PREVALENCE, TESTING AND TREATMENT PATTERNS OF MALARIA; A HOSPITAL BASED FIVE-YEAR ANALYSES BY AGE IN KWAEBIBIREM, EASTERN GHANA

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Abstract

Objective: Malaria, caused by single-celled microorganisms of the plasmodium group, is a mosquito-borne infectious disease that affects humans and other animals. Objectives prioritizing control and elimination led to the T3 policy (i.e., *'Test, Treat and Track*') encouraging scale up of diagnostic testing, treatment and surveillance.[3] This study analyses the prevalence of malaria infection and assesses health institutional compliance with policy directives for testing before treatment of all clinically suspected malaria cases.

Methodology: A 5-year record review of malaria morbidity, 2014-2018, was completed with the DHIMS-2 web-based database using a cross sectional study design.

Results: Despite a downward trend that decreased with increasing age through adolescence, higher proportions of hospital clients aged ≤ 28 days to 17 years were subjected to confirmatory malaria tests. This remained comparatively low among adults. The highest yield of positive malaria tests was observed among patients aged 1 month to 17 years. Malaria's morbidity burden remained highest among hospital clients aged 1 month to 15 years of age while the highest proportion of hospital clients treated without prior confirmatory tests was observed among the ages of 18 to 70 years and above. Proportion of patients treated for malaria without prior confirmatory tests therefore increased with increasing patient age.

Conclusion: Isolated cases of presumptively treated malaria suggest that universal compliance with the first T of the T3 policy is yet unattained, potentially invalidating quality of the other Ts.

Recommendations: Correlates for presumptive treatment should be investigated to facilitate acceleration towards attainment of universal compliance with the T3 policy.

Key Words: *Malaria, testing, treatment, policy, diagnosis, rapid diagnostic test, microscopy*

Introduction

Malaria, caused by single-celled microorganisms of the Plasmodium group, is a mosquito-borne infectious disease that affects humans and other animals. It is typically, but not invariably, characterized by recurrent episodes that may be experienced if not properly treated, while survival of recent infection sufficiently induces a partial resistance associated with milder symptoms during subsequent infections.[1,2] Acquired partial immunity may, however, be lost over months to years without continued exposure.[1,2] Efforts towards control and elimination led to the T3 policy in 2012 i.e. *'Test, Treat and Track*' initiative urging endemic countries, donors and the global malaria community to scale up diagnostic testing, treatment and surveillance for malaria.[3]

The United Nations set the target for the attainment of universal coverages with long-lasting insecticidal nets in 2008 coupled with other essential malaria control interventions by the end of 2010.[4] Significant progress towards achievement of the target of universal coverage was made with the distribution of over 290 million nets in Africa between 2008 and 2010.[4] Control interventions have typically been scaled up with aims to cut malaria morbidity and mortality in high-transmission areas.[4] The scale-up of diagnostic testing, treatment and surveillance has comparatively not received the same degree of attention.[4] Availability of resources required to strengthen these three fundamental pillars of the existing global strategy to fight malaria is likely to be a future challenge in many resource constrained countries.[4] T3 supports malaria-endemic countries to achieve universal coverage with diagnostic testing and antimalarial treatment, as well as strengthening malaria surveillance systems.[4] Endemic countries are contextually within this policy framework to ensure that *every suspected malaria case is tested*, that every confirmed case is treated with a quality-assured antimalarial medicine, and that the disease is tracked through timely and accurate surveillance systems to guide policy and operational decisions.[4] Despite the Africa's non-universal access to diagnostic testing, availability of high quality, inexpensive RDTs has significantly expanded diagnostic testing.[4] Microscopic examination, however, remains the "gold standard" for laboratory confirmation of malaria though their reliability is subject to quality of the laboratories performing the tests.[5] Despite current ratification of the test and treat policy in an estimated 97 countries, health worker compliance remains inconsistently problematic leaving some suspected cases untested but treated with antimalarial medication.[6]

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Conflict of Interest: None Declared

