The Tenth Ethiopian Malaria Research Network Symposium Proceeding

Hosted by:

St. Paul's Hospital Millennium Medical College

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Acknowledgement

The 10th Malaria Research Network Symposium was conducted by the collective and unreserved efforts of various organizations and individuals. The Malaria Research Network of Ethiopia would like to extend its heartfelt appreciation to those organizations and individuals who participated in organizing this symposium. First and foremost, the network acknowledges the involvement of the Federal Ministry of Health/Ethiopian Public Health Institute (FMoH/EPHI) in providing guidance and active participation of all the events of the network in general and the 10th symposium in particular and Armauer Hansen Research Institute (AHRI) for joining the network with active participation in the symposium. Our special thanks goes to St. Paul's Hospital Millennium Medical College (SPHMMC) for hosting the symposium with great hospitality, Addis Continental Institute of Public Health/President Malaria Initiative-Strengthening Malaria Monitoring and Evaluation Systems (ACIPH/PMI-SMMES) project for the well-organized coordination of the symposium, the junior and senior researchers who presented their research work and all other participants of the symposium. Finally, our sincere gratitude goes to PMI, this network in general and the current symposium in particular, wouldn't be a reality without the generous financial and technical support of PMI-Ethiopia team who have supported the network since its inception.

Acronyms

AAU	Addis Ababa University
AAU/SPH	Addis Ababa University School of Public Health
ACIPH	Addis Continental Institute of Public Health
ACT	Arteminisin Combination Therapy
AHRI	Armauer Hansen Research Institute
G6PDd	Glucose 6 Phosphate Dehydrogenase Deficiency
AOR	Adjusted Odds Ratio
CI	Confidence Interval
DDMS	Disease Data Management System
EFETP	Ethiopian Field Epidemiology Training program
EIA	Enzyme Linked Immuno Assay
ELISA	Enzyme Linked Immuno Sorbent Assay
ENACT	Enhanced Climate Service
EPHI	Ethiopian Public Health Institute
FGD	Focus Group Discussions
FMOH	Federal Ministry of Health
FTAT	Focal Test and Treat
GPS	Global Positioning System
HRBCs	Healthy Red Blood Cells
DHSS	Health and Demographic Surveillance Sites
ITN	Insecticide Treated Nets
IRS	Indoor Residual Spray
IVM	Integrated Vector Management
KII	Key Informant Interview
LAMP	Loop Mediated Isothermal Amplification
LLIN	Long Lasting Insecticide Treated Nets
MRNE	Malaria Research Network of Ethiopia
MRNS	Malaria Research Network Symposium
NMA	National Meteorology Agency
NMPCEP	National Malaria Prevention, Control and Elimination Program
OPD	Outpatient Department

OR	Odds Ratio
MACEPA	Malaria Control and Elimination Partnership in Africa
PFSA	Pharmaceutical Fund and Supply Agency
PMI	President's Malaria Initiative
RBM	Roll Back Malaria
RCD	Reactive Case Detection
RDT	Rapid Diagnostic Test
RHB	Regional health Bureau
SBCC	Social Behavioral Change Communication
SMMES	Strengthening Malaria Monitoring and Evaluation Systems of Ethiopia Program
SPHMMC	St. Paul's Hospital Millennium Medical College
USAID	United States Agency for International Aid
WHO	World Health Organization

Introduction

The 10th Ethiopian Malaria Research Network Symposium with a theme: ***"Strengthening Malaria Surveillance in the Context of Malaria Elimination"*** was held on December 19 and20, 2018 at St. Paul's Hospital Millennium Medical College – Addis Ababa, Ethiopia. The symposium was organized in collaboration with ACIPH/PMI-SMMES project, EPHI and SPHMMC. The Symposium brought together high-level experts from PMI, FMoH, EPHI, PMI-SMMES, SPHMMC, AHRI, researchers from different Universities and different implementing partners working on malaria in the country. The two-day Symposium was organized as a platform to strength communication between researchers and program persons; to maximally make use of research results in improving the program and realizing malaria control and elimination in the country.

The Symposium presented a combination of inspiring speakers delivering messages and scientific sessions reporting results using oral and poster presentations. a total of ___oral and four poster presentations of different malaria thematic areas were presented and discussed by the researchers and program persons. The symposium creates and opportunity to junior and senior researchers to present their research work to fellow researchers, program persons and donors, who were attendees of the symposium. The traditional business meeting was also conducted focusing on the future of Malaria Research Network of Ethiopia with emphasis on ensuring the sustainability of the network. There were eight sessions clustered into different malaria thematic areas like epidemiology, vector control, case management, etc. and moderated by senior malaria experts from different Universities in the country. Eighty-nine participants from different institutes (research as well as program) have actively participated in the symposium and made the discussion lively.

Session I. Opening Ceremony

The first day of the Symposium was commenced by a welcoming address from Prof. Markos Tesfaye, Research Directorate Director of SPHMMC.

Prof. Markos extended a warm welcome to symposium participants on behalf of SPHMMC and the organizing committee. He briefly explained the mandate of St. Paul's Hospital Millennium Medical College and the value of the contribution of the college in research activities and overall training of health professionals. He stressed that most of the trainees will be deployed to areas where malaria is common and also take administrative positions in various areas which put them in a position where they can make decisions in malaria control and elimination. Prof. Markos added that such collaborative symposium is great opportunity to collaborate with researchers within and out of the country to inform malaria research results with program people. Finally, he thanked Addis Continental Institute of Public Health, Ethiopian Pubic Health Institute, Federal Ministry of Health and all who took part in organizing this Symposium. He also thanked PMI for providing financial support in organizing the symposium.

Next to the welcoming speech, Dr. Matthew Murphy-PMI Ethiopia, CDC-resident advisor delivered a keynote address representing the PMI-Ethiopia team. Dr. Murphy noted that PMI's collaborative effort is to strengthen malaria prevention, control and elimination missions and related activities of Ethiopian FMoH. Recommending development and sustainability of the network, he applauded presence of the network in Ethiopia, as it will facilitate opportunities for creating dialogue forum among researchers, policy makers, front line managers and practitioners. He also noted that this approach will help to communicate key messages and stressed on the

importance of making appropriate linkages and cooperating for the achievement of common goals. Clearly illustrating the need for an integrated approach to the program, Dr. Murphy further explained that it really takes collaborative effort of private and public communities to realize the nationally set malaria related goals. Appreciating the determination in organizing this symposium and participation of researchers in presenting their research works, he prompted that FMoH, PMI and all other stakeholders are looking for the scientific research results to make evidence based decision in strengthening the program. He concluded his speech by wishing fruitful discussions.

Professor Yemane Berhane, Director of ACIPH, has delivered keynote address representing PMI-SMMES. Professor Yemane warmly welcomed the symposium participants and thanked SPHMMC for hosting this 10th MRN symposium. Professor Yemane mentioned that a record of 67 different papers were received for this symposium, which he believe is an evidnce to show how much malaria related research is increasing in the country. He also appreciated the quality and diversity of malaria researches carried out on malaria surveillance, outbreak management, magnitude of malaria, testing and treatment strategies. He also praised the participation of diverse group of researchers from different research institutes and public Universities, including the third generation Universities. He noted that Ethiopia is fortunate to have PMI support in fighting against malaria in general and this network in particular in her effort of strengthening malaria program with better and stronger evidences. Professor Yemane added the importance of promoting regional and international collaboration and consideration of expanding the mandate to other vector borne diseases so that the programs may use similar strategies to benefit from different research works in specific areas. As there is participation of diverse expertise, using this platform, he suggested research capacity building for the young researchers, joint grant writing and research works so that the next generation of malaria research works be more comprehensive and deeper. Finally,

Professor Yemane thanked the event organizers: ACIPH, SPHMMC, EPHI and FMoH. His special thanks goes to PMI for making the symposium possible through their strong technical and financial support.

Next to that, Dr. Adugna Woyesa from EPHI delivered a keynote address representing EPHI. Dr. Adugna started by stressing the major ultimate goal of the MRNE, which is enhancing knowledge sharing and networking of younger and senior malaria researchers. He strongly supported Professor Yemane's suggestion on the importance of research capacity building for the younger researchers. Dr Adugna noted that EPHI is contributing a lot in malaria research as a research wing of FMoH, which according to Dr. Adugna is intensifying its effort in eliminating malaria from the country by creating strong collaboration among all malaria stakeholders. He stressed that malaria is a focal infection for which we have to generate focal evidence to inform decision makers. Dr. Adugna concluded his key note address by appreciating SPHMMC in hosting this symposium and thanking the organizers and reiterating the importance of strengthening such platforms to inform policy makers.

