GENOTYPE AND ABO BLOOD GROUP ASSOCIATION WITH PREVALENCE OF MALARIA AMONG PATIENTS IN UNIVERSITY OF NIGERIA MEDICAL CENTER: A CROSS-SECTIONAL EVALUATION

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ABSTRACT

Objective: The aim of this study was to evaluate the prevalence of malaria and its relationship with the ABO blood group and genotype at the University of Nigeria Medical Centre.

Methods: The study had a prospective cross-sectional design in which malaria status and blood groups and genotype were determined. All collected data were analysed using Statistical product and services Solution (V.21). Frequencies and percentages were used to describe the data while Chi-square and Pearson correlation were used to determine associations between malaria prevalence and patients' demographic and clinical characteristics. Statistical significance was considered for p<0.05.

Results: Three hundred and twenty-three (323) patients were tested for malaria, 245 (75.9%) of whom tested positive. The prevalence was highest for patient's aged 19-25 y (28.5%). The difference was statistically significant for age; $\chi^2(5) = 33.60, p = 0.0005$. There were more blood group O (57.6%) among the patients, while AA genotype was the majority (72.4%). Those with blood group O had the highest prevalence of malaria (33.7%) and it was statistically significant ($\chi^2(5) = 72.10, p = 0.0005$). Correlation showed that the association between blood group and malaria prevalence was moderate (R = 0.457). The AA genotype had more incidence of malaria (54.5%), but the difference was not statistically significant.

Conclusion: The prevalence of malaria was high among the patients surveyed. Its association with the patients' ABO blood group was established to be statistically significant, with blood group O having the highest incidence. Although AA genotype was observed to have the highest cases of malaria, the relationship was found not to be significant.

Keywords: ABO Blood Group, Genotype, Malaria, Prevalence

INTRODUCTION

Malaria remains an important global public health disease, despite many multinational efforts towards its treatment and eradication. The World Health Organization (WHO) reported that while 1.2 billion people were at high risk of being infected and developing the disease in 2015, an estimated 3.2 billion people in 95 countries and territories were at risk [1]. In the same year, World Malaria Report indicated that there were 214 million cases of the disease and 438 000 related deaths [1]. The prevalence increased to 216 million cases (in 91 countries) in 2016 [2]. Death from the disease remained around 445 000 between 2015 and 2016. In all reports, Africa had the highest burden of the disease, with 90% of cases and 91% deaths being from the region in 2016. Two-thirds of all reported deaths were among children aged under 5 y [2]. To control and eliminate this top killer disease, an estimated US$ 2.7 billion was spent in 2016, with governments of endemic countries contributing just about 31%. Artemisinin-based combination therapies (ACTs) are currently the drugs of the first choice in the management of malaria, but concerns about the tastes of the oral preparation often affects compliance to prescribed regimens [3], apart from accessibility and affordability.

A good understanding of the aetiology of malaria will play a vital role in its elimination. It is the foundation of many researches on vaccinations against the disease [4–6]. Vector and host factors determine susceptibility to the disease. An example of vector factor is their feeding pattern which varies through the hours of a day, and even the seasons of a year. Some host factors (such as the region of residence and lifestyles like personal hygiene that expose individuals to the vector) and cooperation in control and eradication operations are modifiable [7, 8]. Hereditary and acquired factors are host-related factors that are not modifiable. Human blood groups and genotypes are two examples of hereditary and host-related factors that have been established to be related with susceptibility to some diseases [9]. The prevalence of malaria in the human population has been studied on the basis of these factors with no definite conclusion [10]. The co-adaptation of various human populations with widespread malaria parasites is clearly due to genetically-based alterations that confer protection against the disease [11, 12]. This study sought to determine the prevalence of malaria and its association with genotypes and ABO blood groups among patients at the University of Nigeria Medical Centre.

MATERIALS AND METHODS

Design

This was a three-month prospective cross-sectional study that involved the collection of data from patients who were tested at the laboratory of the university medical center.