Health worker compliance remains a key aspect of the sequential components that determine proportion of clinical events that are effectively treated by the formal health care sector.[6] Extant WHO guidelines emphasize a universal "test and treat" strategy for malaria mainly by use of rapid diagnostic test (RDT) in all areas.[7] Ghana, having subscribed to WHOs test, treat and track policy in 2013 (with aims to replace presumptive treatment with targeted treatment), records better compliance with the policy at community clinics (i.e. CHPS) than hospitals and health centers.[8] Poor compliance is partly attributed to poor clinician compliance with negative tests across all age groups; this is typically premised on a hypothetical concern that 'negative tests do not definitively rule out malaria'.[9] Evidence indicates that some healthcare practitioners in Ghana, (despite increased access to confirmatory diagnostic testing with RDTs in resource-constrained primary health facilities with weak infrastructure for microscopy) still treat febrile patients without testing, or without regard for negative malaria test results.[10] This study aimed to investigate the prevalence of *p. falciparum* malaria cases and assess district health institutional compliance with the WHO policy for confirmatory malaria testing before treatment for all clinically suspected cases in Kwaebibirem, Eastern Ghana.

Materials and Methods

The study was carried out at the Kade District Hospital, Eastern Ghana, through a review of institutional records on malaria morbidity for the period 2014-2018 using a cross sectional study design. Data were abstracted in accordance with the already available DHIMS-2 categorizations for the variable of age group units of the persons reporting to the hospital's Out Patients' Department (OPD). The summary age categorizations could not be disaggregated as the web-based data source does not make provision for any further break down of age groups. Information abstracted for analyses included the institutional malaria morbidity burden, age groups of patents who sought care over the same period, number of cases clinically suspect for malaria and number of cases treated for malaria with or without prior confirmatory testing. Pre-existing age groups from the DHIMS-2 dataset were analyzed across all the above listed variables to identify proportions of clinically suspected cases by age *tested and treated* and *not tested but treated*. The DHIMS-2 web-based health datasets repository comprised the key data source for the record review and subsequent analyses with the intermittent use of Microsoft excel. Permission to carry out the study at the hospital was granted by the hospital's medical superintendent; this was deemed sufficient for completion of the study as datasets used were secondary and devoid of any identifying or traceable variables.

Results

Patterns of clinical suspicion of malaria among OPD attendants with subsequent conduct of confirmatory testing for the disease, 2014-2018, varied across all the studied age categories of patients who sought health care at the hospital's OPD. Subsequent testing for malaria among clinically suspected OPD cases was observably highest among patients aged ≤ 28 days to 17 years of age. Testing, however, declined inversely with increasing patient age through to adolescents of 15-17 years who recorded the lowest testing proportions across this age category.

Clinical suspicion for malaria with subsequent confirmatory testing among patients aged 18-70 years or older over the period 2014-2018 steadily declined from 73.5%, (the highest proportion for this age category suspected and subsequently tested), to adult OPD attendants aged 35-49 years. A plateaued trend, however, further defined the testing patterns for clinically suspected malaria cases among older OPD.

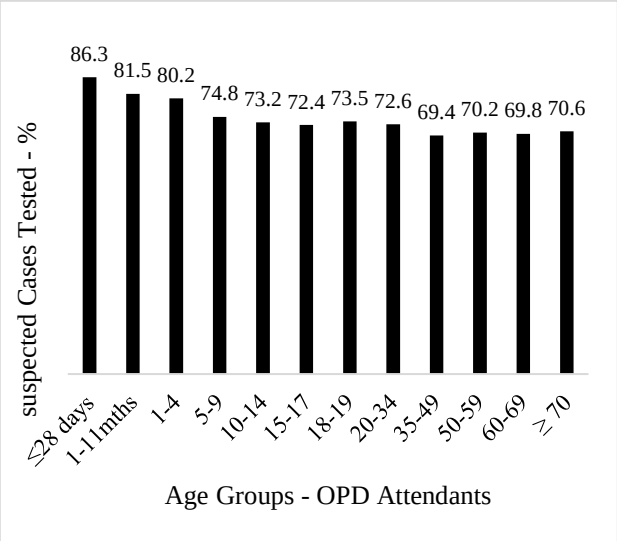

Fig. 1.0: Clinically suspected malaria cases tested for confirmation before treatment, analyzed by age, 2014-2018.

