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ORIGINAL ARTICLE

Performance evaluation of a popular malaria RDT in Nigeria compared with microscopy

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Abstract Malaria remains a public health problem in Sub-Saharan Africa. Prompt diagnosis and effective treatment are important in reducing morbidity and mortality associated with malaria especially among high-risk groups. This study evaluated the diagnostic performance of one of the popular malaria rapid diagnostic test (RDT) kit in Nigerian market which has not been investigated before in field-condition compared with microscopy as the gold standard. A total number of 250 children of 10 years and below were examined for malaria parasites using both microscopy and RDT in Uhogua community in Edo state and data were analysed using SPSS version 22. The prevalence of malaria by microscopy was 99.2% while only 55.2% were positive by RDT. Majority of the study populations were asymptomatic for malaria infection. RDT sensitivity and specificity compared to light microscopy was 69.08% and 66.67% respectively while the positive predictive value and negative predictive value were 99.6% and 1.77% respectively. The RDT accuracy was less than 70%. RDT cannot be relied upon alone for malaria diagnosis. Microscopy remains the gold standard for malaria diagnosis.

Keywords Malaria · Microscopy · Rapid diagnostic test (RDT) · Asymptomatic · Nigeria

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Introduction

Malaria disease burden in sub-Saharan Africa is almost 90% with children below 5 years accounting for more than 78% of global malaria deaths (Hay et al. 2007). Prompt diagnosis and effective treatment are important in preventing complications associated with deaths due to malaria especially among high-risk groups (WHO 2015).

The most prominent of the many clinical signs and symptoms associated with malaria is fever often accompanied by chills, perspiration, headache, vomiting and malaise. People living in endemic areas have frequently experienced this symptoms and out of familiarity presume that they have malaria based on the symptoms. They often buy widely available and inexpensive antimalarial drugs without malaria testing resulting in self-diagnosis and treatment (Bell et al. 2006; D'Acremont et al. 2009). This leads to the emergence and spread of drug-resistance (White 2004).

A major factor responsible for this self diagnosis and treatment is the unavailability of high quality laboratory diagnosis especially in rural areas. This is due to the absence of necessary materials such as satisfactory microscopes, good quality reagents; enabling environment in terms of water supply and electricity as well as technical expertise. In urban areas with microscopic facilities, patients find laboratory diagnosis as time wasting as heavy case loads resulted in long laboratory waiting times (Boadu et al. 2016). Testing was often arbitrary, or for detained or admitted patients, who often received treatment before results became available (Mokuolu et al. 2018). Despite these short comings, microscopy still remains the gold standard for malaria diagnosis in Nigeria.

Rapid diagnostic tests for malaria (RDTs)—antigen-detecting tests based on immunochromatographic

methods—offer a new diagnostic alternative for health professionals. Since 2010, the recommendation by the WHO is that diagnostic testing must be done either by microscopy or rapid diagnostic tests (RDTs) to confirm malaria before treatment of suspected cases (WHO 2011). RDTs do not require much infrastructure or technical expertise and as such can be done easily in remote rural settings, hence discouraging the presumptive treatment of malaria in the absence of microscopy. RDTs exist in different formats. The major difference between them is in the antigen type detected by the kit. The histidine-rich protein 2 (HRP-2) is specific for the detection of *P. falciparum*, aldolase for detection of *Plasmodium spp* in general and plasmodial lactate dehydrogenase (pLDH) either for *P. vivax* (Pv-pLDH), *P. falciparum* (Pf-pLDH) or *Plasmodium sp* in general (pan-pLDH) (Kennedy and Otokunefor 2017). HRP-2 can detect the presence of the plasmodium protein whether dead or alive and so tends to be very sensitive, but less specific because of it results in false positive occasionally (FMOH 2015). At present, more than 90% of RDT in use are the most common assays that detect HRP-2 (Mouatcho and Goldring 2013). These assays are valuable in Sub Saharan Africa where the main causative agent of malaria is *P. falciparum*.

However, within the period of rapid uptake, three RDT-associated challenges emerged: (a) varying performance of RDT products in field use, (b) a confusing range of products on the market, and (c) limited acceptance of results by health workers and patients (e.g. so that they prescribe or take medicines in spite of a negative result due to a lack of trust in the new technology, or simply continuing with clinical habits). Since 2002, WHO has used different strategies to address these challenges (WHO 2010). In Nigeria, the use of RDTs has continued to increase. However the usage of RDT is higher in health facilities compared to privately owned facilities as confirmed by a study done by Bamiselu et al. (2016). A study by Mokuolu et al. (2016) carried out on private health facilities reported that about 50% of diagnosis of malaria was confirmed by use of RDTs. It has been recommended by the WHO that standard RDT must have a sensitivity of 95% for the detection of 100/µl of *P. falciparum* and 95% specificity (WHO 2006). However, this benchmark values have been discovered to vary in different areas necessitating the need to determine the performance of different RDTs in different regions. There is therefore a need to continue to determine the performance of the different RDTs found in Nigerian markets. This study was carried out to determine the performance of Biocheck RDT in field conditions.

Methods

Study site

The study site is in Uhogua community, Ovia north-east local government area of Edo state which accommodates internal refugees from the north-eastern states (Mouatcho and Goldring 2013). The area has a tropical climate with an average annual rainfall which ranges from 500 to 2780 mm and temperature between 24 and 33 °C. The study was carried out among pre and school-age children of both sexes aged 3 months to 10 years old in the Internally Displaced Persons (IDP) Camp.

