main public health challenge in more than a hundred countries across the globe with more than 2.5 billion people at the chance, causing a few million deaths yearly.[1] A recent study has shown a correlation between *Plasmodium* infection and blood glucose levels. *Plasmodium* depends exclusively on an exogenous supply of glucose for survival due to the inability to store energy in form of glycogen.[2] On the other end, diabetes mellitus (DM) is one of the most well-known non-transmittable diseases, that has an absolute or relative insulin lack.[3] Diabetes is a degenerative disease characterized via disordered metabolism and hyperglycemia due to insufficient levels of the hormone insulin with or without additional resistance of insulin's impact on many body cells.[4] There is insulin-dependent diabetes mellitus (IDDM) which is generally alluded to as type 1 diabetes, and insulin-independent diabetes additionally referred to as type 2 diabetes. Type 2 DM is found in around 70–90% of diabetic cases and normally impacts humans aged 30 years and above.[5,6] Evidence has clearly stated that DM will be pandemic in many developing and industrialized nations, attributable to the western-style diet.[3]

In tropical Africa, malaria poses a dangerous

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wellbeing danger for quite a long time more than some other ailment, with 80% of malaria cases and mortality going on in Africa, affecting both young and old. Regardless of extra special development in medical sciences, malaria and DM continue to be a chief killer.[7,8] Anemia is two times as common in DM in comparison with non-diabetic.[9] Anemia is described as a condition where the hemoglobin (HGb) level is reduced, which diminishes the oxygen-carrying limit of red blood cells to tissues. It is likewise a worldwide general health problem affecting both advanced and developing nations.[9] Despite all these scientific shreds of evidence, anemia is not associated with about 25% of diabetic patients. Moreover, the danger of anemia is better in people with diabetic nephropathy in comparison with individuals with nephropathy from other sources as this is associated with a greater speedy decline in the glomerular filtration rate (GFR). There is a significant correlation of anemia with exceptionally low serum erythropoietin in men and women with either type 1 or type 2 diabetes, even without advanced kidney ailment or overt uremia.[10] The etiology of anemia in diabetes is multi-factorial and these encompass nutritional deficiencies, concomitant autoimmune diseases, drugs, inflammation, and hormonal changes further to kidney disease.[11]

Anemia and malaria parasitemia is endemic in developing nations among others in Nigeria. It is therefore important to diagnose malaria in DM patients and further determine the correlation between the degree of anemia and severity of malaria infection in DM to oversee it fittingly. Subsequently, this study is aimed to overcome any barrier in information and providing useful data to the medical and scientific community in the management of DM infected with Plasmodium falciparum.

Methods

This was a case-control study, performed between January to August 2019, including 100 subjects from Owo Metropolis-Nigeria, comprised of DM patients infected with malaria (n50) and non-DM patients as a control group. Fasting plasma glucose levels greater than 7.0 mmo/l on two or more occasions were designated as DM.[3] The control was further regrouped as non-DM patients infected with malaria (n25) and non-DM without malaria parasitemia (n25). All the participants were aged between 30–70 years old. The medical and personal information had been obtained via a comprehensive questionnaire. Exclusion criteria were diabetic patients with medical complications, including hypertension, human immunodeficiency virus (HIV), hepatitis, and cancer. Pregnant and breastfeeding mothers were also excluded from the study. Participants in this study had been fully briefed on the study protocols inside the health facility and then they were required to sign a written consent. Ethical approval with registration number FMC/OW/380/VOL.LXX/66 was obtained from the Ethical Review Committee, Federal Medical Centre, Owo-Nigeria.

Six milliliters (6 ml) of venous blood was aseptically collected from the median-cubital vein after 12 hours of fasting. Three milliliters (3 ml) of collected venous blood was dispensed into a fluoride oxalate bottle, gently mixed, and thereafter used for the determination of fasting blood sugar to confirm diabetic condition. Blood levels of fasting blood sugar were estimated using the standard spectrophotometric technique.[12] The remaining 3 ml of venous blood was dispensed into an ethylene diamine tetra-acetic acid (EDTA) bottle for determination of packed cell volume (PCV), hemoglobin concentration, and malaria parasitemia.