The final keynote address was delivered by Mr. Mebrahtom Haile, NMCEP team leader, make the opening speech Mr. Mebrahtom welcomed the symposium participants and started his opening speech by praising the achievements made so far in fight against malaria in the country and by reminding the audience that there is a lot more to go as malaria remains to be one of the public health problems in the country. He also stressed that the government, motivated by the achievements so far, has intensified antimalarial interventions in recent years aiming at nationwide malaria elimination. Among the challenges faced in achieving this holy goal, the two most important ones according Mr. Mebrahtom were: insecticide resistance and the on-off instability issues seen in the country. Recognizing the efforts made in fight against malaria by all

stakeholders, he called for continued technical as well as financial support from all stakeholders and assure the commitment of the FMoH to work with all. He concluded his keynote address by thanking the organizers of the symposium for their unreserved effort to make this symposium happen and SPHMMC for hosting the symposium and wish all a successful deliberations,

Opening speech was delivered by Dr. Wondwossen, representing the host SPHMMC, delegated by the school provost. Dr. Wondeson began by thanking the organizers for the invitation and briefely introduced SPHMMC, which is the youngest and the first medical college that initiated Integrated Modular Curriculum for the first time in the country. He added that currently the college runs more than 15 post graduate programs where students are required to conduct researches, hence, the relevance of organizing such symposium in the campus which will be a good opportunity for the students to learn from this platform. Wishing very fruitful and enjoyable stay for the participants, he declared that the symposium is officially opened.

Session II: Malaria Surveillance in the context of Malaria Elimination.

Prof. Ahmed Ali from Addis Ababa University moderated the session. In this session, three presentations related to the theme: *Malaria surveillance in the context of Malaria Elimination* were made.

Presentations

- ***Updates on activities of the sentinel surveillance sites and the national surveillance system*** *by Dr. Adugna Woyesa (Ethiopian Public Health Institute) and Mr. Dereje Dillu (Federal Ministry of Health).*

The presentation was made by Dr. Adugna Woyesa; from Ethiopian Public Health Institute and Chairman of Malaria Research Network. He presented an update the activities of the sentinel surveillance sites and the national surveillance system. He described that the general purpose of sentinel surveillance in Ethiopia is to shade a light on generating local information on malaria burden, at the same time; to strengthen the local capacity to help evidence based decision with the context of malaria elimination. Dr. Adugna explained that 25 sentinel surveillance sites selected from various eco-epidemiological settings from eight regional states and City Administrations. He then provided an update of the sentinel surveillance for the participants. Finally, calling for potential collaboration between National Malaria Control and Elimination Program and other Institutions with research capacity, he concluded his presentation.

The full abstract is contained in Annex III**.**

- ***Strengthening malaria surveillance in the context of Malaria Elimintaion*** *by Prof. Joe Keating, Associate Dean of Tulane University, SPHTM*

Prof. Joe Keating, Associate Dean of Tulane University, SPHTM, made the second presentation of the second session. Prof. Joe started his presentation by briefing the cornerstone considerations for effective and sustained malaria elimination including the important issues to consider during elimination. He also highlighted about operational aspects of malaria elimination noting that surveillance can be done at different levels of the health care system with different detection systems and sampling strategies. His presentation also included malaria surveillance for elimination in theory and in practice, how to strengthen malaria surveillance and the key activities

of elimination surveillance system. He then briefed some case studies conducted in different countries related to the process of malaria elimination and identifying imported cases and China's 1-3-7 surveillance system as lessons for the country. Finally, he presented about the ideal information surveillance system needed and ended his presentation.

The full abstract is contained in Annex III**.**

- ***Update on Vector Surveillance and Insecticide Resistance Monitoring Activities in Ethiopia*** *by Delenasaw Yewhalaw, Director, Tropical and Infectious Diseases Research Center, Jimma University*

Prof. Delenasaw Yewhalaw presented the third and final presentation of the session on vector surveillance and insecticide resistance (IR) monitoring activities conducted in Ethiopia. Highlighting about different vector borne diseases in Ethiopia, he noted that malaria historically accounts for most of the cases and deaths from vector borne diseases in the country. He then briefed about the current national malaria context and goal of the NMCEP. Prof. Delenasaw also prompted about vectors of malaria in Ethiopia, including a surprise finding related to emergence of suspected new vector called *Anopheles coustani.* He then presented updates of malaria vector surveillance in different parts of the country including IR monitoring activities. He summarized his presentation by discussing IR mechanisms and the toxicity evaluation of novel insecticide candidates against mosquito populations in the country. Finally, he informed the challenges of vector surveillance and IRMM in Ethiopia.

The full abstract is contained in Annex III**.**

Session Discussions

There was concern over the resting and biting practices of *Anopheles gambie* in general and intensity of the evidences related to outdoor biting style of this species. Professor Delenasaw noted that, in Ethiopia, there are two-member species of *Anopheles gambie*: *Anopheles arabiensis* and *Anopheles pharoensis*. He then briefed that there are only few reports in the country that indicate *Anopheles arabiensis* are more endophilic than exophilic but it is difficult to tell that these species are both endophilic and endophagic with this very limited evidences. He added that neither enough surveillance nor sufficient studies are conducted to differentiate this. He noted that depending on few observations they had in some of the surveillance sites, there seems that they the resting and biting practice of the mosquitoes is becoming more outdoor than indoor and also that there is a change in resting and biting practice of Anopheles mosquitoes.

Prof. Delenasaw was also asked: What is your proof to say *Anopheles stephensi* is an introduced vector? He responded that there are reports indicating that this vector has been a malaria vector typically in the Middle East, and recently found in Djibouti. He said that he questioned *Anopheles stephensi* is an introduced vector depending on recent study conducted in East Ethiopia, which for the first time, confirmed distribution of *Anopheles stephensi* in the country. He added that the researchers said that it has been introduced from the Middle East and Djibouti but there is no solid information to say that this vector is transmitting malaria. He reminded all should take this as an assignment.

Participants expressed also their worries whether the selected 25 sentinel surveillance sites are enough and asked what the Ministry of Health is thinking in this regard. Admitting that these 25 sites are might not be enough to generate adequate information on malaria burden of the country, Mr. Dereje, from Ethiopian Ministry of Health, noted that this would be the start and that there are

reflections the sites would be expanded. He noted that collaboration between local NMCEP and Institutions is needed in mounting the sites as the activities are resource intensive.

Participants also asked whether the Ethiopian Malaria Control program and malaria community have feasibility study for the 1-3-7 surveillance, Mr. Dereje responded that they don't have any and pointed out that some African countries like Zimbabwe are using this 1-3-7 surveillance. He then emphasized that, relatively, Ethiopian Ministry of Health has better opportunity (Health Extension Program) to implement this system. He assured the MOH will only expand once it pilots and see the results depending on the actual situation of the country.

Session III. Malaria Epidemiology

Dr. Elias Senbeto and Dr. Endalamaw Gadisa moderated this session. A total of 04 abstracts focusing on Malaria Epidemiology were presented. The presented papers were: ***Malaria Surveillance System Evaluation result of Benchi Maji Zone, Southern Ethiopia, 2018*** *by Biniam Dagito****, Malaria Outbreak Investigation in Ganta-Afeshum District, Tigray, Ethiopia, 2016*** *by Mesfin Wubishet,* ***Malaria Prevalence and Associated Factors among pregnant Mothers in***

Sherkole District *by Girma Bekele and* ***A 17 year trend analysis of Malaria at Adi Arkay District*** *by Habte Tesfa.*

Session Discussions

The session was followed by a lively discussion. The first presenter was asked: Given the results from this study showing the malaria surveillance system evaluation of Benchi maji zone, was your surveillance system evaluation based on PHEM or other data source? At the same time coming to the credibility of the data quality, how do you get it? Biniam responded that he used PHEM data, emphasizing that majority of the HEWs usually report surveillance using phone. Regarding to credibility of the data, admitting possibility of quality issues, he said that only recorded PHEM data were used for evaluation. Biniam was also asked why he preferred his study period from October to March and responded that he selected the study period simply because he conducted the evaluation in April after he had been tracing for the range of six months; which means October to March. He explained that the reason is to get to get the previous six-month data.

The next questions were forwarded for Mesfin Wubshet. He was asked, at the time, what makes the year particular for the occurrence of the outbreak in Ganta Fashom district? Mesfin appreciated the question and noted that he was interested to know the reason whether the surveillance system was weak or anything else. He insisted such reasons were made him to study ad that he founded the reasons as the climatic changes, which resulted in high rain, fall at the time. He mentioned that this again was the reason for the appearance of stagnant water, which made comfortable situation for the breading of mosquitoes. Mesfin was also asked: Why *Plasmodium vivax* was high during the outbreak? Mentioning that *P. vivax* was dominant during the outbreak in the study area, apart from this, he noted that he did not know the reason behind. He said that he got the data from

registration books and that the data were checked for consistency and completeness. Asked whether he had tried to identify the time when IRS was implemented in that specific area because absence of IRS implementation previously might be the reason for the outbreak, he responded that he did not consider that. Appreciating the comment, he said absence of IRS implementation might even be the reason for the outbreak. Mesfin was also asked: Do you think convenient sampling technique generalizes your result as you have both cases and controls? Mentioning that cases were randomly taken from Bizet HC, he responded he used the convenient sampling techniques only for controls. One of the audience then said he knows most of the kebeles in Ganta Fashom district are above 2200m above sea level. For the reason that he asked the researcher why the outbreak happened there. He also added whether the researcher included Adigrat in his study, and used matching. Mesfin replied that he did not use matching; which he accepted as a comment andn also that he did not include Adigrat in his study mentioning that Adigrat is town Administration. Memorizing that previously there was malaria outbreak in some parts of Tigray region especially in Aferom district, he said what makes Ganta fashom district unique was that there was no malaria outbreak previously as it is highland.