Design and setting of the study

Prior visits were made to the community to obtain informed consent from the camp coordinator and participants. Children 10 years old and below were asked to gather at the data collection venue. Following a brief explanation of the purpose and procedure of the sampling, demographic characteristics were taken and blood sample was collected for each child for malaria parasite test. The sample size was calculated using 50% prevalence of malaria in children in the study area using the formula described in a manual by Centres for Disease Control and Prevention/World Food Programme (CDC/WFP 2005).

Laboratory methods

For the detection of malaria parasite by microscopy, venous blood was collected from the children. Thick blood films were prepared, stained and examined under the microscope by two experienced medical laboratory scientists. A third expert scientist also crosschecked randomly selected slides. The malaria rapid diagnostic test kit was performed on the field during survey to detect malaria infection using Biocheck RDT (sensitivity $> 99.0\%$ and specificity 99.7% according to manufacturer, Year of Manufacture: 2018) according to WHO guidelines. The test kits lot number was Cat: IMA-402.

Statistical analysis

Data were analysed using the IBM-Statistical Package for Social Sciences (IBM-SPSS) version 22. Pearson's Chi Square ($\chi 2$) was used to evaluate differences in proportions. Sensitivity, specificity, positive and negative predictive value were calculated for *P. falciparum* at 95% CI.

Ethics approval and consent to participate

Ethical clearance was gotten from the ethical review committee of the University of Benin Teaching Hospital. Informed consent was also obtained from the IDP Camp coordinator. Verbal consent was obtained from the parent/caregivers after explaining the purpose, risks, and benefits of the study. Microscopically-confirmed malaria positive study participants were referred to the nearest healthcare facility.

Results and discussion

An overall number of 250 children were tested by both microscopy and RDT. The age of the participants ranged from 6 months to 10 years old and 70% were females. The overall prevalence of malaria by RDT and microscopy was 55.2% and 99.2% respectively. More than 90% of the study populations were asymptomatic for malaria infection (Tables 1, 2).

The sensitivity and specificity of RDT compared to light microscopy was 69.08% and 66.67% respectively while the positive predictive value (PPV) and negative predictive value (NPV) were 99.6% and 1.77% respectively. The accuracy was 69.06%.

The prevalence of malaria by the gold standard was 99.2%. Majority of the study population were asymptomatic for malaria infection. This high rate of asymptomatic malaria calls for concern. There is a high reservoir of parasites which can be responsible for high transmission of parasite from infected to uninfected persons in the study area. Several high prevalences of malaria have been recorded in Nigeria but this is higher than previous records (Okonko et al. 2009; Kalu et al. 2012; Adekunle et al. 2014). Generally, malaria infection was higher among females and in the age group 6–10 years but was not statistically significant using microscopy method of diagnosis.

Table 1 Prevalence of malaria according to age and sex by RDT

Parameter	No examined	Prevalence (n)	*P* value
Age (years)			
0–5	75	41.3 (31)	
6–10	175	61.1 (107)	0.004*
Sex			
Female	156	53.2 (83)	0.414
Male	94	58.5 (55)	

*Significant

Table 2 Prevalence of malaria according to age and sex by microscopy

Parameter	No examined	Prevalence (n)	*P* value
Age (years)			
0–5	75	98.7 (74)	
6–10	175	99.4 (174)	0.535
Sex			
Female	156	99.4 (155)	0.716
Male	94	98.9 (93)	

Malaria RDT was able to detect 55.2% out of the 99.2% truly positive for malaria. The malaria RDT recorded only 1 false positive and 111 false negatives. The sensitivity and specific values (69.08% and 66.67%) were lower compared to that observed in previous studies by (Ameh et al. 2012; Oyeniran et al. 2014; Ilesanmi et al. 2017) who recorded higher sensitivity and specificity for Bioline SD. The positive predictive value of 99.6% was high compared to the negative predictive value of 1.77%. A high prevalence has been severally reported to lead to a high positive predictive value and low negative predictive value which was the case in this study. The high predictive value recorded in this study shows that RDT is useful in resource limited settings for diagnosing malaria infection and those positive can be classified as truly positive. However the low negative predictive value reveals the need for further testing for malaria negative patients if the means are available. The sensitivity and specificity value recorded in this study is lower than the WHO recommendation of 95% sensitivity and 97% specificity for malaria RDT. This is a major issue to be considered when using RDT in diagnosis of malaria in primary health care or for malaria control programmes.

Several factors have been reported to be responsible for low performance of RDT in field conditions which includes effect of environmental conditions such as high temperatures during transportation and storage, quality issues, disease related factors e.g. parasite species and density etc., and also host factors such as treatment history (Emmanuel et al. 2018).

The Federal Ministry of Health, National Malaria and Vector Control Division, Nigeria has recommended that RDT cannot be used to replace microscopy as the only means of diagnosis for malaria (FMOH 2015). This is because there are variations in the performances of RDTs. The effect of high temperature and humidity which is characteristic of tropical regions on RDTs is a serious limitation. As such, microscopy remains the gold standard for malaria diagnosis and should be used for diagnosis of malaria where possible especially in severe illness where malaria is suspected.

In conclusion, RDTs are very useful in areas where microscopic diagnosis of malaria is not feasible however they should not be used to replace microscopy. There is need for further investigation on the RDT used in this study to determine the reason for the low specificity and sensitivity recorded.

Limitations

Parasite density which could have affected the sensitivity of the RDT was not measured in this study.

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Authors' contributions AOG AND IMR designed the research concept and analysed the data. AOG wrote the manuscript and IMR proofread and corrected the manuscript. Both authors read and approved the manuscript.

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Data availability All data generated or analysed during this study are included in this published article.

Compliance with ethical standards

Conflict of interests The authors declare that they have no competing interests.

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