The packed cell volume (PCV) and hemoglobin concentration were determined by the manual method as described by Cheesbrough.[12] The malaria parasite density test was determined from Giemsa stained peripheral blood smear.[12] The level of parasitemia was in a microliter (ul) of blood thick film preparation, graded as low or + (1 to 999/ul), moderate or ++ (1000 to 9999/ul) and severe or +++ (> 10,000/ul), based on WHO criteria[13] and Al-Salahy et al.[14]

Malaria parasite density was estimated by counting parasites against white blood cells. The number of parasites per microliter was calculated as follows.

$$\text{Number of parasite per microliter} = \frac{\text{WBC count x } \textit{parasite counted against white cells}}{100}$$

One way analysis of variance (ANOVA) was used for comparison within the groups. A correlation was used to test the association between variables among DM with malaria. Data were presented using mean±standard deviation (mean±SD) for all quantitative values. The level of significance was taken as a 95% confidence interval and p values less than or equal to 0.05 were considered significant. A statistical package for social sciences (SPSS) v.23.0 was used for the analysis of the data.

Table 1 Presentation of Age and Haematological Parameters on Control and Study Subjects in Means±Standard Deviation

	DM	Non-DM	
	With malaria (n=50)	With malaria (n=25)	Without malaria (n=25)
Age (Years)	50.9±17.48 a,b	39.12±11.35 c	39.40±10.33 c
HGb (g/dl)	12.43±1.59 a	10.74±1.68 b,c	13.64±1.16 a,c
PCV (%)	35.67±6.84 a,b	32.12±5.04 b,c	40.78±3.39 a,c

Note: * significant at p≤0.05, a = significantly different from non-DM with malaria; b = significantly different from non-DM without malaria; c = significantly different from DM with malaria, HGb= Hemoglobin, PCV= Packed cell volume

Results

The mean age among respondents was as followed: DM with malaria was 50.9 years old ±17.48, non-DM with malaria 39.12 years old ±11.35, and non-DM without malaria 39.40 years old ±10.33, respectively. The Hb and PCV values were compared between groups as shown in Table 1. There was a lower significant value of PCV and hemoglobin in DM with malaria when compared with non-DM without malaria. Furthermore, there was statistically significant higher hemoglobin and PCV in diabetic subjects with malaria than non-DM patients with malaria ($p<0.05$).

In Figure 1, there was a statistically significant higher blood glucose concentration in diabetic subjects when compared with non-diabetics with and without malaria. Figure 2 shows that the mean parasite density in diabetic subjects with malaria was significantly lower than in the non-diabetic group with malaria. Figures 3 and 4 show the correlation between malaria parasite densities and packed cell volume ($p=0.844$, $r=0.029$) and hemoglobin ($p=0.952$, $r=-0.009$) respectively, and no statistically significant correlation was observed.

Discussion

The association of malaria with either hyperglycemia or hypoglycemia has been documented in several studies since there is a dependency of malaria parasites on an exogenous supply of glucose for survival due

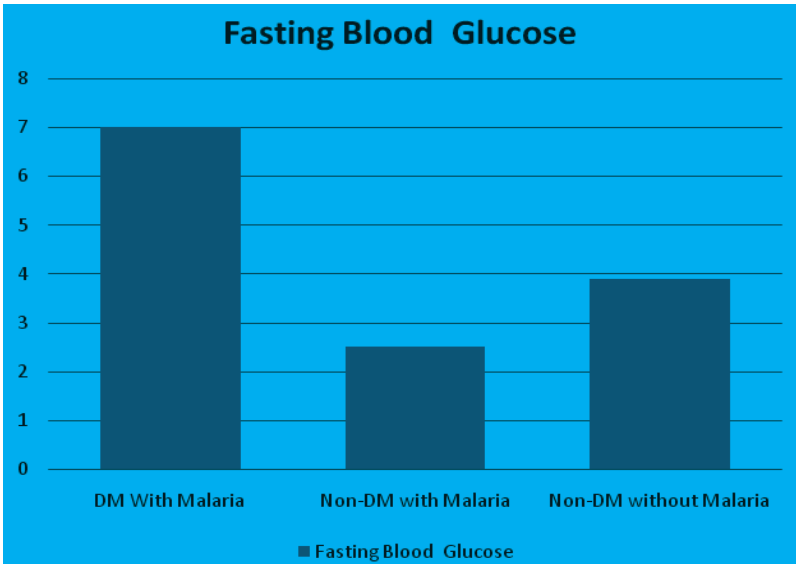

Figure 1 Fasting Blood Glucose (FBG) among DM with Malaria, Non-DM with Malaria, and Non-DM without Malaria