The third presenter, Girma Bekele, was asked if he can tell more about the tool he used in evaluating utilization of bed net, because bed net utilization was high but there is high malaria prevalence on the study area. Girma admitted that this is one of the limitation of Cross sectional study. He then mentioned that the utilization of bed net was assessed during the study period and that the result of the incidence may be associated with the life style of the community; mentioning that most of the time the community travel and stay outside of the study area. He added that they might have been infected by the parasite and come back during the incubation period and this can

be another reason why bed net utilization and malaria prevalence did not reflect the expected association.

The other questions forwarded for the fourth presenter were: In 17 years' analysis you was showed that older pregnant ones develop immunity which protect them from Malaria infection. How do you compare this for example with under 15s? Have you read any literatures that supported this? Habtie Tesfa responded that he has referred different literatures from Ethiopia and sub Saharan African countries especially in high malaria transmission areas. He added that the literatures support that as age increase; people will get higher exposure to be bitten with malaria vectors, which helps them to develop partial immunity. Asked why he considered multi stage sampling while for a single district, he responded that the district has 20 kebeles out of which he had to select 8. He added that he had to select households to recruit pregnant mothers.

Session IV. Malaria Prevention and Control Interventions

This session was moderated by Dr. Mattew Murphy and Mr. Mebrathom Haile. A total of 4 presentations were made. The abstracts presented were: ***The Role of Mathematics in fighting against Malaria*** *by Woldegebriel Assefa,* ***Travel to Farms in the lowlands and inadequate information on malaria significantly predict malaria in villages around lake Tana*** *by Asmamaw Malede,* ***Serological Evidenece for a decline in Malaria Transmission following major scale up***

of control eeforts *by Migbaru Keffale* ***and Use of ITN and care seeking behavior for febrile children by care takers*** *by Zewdie Berhanu.*

Session Discussions

Following the presentations, the floor was made open for discussions. The first presenter, Woldegebriel Assefa, was asked: Is the mathematical model you used applicable for transmission of other diseases like Tuberculosis? Before saying either applicable or not, Woldegebriel tried to make clear about and types of transmissions. The first one is epidemiological model, which sees transmission of diseases between individuals or groups of individuals. The second one is immunological or microscopic modeling that sees what will happen after parasites inter in an individual. Then, illustrating the difference between the life cycles of malaria parasite and Tuberculosis in human body, he said that the model might not be applicable in other infectious diseases like Tuberculosis because, the dynamics of life cycles of each are different. Asked whether the mathematical Modeling was applied for with *P.vivax,* he replied the mathematical model is applied only for falciparum. For this, he reasoned out that the Numerical values of the average number of Merozoites released from bursting cells, it is not the same for *P. falciparum* and *P. vivax*. He also added that the maturation time of gametocytes is different for *P. falciparum* and *P. vivax*. Because of this, he replied the mathematical model was applied only for *P.falciparum*. Woldegebriel was asked: Because the rate of infection of *P. falciparum* is not mostly dependent only on the density of parasite, could it not be challenging the model? He responded that somehow, the transmission is related with the rate of infection. He admitted that this is one of the challenges in using mathematical model. He then added assuming one individual who have the parasite inside his body, the rate of infection/transmission takes in to account in the dynamics of parasite inside the individual, which is probably the rate of gametocytes in the blood. He further

explained that most of the time when we talk about mathematical modeling what comes to people mind is an epidemiological modeling where the disease is transmitted from one person or group to another. But in the case of mathematical model it sees how the parasite is developing and the possible ways in reducing the growth of the parasite inside human body. He also noted that mathematical modeling does approximation; not exact representation that gives many insights for prediction. Asked how far he went practically on the ground and what kind of effort he did to create collaboration, he responded that he has some collaborations, of these, one is with his co-supervisor during his PhD studies in one of USA Universities. He pointed out that the problem is since they do on human host, it is difficult for them to get data; for example, the acquired/adaptive immunity after infection in endemic areas. Another problem in acquired/adaptive immunity in terms of malaria is it can disappear after certain period. For example, one thing they want to estimate the rate of adaptive immune system in terms of reducing the effectiveness of the parasite; but the problem is there was no data in under 5 for example. He said that this shows that if there was data, it would be possible to see how adaptive immunity works against malaria parasite. Woldegebriel was asked if he had ever used laboratory and he replied that mostly, the model is dependent on the existing biological literatures and he tried to use the recent biological factors. On the other side, he added what he understood at the end of his PhD was he had to go back and remodify about dissertation question: about the ability of adaptive immune system inhibiting fertilization inside mosquitoes.

Lastly, he was asked: What new parameters are there in your model? In his response, he mentioned some parameters in mathematical model like proportion of merozoites developed to gametocytes. He added the role of the immune system to affect the load of parasite inside human host and that

when adaptive immune system is developed in human body; it either inhibits the development of merozoites inside the cell or decrease the contact rate between the cell and merozoits.

The next questions were forwarded to Asmamaw Malede. He was asked: How do you define locally acquired and imported malaria? Asmamaw demarcated locally acquired malaria as indigenous one, which is transmitted by local malaria vector. He then defined introduced Malaria as a malaria case that is transmitted by malaria vector from imported case. In case of imported malaria, it might be associated with travel history that is outside of the study area he said.

The third presenter, Migbaru Keffale was asked what are the factors that shows progressive transmissions in *P.falciparum*? Migbaru replied different reasons are elaborated by different scholars and that the biological differences between the two parasites as *P. vivax* prefers reticulocytes specifically CD7T1 positive reticulocytes. If so, reticulocytes will be deformed and detected by immune system as a foreign and cleared through spleen while the others may be sequestered in bone marrow. He added, because of this, density of parasite might be reduced inside individuals so as it might be hardly detected by standard microscope. He was also asked how blood sample collected and responded the blood sample was collected for Blood Film and DBS (Dried Blood Sample) preparations.

Session V. Malaria Entomology

This session was about malaria entomology. In this session, four abstracts focusing on the entomology were presented and Dr. Meshesha Balkew moderated the session

The title of the paper presented were: ***Exploring the impact of house screening intervention on entomological incidence of mMalaria*** *by Solomon Kinde,* ***Impact of wall surface types and spray application quality on eeficay of Propoxur*** *by Zerihun Desalgn,* ***Species Composition, abundance and distribution of Anopheles mosquito in Jibatehnun district*** *by Getnet Atnafu* ***and***

Integrated Vector management implementation for malaria control in Tolay *by Abebe Asale.* The summary of the discussion points was as follow.

Session Discussions

During the discussion, questions and comments were raised for each presenter. The first question was forwarded to Zerihun Desalegn. He was asked his objection for taking only 30 households as sample size for spray; and whether the sample size was adequate. Zerihun explained that the sample size is adequate and was determined purposefully mentioning the difficulty in entomology to use larger sample size. For example, if we take 100 households it is difficult to read that much mosquitos for all those 100 households. So, the sample was taken purposefully because the other studies also used not more than that like in Tanzania, Cameron and somewhere.

The next question forwarded to Zerihun was: You categorized or classified spraying walls as smooth, plane and painting. Your result shown us good with painting surface, did you consider the type of paint? What type of painting is effective? He was also commented on the importance of clearly operationalizing type of spray rather than say standard or routine spray. Related to the point raised about the type of wall paint; he replied he hasn't assessed its consistency and finally, he took the comments on operational definition of standard and routine spray.

Next to Zerihun, questions were forwarded to the second presenter, Abebe Asele. Participants raised their concerns related to the source of data for case reports, Abebe explained that the source of data for case repot was collected from health facilities including health posts and health center. Abebe was also asked if he think the country need to control tools like Net and IRS now for malaria elimination in Ethiopia and explained that to eliminate malaria in Ethiopia we need other control tools like net and IRS because we mostly really on these tools; indicating that both of them are for

indoor mosquitos. Mentioning that mosquitos are changing their behaviors in early and outdoor biting which means before they get inside the net, he urged earnestness of coming with new tools that can target residual transmission.

Session VI: Malaria Case Management I.

In this session three papers were presented focusing on malaria case management. Dr. Kebede Etana from FMoH and Dr. Maude Dinkiye moderated this session. Titles of the papers and their presenters were: **Therapeutic efficacy choloroquine for the treatment of *P. vivax* in Gurage: A one-arm prospective study** by Teha Shumbej, **Antimalarial treatment outcomes in Ethiopia-Systematic review and meta-analysis** by Eyob Alemayehu, and **Low and heterogeneous prevalence of G6PD deficiency in different settings of Ethiopia: A cross sectional survey** by Getasew Shitaye. The summary of the discussion points was as follows.

Session Discussions

During the discussion questions and comments were raised for each presenter. The first question was forwarded to Getasew Shitaye. He was asked if he is assuming that the sample size is representative and how he calculated the sample size for the study. Getasaw explained the he considered to calculate the sample size by using a prevalence of 7.5 that is phenotypically reported in Gambela region. He added that they screened around 350 the minimal sample and 400 individuals in the same region, but for the rest, they didn't consider the 7.5 prevalence. Asked how they did RDT validation for their result, he said there are some limitations because it might be

prone to subjectivity for interpretation and it may cause false positive and false negative results but it is good to have information about this sever deficiency. He also recommended that it may be good to use other screening test.

