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RESEARCH ARTICLE

Plasmodium falciparum Infection among Febrile Patients Attending a Tertiary Healthcare Facility in Central Nigeria: Prevalence, Hematologic and Sociodemographic Factors

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Abstract

Introduction: *Plasmodium falciparum* infection remains a leading cause of global morbidity and mortality, causing about 3,000 daily deaths. This study intended to document the prevalence, and the associated factors of *P. falciparum* infection among febrile patients attending Federal the Medical Centre Keffi, Nigeria.

Methods: After ethical clearance, 400 whole blood samples were collected from patients who gave informed consent and completed a self-structured questionnaire from July 2015 through January 2016. The blood samples were examined for the parasitic infection and hematological parameters, using standard laboratory techniques.

Results: The overall prevalence of *P. falciparum* infection was 227/400 (56.8%). The prevalence with respect to patient's categories was children (68.1%), pregnant women (67.0%), male adult (47.1%) and female adult (42.0%). The infection was high among genotype AA (83.0%), blood group A (90.8%), females (57.7%), rhesus factor positive (57.7%), age < 15 years (72.4%), those who use insecticide-treated mosquito nets (55.8%) and those with PCV range 20-25 (86.7%). Genotype, blood group, and age were statistically associated with *P. falciparum* ($p < 0.05$). In this study, categories of patients, gender, rhesus factor, use of insecticide-treated mosquito nets (ITNs) and packed cell volume (PCV) ranges were not associated statistically with the infection ($p > 0.05$).

Conclusion: This study reported a high prevalence of *P. falciparum* among patients and as such further studies on molecular characterization of the parasite should be carried out in the population. General awareness and continuous laboratory screening of the public to stop the acquisition of the parasite among population are strongly suggested.

Keywords

Plasmodium falciparum, Prevalence, Patients, Central Nigeria, Malaria

Introduction

Plasmodium falciparum infection remains a global public health challenge and still considered globally as a leading parasitic cause of morbidity, and about 93% of all global malaria deaths occur in WHO African region with Nigeria carrying the highest burden of 19% in 2017 [1]. Malaria is caused by a parasitic protozoan of the genus *Plasmodium* and it is transmitted through the bite of an infected female *Anopheles* mosquito. The parasites move to the liver where maturation and reproduction takes place [2,3]. The infection arises from the division of *Plasmodium* parasites in the red blood cells, causing symptoms which include a headache and fever, and in severe cases progress to coma and death. The infection is endemic in the tropical and subtropical areas which include; Sub-Saharan Africa, Asia, and America [2,3]. Five species of malarial parasite causes infection in humans. *P. falciparum* often causes severe disease and most commonly identified in Nigeria while other species

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such as *P. ovale*, *P. vivax* and *P. malariae* are mild and seldom fatal [4]. *P. knowlesi* is implicated to macaque's malaria and also man (zoonosis). Malaria remains a life-threatening vector-borne disease and has a significant impact on the economic development of most endemic countries [1,5,6]. Those who are at high risk are young children especially under five years, pregnant women and immunocompromised people [1,7]. Malaria infection during pregnancy is a challenge in the tropics and subtropics too, affecting approximately 24 million pregnant women [8].

Malaria transmission can be reduced by preventing mosquito bites by distribution of Insecticidal Treated Nets (ITNs) and insect repellants, spraying insecticides and unblocking stagnant water channels [1]. There is no vaccine offering a high level of protection exists but efforts in developing such are ongoing. Although, number of medications are available for prevention especially among travelers traveling to malaria-endemic regions [1,9]. The World Health Organization currently suggests that all cases of the parasitic infection must carry out laboratory parasite-based test before therapy due to inadequate data on the effectiveness of presumptive tests [9].