Study site

The University of Nigeria Medical Centre (UMC) Nsukka is a secondary level healthcare institution. It provides care primarily for staff (and their immediate families) and students of the university at its main campus. It is a 20-bed capacity hospital which provides outpatient/emergency services to patients and specialty care for some diseases. Referrals are made to the University of Nigeria Teaching Hospital Enugu where necessary.

Ethical considerations

Ethical clearance was obtained from the institutional review board of the institution before this study was conducted (Ref. No.:...
Sampling procedure

Only patients whose malaria tests were conducted in the laboratory of UMC were included in the study. Their genotype and ABO blood group determinations had to be determined at the UMC’s laboratory as well. Patients (or guardians of minors) who refused to provide oral consent to participate in the study were not included.

Data collection

Qualified laboratory staff conducted the tests on eligible patients. Malaria test was conducted using the thick and thin film method as described by the WHO [13, 14]. Genotype and ABO blood groups were determined using electrophoresis. Results of the tests were recorded in a data collection form designed for the purpose. The patients’ demographic characteristics were also documented. The study was conducted from July to September 2017.

Data analysis

The collected data was first entered into Microsoft Excel (2016) and checked for correctness. It was then exported into Statistical Product and Services Solutions (Version 21) for Windows which was used for appropriate descriptive and inferential analyses. Frequencies and percentages were used to present the different laboratory results. The association between the malaria results and the patients’ demographic characteristics was determined using Chi-square. Chi-square test and Pearson correlation were used to determine the relationship between the prevalence of malaria among the patients and their genotype and ABO blood groups. Statistical significance was considered for tests with p values less than 0.05.

RESULTS

Three hundred and twenty-three (323) patients were tested for malaria during the period of the study. Many of the patients were students (59.8%), while the majority (95%) were females. Other demographic characteristics are presented in table 1.

| Table 1: Demographic characteristics of the patients |
|-----------------------------------------------------|
| **Age (Years)** | **Percentage** |
| Less than 14 | 1.5 |
| 15-18 | 1.9 |
| 19-25 | 30.3 |
| 26-30 | 29.7 |
| 31-35 | 28.5 |
| Greater than 35 | 8.0 |
| Total | 100.0 |
| **Gender** | |
| Male | 5.0 |
| Female | 95.0 |
| Total | 100.0 |
| **University Status** | |
| Student | 59.8 |
| Staff | 39.0 |
| Others | 1.2 |
| Total | 100.0 |
| **Pregnancy Status** | |
| Pregnant | 75.5 |
| Non-pregnant | 24.5 |
| Total | 100.0 |

Of the 323 patients, 245 (75.9%) tested positive for malaria. The prevalence was highest for patients aged 19-25 y (28.5%). When compared to the other age groups, the difference was statistically significant (χ² (5) = 33.60, p = 0.00). There were more patients with blood group O (57.6%) than those with other blood groups. Patients with AA genotype were the majority (72.4%) in the population. Table 2 shows the clinical characteristics of the population while table 3 shows the relationship between the patients’ independent characteristics and the malaria test results.

| Table 2: Clinical characteristics of the patients |
|------------------------------------------------|
| **ABO Blood Group** | **Percentage** |
| A | 21.4 |
| B | 19.2 |
| AB | 1.9 |
| O | 57.6 |
| Total | 100.0 |
| **Genotype** | **Percentage** |
| AA | 72.4 |
| AS | 26.6 |
| SS | 9 |
| Total | 100.0 |
| **Malaria Test Result** | **Percentage** |
| Positive | 75.9 |
| Negative | 24.1 |
| Total | 100.0 |
Table 3: Association between malaria status and demographic characteristics

| Age (Years) | Patient’s malaria test result | Total |
|-------------|-------------------------------|-------|
|             | Positive | Negative |       |
| Less than 14| 4(1.2)    | 1(0.3)   | 5(1.5) |
| 15-18       | 5(1.5)   | 1(0.3)   | 6(1.9) |
| 19-25       | 92(28.5) | 6(1.9)   | 98(30.3)|
| 26-30       | 67(20.7) | 29(9.0)  | 96(29.7)|
| 31-35       | 55(17.0) | 37(11.5) | 92(28.5)|
| Greater than 35| 22(6.8)  | 4(1.2)   | 26(8.0) |
| Total       | 245(75.9)| 78(24.1) | 323(100.0)|