Next, Eyob Alemayehu was asked: You said that drug resistance emergency is inevitable. Is there any study that shows anti malaria drug resistance? Eyob replied that there are reports in South East Asia and few reports in Africa, which will make our country prone to acquire the resistance from other area. My suggestion is that we have only limited options in the current treatment guideline. What we have is the Arithimetrin based regimens and chloroquine and if these drugs fail, we do not have another alternative. Therefore, it is good to have multiple treatment options. Also asked how he defined heterogeneity in sample size, he said that he mean that the sample size is highly variable; from 69-400. Therefore, there is variability on treatment outcome rate and efficacy rate he said. Eyob was also asked why he didn't include inclusion criteria in his presentation and how he avoids bias, he replied these things are considered in the main paper and that starting from the title selection two individuals independently assessed for the eligibility and quality assessment is also done independently.

Teha Shumbej was also asked why he said the study is conducted in Gurage zone while only three health centers are selected from three different districts. He then replied, during design, just they reviewed zonal health reports reported in previous years of the study period and purposely selected those health centers having a high report of *Plasmodium vivax*. Asked what he mean by mean parasitic density of 2270 per micro liter; which he mentioned in his results, he replied for *Plasmodium vivax* study the individuals having plasmodium mono infection were considered eligible when the asexual parasitic count is greater than 250 per micro letter. However, for

Plasmodium falciparum the number was large and it should be exceeding greater than 10,000 because parasitemia is higher in case of *Plasmodium falciparum*.

Session VII: Malaria Case Management II.

The AHRI team was presenters of the research findings in this session except one which was from ALIPB. The session mainly focused on antimalarial activities. Dr. Abebe, the Director General of AHRI took the floor and chaired the session. In his talk he has shared to the participants about the experiences he has abroad and stressed that a simple presentation can trigger something big, so don't hesitate to present about the researches being done in Ethiopia.

Three papers were presented here. The first presentation was done by Lemu Golosa ***Ultrasensitive rapid tests detected six-fold more asymptomatic malaria reservoirs than microscopy***. His main conclusions include; uRDT does better than traditional RDTs in detecting asymptomatic malaria, Traditional RDTs and microscopy vastly underestimate the true infectious reservoir. Finally, He has recommended that further studies are required to identify the optimal diagnostic test for interrupting malaria transmission in elimination studies. The Second presenter was Fitsum with a title of the ***relative contribution of symptomatic and asymptomatic P.Vivax and P.falciparum infections to the infectious reservoir in Ethiopia.*** The conclusions from the finding included, asymptomatic infections are highly prevalent and form an important source of mosquito infections in Ethiopia, Early identification and treatment of asymptomatic infections might accelerate elimination efforts, the relative contributions of populations may differ between times during the season, and settings (temporal and spatial variation) so good to consider these situations. Finally, he recommended for other studies to reach in to final conclusion. In the meantime, Dr Abebe, the chair person, summarized the two presentations by saying that, both of the presentation directly

focuses on the malaria elimination goal that our country Ethiopia is working. In addition to this he has also passed a message that research is collaboration, so everybody should focus on collaboration rather than working alone. The third presenter, was Elfagede and his title of presentation was ***Prevalence of Pfcrt and Pfmdr1 alleles among asymptomatic Plasmodium falciparum malaria carrier study participants in different transmission settings in Ethiopia.*** The results include, Pfcrt-76T distribution was varied significantly across sites, increase in the Pfmdr1-86N haplotypes and a decline of the Pfmdr1-86Y in the study sites. The recommendations emanated from this finding includes the need for country wide assessment of drug resistance markers and other Pfmdr1 codons. The last presentation of the session was presented by Endalemaw and his title of presentation was Substantial ***household level clustering and genetic readiness of sub-patent P.falciparum and P.vivax infections in a low endemic setting in Ethiopia.*** The conclusions from the presentation included that, Clustering was detected in index & RDT+ households, Infected individuals located around RCD cases had more complex & diverse infections than control cases, Genetically related infections were identified within households & declines with space and time, Within household & fine-scale focal transmission was identified, Parasite genotyping identified hot spot of focal transmission beyond the household that was not detected through the case clustering.

Discussion Session

During the discussion session, several questions were raised by the symposium participants. The first the question was from Prof Ahmed Ali, it was a kind of comment and advise, he said that starting from the day one of the symposium I am glad that we have seen many presentations on malaria elimination and these findings can directly feed the FMoH/NMCP. He added that, most of

these researches are particularly done to get PhD hence the need for continuity has to be our main concern. The next chance was given to Prof Delnesaw. He started by congratulating the presenters for their world class research they presented for the audience. One of his question goes to Lemu, did you use the same blood sample as well as sample collection system to assess the level of detection of all these diagnostic tools. The other question from the participants was what was the competence of lab professionals as well as what type of microscopy did you use. The other question was how did you classify the area as low endemic area.

The presenters responded accordingly to the questions raised by the participants; regarding the skills of Microscopists they have deployed to compare the results of different malaria diagnostic tools, they said that they have used highly proficient and WHO certified. The question regarding the stratification of levels of endemicity was address by Mr Dereje (NMCP) as, the stratification was done in to four strata based on WHO criteria. When the district has API of Zero, we call it low stratum or malaria free. If the API is between 1-5, we call it low stratum. The moderate one is API from 5-100 and the high strata is when the API is greater than 100. The remaining questions were entertained accordingly.

Finally, before the end of the session the chair person has summarized the major points. He has obliged him self as well as the presenters to sustain and further strengthen the researches to be done on malaria program. In his message he has emphasized that, we all should not be driven by grant rather we should be guided by research agenda. Regarding the competence level of microscopists as it is an alarming sign, giving refresher course as well as working on other things should be also done by all partners in line with ministry of health.

Session VIII: Business Meeting

The activities done so far and the way forward on Malaria Research Network of Ethiopia.

This was the last session of the symposium and focused on discussion regarding the activities carried out so far as well as the future directions of the network. The session was moderated by chair of the network (Dr Adugna from EPHI) and the secretariat (Dr Ayele from ACIPH/PMI-SMMES Project).

Dr Ayele started by making note on the wide participation of all concerned institution in this 10th MRN. ACIPH/PMI-SMMES project is PMI funded 5 years project and has been responsible to organize this annual symposium and support MRNE since the 4th symposium which was held in Mekelle. He stressed that the main purpose of the network and the symposia organized is to bring together the researchers with the program people and hence use evidence generated by the research for decision making and program improvement

Dr Adugna took the floor and highlights the network achievements, the overall situation of the 10th MRN as well as the proposed way forward. Accordingly, he talked about the progressive increase in the number of attendants and stated that the approximate number of attendees of the current symposium is close to 100. More than 60 abstracts submitted for selection, which is a record number for the symposium organized by the network. Dr. Adugna has emphasized the need to engage different institutes in strengthening the network and brought the suggestion of the organizers to establish different sub-committees, which will contribute in strengthening the network. Accordingly, three sub-committees were suggested and brought to participants for discussion. The suggested sub-committees were: Scientific and grant writing, membership and recognition and documentation and communication. According to Dr. Ayele, the secretary of the network, the need for the sub-committees is for the network to go beyond organizing these symposia, which is what the network be able to achieve so far, as indicated in the ToR and by-

laws of the network. He briefly described the role and responsibility of each sub-committee and the floor is made open for discussion by the participants.

During the discussion session various points have been raised by the symposium participants.

Prof Delenasaw (from Jimma University) has agreed on the establishment of sub-committees. He said thatsuggested to broaden the scope of the scientific committee to include thematizing the research areas. Prof. Delenasaw also suggested the initiation of activities, like production of bulletin, establishment of websites and having the network logo, that introduce the network to the wider malaria community, He also suggested to discuss the issue of membership, whether it is institution based or individual based. He also suggested the recognition team to work hard in recognizing contributors. He then expressed his strong desire to contribute in strengthening the network and willingness to be assigned in any of the sub-committees representing Jimma University.

The representative from FMoH/NMCEP, Mr Dereje has reminded the need to create sense of ownership by working together during article selection. In addition to this he has also mentioned the need to share experience from other strong program networks like tuberculosis. In addition, he suggested the ultimate goal of this network be thoroughly discussed and the outputs must be synthesized and used for policy briefing. The other point that Mr. Dereje raised is the issue of creating and regularly updating database, which shows the work done by the network.

Different participants has echoed the idea of recognizing individuals and/or institutes that contribute a lot to malaria prevention, control and elimination in the country at least by creating the bibliography of the contributors.

Dr Abebe (AHRI Director General) has recognized the organization of the symposium annually without interruption as a great success. He also shared the positive experience of the TB TRAC in

advising the ministry on topics related to tuberculosis. He stressed the need to provide policy brief to the beneficiary on regular basis as deemed necessary. Regarding the establishment of sub-committee, he expressed his agreement in establishing the sub-committees but suggested two, Scientific and grant writing and membership and recognition sub-committees, than three. He emphasized the deed for strong communication among the malaria community, which will help minimize duplication of effort and use expertise from different institutes. Finally, he indicated his institute (AHRI) will be happy to be engaged in strengthening the network activity by being member of the scientific and grant writing sub-committee member. Dr. Abebe's ideas and suggestion was echoed by Dr. Endalemaw (From AHRI).

