

Plasmodium falciparum malaria cases detected for prompt treatment by rapid diagnostic tests in the Ho Teaching Hospital of the Volta Region of Ghana

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ABSTRACT

Background: Prompt diagnosis and effective treatment of malaria cases with efficacious drugs is an important strategy in the management and control of malaria in endemic populations. As part of a study investigating the factors modulating the development of *Plasmodium falciparum* gametocytes in the human host, we assessed the rate of RDT positivity of patients in different departments of the Ho Teaching Hospital and the relation with age and anaemia.

Materials and methods: Eight-hundred and ten individuals attending clinic at various departments within the Ho Teaching Hospital were screened for malaria antigenaemia using RDT as a point-of-entry investigation. RDT positive individuals were immediately treated for malaria whereas RDT negative individuals were treated for other ailments. Haematological analyses were performed for 69 of these patients and the relationship between RDT results and haemoglobin levels were investigated.

Results: The overall RDT positivity rate was 19.8% (160/810) of all individuals screened. There was no significant difference in the haemoglobin levels of RDT-positive and RDT-negative individuals (p value = 0.272). The highest number of attendees screened was children in the paediatric outpatient department and paediatric ward, 62% (507/810), with RDT positivity rate of 17% (91/507). We found the highest RDT positivity rate of 51% (19/37) in the male medical ward.

Conclusions: This study shows that RDT is a useful tool in promoting prompt diagnosis and management of malaria and though children form a majority of hospital attendees and malaria infections, the frequency of malaria detection may be higher in adults as compared to children.

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1. Introduction

Four hundred and forty-five thousand people were killed by malaria from among 216 million clinical cases in 2016, and most of these were children under 5 years [1]. This burden is borne largely by Africa, where despite some achievements in controlling malaria, a vast majority of the African population still live in areas of moderate to intense malaria transmission [2]. Malaria is caused by *Plasmodium* species and is the most important protozoan parasitic disease of man [3]. Six species of *Plasmodium* infect and cause malaria in human beings, namely, *P. ovale curtisi*, *P. ovale walikeri*, *P. malariae*, *P. vivax*, *P. knowlesi* and *P. falciparum* [1, 4, 5]. The latter, *P. falciparum*, causes the most malaria burden and is responsible for a majority of malaria deaths in sub-Saharan Africa due to its virulence [6, 7]. The Ho Teaching Hospital records for the past 3 years (2014–2017) show that malaria is associated with 2–3% of deaths among children <5 and 1–4% among persons older than 5 years (Supplemental Table 1) [8].

Prompt diagnosis and effective treatment and management of malaria remain key component in the malaria control and elimination agenda [8]. Rapid treatment of malaria cases, vector control through the use of long lasting insecticide treated nets, and indoor residual spraying have contributed to the substantial reduction in the global morbidity and mortality associated with malaria [2]. In addition, the number of individuals who develop severe anaemia due to malaria infections has also been on the decline.¹ In compliance with this essential guideline, the Ho Teaching Hospital in the Volta Region of Ghana subjects all suspected malaria cases to rapid diagnostic testing (RDT) regardless of the patient point of entry into the hospital. The RDT is performed by trained health persons at the various departments of the hospital. RDT, compared to microscopy, is less time consuming and does not require any specialized training in order to perform and thus contributes to efficient management of malaria cases in clinics and hospitals. Since 2014, there has been a tremendous increase in the use of RDTs as first line malaria diagnosis with a positivity rate of 20–35% among suspected malaria cases in the Ho Teaching Hospital (Supplemental Table 2) [8].

When suspected malaria patients are promptly diagnosed and treated, not only is their suffering alleviated but the intervention reduces the chances of continuous transmission in the population [9]. In addition, the development of severe malaria or even death is also reduced when prompt treatment with efficacious drugs is available [10]. The likelihood of anaemia, which is often associated with delayed treatment of malaria, is also limited [10].

As an ancillary analyses of a study investigating the development of the transmission stages of malaria parasites in the human host (Dinko et al., 2018, AJTMH, Accepted), we sought to determine the rate of RDT positivity among patients in different departments of the Ho Teaching Hospital and whether RDT positivity related to the level of patient haemoglobin and age. In this study we analysed RDT positivity rates among patients diagnosed at the various departments where RDT testing was available.