The mean proportion of clinically suspected malaria cases among OPD attendants who subsequently tested positive for malaria aged ≤ 28 days to 17 years over the period 2014-2018 showed the highest yield of malaria positive test results for patients aged 1-11 months through to adolescents aged 10-14. A gentle decline was then observed to 43.6% of the hospital's adolescent OPD patients aged 15-17 years testing positive for malaria. The mean proportions of adult OPD patients clinically suspected for malaria who subsequently tested positive over the period 2014-2018, (i.e. patients aged ≥ 18-70 years), varied insignificantly across patients of

this age category. A marginal comparatively high yield of positive malaria tests was, however, observed among OPD attendants aged 18-19 while that of the remaining older age categories plateaued through to OPD attendants aged ≥ 70 years. At least, 32904, out of the total 66421, i.e. 49.5% of all the clinically suspected cases of malaria, 2014-2018, eventually tested positive to microscopy and RDT used over the period.

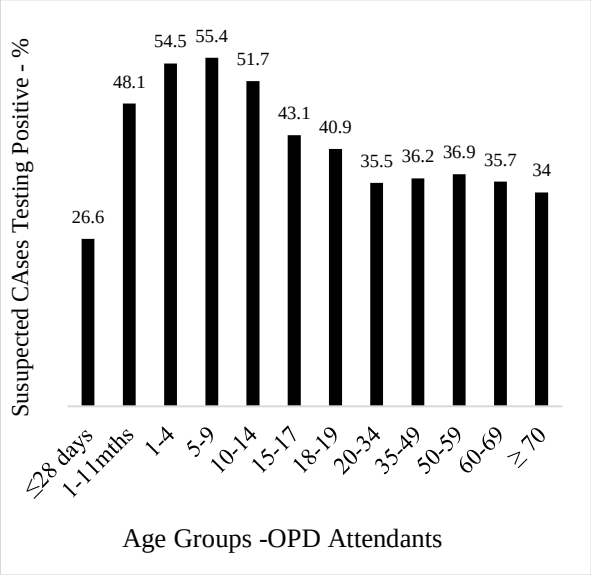

Fig. 2.0: Clinically suspected malaria cases testing positive analyzed by age, 2014-2018

Age group-specific analyses of proportions of OPD attendants who were diagnosed with confirmed malaria (by thick and thick blood film microscopy or Rapid Malaria Diagnostic Testing) among patients aged ≤ 28 days to ≥ 70 years in 2014 showed that hospital clients aged 1 month to 17 years observably recorded the highest malaria infection morbidity burden in 2014. This notably peaked among OPD attendants aged 10-14 years while a gradual decline was recorded for OPD attendants from 15 years to ≥ 70 years. The morbidity burden of confirmed malaria cases among OPD attendants in 2015 showed the highest prevalence of the confirmed malaria morbidity among OPD attendants in the age group of 5-9 years. Patients aged 10-14 years were second in this series while patients aged 1-4 years were third in this series. Occurrence of confirmed malaria among OPD attendants aged 18 years, i.e. adolescents, remained comparatively lower than what was observed for patients aged 1 month to 17 years.

The distribution of confirmed malaria's morbidity burden among OPD attendants in 2016 was similar to that of 2014 and 2015. The peak morbidity burden of confirmed malaria among age-specific OPD attendants was recorded among patients aged 5-9 years while patients aged 10-14 years were second in this series. OPD patients aged 1-4 years ranked third observably while the confirmed malaria cases among OPD patients aged 18 years or older remained comparatively low over the period observed, declining steadily with increasing age. The 2017 distribution of the morbidity burden of confirmed malaria among OPD attendants remained similar to what was previously observed 2014-2016. OPD patients aged 5-9 years recorded the highest proportionate case burden of OPD attendants with confirmed malaria while second in this series was the age category of patients aged 10-14. OPD attendants aged 1-4 years ranked third consistently with observations of the previous years. Contrary to the observed malaria morbidity trend from 2014-2016, a comparatively high malaria morbidity burden was sustained through to the age group of OPD patients aged 19 years. On account of this observed change in morbidity pattern, the prior characteristic, comparatively lower malaria morbidity burden for patients above 17 years was now observed from 19 years in 2017.