Gender ($\chi^2(1) = 0.27, p = 0.61$)

| Gender | Positive | Negative | Total |
|--------|----------|----------|-------|
| Male   | 13(4.0)  | 3(0.9)   | 16(5.0)|
| Female | 232(71.8)| 75(23.2) | 307(95.0)|
| Total  | 245(75.9)| 78(24.1) | 323(100.0)|

Status in the University ($\chi^2(2) = 9.62, p = 0.01$)

| Status                | Positive | Negative | Total |
|-----------------------|----------|----------|-------|
| Student               | 158(48.9)| 35(10.8) | 193(59.8)|
| Staff                 | 84(26.0) | 42(13.0) | 126(39.0)|
| Others                | 3(0.9)   | 1(0.3)   | 4(1.2) |
| Total                 | 245(75.9)| 78(24.1) | 323(100.0)|

Pregnancy Status ($\chi^2(1) = 3.38, p = 0.07$)

| Pregnancy Status | Positive | Negative | Total |
|------------------|----------|----------|-------|
| Pregnant         | 179(55.4)| 65(20.1) | 244(75.5)|
| Non-pregnant     | 66(20.4) | 13(4.0)  | 79(24.5) |
| Total            | 245(75.9)| 78(24.1) | 323(100.0)|

Malaria prevalence was highest among patients with blood group O (33.7%) compared to other groups. Chi-square test indicated that the difference was statistically significant ($\chi^2(3) = 72.10, p = 0.00$). Pearson correlation showed that the association between blood group and malaria prevalence was moderate ($R = 0.457$). Patients with AA genotype had more incidence of malaria (54.5%). When compared to other genotypes, the difference was not statistically significant. Pearson correlation showed a weak relationship between malaria prevalence and genotype, as shown in table 4. Table 5 shows the prevalence of malaria based on the blood group and genotype combination. The least susceptibility to malaria was in the combination of all genotypes and blood group A (0.00).

Table 4: Association between the prevalence of malaria and patients’ clinical characteristics

| Blood Group | Patient’s malaria test result | Total |
|-------------|-------------------------------|-------|
|             | Positive | Negative |       |
| A           | 69(21.4) | 0(0.0)    | 69(21.4)|
| B           | 62(19.2) | 0(0.0)    | 62(19.2)|
| AB          | 5(1.5)   | 1(0.3)    | 6(1.9) |
| O           | 109(33.7)| 77(23.8)  | 186(57.6)|
| Total       | 245(75.9)| 78(24.1)  | 323(100.0)|

Genotype ($\chi^2(2) = 0.30, p = 0.82$) $R = 0.02$

| Genotype | Positive | Negative | Total |
|----------|----------|----------|-------|
| A        | 176(54.5)| 58(18.0) | 234(72.4)|
| AS       | 67(20.7) | 19(5.9)  | 86(26.6) |
| SS       | 2(0.6)   | 1(0.3)   | 3(0.9)  |
| Total    | 245(75.9)| 78(24.1) | 323(100.0)|