2. Materials and methods

2.1. Study area and site

The study was conducted at the Ho Teaching Hospital, Ho, in the Volta Region of Ghana. This study site and region has been described previously [11]. The Ho Teaching Hospital serves as the main referral point for tertiary healthcare in the Volta Region but provides both primary and secondary healthcare to all kinds of patients. It is located in Ho, which is the regional capital of the Volta Region. Ho is one of the towns located in the central part of the Volta region and the population of the municipality was estimated at around 70,000 inhabitants [8]. Malaria transmission in the municipality is continuous with some seasonal peaks coinciding with the rainy seasons. The major rainy season lasts for 4 months, from April to July, and the minor rainy season is usually from September to November [12]. Minimal cases of malaria are recorded during the dry periods intervening the wet seasons, but the highest malaria cases are seen 1 month after the beginning of the rainy season.

2.2. Sampling and rapid diagnostic testing

During the period of March 2015 to May 2016 patients attending hospital at the Ho Teaching Hospital (formerly Volta Regional Hospital) were tested for malaria by rapid diagnostic tests (RDTs) (Standard Diagnostics Inc., Korea) at the various departments within the hospital. The departments included: 1) casualty ward 2) diabetic and surgical outpatient department 3) female medical ward 4) gynaecology ward 5) male medical ward 6) medical outpatient department 7) general outpatient department 8) paediatric ward 9) paediatric outpatient department and 10) psychiatric ward. It is the arrangement within the Ho Teaching Hospital to test all individuals suspected of malaria with fever, temperature > 37.5 °C and convulsions via RDT in order that prompt antimalarial treatment can be administered. To achieve this, the diagnostic laboratory within the hospital supplies these wards and outpatients' departments with RDTs for prompt screening of patients by well-trained medical staff stationed in the respective departments. In some departments, the tests were performed by the attending physician while trained nurses carried out the tests in other departments. The results obtained were entered into a form which were later entered into the hospital database. Once test results were obtained RDT positive individuals were given prompt treatment and later referred to the laboratory for further tests. All RDT-positive individuals were provided with 3 daily dose of artemether-lumefantrine while RDT negative individuals were treated for other ailments. We collected and analysed the data presented here as part of our studies of *P. falciparum* gametocytes.

2.3. Determination of haematological indices

Upon the attending physician's request, the haemoglobin levels, erythrocyte indices (red blood cell counts, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) and red cell distribution width (RDW), leucocyte indices (total white blood cell (WBC) count, percent lymphocytes (LYM%), percent monocytes (MON%), percent granulocytes (GRA%), percent eosinophils (EOS%), percent neutrophils (NEU%), percent basophils (BAS%) and platelet indices (platelet count (PLT)), mean platelet volume (MPV), and platelet distribution width (PDW) were analysed using a haematology analyser (Sysmex America, USA) as described elsewhere [13].

Ethical approval to conduct this study, and to use the patient samples and information for these analyses were obtained from the Ghana Health Service Ethics Review Committee in Accra (ID No: GHS-ERC: 03/05/15).

2.4. Data analysis

All summary and descriptive statistics and analyses were performed on Stata version 14 (Stata Inc., USA, 2016). Categorical variables of haemoglobin levels were obtained by using the WHO definition of anaemia as severe, moderate and mild and these were used to classify the patients with haematological data [14, 15]. Pairwise comparison of means was used to test for differences between haemoglobin levels of RDT positive and negative individuals. The Wilcoxon rank sum test was used to test for association between RDT positivity and age of participants. RDT was analysed as a binary variable whereas age was analysed as a continuous variable. Haemoglobin levels were analysed as either continuous or categorical depending on the situation.

3. Results

Eight hundred and ten individuals suspected of malaria presented for RDT testing in 10 departments/wards. The distribution of the number (*n*) of individuals within the various wards and departments were as follows: casualty ward *n* = 33, diabetic and surgical outpatient department *n* = 48, female medical ward *n* = 21, gynaecology ward *n* = 47, male medical ward *n* = 37, medical outpatient department *n* = 46, general outpatient department *n* = 49, paediatric ward *n* = 251, paediatric outpatient department *n* = 255, and psychiatric ward *n* = 23. Overall, the age ranged from 11 months to 81 years with a median of 9.5 years (IQR = 2–30 years) and 52% of the total participants were female.