The institutional prevalence of confirmed malaria cases among OPD attendants aged 5-9 years remained highest in 2018. The 2018 malaria morbidity burden among OPD attendants aged 17-19 years remained comparatively high consistently with observations for 2017. While OPD attendants aged 10-14 years recorded the second highest age-group specific malaria morbidity, patients aged 1-4 years ranked third in this series. The trend of confirmed malaria cases among OPD attendants, analyzed to show the pattern of occurrence and distribution of malaria infection from the health facility-based perspective, 2014-2018, showed that the morbidity distribution and spread analyzed by age of OPD patients remained essentially unchanged over the five years i.e. 2014-2018. Malaria's morbidity burden remained highest among OPD attendants aged 1 month to adolescents of 17 years. The decline in the morbidity burden across the older patients with increasing age was sustained through all the years from 2014-2018.

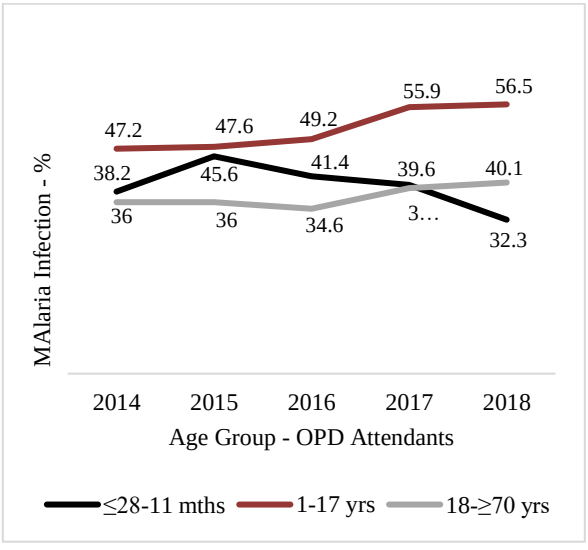

Fig 3.0: Malaria morbidity burden among OPD attendants analyzed by age, 2014-2018

Malaria cases, treated without compliance with policy directives for *confirmation before treatment* were analyzed. This showed that the tendency for treatment of clinically suspected malaria cases not subjected to any confirmatory clinical/laboratory tests (but treated presumptively) increased commensurately with increasing patient age. This trend sharply rose from patients aged 10-14 to patients aged 35-49 after which it observably plateaued through to patients aged ≥ 70 years.

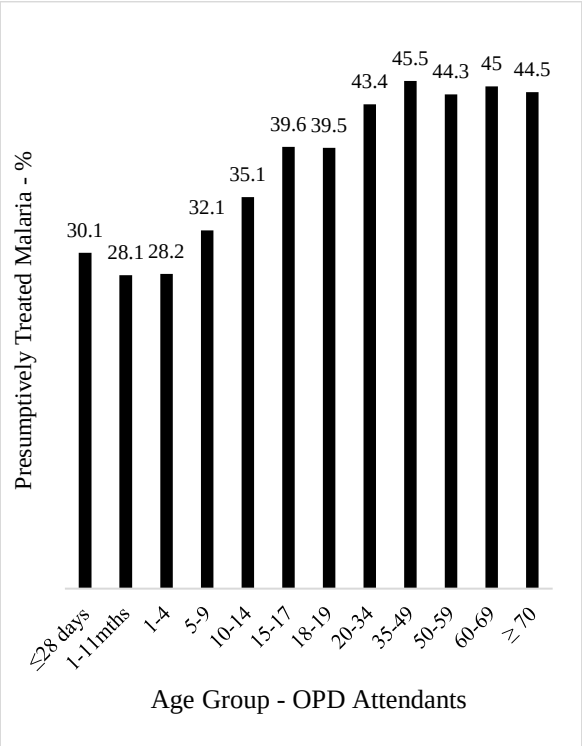

Fig. 4.0: Mean proportion of malaria cases not tested but treated for malaria by age, 2014-2018

The proportions of OPD attendants clinically suspected for malaria and subsequently tested (consistently with current malaria control policy directives) was assessed. This compared with the proportion of the same sub population that was not tested but treated (i.e. treated presumptively for malaria) yielded an inverse relationship. The proportion of OPD attendants treated for malaria without testing increased inversely with decreased confirmatory testing for clinically suspected malaria cases. An increase in proportions of OPD attendants treated without confirmatory malaria testing was observed among hospital clients aged 19 years through to ≥ 70 years. Testing of clinically suspected malaria cases was comparatively lower than was recorded for patients in the younger age categories among such patients.