Table 5: Malaria susceptibility based on blood group genotype combination

| Blood Group | Genotype | Patient’s malaria test result | Total |
|-------------|----------|-------------------------------|-------|
|             | Positive | Negative |                   |
| A           | AA       | 50(72.5) | -                  | 50(72.5)|
| A           | AS       | 19(27.5)| -                  | 19(27.5)|
| A           | Total    | 69(100.0)| -                  | 69(100.0)|
| B           | AA       | 47(75.8) | -                  | 47(75.8)|
| B           | AS       | 15(24.2)| -                  | 15(24.2)|
| B           | Total    | 62(100.0)| -                  | 62(100.0)|
| AB          | AA       | 3(50.0) | 1(16.7)            | 4(66.7)|
| AB          | AS       | 2(33.3) | 0(0.0)             | 2(33.3)|
| AB          | Total    | 5(83.3) | 1(16.7)            | 6(100.0)|
| O           | AA       | 76(40.9)| 57(30.6)           | 133(71.5)|
| O           | AS       | 31(16.7)| 19(10.2)           | 50(26.9)|
| O           | SS       | 2(1.1)  | 3(0.5)             | 3(1.6)|
| O           | Total    | 109(58.6)| 77(41.4)          | 186(100.0)|
This study was conducted in a university medical centre to determine the relationship between the prevalence of malaria and the patients’ genotype and ABO blood groups. Most of the patients were middle-aged and almost all were females. Majority of the population were pregnant, and there were more students than staff among them. Laboratory results showed that more than half of the patients had blood group O. AA was the most observed genotype in the population. Majority of the patients who participated in the study tested positive for malaria. Patients’ age and status in the university were the demographic characteristics that had a statistically significant relationship with their malaria test results. Blood groups showed a significant but moderate association with the prevalence of malaria. The prevalence of malaria among the patients had no significant association with their genotypes.

The demographic characteristics reported in this study compare reasonably with those of other studies conducted in similar settings. The reported middle age of most of the participants is understandable, as the majority of them were students. Most undergraduate students in Nigerian universities are about this age group, as shown in studies from different regions of the country [15–23]. The marital status of the participants in the study was not obtained. Thus, the high proportion of pregnant ones cannot be properly classified and attributed to any factor. It is worth noting that students in Nigerian universities have been reported to be highly sexually active [16], but with fair knowledge of emergency contraception [16,20,21,23]. Suffice it to mention however that in almost all endemic countries, malaria is more of a problem among under-five children [24].

The diagnosis of malaria is reliably done using rapid diagnostic tests in most cases settings at present, and it is as specific and sensitive as the peripheral blood smear test [25]. Many studies have reported the higher prevalence of malaria among blood group O patients compared to others. Zerihun et al., in Ethiopia, reported that most of their population that were confirmed to have malaria were of blood group O [26]. Their study established a significant relationship between the two variables, as in the present study. Another study in the same country presented a similar result in terms of the higher incidence of malaria among blood group O patients. A similar result was reported in a study among students of a university in Cameroon. In that study, blood group O had the higher incidence of malaria, but with no significant difference [31]. Nonetheless, blood group O has also been documented in other studies to confer protective advantage against severe malaria [27,29].

The relationship between genotype and incidence of malaria has also been the subject of research by many authors. As in this study, a higher prevalence of malaria among patients with AA genotype was reported in Nigeria [28]. Unlike in this study, the observed difference was reported to be statistically significant. Another study in Nigeria presented a similar result [9]. While the study reported that the least susceptibility to malaria was in the combination of genotype AS and blood group O, the combination of all genotypes and blood group A was observed in the present study.

As studies present conflicting results, suffice it to repeat that the relationship between the prevalence of malaria and genetic factors will remain controversial. While some studies describe the prevalence of malaria in their population, some went deeper to classify the severity of the malaria or differences based on the causative organisms [33]. The present study did not classify the malaria and it is an apparent limitation. The study contributes to the body of knowledge about the prevalence of malaria and it is a fulcrum for further researches.

This study concludes that the prevalence of malaria was high among patients tested at the University of Nigeria Medical Centre. The association between the malaria prevalence among the patients and their ABO blood group was established to be statistically significant, with blood group O having the highest incidence. Although AA genotype was observed to have the highest cases of malaria among the patients, the relationship between malaria prevalence and genotype was found to be not significant.

**AUTHORS CONTRIBUTIONS**

Abduluminu Ishal conceptualized the study, modalities of data collection and analysis. Chiibuzo Aonsike drafted the manuscript, Chukwuma Ogodo Stephen and Charles Obinna Emeka collected the data and participated in data analysis, Chukwumemka Sylvester Nworo revised the manuscript. All authors approved the manuscript for publication.

**CONFLICTS OF INTERESTS**

Declared none

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