Anemia has been known to be the usual sign of the parasitic infection in endemic malaria areas. *P. falciparum* is an important contributor to anemia in pregnancy [10]. Studies have shown that the ABO blood grouping has come up under a great selection pressure in primates and man having challenge to provide a preferred vulnerability to persons that have a certain blood group. The role of ABO blood group in pregnancy susceptibility to malaria is not fully studied [11,12]. Although, Malaria is endemic in Nigeria (Keffi inclusive), the prevalence of the parasitic agent among patients is poorly understood in Keffi in spite of its significance in planning intervention strategies. Therefore, in this study we evaluated the prevalence of *P. falciparum* infection and analyzed associated hematologic and socio-demographic factors among febrile patients attending a tertiary healthcare facility in Central Nigeria. We found that the prevalence of *P. falciparum* infection was high and few probable risk factors for its transmission, denoted by the prevalence of the parasite in this population, was significant. Our findings will enhance epidemiologic understanding of the parasite in Nigeria with implications for control measures

Materials and Methods

Study area

This study was conducted in Keffi. Keffi is 68 Km from Abuja, the Federal Capital Territory and 128 Km from Lafia, Nasarawa State. It lies in Latitude eight 5'N of the equator and Longitude seven 8'E, it also situates on altitude of 850 M above sea level [13]. The average annual rainfall in Keffi is ± 2,000 millimeters (79 in), and is often heavier during the rainy months having its peak around July through September [14]. Most of the populace in this area are traders, farmers, civil servants, and students.

Study population

The study population comprises of febrile patients who were children, adults and pregnant women attending the facility that agreed to participate in the study from July 2015 through January 2016. Structured questionnaires were administered to the four hundred (400) participants recruited for the study. Participants who could not read or write in the English Language were interviewed orally in Hausa. Representative sample size was determined using the formula propounded by Swinscow and Campbell [15]. The instrument was developed to provide data on hematologic and sociodemographic risk such as blood group, PCV, rhesus factor, age, gender and use of ITNs.

Inclusion and exclusion criteria

Patients with a history of fever or body temperature of > 37.5 °C in both adults and children who agreed to participate in the study at Federal Medical Centre Keffi were included while those on antimalarial treatment or any who had received treatment of malaria three weeks before the study were excluded.

Sample collection

Blood sample was collected from each participant by venipuncture following the protocol of Kalu, et al. [11].

Laboratory analysis

Rapid diagnosis of malaria parasite: Screening for malaria was performed using Care Start™ malaria HRP2 (Pf) rapid test for *Plasmodium falciparum* malaria ML no: 338 (Orchid Biomedical System, India) following the manufacturer's instructions.

Microscopic examination of the malaria parasite (Gold standard): Thin and thick blood smears were used as confirmatory test for the parasite in the target population. The both smears were stained using 3% Giemsa technique as described by Cheesbrough [16].

Determination of genotypes: The genotype of each participant was determined as described by Ochei and Kolhatkar [17]. Briefly, the anticoagulant blood was centrifuged at 2500 rpm for 5 minutes. The supernatant discarded and packed cells washed with normal saline three times. The red cells were lysed by adding an equal volume of distilled water, one quarter (1/4) of toluene and a drop of 3% KCN after the final wash. It was then mixed properly.

Determination of blood groups: The ABO blood group of each subject was determined using cell grouping Antisera as by Rosenfield [18] and Cheesbrough [19]. Monoclonal Antisera A, B, and D (Agappe Diagnos-

tics Ltd, India) were used for the assay.

Packed cell volume (PCV) determination: Packed cells volume was determined by the micro haematocrit protocol as described by Coles. The blood samples were collected into capillary tubes, sealed at one end in Bunsen flame and centrifuged at 10,000 rpm for 5 minutes using a micro hematocrit centrifuge. Using a microhematocrit reader, the PCVs were read and recorded.

Data analysis

The data gathered were statistically analyzed using the Smith's Statistical Package (SSP version 2.80, Claremont, California-USA). Chi-square statistical test was used to determine differences and values obtained were considered statistically significant at $p \leq 0.05$.