Of the 810 individuals who had RDT test results, 69 of these had results for haematological analyses. The median haemoglobin for all these individuals was 10.7 g/dL (IQR = 8.9–11.7) and the haemoglobin ranged from 4.7 to 16.9 g/dL. Among the individuals tested by RDT, 19.8% (160/810) were found to be positive and 57.5% (92/160) of all RDT positive individuals were male. In addition, 62% (507/810) of all individuals tested were children attending either the paediatric OPD or were on admission in the paediatric ward. Among these children, 17% (91/507) were found to test RDT positive who were subsequently treated (Fig. 1). The remaining 37% (303/810) of RDT-tested individuals were spread somewhat evenly among the other 8 departments. The male medical ward recorded the highest RDT positivity rate of 51% (19/37) followed by patients in the diabetic and surgical OPD with 29% (14/48), while patients in the paediatric OPD recorded the lowest positivity rate of 8% (21/255) (Fig. 1).

In the malaria endemic area, anaemia is commonly associated with patients infected with malaria, especially children [16–18]. Nineteen out of the 69 patients (27%) whose haemoglobin levels were determined were found to be RDT positive. However, using a pairwise comparison, we did not find any significant difference in haemoglobin levels between RDT positive and RDT negative individuals (*P* value = 0.272) (Table 1). However, 91% (63/69) of patients with haematological data had some form of anaemia ranging from mild to severe as classified by the World Health Organization (WHO, 2011) and 67% (42/63) of these were from the

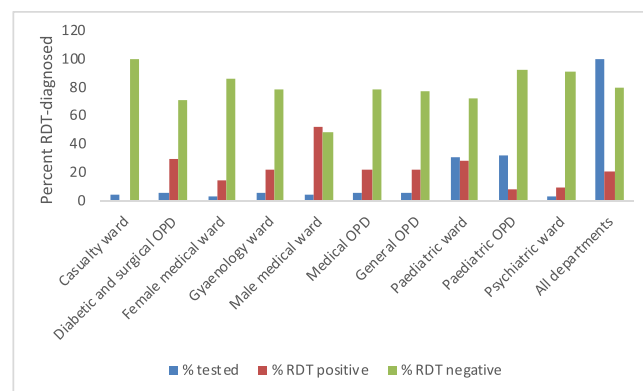


Fig. 1. Proportion of individuals tested for malaria by RDT in the various departments and the rate of RDT positivity within each department in the Ho Teaching Hospital. The percent tested denotes the proportion of individuals tested in the various department relative the total number (810) while percent RDT positive and negative refers to the proportion of patients testing positive or negative relative to number tested for the respective department.

Table 1

Lack of difference in haemoglobin levels between RDT positive and RDT negative individuals.

	Number	Mean (g/dL)	95% CI	P value
RDT positive	19	9.6	8.4–10.8	0.272
RDT negative	19	10.4	9.7–11.1	

paediatric OPD and ward combined (Table 2). We found 17% (12/69) and 42% (29/69) of the participants with haematology data to be severely and moderately anaemic respectively while 31% (22/69) had mild anaemia (Table 2).

As malaria affects mostly children under the age of 5 years and pregnant women [16–18], we tested for an association between RDT positivity and age. There was no association between the age of the participants and the probability of testing positive via an RDT test (P value = 0.508).

Given that 80% of the patients investigated tested negative for *P. falciparum* antigenaemia by RDT, we were curious to know the kinds of treatment administered to these individuals. We were able to obtain the treatment for 305 patients out of the 648 RDT negatives. A total of 75 medications were administered either in combination with other drugs or sole prescriptions and among these the occurrence of paracetamol, an analgesic, was the highest with 17%. Artemether-lumefantrine, an antimalarial, was ranked second with 10% of the RDT negative patients receiving it. There were various kinds of other treatments given to the RDT negative patients and antibiotics formed a majority of the remaining 63% of participants.