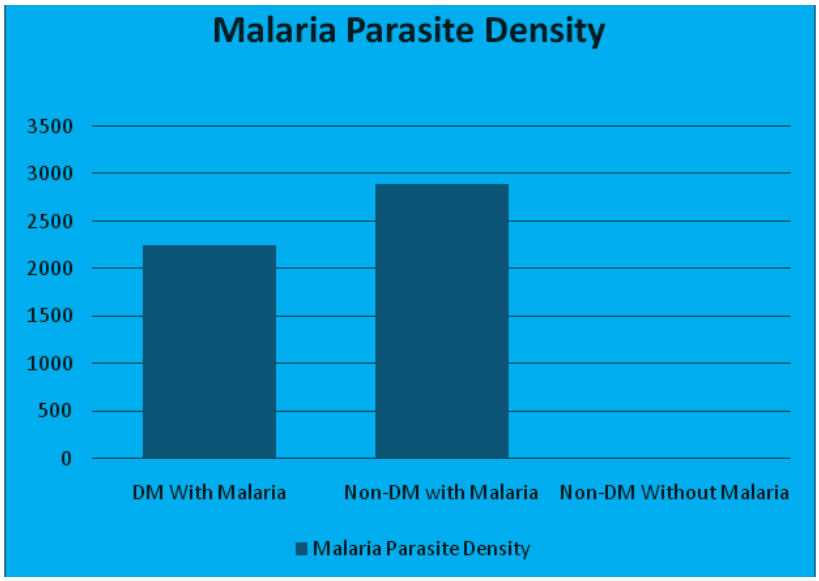

Figure 2 Malaria Parasite Density among DM and non-DM Patients with Malaria

to the inability to store calories in form of glycogen.[2,15] Diabetes and malaria are common in developing countries with high fatalities and are thus major public health problems.[15]

Approximately 216 million cases of Plasmodium falciparum malaria has been documented in 2016 and induced an estimated 445,000 deaths, frequently among children residing in sub-Saharan Africa.[1,11] Malaria is one of the major causes of anemia in endemic areas, which is one of the inceptive factors for blood transfusion in those regions. The

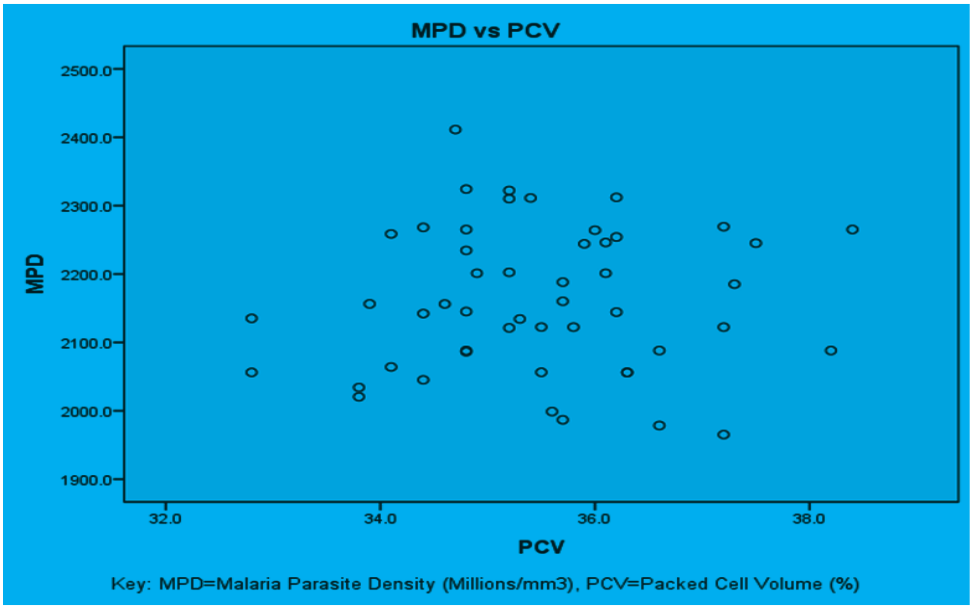

Figure 3 Correlation between Malaria Parasite Density and Packed Cell Volume in Diabetic Patients with Malaria