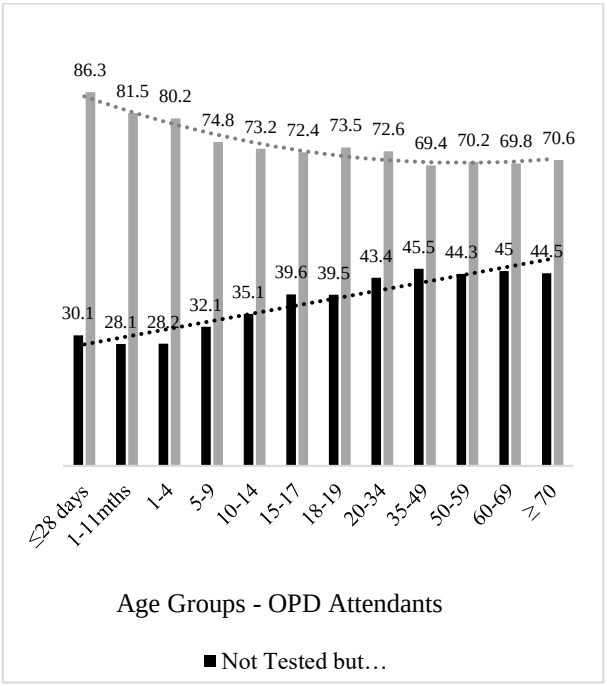

Fig. 5.0: Proportion of malaria cases not tested but treated compared with clinically suspected cases tested before treatment

DISCUSSION

Treatment for malaria, prior to ratification of policy directives recommending confirmation before treatment, was largely based on empirical or presumptive administration of antimalarial medication for all persons who reported to hospitals with conditions characterized by febrility.[8] Testing rates for confirmation of clinically suspected cases, despite notably significant increments, are yet to attain 100% in many malaria endemic areas.[4, 6, 7] Increased availability to testing with Rapid Diagnostic Tests, *RDTs*, for malaria has significantly increased access to confirmatory testing. Thick and thin blood film microscopy, however, remain a resource constrained clinical investigation with comparatively limited access.[4, 7, 8] Confirmatory testing of clinically suspected cases remained observably higher among patients from one month of age through to adolescents who recorded comparatively lower proportions of suspected cases tested. Adults, over the period, presenting with conditions clinically suspected for malaria-maintained testing trends that declined with increasing age. The WHO recommends early and accurate diagnosis of malaria infection (through the conduct of standard malaria infection confirmatory tests i.e. thick and thin blood film microscopy and RDT) to facilitate effective case management and case surveillance; this is adopted in 97 countries.[11] *High-quality* malaria diagnosis further remains universally important as misdiagnosis may affect the accuracy of data on morbidity and mortality.[11] WHO therefore recommends prompt parasitological confirmation of diagnosis either by microscopy or

malaria rapid diagnostic testing, RDT, in all patients suspected to have malaria before treatment is administered. Current evidence attributes factors (that include patient case-load, availability of skilled laboratory technicians, availability of logistics for testing etc.) to challenges opposed to attainment of 100% testing rates.[11] Universal confirmatory testing in endemic areas will significantly impact quality of management of patients with febrile illnesses. It would help identify true positive malaria cases and facilitate adequate clinical attention to non-malaria febrile illnesses.[11] Universal testing further bears cost-effective implications as it limits antimalarial treatment to positive cases while negative cases are further thoroughly assessed for other causes of fever.[11] Since 2010, testing rates have substantially increased and surveys in sub-Saharan Africa indicate an estimated 59% in 2015-2017 from 33% 2010-2012.[11]

