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Reliability of Urine Malaria Test (UMT) for Malaria Diagnosis

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Authors' contributions

This work was carried out in collaboration between all authors. Author JAO designed the study, performed the statistical analysis, wrote the protocol and first draft of the manuscript. Author EMO managed the analyses of the study. While author CEA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Although an accurate diagnosis of malaria is key to effective rational malaria therapy, it has been the most neglected area of Malaria research. Thick blood film microscopy, Blood rapid diagnostic test (bRDT) and Urine Malaria Test (UMT) was comparatively used to study malaria prevalence as well as their sensitivity, specificity and predictive values in diagnosing malaria. A total of 100 samples were collected from patients attending University of Agriculture Makurdi health centre from September 2016 - January 2017 and analysed appropriately using standard procedures. The highest malaria prevalence 86(86%) was recorded in microscopic diagnosis followed by UMT 57(57%) while Blood Rapid diagnostic Test b(RDT) recorded the least malaria prevalence 50(50%).

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There was no significant difference (P > 0.05) in the prevalence of malaria in the different diagnostic methods used. Microscopic diagnosis recorded sensitivity and specificity of 100%, UMT recorded sensitivity of 79% and specificity of 100% while bRDT recorded sensitivity of 76% and specificity of 100%. There was a significant difference (P< 0.05) in the sensitivity and specificity among the different diagnostic methods used. The positive predictive value (PPV) and negative predictive value (NPV) microscopic diagnosis was 100% while bRDT also recorded a positive predictive value (PPV) of100% and a negative predictive value (NPV) of 75%. UMT equally had a positive predictive value (PPV) of 100% and a negative predictive value (NPV) 55.5%. The assessment of attributable fraction of fever associated with malaria among the participants showed that out of 86 malaria positive participants, 19 of had fever while 67 of them had malaria without any sign of fever.

Keywords: Malaria; Urine malaria test (UMT); reliability; UAM Health Centre.

1. INTRODUCTION

Malaria remains one of the world's greatest childhood killers and is a very significant obstacle to social and economic development in the tropics [1]. The malaria burden faced by African countries continues to be a challenge for national government with Nigeria inclusive [2] . It is a life threatening disease characterized by paroxysms of chills, fever, sweating, splenomegaly, fatigue headache and a chronic relapsing course [3]. It is a disease that has had a major impact on the development of life and health of humanity.

Malaria is not just a disease associated with poverty. Evidence suggested that it is also the cause of poverty and a major hindrance to economic development. Throughout history, the contraction of the disease has played a prominent role in the fate of government rulers, nation states, military personnel and military actions.

Malaria is a disease of the tropical and subtropical region of the world especially in sub-Saharan Africa, China/India, and Central America. It is estimated that the disease causes about 207 million clinical episodes and about 627,000 deaths annually, mostly in Sub-Saharan Africa. It accounts for 25% of infant mortality and 30% of childhood mortality in Nigeria thereby imposing a great burden on the country in terms of pains suffered by victims as well as loss in output and expensive treatment [4]. It is documented that children in their countries of origin import malaria from Nigeria and other hyper endemic countries to non endemic countries.

One of the factors that have ensured the persistence of malaria morbidity and mortality has been the failure of definitive diagnosis and prompt treatment of the disease [5]. In recent times, with the relatively high and increasing incidences of resistance of malaria parasites to antimalaria drugs, it has become very necessary to confirm the diagnosis of malaria using rapid laboratory test methods for enhancing prompt treatment of the disease. Urine Malaria Test (UMT) diagnosis method is one of the rapid diagnostic test methods in current use for prompts diagnosis of malaria. It is imperative therefore to evaluate the reliability of the UMT method through a comparative study with other standardized laboratory test methods. Furthermore, the non-invasive rapid malaria diagnostic test methods are very convenient for use but their reliability ought to be checked against other conventional methods to validate their accuracy.

This recent research therefore aimed at evaluating the reliability of UMT kit (Fyodor Test Kit) in diagnosing of Malaria.

2. MATERIALS AND METHODS

2.1 Study Area

The study was carried out in the University of Agriculture Makurdi Health Center (Fig. 1) which is located in the middle core of the University. The University was established in 1988, following the recommendations of a 1987 Federal Government White Paper on Higher Education curriculum and development in Nigeria [6]. The University is 10 km away from the Federal road leading to Lafia-Engu across Benue. It has a land mass area of 8,048 hectares and share common boundaries with the River Benue and Makurdi town in the South, Federal Housing Estate in the west, Tyodugh village in east, \Agan village in the north and Guma Local Government Area in the North-east.