Prof Ahmed (from AAU SPH) has suggested to add one more sub-committee in addition the two sub-committees suggested by Dr. Abebe and named the suggested sub-committee, ***documentation and communication*** which will make the collaboration transparent, ensure the sustainability of the network and finally will facilitate the emanation of policy briefing from the database.

After a thorough discussion, it was decided that three sub-committees be established and membership of the sub-committes should be institution based, which will ensure the sustainability of the network. The sub-committes and the suggested member institutes are:

1. Scientific and grant writing sub-committee: AHRI, ALIPB and Jimma University
2. Membership and recognition sub-committee: Wollo University, Gonder University and Arba Minch University
3. Documentation and Communication sub-committee: Mekelle University, Wollega University and Debre Markos University

Finally, closing remarks were given by representatives from FMoH/NMCEP, EPHI and ACIPH/PMI-SMMES. All the speakers took the opportunity to thank all participated in strengthening the network in general and those contributed for the success-ful deliberation of the current symposium and call upon all the participants to continue their participation and work on strengthening the network, which has a long way to go to be a strong network and contribute to the countries effort in elimination malaria nationally by 2030.

At last, Debremarkos University volunteered to host the 11th malaria research network symposium and the colorful 10th malaria research symposium was concluded.

Annex

Annex I. List of Participants

SN	Name	Institution

1	Elifaged H/meskel	AAU
2	Lemu Golassa	AAU/ALIPB
3	Prof Ahmed Ali	AAU/SPH
4	Prof. Yemane Berhane	ACIPH
5	Dr. Ayele Zewdie	ACIPH
6	Honelgn Nahusenay	ACIPH
7	Eyob Seife	ACIPH
8	Ashetu Hunduma	ACIPH
9	Samir Awol	ACIPH
10	Yonas Kebede	ACIPH
11	Endalemaw Gadisa	AHRI
12	Fitsum Girma	AHRI
13	Abebe Genetu	AHRI
14	Solomon Kinde	Arba Minch University
15	Zerihun Desalegn	Arbaminch University
16	Sintayehu Tsegaye	Arbaminch University
17	Masfin Wubishet	Arsi ZHO
18	Tadesse Hailu	Bahirdar University
19	Getasew Shitaye	Bahirdar University
20	Nitsuh Tadese	Benishangual Gumuz RHB
21	Girma Bekele	Benishangual Gumuz RHB
22	Bayou Belandi	Bruysa Bayer
23	Dr. Getnet Atenafu	Debre Markos University
24	Dejene Getachew	Dire Dawa University
25	Alemayehu Keberku	East Hararghe ZHD
26	Ashenafi Asefa	EPHI
27	Dr Geremew Tasew	EPHI
28	Fekadu Gemechu	EPHI
29	Alemnesh H /mariam	EPHI
30	Adugna Abera	EPHI

31	Adugna Wayesa	EPHI
32	Tesfahun Abya	EPHI
33	Dereje Dillu	FMoH
34	Degu Mehari	FMoH
35	Mebrahatom Haile	FMoH
36	Samson Tadiwos	FMoH
37	Seife Bashaye	FMoH
38	Achamelesh Sisay	FMoH
39	Tilahun Kebede	FMoH
40	Gashu Fenie	FMoH
41	Dr Kebede Etana	FMoH
42	Jay Orem	Gambella RHB
43	Dr Migbaru Kaffale	Haramaya University
44	Biniam Degito	Hawassa University
45	Feleke Belachew	ICAP
46	Abaya Mulgeta	ICAP
47	Negash Seyoum	ICAP
48	Mekonnen Tadesse	ICAP-CU
49	Abebe Asale	ICIPE
50	Prof Delenasaw Yewhalaw	Jimma University
51	Zewdie Birhanu	Jimma University
52	Zelalem Kebede	Malaria Consortium
53	Mekonen Yohannes	Mekelle University
54	Woldegebriel Assefa	Mekelle University
55	Gezahegn Tesfaye	PATH
56	Dr Matt Murphy	PMI
57	Meshasha Balkew	PMI Vector Link
58	Dr Beka Aberra	SPHMMC
59	Dr Tesfaye Deresse	SPHMMC
60	Dr Getachew Bizuneh	SPHMMC

61	Dr Sisay Sirgu	SPHMMC
62	Awol Dawed	SPHMMC
63	Wondwossen Tsegaye	SPHMMC
64	Mebratu Abraha	SPHMMC
65	Daniel Razzanu	SPHMMC
66	Ermias Abraham	SPHMMC
67	Bamlak Gashaneh	SPHMMC
68	Binyam Tariku	SPHMMC
69	Bemnet Yazew	SPHMMC
70	Tsion Yewalashet	SPHMMC
71	Azeb Mulgeta	SPHMMC
72	Damtie Lenrar	SPHMMC
73	Hilina Worku	SPHMMC
74	Kasahun Dameke	SPHMMC
75	Yosef G/Egziabher	SPHMMC
76	Zelalem Demissie	SPHMMC
77	Solomon Dinku	SPHMMC
78	Mamude Dinkiye	SPHMMC
79	Prof Markos Tesfaye	SPHMMC
80	Aman Safewu	SPHMMC
81	Joseph Keating	Tulane University
82	Eyob Alemayo	University of Gonder
83	Asmamaw Malade	University of Gonder
84	Habtie Tesfa	University of Gonder
85	Dr Kassahun Alemu	University of Gonder
86	Tsion Demissie	USAID-PMI
87	Worku Bekele	WHO
88	Teha Shumbej	Wolkite University
89	Mebratu Dufera	Wollega University

Annex II. Schedule

MALARIA SURVEILLANCE IN THE CONTEXT OF MALARIA ELIMINATION

10th Ethiopian Malaria Research Network Symposium

December 19-20, 2018, St. Paul Hospital Millennium Medical College

Time	Topics	Presenters
Day 1		
08:00- 09:00	Registration	ACIPH/SPHMMC
Session I: Moderator and Master of Ceremony: Dr. Ayele Zewde		
09:00- 09:10	Welcoming Address	Prof. Markos Tesfaye – St. Paul's Hospital Millennium College, Research Directorate Director
09:10 -09:20	Key note address	Dr. Matthew Murphy – PMI Ethiopian Program
09:20- 09:30	Key note address	Prof. Yemane Berhane – Director, ACIPH
09:30- 09:40	Key note address	Dr. Adugna Woyessa – EPHI Representative
09:40- 09:50	Key note address	Mr. Mebrahtom Haile – Team Leader, NMCEP, FMoH
09:50- 10:00	Opening speech	Dr. Wondimagegne Gezahagne – Provost, St. Paul's Hospital Millennium College
10:00-10:30	**Tea Break**	**Organizers**

Session II: Malaria surveillance in the context of malaria elimination; Moderator: Prof. Ahmed Ali/Dr. Gunawardena Dissanayake		
10:30-11:00	Update on activities of the sentinel surveillance sites and the national surveillance system	Dr. Adugna Woyessa- EPHI and Mr. Dereje Dillu, FMoH
11:00-11:40	Strengthening malaria surveillance in the context of malaria elimination	Prof. Joe Keating, Associate Dean Tulane University, SPHTM
11:40-12:00	Update on Vector Surveillance and Insecticide Resistance Monitoring Activities in Ethiopia	Prof. Delenasaw Yewhalaw, Director, Tropical and Infectious Diseases Research Center, Jima University
12:00-12:30	**Discussion**	**Participants**
12:30- 01:30	**Lunch break**	**Organizers**
Session III: Malaria Epidemiology; Moderator: Dr. Elias Senbeto/Dr. Endalamaw Gadissa		
01:30 -01:45	Malaria surveillance system evaluation result of Bench Maji Zone, Southern Ethiopia, 2018	Biniam Degito
01:45 -02:00	Malaria Outbreak Investigation in Ganta-Afeshum District, Tigray, Ethiopia, 2016	Mesfin Wubeshet
02:00 -02:15	Malaria prevalence and associated factors among pregnant mothers in Sherkole District	Girma Bekele
02:15 -02:30	A 17 year trend analysis of malaria at Adi Arkay district	Habte Tesfa
02:30-03:00	**Discussion**	**Participants**
03:00-03:20	**Tea break**	**Organizers**
Session IV: Malaria Prevention and Control Interventions; Moderator: Dr. Matthew Murphy/Mr. Mebrahtom Haile		
03:20-03:35	The role of mathematics in fight against malaria	Woldegebriel Assefa
03:35-03:50	Travel to farms in the lowlands & inadequate information on malaria significantly predict malaria in villages around Lake Tana	Asmamaw Malede