An estimated 49.5% of all clinically suspected malaria cases, 2014-2018, eventually tested positive to microscopy and RDT used over the period. Testing rates among clinically suspected cases remained comparatively low among adult OPD attendants and showed an increase with increasing age. Malaria test positivity rate (TPR) is defined as the number of laboratory-confirmed malaria tests per 100 suspected cases examined; it comprises one of WHO's ten core indicators for malaria surveillance in the control phase.[12] It is widely used by malaria surveillance programs as one of several key indicators of temporal trends in malaria incidence.[12] TPR, increases in significance when percentage of suspected cases tested is above 90%.[12] Computation of diagnostic method-specific TPR (microscopy- and RDT-specific TPR) remained a challenge in this study on account of data challenges.[12] The indicator ,TPR, may be used to define malaria endemicity, assess temporal trends in malaria incidence and evaluate impact of malaria control interventions.[13] TPRs of <5% characterize malaria endemic areas moving towards elimination.[13] Microscopy remains the gold standard for diagnosis.[14] The accuracy of clinical diagnosis varies in accordance with the level of endemicity, malaria seasonality and age group, over-diagnosis; RDT thus remains relevant for objective diagnosis of malaria.[14] WHO recommends that parasite-based diagnosis should be used in all cases of suspected malaria with the possible exception of children in high-prevalence areas and certain situations.[14] The use of RDT is, however, recommended by WHO for areas where microscopy is not available.[14]

The peak prevalence of malaria infection 2014-2018 was notably highest among OPD attendants aged 1 month to 14 years followed by adolescents who, in turn, recorded a moderately higher morbidity burden than adults. The adult age category recorded a comparatively lower prevalence that decreased with increasing age over the period. The peak prevalence of severe *p. falciparum* malaria is typically skewed towards younger age groups as the intensity of transmission increases. Evidence of such patterns for uncomplicated malaria, however, remains limited.[15] This peak prevalence age range, aside severe malaria, has also been described for other infections against which immunity is acquired.[15] It bears control implications as, firstly, identification of the age groups with the greatest burden of clinical malaria for a given transmission setting would enable interventions to be targeted to those worst affected. Secondly, it implies that reported declines in malaria transmission intensity and future progress towards malaria elimination, will result in a shift of malaria morbidity towards older children.[15] Evidence, however, also further suggest that hospital patients with malaria parasites are more concentrated in younger children than is clinical malaria in all settings.[15] These severe cases become more concentrated in younger ages with increasing transmission intensity and less seasonality.[15] The institutional in-patient malaria-specific morbidity burden is therefore concentrated in children under-5 years of age in all settings.[15] This trend further shows a shift towards younger ages with increasing intensity of malaria transmission.[15]

Malaria-associated mortality is higher in younger children under-5 years of age than admissions with malaria among older patients, in all settings for which there are comparable data irrespective of transmission intensity.[15] Findings in Ethiopia identified migrant laborers who travel to endemic areas, children under-5 years old, and pregnant women are among high-risk groups affected by a high morbidity burden of malaria.[16] Wide evidence consistently identifies children under-5 years, pregnant women, people living with HIV/AIDS, non-immune migrants and travelers as a high risk sub populations for malaria infection.[17] Children under-5 years of age, the most vulnerable group, further accounted for an estimated 67% of all malaria deaths worldwide in 2018.[17]

Despite notably significant and established increased compliance with policy directives for the conduct of confirmatory tests before treatment, available data indicates some clinically suspected cases are still empirically treated without laboratory confirmation.[4] Testing patterns for clinically suspected OPD attendants decreased as age increased. This eventually translated into higher proportions of OPD attendants who were treated without health facility compliance with the policy for testing before initiating treatment with antimalarial medications. An inverse relationship was established between proportions of OPD attendants clinically suspected for malaria and subsequently tested (consistently with current control policy directives) and the proportion of the same population that was not tested but treated. Identification of explanatory factors that underlie a continued degree of non-compliance with policy directives recommending the conduct of confirmatory tests before treatment was beyond the scope of this study. The WHO T3 policy (for testing before treating and then tracking) is recommended for every suspected malaria case without exception.[4] While

febrility, (prior to increased access to testing facilities), in many endemic countries was typically equated with malaria, recent control efforts have significantly reduced the malaria burden even in high transmission areas in Africa.[4] Continued presumptive treatment could lead to drug wastage and under-treatment of other febrile illnesses that must be investigated further in the event of negative malaria tests.[4]

