Quality Control of Malaria Rapid Diagnostic Tests in Zanzibar

Introduction

Historically, malaria has been a major health problem in areas of Sub-Saharan Africa like Zanzibar. Currently, most of the cases in Zanzibar are caused by the P. falciparum malaria parasite. According to the World Health Organization, morbidity and mortality rates of malaria has decreased substantially in recent years. The reasons include the increase of use of long lasting insecticidal nets (LLINs)/ Insecticide-treated nets (ITN), indoor residual spraying (IRS), and artemisinin-based combination therapy (ACT) [1/2]. In addition, the government has made malaria rapid diagnostic tests (mRDTs) available for people of all ages. According to data from the Zanzibar Malaria Elimination Program (ZAMEP), 300,892 mRDTs were used in Zanzibar in 2015. Overall prevalence is defined as the total number of cases divided by the total population. Many surveys have been conducted since 2006 that show the overall prevalence is under 1% in Zanzibar [3]. However there are still areas with increased prevalence on both Unguja and Pemba, as displayed in Figure 1, and increased prevalence also occurs seasonally. Sustainability of these low numbers is made possible through ZAMEP, with the goal of "Zero locally acquired malaria cases by 2017." ZAMEP policy is to test every family member if a positive case of malaria is identified, to ensure all malaria cases are detected early and treated accordingly.

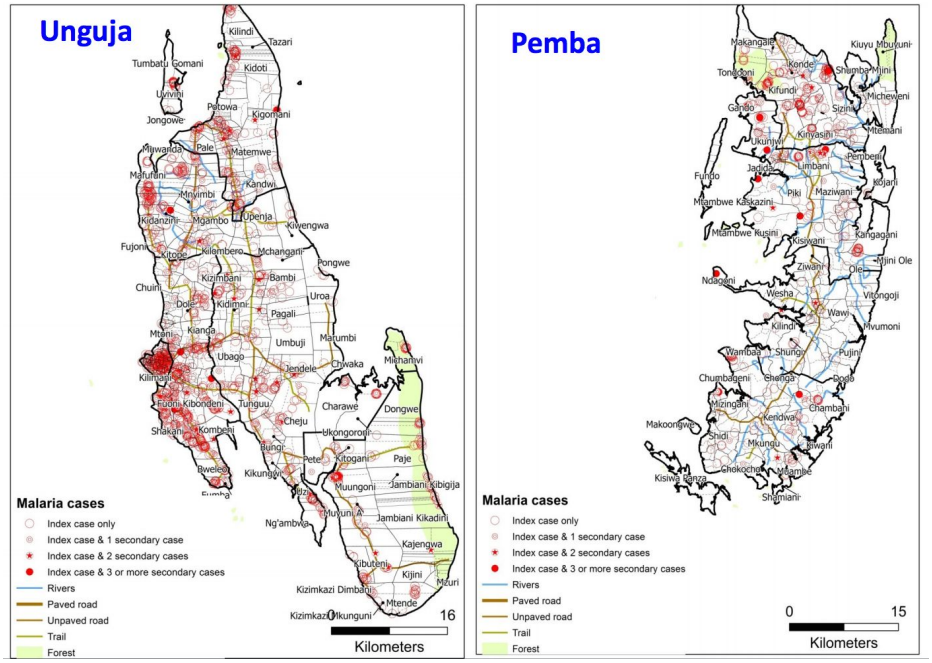

Figure 1: Malaria prevalence on Unguja and Pemba in 2013 (ZAMEP)

Methods

Three health facilities in two districts on Unguja were visited for imaging of mRDTs. Mwembeladu Maternal and Child Health (MCH) Clinic and Rahaleo Primary Health Care Unit Plus (PHCU+) were visited in the Urban District, and Fuoni PHCU+ was visited in the West District. Each facility was visited over a three day period. Imaging was mostly performed at antenatal care (ANC) clinics where women receive preventative screening due to low numbers in outpatient testing.

Six images of each mRDT were taken with a ProScope microscope attachment on an iPhone 6, both before the blood sample was taken and after the test had completed, for a total of 12 images for each test. Images were captured at the buffer well, the sample well, three points along the nitrocellulose strip that includes the control and test lines, and the conjugate pad. Data were captured on the imaging times, and a checklist was used for each mRDT as related to the WHO guidelines for mRDT testing.