Ethical clearance

In line with the Helsinki Declaration which specifies the code of ethics for biomedical research involving human samples, clearance for the study was obtained from the Ethical Committee on Health Research of Federal Medical Centre, Keffi, Nigeria. Formal consents were retrieved from adult and pregnant women directly while children below 16-years-old consent were obtained from their parents/guardians using a consent form prior sample collection.

Results

Out of 400 subjects examined, 227 (56.8%) were infected with *Plasmodium falciparum*. The malaria prevalence in respect to patient's categories was children (68.1%), pregnant women (67.0%), male adult

Table 1: Distribution of *Plasmodium falciparum* infection among febrile patients attending Federal Medical Centre Keffi, Nigeria in relation to sociodemographics and hematological parameters.

Parameters	No. Examined	No. Positive	Prevalence (%)	χ^2	*P* value
Categories of Patients					
Children	116	79	68.1		
Male adult	102	48	47.1	6.1219	**0.1057**
Female adult	88	37	42.0		
Pregnant women	94	63	67.0		
Genotype					
AA	106	88	83.0		
AS	151	72	47.7	10.2046	**0.0059**
SS	143	67	46.9		
Blood group					
A	87	79	90.8		
B	87	67	77.0	41.1801	**< 0.0001**
AB	56	41	73.2		
O	170	40	23.5		
Gender					
Male	128	70	54.7	0.0907	**0.7633**
Female	272	157	57.7		
Rhesus factor					
Positive	364	210	57.7	0.4273	**0.5133**
Negative	36	17	47.2		
Age (Years)					
< 15	87	63	72.4		
16-30	150	98	65.3	8.8123	**0.0317**
31-45	145	58	40.0		
> 46	18	8	44.4		
Use of ITNs					
Yes	260	145	55.8	0.0799	**0.7774**
No	140	82	58.6		
PCV range					
15-20	40	34	85.0		
20-25	30	26	86.7		
25-30	60	38	63.3	10.2595	**0.0681**
30-35	180	93	51.7		
35-40	63	28	44.4		
> 40	27	8	29.6		

(47.1%) and female adult (42.0%). The infection was high among genotype AA (83.0%), blood group A (90.8%), females (57.7%), rhesus factor positive (57.7%), age < 15 years (72.4%), those who use insecticide-treated mosquito nets (55.8%) and those with PCV range 20-25 (86.7%). Genotype, blood group, and age of the participants did not show any statistical difference with *P. falciparum* infection ($p < 0.05$). In this study, categories of patients, gender, rhesus factor, use of ITNs, and PCV ranges were not associated statistically with the infection ($p > 0.05$) (Table 1).

Discussion

An overall prevalence rate of 56.8% *P. falciparum* was reported among febrile patients attending the tertiary healthcare facility in North Central Nigeria which is in agreement with the reports in parts of the countries. It was 69.19% among patients in Niger state [2], 64.9% among patients in Kano [5], 39.5% among patients in Benue state [20], 15% among febrile patients in Jos [3], 65.0% among people living with HIV/AIDS in Keffi [21], 31.6% among children in Abeokuta [7] and 38.4% among students in Igbinedon University Okada [22].

Lower rates compared to findings in the present study have been reported in other countries such as 9.8% among students [23], 25% among adults [24], 12.3% among pregnant women [25].

Higher rates than report of this study have been found in some parts of the country [2,5]. The relatively high prevalence of *P. falciparum* infection reported in this study might relate to the prevailing environmental conditions that enhance the breeding of the vector of the parasite. The major strength of this study lies in the unprecedented categories of study subjects incorporated in this study. No significant difference statistically between the prevalence of *P. falciparum* infection, and categories of patients studied ($p > 0.05$). The parasitic infection was highest among children subjects (68.1%) and lowest among female adults (42.0%) respectively. Children, especially under five years old are the most vulnerable group affected by the parasitic infection [1]. Several researchers have reported different prevalence based on their selected study subjects [23-26].