Makurdi is the capital city of Benue State in north central Nigeria. It lies between latitude 7°44N and longitude 8°54E. It is located within the flood plain of lower River Benue valley. The physiographic characteristics span between 73-167 m above sea level. Due to the general low relief, sizeable portions of Makurdi are water logged and flooded during heavy rainstorms. This is reflected in the general rise in the level of groundwater in wells during wet season. The drainage system is dominated by River Benue which traverses the town into Makurdi North and South banks. Temperatures are generally high throughout the year due to constancy of isolation with the maximum of 32°C and mean minimum of 26°C. According to [7], the hottest months are March and April. The rainfall here is convective, and occurs mostly between the months of April and October and is derived from the moist and unstable southwest trade wind from St. Helena Subtropical Anticyclones (STA). Mean annual rainfall total is 1190 mm and ranges from 775-1792 mm. Rainfall distribution is controlled by the annual movement and prevalence of Inter-Tropical Discontinuity (ITD). The mean monthly relative humidity varies from 43% in January to 81% in July-August period. Makurdi town which started as a small river port in 1920 has grown to a population of 297,393 people [8].

The vegetation of Makurdi town is the guinea savannah type. This vegetation type has been

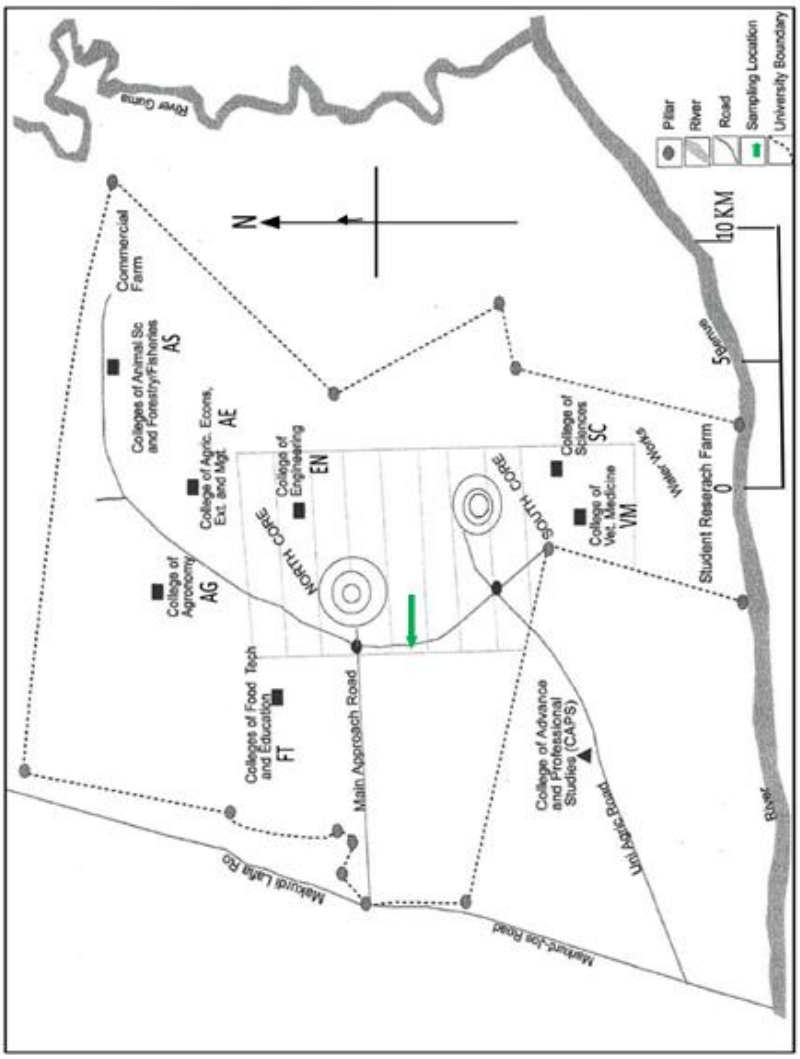

Figure 1. University of Agriculture Makurdi showing the study area [9]

adversely affected by human activities leading to the clear-cutting of tree cover in many parts of the town. Due to this, artificial vegetation has replaced natural secondary vegetation. Makurdi town is inhabited by many tribes with a population of 297,398 to 157,295 males and 140,103 females [10]. These tribes include the Tivs, Idomas, Etilos, Jukuns, Egede, Hausas, Yorubas and Igbos. The Tivs are the dominant tribe. Makurdi town is made up largely of people who engage in civil service duties, commercial activities and agrarian peasantry. Makurdi town is a built up area with the highest concentration of people in high level and Wadata. Dense population also exists in some low-lying parts of the town such as Wurukum.