Results

A total of 1,284 images were captured of 107 mRDTs at the three facilities: 22 at Rahaleo, 21 at Mwembeladu, and 64 at Fuoni. All facilities used First Response pLDH/HRP2 combination malaria kits. The majority of mRDTs were performed on pregnant adult females, with 1,212 images taken of 101 mRDTs at ANC clinics. Before and after images were also taken from five mRDTs performed on children (3 children under 5 years old) in outpatient clinics and one mRDT performed on an adult nonpregnant female in an outpatient clinic.

Additionally, 84 used mRDTs from Fuoni were imaged at the ZAMEP quarterly quality control check and eight used mRDTs performed one day earlier were imaged at Rahaleo. As these mRDTs were well past the recommended time for reading, these numbers were not included in the total count.

Discussion

The first week in Zanzibar was spent with the ZAMEP to learn about current malaria control methods as well as the procedures for quality control. The Central Medical Store outside of Stone Town was also visited to understand quantities of mRDTs coming through Zanzibar and in-country quality control checks being performed. According to CMS and the Ministry of Health, SD Bioline is the preferred brand for mRDTs, however First Response was the only brand in use in all facilities visited.

ZAMEP's efforts have thus far proved successful in reducing malaria prevalence to under 1%, and Zanzibar is currently in a pre-elimination phase [3]. It is important to note, however, that ZAMEP and the Ministry of Health lack proper death audits, and actual prevalence as well as morbidity may be higher than published reports suggest.

Where microscopy is available, blood smears are the only detection method used for malaria diagnosis. Only in cases where laboratories do not have electricity or proper supplies will mRDTs be used. Though it is good to see availability of microscopy, some facilities with higher outpatient numbers could not be included in this study. Due to limited time frames and a need for large image quantity, many of the images taken were in the ANC clinics where mRDTs are used for preventative screening.

Zanzibar currently does no quality control testing of mRDTs either at the facilities or at CMS. ZAMEP's Quality Control department performs quarterly *quality assurance* at every health facility, and focuses more on user error than device performance. A ZAMEP quality control officer examines each used mRDT from the quarter and checks for Patient ID, Date, Validity (Control Line), Incubation time labeling, color of test zone, and excessive red test zone. ZAMEP does keep data on lack of control line

which falls under quality control, however their data collection is still intended to monitor worker performance and ensure a second test was run.

Positive blood smears are sent to ZAMEP for confirmation as an additional method of quality assurance. ZAMEP is currently working with the Karolinska Institutet to train workers on polymerase chain reaction (PCR) assays in an effort to begin quality testing of mRDTs.

After imaging mRDTs at the three different facilities, user error seems to be the cause of many anomalies. This was especially the case with tests conducted at Fuoni PHCU+. Many of the mRDTs still had a red background after the recommended 20 minute read time. For these tests either too much blood was drawn or there was poor blood migration. Poor migration could be due to problems with the test itself, or user error. These errors include no buffer added or incorrect placing of the blood sample. Other common errors included not allowing the patient's finger to dry between swabbing with alcohol and pricking with the lancet and adding the incorrect amount of buffer. In addition to the excessive amount of blood placed onto the mRDT, the health worker administering each mRDT would firmly press each blood sample into the blood well, possibly affecting the absorbance of the blood into its designated placement section.

Variations in the mRDTs themselves were also noted. Before a sample is added, sample wells in mRDTs should be a purple, blue, or pink color. The First Response brand used for all images has purple colored sample wells, but discoloration of varying degrees was noted around the edges of many sample wells.

The process of drawing blood from the patient varied by health worker and facility. Standard testing procedures call for pricking of the ring finger of the non-dominant hand. In most cases this should be the left hand but the nurses almost always used the right hand for blood samples. Some health workers chose to draw blood from whichever finger was presented by the patient.

Our work here in Zanzibar was beneficial in understanding the malaria situation, mRDT usage, and the need for quality control of the devices. Though we had hoped to confirm our mRDT tests with microscopy tests, this was not possible given limiting resources and the fact facilities with microscopes did not use mRDTs. We were able to image mRDT tests before and after the tests were taken. Going forward, we look to analyze the 1,284 images taken in Zanzibar. However, many more images will be needed to conduct significant analysis using machine learning. In the future, a refresher training for health workers on proper administration of mRDTs is recommended prior to commencement of imaging to reduce the amount of anomalies in the data that result from user error.

References

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