This study further revealed a statistically significant association between the prevalence of the parasitic agent and genotype ($p < 0.05$). The malaria infection was highest among patients who had AA genotype (83.0%), followed by AS (47.7%) and lowest among patients with SS genotype (46.9%). A related study was done by other researchers [27]. The high prevalence among the AA genotype might be because of their high percentage of oxygen and a large amount of hemoglobin in which the parasite thrives better in such environment.

In this study, blood group appeared to be an associated factor for the protozoan agent ($p < 0.05$). Patients with blood group A had the highest prevalence (90.8%) while those with blood group O had the least prevalence of the infection (23.5%). There were disagreements with findings of Otajevwo [22] and Akhigbe, et al. [28] in Nigeria while, Bamou and Sevidzen, [23] in Cameroon reported highest prevalence in blood group O and Kuesap and Na-Bangchang, [27] in Thailand which reported the highest prevalence of the infection among B blood group. The high epidemiology of *P. falciparum* with blood group A might suggest that A antigen is more susceptible to malaria infection.

This study findings showed that the prevalence of *P. falciparum* infection is higher in females (57.7%) than males (54.7%), which are consistent with the reports of Houmsou, et al. [20] and Olasunkanmi, et al. [7] in Nigeria but contradicts with findings within Nigeria and other countries [2,5,24,29]. No association between gender and the prevalence of the infection was reported in this study. A predominance of malaria infections in males has been reported in epidemiological studies, although no scientific evidence documented to prove the higher prevalence was associated to sex susceptibility that malaria infection does not have any significant influence with sex [7,30].

There was no statistically significant association between rhesus factor and the prevalence of the parasitic infection ($p > 0.05$). It was 57.7% among positive rhesus factor patients while 47.2% prevalence was reported among patients with negative rhesus factor. This finding agreed with a similar study in Cameroon [23] and Nigeria [22]. There is no obvious reason for this outcome.

In this study, the prevalence of the infection was highest among patients aged less than 15-years-old (72.4%). Epidemiology of malaria infection in lesser age groups have been reported [2,20] while other findings disagree with this report [3,5,24,31]. There is an association between the parasitic infection and age of the patients ($p < 0.05$). Therefore, age was a probable risk factor for the acquisition of the infection in this study. Weak immunity and improper use of control strategies e.g. ITNs usage might be the reason for a high prevalence among those aged < 15 years.

In this study, no significant association statistically was observed among patients who use ITNs ($p > 0.05$). The prevalence of the infection was higher among patients that do not use ITNs (58.6%) than those who use ITNs (55.8%). Findings in this study was also recorded in related researches in Nigeria and other countries [5,25,31]. Appropriate utilization of ITNs is one of the major interventions for the prevention of malaria.This finding is a clarion call to Federal and State Governments for provision and distribution of ITNs to the vulnerable population. Continuous awareness

campaign on its importance and usage should also be at play.

Evaluation of *P. falciparum* infection based on PCV range by the patients shows a gradual increase in the prevalence of the infection with PCV range (85.0% in those patients with PCV range from 15-20 to 29.6% in those with PCV range greater than 40). PCV was once an indicative tool of malaria control and its prevalence among a particular group and it is used to assess the efficacy of intervention programmes. Similar findings were reported in Liberia [25] and in Thailand [27].

Conclusion

This study reported a high prevalence of *P. falciparum* infection among the study population. Genotype, blood group, and age of patients were associated statistically with the infection ($p < 0.05$). In this study, categories of patients, gender, rhesus factor, use of ITNs, and packed cell volume (PCV) ranges did not show any significant difference statistically with malaria ($p > 0.05$). Therefore, further studies on molecular characterization of resistant strains of the parasite should becarried out in the population. General health awareness and continuous laboratory screening of the public to stop the acquisition of the parasite are strongly suggested.

Limitations

Molecular analysis (Polymerase Chain Reaction) of the identified parasites was not done due to limited resources and availability of the technology. Further studies that will capture a wider population and facilities as well as determination of the fever that is attributable to malaria parasite should be carried out, since agents like dengue and other arboviral diseases shows similar symptoms with malaria.

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Conflict of Interest

There are no conflicts of interest.

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