Enhancing efforts towards attainment of universal testing of all clinically suspected cases (through universal health worker compliance with malaria control protocols) would present unprecedented opportunities for improvement in the accuracy of malaria surveillance data.[4] This would help malaria control programs to specifically respond to surges.[4] The established global shift in malaria case management, observed among health workers in medium- to high -malaria transmission regions indicates a shift from a presumptive treatment approach to a 'test and treat' approach.[6] It further therefore enhances the availability of quality surveillance data.[6] In many countries that have adopted the test and treat protocol, fewer than 50% of ailments characterized by febrility are tested for malaria infection by microscopy or RDT.[6] Health worker compliance, (according to the 'systems effectiveness model), is one of a number of sequential components that collectively determine the proportion of clinical events that are effectively treated by the formal health care sector.[6] The evidence for the 'test and treat policy' has, however, been questioned as there is a risk of over-reliance on parasitological diagnosis in high transmission situations, which still exist.[7] The presence of plasmodium species neither reliably confirms malaria as the cause of fever nor excludes the possibility of other diseases in such areas when a patient has fever or other malaria symptoms.[7]

Evidence suggests that compliance with the T3 strategy in some malaria endemic areas in Ghana is better at community clinics, (i.e. CHPS compounds), than Hospitals and Health Centers.[8] Evidence also further shows that some public primary health care facilities still largely lack diagnostic facilities including microscopes.[8] In situations where testing facilities are available, personnel to cope with the high volumes of work may be inadequate.[8, 9] While facilities for thick and thin blood film microscopy may be limited, availability of RDTs, (at increasingly competitive prices and their improved quality), has substantially simplified and expanded diagnostic capacity in endemic areas.[18] Their use at peripheral facilities and shops and by trained community health workers (CHWs), to whom patients come for care, is currently commonplace.[18] A recent systematic review estimated 78% and 97% health worker compliance with testing before treatment in some endemic areas using RDTs.[18] The review further indicated that an estimated 95% of Community Health Workers, (CHWs), were likely to comply with negative RDT results compared with an estimated 75% of clinicians and nurses at higher levels of heath care service delivery.[18]

Extant literature on malaria diagnosis for improved pediatric fever management in sub-Saharan Africa, however, contrarily emphasizes the need to shift from malaria-focused '*test and treat'* strategies toward Integrated Management of Childhood Illnesses, (*IMCI*).[22] Testing, within an IMCI context, can be used to improve quality care and rational use of both antimalarial and antibiotic medicines.[22]

Conclusion

The study was carried out to investigate the prevalence, testing and treatment patterns of malaria-associated morbidity using a cross sectional record review of health facility-based data covering a period of five years. Findings showed that full compliance with the policy recommending indiscriminate confirmatory malaria testing prior to initiation of treatment is yet to attain universal compliance despite sustained high proportions of tested OPD attendants. Establishing explanatory factors for the sustained failure to attain 100% testing rates for clinically suspected malaria cases was beyond the scope of this study. The conduct of confirmatory malaria tests was higher among younger patients aged 1 month to at least 15 years who commensurately recorded a higher subsequent yield of positive malaria test results. OPD attendants aged 1 month to 15 years therefore recorded the highest yield of positive malaria tests and commensurately therefore recorded the highest malaria morbidity over the period of study. Adult OPD attendants recorded the highest proportions of hospital clients presumptively treated for malaria without the conduct of confirmatory tests which may be explained by the comparatively lower confirmatory malaria tests recorded for the older sub population. Universal coverage for the first T of the T3 policy is yet to be attained.

Recommendations

Research to establish explanatory factors that underlie differential testing patterns among younger and adult clinically suspected cases of malaria should be prioritized. This should further aim to investigate the consistently higher prevalence of malaria infection among children and adolescents despite a myriad of malaria control interventions that particularly target children and pregnant women. Individual health worker tendencies predicting differential confirmatory testing patterns among clinically suspected malaria cases should be further investigated. Identification of correlates for treatment without carrying out confirmatory malaria testing remains key. This may facilitate acceleration of progress towards attainment of universal compliance with policy directives that recommend the conduct of confirmatory testing before initiation of treatment.

Acknowledgement

I would like to acknowledge the support of the Medical Superintendent and the entire management body of Kade Government Hospital.

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