2.2 Sample Collection

2.2.1 Blood

The method of sample collection was venepuncture technique [11]. A tourniquet was fastened to the upper arm of the patient to enable him/her feel a suitable vain. The punctured site was then cleansed with methylated spirt (methanol) and venepuncture mode with the aid of a 21 g needle attached to a 5ml syringe. When sufficient blood was collected the tourniquet was released and the blood was transferred into an ethylenediamine tetra-acetic disodium acid (EDTA) bottle to prevent clotting.

2.2.2 Urine

Patient`s early morning urine was collected to detect the presence of malaria parasites using Urine Malaria Test kit (UMT). Biological data (gender, age and temperature range) of the patients were collected from patient clinical records.

2.3 Laboratory Analysis of Samples for Malaria

2.3.1 Rapid diagonstic test

The rapid diagnostic test was performed according to [12]. Five µl of whole blood was added into sample well in the *pf/pv* antigen test kits and two drops (80 µls) of assay buffer was added into the developer well. Then the results were read in 20 minutes as shown in The presence of two colour bands “C” and “pf”, indicate a positive for *P. falciparum,* Two colour band”C” and “Pv” indicate a positive result of *P. vivax,* three colour bands indicate a positive result for *P. falciparum and P. vivax.* The presence of only band “C” within the result window indicate a negative result, as manufacturers instruction(Rapid Malaria pf/pv Antigen Test) .

2.3.2 Urine malaria test

The malaria test was performed according to the manufacturer’s guidelines [13]. Patients urine was collected in a universal bottle (Plate 2b), and later turned into the sample cup (provided in the kit), and the urine was filled up to the ridges (Plate 3a). The test strip was removed from packaging pouch, white end of the strip was dipped into a freshly collected urine specimen, with arrows pointing downward, strip was allowed to stand in sample urine for 25mins the result was being read.

The result was read visually: one coloured band indicates the absence of *Pf* malaria; two coloured bands indicate the presence of *Pf* malaria. The tests were interpreted by the presence or absence of visually detectable pink or purple coloured bands as outlined in the manufactures manual.

2.4 Malaria Microscopic Test

2.4.1 Thick blood film

Thick film blood smear was prepared according to [14]. A little drop of blood was placed on a clean dry glass slides and emulsified (spread) to the size of a small coin and left to dry After allowing it to dry for almost a whole day to get accurate result the slide was dipped into a Giemsa stain and allowed to dry on the staining rack, for 30 minutes and rinsed in water to remove excess stain, the stain was allowed to air dry before viewing under the microscope (x100) objective using immersion oil.

2.4.2 Determination of sensitivity and specificity

The sensitivity and specificity was calculated using the formula

Sensitivity (%) = $\frac{TP}{TP + FN} x\ 100$, where = TP True positive, FN = False negative

Specificity % = $\frac{TN}{TP + FP} x\ 100$,

where TN = True negative, TP = True positive, FP = False positive.

2.4.3 Determination of Positive and Negative Predictive Value

$$PPV = \frac{TP}{TP + FP} X100$$

$$NPV = \frac{TN}{TN + FN} X100$$

Tp = True Positive
Tn =True Negative
Fp =False Positive
Fn =False Negative
Ppv = Positive Predictive Value
Npv = Negative Predictive Value

2.5 Statistical Analysis

ANOVA was used to test the significant difference between prevalence of malaria using different diagnostic methods among different age groups. While (Chi-square x^2) was employed to show the significant relationship between the sensitivity and specificity, positive and negative predictive value, mean temperature and attributable fraction of fever related to malaria.

3. RESULTS

3.1 Comparative Prevalence of Malaria Based on Age Group by Using Different Diagnostic Methods (bRDT, UMT, Microscopy)

Prevalence of malaria based on age group using different diagnostic methods (bRDT, UMT and Microscopy) is shown in Table 1. The overall age group related prevalence based on the different diagnostic methods used showed a highly prevalent (100%) of malaria parasitaemia in the age group of 71-75. The highest prevalence (86%), malaria parasiteamia was recorded in microscopic diagnostic method, followed by UMT 57 (57%) while the least prevalence 50 (50%) was recorded in bRDT diagnostic methods. There was no significant difference ($P > 0.05$) in the prevalence of malaria base on different diagnostic methods used among the different age groups

3.2 Sensitivity and Specificity of UMT Kits in Relation to Microscopy and bRDT

Sensitivity and specificity of UMT kits in relation to Microscopy and bRDT is shown in Table 2. The Microscopy diagnosis recorded the highest sensitivity 100% and specificity (100%) followed by UMT sensitivity (79%) and specificity (100%) and bRDT recorded sensitivity (76%) specificity (100%) respectively.