4. Discussion

RDT was used to screen individuals of all ages attending clinic in different departments of the Ho Teaching Hospital as part of routine methods to identify *P. falciparum* malaria-infected individuals for prompt treatment. In this child-dominated population, the prevalence of malaria was recorded as approximately 20% and more than half of these were male. Interestingly, the highest rate of RDT positivity was found among adults in the male medical ward whereas children in the paediatric OPD showed the lowest. There was no significant difference in haemoglobin levels between RDT positive and RDT negative individuals and we found no association between RDT positivity and the age of participants. We found analgesics, antimalarials and antibiotics to be the most frequently administered drugs to patients who tested negative for malaria by RDT.

Though the highest number of individuals suspected with malaria and were subjected to RDT screening were from the paediatric ward and paediatric OPD, these two departments together recorded the lowest number of positive cases per number screened. This is an interesting and important observation that is worth noting. Children form part of an important group that are most vulnerable to malaria due to the fact that their immune systems have not been adequately primed to protect them from malaria [17–19]. It is therefore surprising that in this survey they have the lowest rate of testing positive by RDT. Nevertheless, this observation confirms the position that not all “malaria-like” symptoms are due to *Plasmodium* species infections. Several studies have shown that febrile illness commonly seen in children in most cases is not caused by malaria parasites [11, 20–22]. However, in this advent of intense education on malaria and the availability of effective artemisinin-based drugs, malaria caregivers might sometimes administer anti-malarials to children before actually presenting them at the clinic as reported elsewhere [23]. In such cases RDTs might turn out negative if the number of parasites is below the limit of detection. Therefore, the possible causes of high frequency of hospital attendance in children, if not malaria, could be attributed to other ailments such as pneumonia, influenza, typhoid and so on as observed in Gabon [24].

What then explains the high rate of RDT positivity among adult males in the male medical ward? This is difficult to explain since we have no further information on their medical history. Nevertheless, adults living in areas with stable and slightly seasonal malaria transmission tend to develop strong protective immunity which protects them from clinical malaria [19]. However, in the presence of co-infections with other pathogens such as HIV and TB, common cold or any other infectious agents, which compromise the immune defense, an asymptomatic malaria condition may develop into symptomatic malaria in adults [19, 25, 26]. Poor nutrition status in adults could also contribute to development of symptomatic malaria and this could explain the high prevalence of malaria in our adults in the male ward observed in this study [27].

Table 2

Distribution of anaemia among the 69 participants with haematological data in the various departments of the hospital.

Categories of anaemia	Casualty ward	Diabetic and surgical outpatient department	Gynaecology ward	Male medical ward	Medical outpatient department	General outpatient department	Paediatric ward	Paediatric outpatient department	Total (%)
Severe	0	0	2	3	0	0	5	2	12 (17)
Moderate	1	1	4	2	0	0	16	5	29 (42)
Mild	0	1	2	1	3	0	10	5	22 (31)
Non-anaemic	0	0	1	0	2	1	2	0	6 (8)

There were no haematology data from the female medical and psychiatric ward.

Considering the fact that anaemia closely associates with malaria in the endemic area regardless of parasitaemia levels, it was surprising to observe a lack of significant difference in haemoglobin levels between RDT positive and RDT negative individuals. There are two possible explanations for this apparent contradiction. The sample size for this analysis was unfortunately small as this study was not originally designed to test this hypothesis. In addition, there is no record of follow-up on malaria definitive tests such as microscopy or polymerase chain reactions to ascertain the real positivity or negativity of the RDT results. Such confirmatory tests are necessary because RDTs sometimes displays some level of false-positivity and false-negativity as shown in the same study area [11]. In the absence of a larger sample size and an additional definite malaria test to accompany the RDT results, no final conclusions can be reached on the relationship between RDT positivity or negativity and haemoglobin levels. This also applies to the lack of association between the age of participants and the probability of testing positive by RDT.

5. Conclusions and recommendations

Using RDT as a screening tool for malaria in the hospital environment we found the highest rate of malaria cases in the male medical ward as compared to the paediatric ward. However, the children in the paediatric OPD and paediatric ward together made up more than half of the hospital attendees for the study period while recording the lowest RDT positivity rate. There was no evidence of any association between age and the probability of an individual being RDT positive. A follow up study with larger sample sizes and follow-up malaria definitive diagnostic data from the patients will enable us to ascertain the other causes of hospital attendances, for instance among the children. Larger sample sizes will also afford the opportunity to investigate associations between age, haemoglobin levels (anaemia) and RDT positivity.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.parepi.2018.e00072>.

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