03:50-04:05	Serological Evidence for a decline in malaria transmission following major scale up of control efforts	Migbaru Keffale
04:05-04:20	Use of ITN and care seeking-behavior for febrile children by care takers	Zewdie Birhanu
04:20-05:00	**Discussion**	**Participants**
Day 2		
Session V: Malaria Entomology – vector behavior; Moderator: Dr. Fekadu Masebo/Dr. Meshesha Balkew		
09:00-09:15	Exploring the impact of house screening intervention on entomological incidence of malaria	Solomon Kinde
09:15-09:30	Impact of wall surface types & spray application quality on efficacy of propoxur	Zerihun Desalegn
09:30-09:45	Species composition, abundance & distribution of anopheles mosquito in Jabitehnun district	Getnet Atnafu
09:45-10:00	Integrated vector management implementation for malaria control in Tolay	Abebe Asale
10:00-10:30	**Discussion**	**Participants**
10:30-11:00	**Tea break**	**Organizers**
Session VI: Malaria Case Management I; Moderator: Dr. kebede Etana/Dr. Mamude Dinkiye		
11:00-11:15	Therapeutic efficacy of Arthemether Lumfantrin in management of uncomplicated malaria at OPD	Mesfin Assefa
11:15-11:30	Therapeutic efficacy of Choloroquine for the treatment of P vivax	Teha Shumbej
11:30-11:45	Antimalaria treatment outcomes in Ethiopia – Systematic review and meta-analysis	Eyob Alemayehu
11:45-12:00	Low & heterogenous prevalence of G6PD deficiency in different settings of Ethiopia	Getasew Shitaye
12:00-12:30	**Discussion**	**Participants**
12:30-01:30	**Lunch break**	**Organizers**

Session VII: Malaria case management II; Moderator: Dr. Abebe Genetu/Adugna Abera		
01:30 -01:45	Ultra-sensitive rapid tests detected four-fold more asymptomatic reservoirs than microscopy	Lemu Golassa
01:45 -02:00	The relative contribution of symptomatic and asymptomatic P. vivax and P. falciparum infections to the infectious reservoir in a low endemic setting in Ethiopia	Fitsum Girma
02:00 -02:15	Prevalence of Pfcrt and Pfmdr 1 alleles among asymptomatic P.falciparum malaria cases in different transmission settings in Ethiopia	Elifagede Hailemeskel
02:15 -02:30	Contrasting transmission dynamics and genetic clustering of co-endemic P. falciparum and P. vivax in a low endemic area in Ethiopia	Endalamaw Gadisa
02:30-03:00	**Discussion**	**Participants**
03:00-03:30	**Tea break**	**Organizers**
Session VIII: Business meeting Moderator: Dr. Adugna Woyessa/Dr. Ayele Zewde		
03:30-04:30	Business meeting/ Discussion on Malaria research network future direction	Participants
04:30- 05:00	**Closing Remarks**	**FMoH/EPHI/ACIPH**

Annex III. Abstracts

Malaria surveillance system evaluation result of Bench Maji Zone, Southern Ethiopia, 2018

Authors: Biniam Degito[1*], Mesay Hailu[2]

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Abstract

Introduction: Public health surveillance mainly uses to detect outbreak early and reduce morbidity and mortality. This can be achieved by assessing disease burdens and guiding the action to be taken, the need to review health policy and planning, evaluation of health programs, providing a basis for further research. Malaria is one of the most important parasitic diseases of humans, is among a major disease of public health important and a leading cause of morbidity and mortality in many countries. So, assessing the surveillance system of malaria can identify the effectiveness of the surveillance system to identify possible outbreak or burden of malaria. There was no malaria surveillance system evaluated at Bench Maji Zone previously. Therefore, this study primarily aimed to evaluate level of attributes and functions of surveillance system of Bench Maji Zone in detecting malaria outbreak early and using it for evidence based decision making.

Methods: The study units were Zonal health office, selected woreda health offices, health centers and health posts. The study was conducted from April 12 to April 26, 2018. Data was collected by semi-structured questionnaire (interview), through observation and record review on status of attributes and functions of malaria surveillance system. Data was analyzed using Microsoft Excel 2010.

Result: The overall timeliness of surveillance data at the district was 69%, while the completeness was 87%. However, some of status of the attributes (sensitivity of 49%) and functions of surveillance were below the expected level in detecting malaria outbreak early. In addition, there was incompleteness of malaria case registration, and report of malaria cases in majority of study units. There were also weak feedback and supervision system in health offices and limited access of communication system for surveillance.

Conclusion and recommendation: The overall malaria surveillance timeliness and completeness were below the WHO target (80% and 90%, respectively). The majority of status of attributes and functions of malaria surveillance system are below the expected levels in meeting the objectives of malaria surveillance system. Therefore, we the Bench Maji Zone Department to analyze malaria surveillance data on timely and on ongoing manner to detect and respond to malaria outbreak early, analyze malaria morbidity and mortality trend and use for evidence based decision making and which is also can have significant positive impact on nationally planned malaria elimination activities.

Key words: malaria, surveillance, Bench Maji Zone

Malaria Outbreak Investigation in Ganta-Afeshum District, Tigray, Ethiopia, 2016

Authors: Mesfin W. Kelkile[1*], G. Berhe (PhD) [2], A. Adissu[3]

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Name of FETP: Ethiopian FELTP

FETP Entry: 2015/16

Background: Malaria is endemic in Ethiopia. Despite many control and elimination efforts, unusual occurrence was reported from Ganta-Afeshum District, Tigray, Ethiopia, in June 2016. We investigated the outbreak to assess its magnitude and identify its potential risk factors.

Method: We conducted *a case-control* study during July 14 to 24, 2016. We also *reviewed* different records to assess the magnitude of the outbreak. We defined a case as a malaria patient with positive microscopic or rapid diagnostic test. We randomly selected 115 newly identified cases from Bizet Health Center registers and compared with 115 community controls. Data was cleaned, entered in to *Epi-Info* and analyzed using *SPSS.* Using bivariate logistic regression, multivariate analysis was performed. Odds ratio, 95% confidence interval and p-values were calculated. We also assessed environmental risk factors; identified new cases; and intervened to the outbreak.

Result: Total of 1328 confirmed malaria cases (Attack rate: 39.8 /1000) with no death were reported between June1 and July 24, 2016. Slide positivity rate peaked to 66% during July. Males and greater than 15 years old individuals were more affected (Attack rate 44.7 and 43.1/ 1000 respectively). Attack rate was highest in Wuhidet, Bizet and Simret kebeles. Using multivariate analysis, males were more likely affected (OR: 2.3, 95% CI: 1.23, 4.29). The odds of presence patients with similar to malaria signs in home (OR: 4.12, 95% CI: 2.12, 8.0) and stagnant water (OR: 2.27, 95% CI: 1.12, 4.59) were higher among the cases. Indoor residual spray (IRS) had not conducted during the year. We conducted environmental management and treatment of cases.

Conclusion: Presence of patients with similar signs in home, and stagnant water were attributed to the outbreak. Absence of IRS might have also contributed to the outbreak. We recommended strengthening of early case treatment, environmental management, and conducting IRS.

Keywords: Malaria, Outbreak, Case-control, Ganta-Afeshum, Tigray Region, Ethiopia

Word count: 294

Authors: Girma B. Gonitie[1], F. Haileab[2]
Authors Affiliation: [1] Ethiopian field Epidemiology training program resident [2:] University of Gondar, Biostatics and Epidemiology department lecturer
Address: graisebekele124@gmail.com, Telephone number: +251922360890
Title: Prevalence and Associated Factors for Malaria Infection among Pregnant Mothers in Sherkole District, Benishangul Gumuz Regional State

Introduction- Malaria during pregnancy leads to serious adverse effects on the mothers and their children. Approximately 25 million pregnant women in Sub-Saharan Africa are at risk of malaria infection each year. The aim of this study was to assess the prevalence and associated factors of malaria among pregnant mothers.

Methods - Community based cross sectional study was conducted from July-August 2018 in Sherkole district, West Ethiopia. Multi stage sampling technique was used to select **504** pregnant mothers. Interviewer based semi structured questionnaires were used for data collection. Malaria infection was diagnosed by using Rapid diagnostic test (RDT). The data was entered using EPI info version 7.2.2.2 and transferred to SPSS version 20 statistical package for analysis. Bivariable and multivariable logistic regression models were employed. Odds ratio (OR) with its 95% confidence interval (CI) was computed and variables having p-values less than 0.05 were considered to be significantly associated with the dependent variable.

Results - Of the total 498 pregnant women participated in this study, 10.2% (51/498) malaria cases were found. Of this, 46 (90.2%) were P. falciparum and 5 (9.8%) were P. vivax. Decreasing Age (AOR 0.78; 95 % CI 0.67-0.911), not using insecticide treated bed net (AOR 12.5; 95 % CI 4.86-32.21), first trimester pregnancy (AOR 20.07; 95 % CI 2.03-198) & second trimester (AOR 7.58; 95 % CI 2.84-20.2) compared to third trimester and secundigravidae (AOR 5.99; 95 % CI 1.68-11.44) compared to multigravida were found to be significantly associated with malaria during pregnancy.

Conclusion- Malaria is still a public health issue among pregnant women in Sherkole district. Age of respondents, insecticide treated bed net use, gravidity, and gestation age had significant association with malaria infection. Screening pregnant women for asymptomatic malaria infection and enhance them to use insecticide treated bed net should be provided.