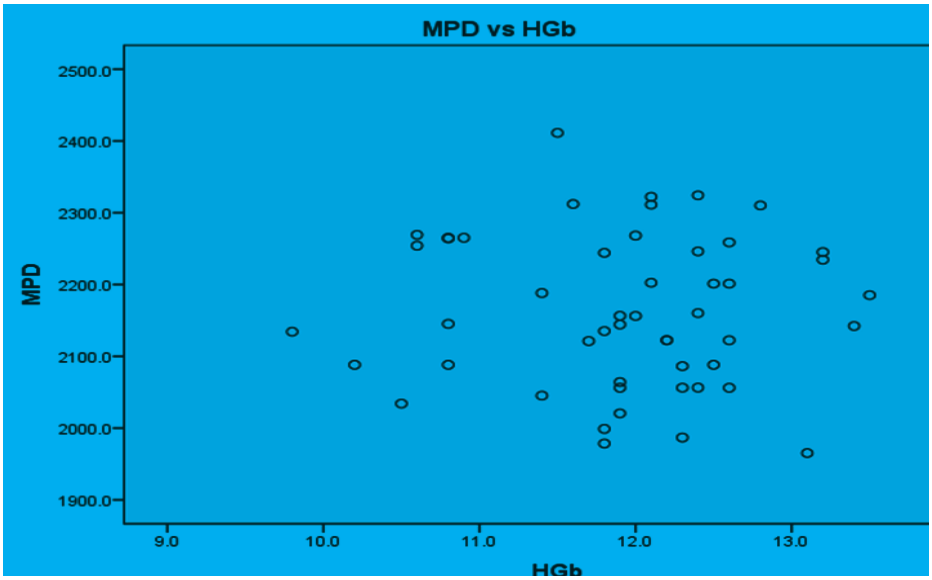

Figure 4 Correlation between Malaria Parasite Density and Hemoglobin in Diabetic Patients with Malaria

majority of fatalities attributed to malaria have occurred directly or indirectly from anemia.[11] Additionally, anemia, an index of malnutrition, is common in *Plasmodium falciparum* infection and has been reported aggravating its complications.[16-17] The result of this study revealed a significantly lower malaria parasite density count in diabetic subjects when compared with control subjects with malaria parasitemia. This is in accordance with a study which revealed a higher parasite density in non-diabetic subjects when compared with diabetic patients,[18] but other study contradicted the result that reported the possibility of high malaria infection in diabetic patients.[19]

Interestingly, there was a significantly higher ($p<0.05$) PCV and hemoglobin in DM with malaria when compared with non-diabetics without malaria. This corroborates earlier reports that malaria is one of the leading causes of anemia.[11] Even though DM has been documented as a diverse group of metabolic disorders that are often related to an excessive disease burden in developing countries such as Nigeria[3], anemia has not been reported as one of its symptoms. In this study, there is no statistically significant correlation between malaria parasite densities, packed cell volume, and hemoglobin in DM patients with malaria parasitemia. In *P. falciparum* malaria, there may be sequestration of red blood cells containing mature parasites in the microcirculation.[11] This simply means the density of the malaria parasite is corresponding to the severity of anemia. Possibly, this is correlated with higher hemoglobin and PCV in DM with malaria in comparison with non-DM with malaria that we found in this study.

Another factor that contributes to reduce the anemia rate among DM patients infected with plasmodium infection is the anti-malarial property of the glucose-lowering drug metformin taken by DM patients. Metformin is the most broadly used oral glucose-lowering drugs and it has been recognized for its anti-malarial properties.[20] In a massive study done in Ghana, metformin used for DM has been discovered to have an appreciably decrease incidence of malaria compared to those without.[20] With the anti-malarial property of this drug, there is a reduced level of red cells that are parasitized. For this reason, few red cells are hemolysed and a reduction in the severity of anemia in diabetes is therefore observed.[15,20]

One of the limitations of this work is that we could not ascertain the anti-malarial properties of metformin. Therefore, similarly, studies need to be executed to assess the anti-malaria properties of anti-diabetic drugs with a larger sample size.

In conclusion, low parasite density, high hemoglobin, and PCV are present in DM

patients infected with *plasmodium*. Hence, there is no correlation between the severity of anemia and malaria parasitemia in DM patients with parasitemia. Further study is needed to explore the anti-malarial properties of metformin.

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Conflicts of Interest

The authors declare that this manuscript was approved by all authors and competing interests did not exist.

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