Table 1. Comparative Prevalence of malaria parasitaemia based on age groups using different diagnostic methods (bRDT, UMT and microscopy).

S/N	Age Group	No. Examined	Different diagnostic methods		
			bRDT	UMT	Microscopy
1	0-5	11	7(64.0%)	8(73.0%)	10(91.0%)
2	6-10	13	5(38.5%)	6(46.2%)	10(77.0%)
3	11-15	14	10(71.4%)	9(64.3%)	13(93.0%)
4	16-20	16	9(56.3%)	8(50%)	13(81.3%)
5	21-25	8	3(38.0%)	5(63.0%)	8(100%)
6	26-30	12	6(50%)	8(67.0%)	11(92.0%)
7	31-35	7	2(29.0%)	4(57.1%)	6(100%)
8	36-40	9	4(44.4%)	3(33.3%)	8(100%)
9	41-45	4	0(0%)	1(25%)	2(50%)
10	46-50	2	1(50%)	2(100%)	2(100%)
11	51-55	2	2(100%)	2(100%)	2(100%)
12	56-60	1	0(0%)	0(0%)	0(0%)
13	61-65	0	0(0%)	0(0%)	0(0%)
14	66-70	0	0(0%)	0(0%)	0(0%)
15	71-75	1	1(100%)	1(100%)	1(100%)
Total		100	50	57	86

Fcal=0.18, Ftab =2.48, df =14, P > 0.05

Table 2. Sensitivity and specificity of UMT kit in relation to microscopy and bRDT methods

Test result	True positive	False positive	True negative	False negative	% sensitivity	% specificity
Microscopy	87	0	13	0	100%	100%
bRDT	49	0	13	39	76%	100%
UMT	55	0	20	25	79%	100%

x^2cal=40.51, x^2tab =18.55, df = 6, P < 0.05

There was a significant relation (P < 0.05) between sensitivity and specificity used with different diagnostic methods used.

3.3 Positive Predictive Value and Negative Predictive Value of UMT Kit in Relation to Microscopy and bRDT

Positive predictive value and negative predictive value of UMT kit in relation to Microscopic and bRDT diagnostic methods is shown in Table 3.The positive and negative predictive value observe for Microscopy were both 100%, bRDT has a positive predictive value of 100% with a negative predictive value of 75%, while UMT has a positive predictive value of 100% and a negative predictive value of 55.5%.

The observe positive predictive value in each of the method used was 100%,while microscopy was observed to have the highest negative predictive value of 100% followed by bRDT 75% and UMT 55.5%. It was observed that there was a significant difference (P < 0.05) in positive and negative predictive value of the different diagnostic methods

3.4 Mean Temperature Range of Malaria Subjects Based on Gender

Mean temperature range of malaria subject based on gender as shown on Table 4:4 1 out of 46 male subject who were diagnosed for malaria had a mean temperature range of 35.6^{o}c, while 45 out of 54 females subject diagnosed for malaria have a mean temperature range of 35.4.This shows that the mean temperature range in male subject was likely higher than female subject, it was also observe that there was a significant difference (p < 0.05) in mean temperature range between male and female subjects.

3.5 Attributable Fraction of Fever Associated with Malaria and Attributable Fraction of fever not Associated with Malaria

Attributable fraction of fever associated with malaria and attributable fraction of fever not associated with malaria according to age range, is shown in Table 5. 19 out of the 86 subjects diagnosed of malaria showed signs of fever while 67 out of 86 subjects diagnosed of malaria showed no sign of fever. It was observed that the attributable fraction of non febril malaria was higher (67) than febril malaria (19). There was no significant difference (P > 0.05).