Key words: malaria, pregnant mothers, sherkole district

Journal name: Malaria Journal (Tesfa *et al. Malar J (2018) 17:155)*

Title: A 17-year trend analysis of malaria at Adi Arkay, north Gondar zone, Northwest Ethiopia

Authors: Habtie Tesfa, Abebe Genetu Bayih and Ayalew Jejaw Zeleke

Abstract

Background: Malaria is one of the leading causes of death worldwide. This study aimed to determine the trend of malaria among febrile patients seeking treatment over 17 year (1997–2013) at Adi Arkay, Northwest Ethiopia.

Methods: A 17-year malaria microscopy data were extracted retrospectively at Adi Arkay health centre. Time series and curve estimation analysis were used to evaluate trends in the data. Pearson's Chi square test was also used to describe associations of variables.

Results: Over 17 years, 20,483 blood flms were requested for malaria diagnosis at the health centre. Out of this, 7428 (36.1%) were microscopically confrmed malaria cases. *Plasmodium falciparum, Plasmodium vivax,* and their mixed infection accounted for 68.85, 28.79, and 2.34% of all malaria cases, respectively. There was a remarkable reduction of overall malaria during the 17 years. Malaria was reported in all age groups of both sexes, but its positivity rate was signifcantly higher in males and in the 15–24 years than their counterparts.

Conclusion: In relative terms, the overall positivity rate of malaria in the area over 17 years showed a significant reduction, but its magnitude as a public health problem is still alarming. *Plasmodium falciparum* played a significant role in the remarkable drop of overall malaria in the area, whereas vivax malaria remained unchanged. Therefore, control measures should continue to strengthen targeting both predominant malaria parasites in the area.

The Role of Mathematics in fighting Against Malaria:

(Modeling of the Immunopathogenesis of the in-host Dynamics of Malaria Parasites, and possible ways to reduce parasite development).

Woldegebriel Assefa (PhD)

Dec 03, 2018

Abstract: Mathematics is playing an increasingly important role in the eld of medicine through the use of models and numerical simulations. The use modelling is increasingly in u-encing the theory and practice of disease management and control. For example, mathematical models of the within human host host dynamics of the malaria parasite play an important role in in understanding the di erent developmental stages including the triggering gameto-cyte development as well as the interaction with the human immune system and even the pharmaco-kinetics of malaria drugs.

In this work, we developed and analyzed mathematical model for the within human dynam-ics of the malaria parasites. The model studied capture the roles played by the main actors responsible for the progression of the infection process both within the human and within the mosquito hosts. Our model for the within human host integrate actors involved in the develop-ment and progression of malaria parasitaemia, gametocytogenesis and mechanisms for innate and adaptive immune response activation culminating in the formation of gametocytes. Our analysis reveals the existence of a threshold parameter which determines conditions for existence and stability of steady states and oscillatory dynamics reminiscent of malaria parasitaemia in humans. Parameters that a ect the e ciency of the process of progression from parasitaemia to gametocytes formation are identi ed. Via global stability analysis, we showed that control of parasitaemia in the human is possible by keeping the identi ed threshold parameter below unity[1].

Mekelle University, CNCS, Department of Mathematics, E-mail: woldegebriel.assefa@mu.edu.et [1]Our work is already published in Bulletin of Mathematical Biology, Springer

Travel to farms in the lowlands and inadequate malaria information significantly predict malaria in villages around Lake Tana, northwest Ethiopia: a matched-case control study

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Abstract

Background: In Ethiopia, malaria has declined in the last decade; only a small number of cases have been reported, primarily from hotspots. The contribution of house proximity to water bodies and the role of migration in malaria transmission has not yet been examined in detail in northwest Ethiopia. Individual and household-level environmental and socio-demographic drivers of malaria heterogeneity were explored contextually in meso-endemic villages around Lake Tana, northwest Ethiopia.

Methods: A health facility-based paired age-sex matched case–control study involving 303 matched pairs was undertaken from 10 October 2016, to 30 June 2017. Geo-referencing of case households, control households, proximate water bodies, and health centres was carried out. A pretested and structured questionnaire was used to collect data on socio-demography, household assets, housing, travel history, and malaria intervention measures. Medians (interquartile range) were computed for continuous variables. Pearson's Chi square/Fisher's exact test was used to detect significant differences in proportions. Principal component analysis was performed to estimate household wealth. Stratified analysis was used to confirm confounding and interaction. A multivariable conditional logistic regression model was used to detect risk factors for malaria.

Results: Of 303 malaria cases, 59 (19.5% [15.4–24.3]) were imported malaria cases whereas 244 (80.5% [75.7–84.6]) were locally acquired malaria cases. In bivariate analysis, marital status, educational status, and bed net ownership were significantly associated with malaria cases. In multivariable adjustment, travel to malarious lowlands in the preceding month (adjusted mOR=7.32; 95% CI 2.40–22.34), household member's travel to malarious lowlands (adjusted mOR=2.75; 95% CI 1.02–7.44), and inadequate health information on malaria (adjusted mOR=1.57; 95% CI 1.03–2.41) were predictors of malaria. Stratified analysis confirmed that elevation of households and travel to malarious lowlands were not effect modifiers. Travel to malarious lowlands had a confounding effect on malaria but elevation of households did not.

Conclusions: In this study, travel to farms in the lowlands and inadequate health information on malaria were risk factors for malaria in villages around Lake Tana. This evidence is critical for the design of improved strategic interventions that consider imported malaria cases and approaches for accessing health information on malaria control in northwest Ethiopia.

Keywords: Locally acquired malaria, Malaria information, Travel, Matched case control study

Serological evidence for a decline in malaria transmission following major scale up of control efforts in a setting selected for *P. vivax* and *P. falciparum* malaria elimination in Babile district, Oromia, Ethiopia

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Abstract

Background: Following successful control during the last decades, Ethiopia set a stepwise malaria elimination strategy in low transmission areas. The level of residual infections, and history of exposures that relate with the impact of previous interventions need to be evaluated in order to guide elimination efforts.

Methods: Cross-sectional survey was conducted in 14 villages in Babile district, Oromia, Ethiopia. *P. falciparum* and *P. vivax* infection status was evaluated by microscopy and nested polymerase chain reaction (nPCR). The prevalence and density of anti-malaria apical membrane antigen-1 (AMA-1) was assessed to generate age-seroprevalence and antibody titre plots.

Results: The current infection prevalence by microscopy and nPCR were 1.4% (16/1144) and 5.0% (57/1144) for *P. falciparum,* and 0.4% (5/1144) and 3.6% (41/1144) for *P. vivax,* respectively. The generated seroconversion curves showed strong indication for a decline in exposure, 15.5 years for *P. falciparum* and 11.5 years for *P. vivax* prior to sampling.

Conclusion: The strong indication of decline in exposure implies effective program. On top the heterogeneous and measurable ongoing local transmission found, argue in favor of the need for continued and tailored efforts to accelerate the stride towards the step wise elimination efforts.

Key words: MALARIA ELIMINATION, SEROLOGY, ASYPTOMATIC CARRIAGE, METRICS OF TRANSMISSION

Caretakers' understanding of malaria, use of insecticide treated net and care seeking-behavior for febrile illness of their children in Ethiopia: Implications for sustained control and elimination

Zewdie Birhanu, Yemane Ye-ebiyo Yihdego, and Delenasaw Yewhalaw

Abstract

Background: Local understandings of malaria and use of preventive measures are critical factors in sustained control of malaria. This study assessed caretakers' knowledge on malaria, use of Long Lasting Insecticide Treated Nets (LLINs) and care-seeking behavior for their children's illness in different malaria transmission settings of Ethiopia.

Methods: Data were collected from 709 caretakers of children of 2–9 years of age during in 2016. A standard questionnaire was used to assess caretakers' perceptions of malaria, use of LLIN and care seeking behavior for febrile illness of children aged 2–9 years.

Results: The caretakers recognized malaria mostly by chills (70.4%, 499/709), fever (45.7%, 324/709) and headache (39.8%, 282/709). Overall, only 66.4% (471) of the caretakers knew that mosquito bite caused malaria and that it was quite heterogeneous by localities (ranging from 26.1% to 89.4%) and altitude ($p < 0.05$). Majority, 72.2% (512), of the caretakers knew that sleeping under LLIN could prevent malaria. Overall knowledge on malaria (mean = 51.2%) was very low with significant variations by localities, altitude and levels of malaria transmission, being low in high altitude and low in transmission areas ($p < 0.05$). Four hundred ninety-one (69.3%, 491/709) of the children slept under LLIN in the previous night. Of malaria related knowledge items, only knowledge of LLIN was associated with net use; non-use of LLN was higher among caretakers who did not know the role of LLIN (AOR = 0.47, 95%CI: 0.28–0.77, $p = 0.003$). Of course, attributing causation of malaria to stagnant water discouraged use of net ($p = 0.021$). Of febrile children ($n = 122$), only 50 (41.0%) sought care with only 17 (34.0%) seeking the care promptly. There was no significant link between knowledge of malaria and care seeking behavior ($p > 0.05$). However, knowledge of malaria had some level of influence on treatment source preference where caretakers with greater knowledge preferred pharmacy as source of care.