Table 3. Positive predictive value and Negative predictive value of UMT kit in relation to microscopy and bRDT

Test result	True positive	False positive	True negative	False negative	Positive predictive	Negative predictive
Microscopy	87	0	13	0	100%	100%
bRDT	49	0	13	39	100%	75%
UMT	55	0	20	25	100%	55.5%

x^2cal = 40.51, x^2 tab = 18.55, df = 6, p < 0.05

Table 4. Mean Temperature range of malaria subjects based on sex

S/N	Sex	No. examined	No. infected	Mean temperature range (^{o}C)
1	Male	46	41	35.6±3
2	Female	54	45	35.4±5

x^2cal=246.54, x^2tab =7.88, df = 2, P < 0.05

Table 5. Attributable fraction of fever associated with malaria and attributable fraction of fever not associated with malaria

Age Group	Febril malaria	Non Febril malaria
0-5	6	5
6-10	0	13
11-15	0	7
16-20	0	16
21-25	5	3
26-30	5	0
31-35	0	7
36-40	0	9
41-45	1	4
46-50	0	2
51-55	2	0
56-60	0	0
61-65	0	0
66-70	0	0
71-75	0	1
Total	19	67

x^2cal = 30.29, x^2 tab = 31.32, df = 14, P > 0.05

4. DISCUSSION, CONCLUSION AND RECOMMENDATION

4.1 Discussion

In order to alleviate the expanding impact of malaria across the globe, as well as its associated increasing drug resistance, establishment of prompt and accurate diagnosis is required. Microscopy has been seen as gold standard for malaria diagnosis especially in under developed nations [15], but in recent years, a number of new techniques have become available for the diagnosis of malaria infection which includes urine malaria test kits and bRDT.

In this present study, the overall age groups related prevalence based on the different diagnostic methods showed that the age group 71-75 recorded the highest prevalence of 1(100%) using different diagnostic methods. A similar prevalence was recorded also in 51-55 years of age group using the different diagnostic methods, while the 46-50 years age group recorded high prevalence 2(100%) using UMT and microscopy. The high rate of infection among these individuals may be as a result of a decline in immunity with age [16].

It may also be as a result of lack of protection against mosquito bite or lack of knowledge about malaria transmission.

Age group of 0-5 year recorded a fairly high prevalence using the different diagnostic methods; 7(64.0%) with bRDT, 8(73.0%) with UMT and 10(91.0%). This result is in contrast with that of [2], who reported lower prevalence of 61.5% among age group 0-5years using microscopy. This recent result obtained may be as a result of lack of transferred maternal immunity or infection acquired through the mother as in case of congenital malaria [2].

Considering the light microscopy as a standard in malaria diagnosis, this study revealed a specificity 100% and sensitivity of 100% in microscopy as against the bRDT specificity 76% and sensitivity 100%, also UMT with a specificity 79% and sensitivity 100%. The result obtained is in agreement with the report by [2], who recorded high values for both sensitivity and specificity using microscopy. This is because microscopy is more efficient in detecting the presence of malaria parasite even in small µl of blood and also it is a differential diagonistic method as compared to bRDT and UMT.

This present study revealed that microscopy has a 100% positive predictive value meaning that patients stand the chance of being correctly diagnosed as positive for malaria. This also applies to bRDT and UMT kit which both has 100% PPV. Also, 100% Npv for microscopy indicate that microscopy can be relied upon in ruling out the chance of malaria .This was however not the case for bRDT and UMT that had Npv of 75% and 55%. This implies that both methods cannot be fully relied upon in ruling out the chance of malaria infection. The high value of Ppv and Npv recorded in this study is however higher than that reported by Anagu et al., (2015) in their study to compare malaria microscopy and malaria rapid diagonistic method (bRDT) in dectection of *P. falciparum.* Also, the temperature range of malaria subjects based on gender showed that the mean temperature range between the male and female subjects was slightly different from each other (35.6°C and 35.4°C). This may be because there was no marked difference in response to malaria infection in male and female patient in terms of temperature changes.

This study also showed that 19 of the patients diagnosed with malaria presented signs of fever while 67 patients who were diagnosed with malaria did not show sign of fever. It was also

recorded that more patients [6] within the age range of 0-5 who were diagnosed with malaria showed signs of fever. This is line with the report of [17] who also recorded similar result among under-fives under reduced malaria infection. The observation that more patient in age group 0-5years diagnosed with malaria had a fever is likely to be as a result of the parasite density in these patients since at this age, their immunity is not fully matured [18].

4.2 Conclusion

The result from this research showed that microscopy still remains the gold standard for malaria diagnosis because of its high accuracy. Both urine malaria test kit and blood rapid diagnostic test kit need to be supplemented with other malaria diagnostic method such as PCR because of their relatively low sensitivity.From this recent study, it was also observed that not everybody presented with fever was actually malarious and vise versa.

4.3 Recommendation

The UMT (Fyodor) should undergo further development and evaluation before the kit can be deployed for malaria epidemiological use. Proper diagnosis of malaria should be carried out before treatment since the wrong diagnosis precludes wrong treatment which may lead to resistance of the malaria parasite

CONSENT

As per international standard or university standard written patient consent has been collected and preserved by the authors.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist

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