Conclusions: Caretakers' understanding of malaria was unsatisfactory with marked heterogeneity by localities. The evidence suggests that knowledge is not sufficient enough to drive malaria preventive behaviors, risking the efforts undertaken for sustained control and moving towards elimination targets. Thus, context-specific health education interventions are important besides ensuring access to necessary preventive tools.

Keywords: Malaria, Caretakers, Malaria Perception, Malaria Knowledge, LLIN, Care Seeking, Fever, Ethiopia

Adapted from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5604495/

The Species Composition, Abundance and Distribution of *Anopheles* Mosquitoes in Jabitehnan District of West Gojjam, Ethiopia

Getnet Atenafu, Asefa Teshal

Malaria is the most important disease transmitted by *Anopheles* mosquitoes. This vector-borne disease often affects vulnerable populations and with limited access to health care services. The objective of the current study was to investigate and determine the seasonal activity patterns of larval and adult *Anopheles* mosquito's abundance, distribution and species composition in Jabitehnan. Longitudinal study design was carried out to investigate abundance, distribution and species composition of *Anopheles* mosquitoes in purposively random selected villages in the districts. In this study 62 larval breeding sites and 30 houses were randomly selected for collecting adults through CDC light traps, PSC and pit shelters in the district. A total of 2,014 adult *An.* mosquitoes were identified of which adult female *Anopheles* mosquitoes 134 (6.65%) were collected using CDC light traps, 118 (5.86%) were by PSC and 113 (4.97%) were in pit shelters and the remaining 1,662 (82.52%) adults were reared from larvae and pupae during four month study. Among 1,662 reared adult identified 537 (32.31%) were males and 1,125 (67.69%) were females. Three *Anopheles* species, *An. gambiae* complex, *An.funestus* and *An. pharoensis* were identified using morphological characters. 1,481 (73.54%) were *An. gambiae* complex, 280 (13.90%) were *An.funestus* and 253 (12.56%) were *An. pharoensis*. There was significant difference between collection seasons and the abundance of *An. gambiae* complex, t = 3.592, P = 0.003 but there was no significant difference between collection seasons and the abundance of *An. pharoensis*, t = -1.891, P = 0.081 and *An. funestus* mosquitoes species, t = -1.621, P = 0.129. Of the three identified *Anopheles* mosquitoes were abundant during study period while *An.gambiae* complex was the most abundant species. Malaria vectors distribution is not restricted in areas below 2000 meter above sea level. From the total *Anopheles* mosquitoes species females were more abundant and distributed than males. The main reason to the species composition, abundance and distribution of *Anopheles* mosquitoes species was the variation of breeding habitats and seasons in Jabitehnan district.

Keywords: *An. gambiae* complex, *An.pharoensis, An. funestus*.

Therapeutic Efficacy of Artemether Lumefantrine (Coartum) In Outpatients With Uncomplicated Plasmodium Falciparum Malaria At Bonosha Health Center Shashogo Wereda, Hadiya Zone Southern Ethiopia By Mesfin Assefa

Abstract

Introduction: The control of malaria relies on chemotherapy, insecticides and use of mosquito bed net. Coartum is the first line treatment of uncomplicated Plasmodium falciparum malaria in Ethiopia. Drug resistance is challenging the control of malaria in different parts of the world.

Objectives: To determine the therapeutic efficacy of Artemether/lumefantrine (Coartum) for treatment of uncomplicated Plasmodium falciparum malaria in outpatients at Bonosha Health Centre Southern Ethiopia.

Methods: A 28 days in vivo drug efficacy study was conducted at Bonosha health centre from April to September 2016. Seventy-nine patients with microscopically confirmed P. falciparum malaria, aged 6 months and above, were enrolled and treated with coartum for three days. Recurrence of parasitaemia and clinical condition of patients were assessed on day 1, 2, 3, 7, 14, 21, &28 during the 28 days follow-up period. The levels of haemoglobin in the study participants were determined at baseline and end of the study.

Results: From 87 patients included in the study, 79 patients completed a 28 days follow up study. Eight patients excluded from the study; 2 participant vomited the third dose of the drug twice at day 2, 1 patients were infected by P.vivax asexual stage on day 14, and 5 patient was lost to follow up on day 14,21 and 28. Among the recruited study participants, males were higher in proportion compared to females (47 were males and 32 were females). The median age of study participants was 23 (range: 4 to 59) (Table 1). During enrolment, 41 (52%) had a history of fever and 38 (48%) had fever. The duration of illness of the patients before enrolment was 3.05 ± 1.41 (mean ± SD) days. In this study, 1(1.3%) patient showed late parasitological failure and the cure rate of Coartem in the study area was 98.7%.The Kaplan-Meier survival estimate showed a 0.013 cumulative incidence of therapeutic failure. The geometric mean of parasite at day 0 was 11,026.6 parasites/µl. Significant (P = 0.01) increase was observed in the haemoglobin level between the baseline and day 28.

Conclusions: The six dose regimen of Coartum showed therapeutic efficacy of (98.7%) in the treatment of uncomplicated P. falciparum. A 1.3% coartum treatment failure, rapid clearance of fever and asexual parasitaemia, improvement in mean haemoglobin level was detected in the study participants.

Recommendations: Regular monitoring of the pattern of resistance, proper instruction and utilization of coartum treatment should be exercised in order to avoid resistance.

Key words: Plasmodium falciparum, Coartum resistance, therapeutic efficacy, Ethiopia

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Therapeutic Efficacy of Chloroquine for Treatment of *Plasmodium Vivax* Malaria Cases in Guragae Zone Southern Central Ethiopia. One-Arm Prospective Study; 2017

Teha Shumbej *et al.*

ABSTRACT

Introduction: Malaria continues to be a public health problem and important cause of morbidity and mortality in Ethiopia. Interventions like anti-malarial drugs to combat malaria in endemic regions are showing a decline in malaria related deaths and morbidity. These gains however, are threatened with the emergency of drugs resistant strains of Plasmodium parasites. Without regular inspection of anti-malarial drug resistance, the disease burden and the economic costs of malaria will rise radically. This study aimed to determine therapeutic efficacy of chloroquine for treatment of *Plasmodium vivax* in Guragae zone, southern Ethiopia

Methods: A one-arm prospective study with recurrence of parasitaemia and clinical conditions of patients evaluated on days 0, 1, 2, 3, 7, 14, and 28 in selected health care centers. Patients with *Plasmodium vivax* mono infection, who met the study inclusion criteria, were recruited. SPSS-21 used for data analysis. Kaplan-Meier survival probability analysis was used to calculate incidence density of failure per person month of follow up and geometric mean used to calculate average haemoglobin. Proportion treatment failure was also calculated.

Results: A total of 81 subjects had completed the follow up. The mean haemoglobin concentration of study participants at day of enrolment was 11.8 g/ dl and 13.8 g/dl on day 28. More than half (57.5 %) had a history of fever and 42.5 % of them had fever at the time of enrolment. The mean body temperature at day of recruitment was 38.2°C and 36.0 ℃ for day 28. Geometric mean parasitemia calculated at day of enrollment was 2270 parasites/µl of blood. 2.5% treatment failure was documented and the 28 day incidence density of failure calculated was 22/1000 person month of follow up.

Conclusion: This study registered a high rate of efficacy of chloroquine among the study participants. Therefore, chloroquine remains efficacious for the treatment of *Plasmodium vivax* in the study area. However, there is a need to monitor chloroquine resistance by employing molecular tools for better evaluation.

Key words: *Plasmodium vivax*, Therapeutic Efficacy, Guragae zone, Ethiopia

Anti-malarial treatment outcomes in Ethiopia: a systematic review and meta-analysis.

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BACKGROUND: Ethiopia is among countries with a high malaria burden. There are several studies that assessed the efficacy of anti-malarial agents in the country and this systematic review and meta-analysis was performed to obtain stronger evidence on treatment outcomes of malaria from the existing literature in Ethiopia.

METHODS: A systematic literature search using the preferred reporting items for systematic review and meta-analysis (PRISMA) statement was conducted on studies from Pubmed, Google Scholar, and ScienceDirect databases to identify published and unpublished literature. Comprehensive meta-analysis software was used to perform all meta-analyses. The Cochrane Q and the I 2 were used to evaluate heterogeneity of studies. Random effects model was used to combine studies showing heterogeneity of Cochrane Q $p < 0.10$ and I 2 > 50.

RESULTS: Twenty-one studies were included in the final analysis with a total number of 3123 study participants. Treatment outcomes were assessed clinically and parasitologically using World Health Organization guidelines. Adequate clinical and parasitological response was used to assess treatment success at the 28th day. Overall, a significant high treatment success of 92.9% (95% CI 89.1-96.6), $p < 0.001$, I 2 = 98.39% was noticed. However, treatment success was higher in falciparum malaria patients treated with artemether-lumefantrine than chloroquine for Plasmodium vivax patients [98.1% (97.0-99.2), $p < 0.001$, I 2 = 72.55 vs 94.7% (92.6-96.2), $p < 0.001$, I 2 = 53.62%]. Seven studies reported the adverse drug reactions to anti-malarial treatment; of 822 participants, 344 of them were exposed to adverse drug reactions with a pooled event rate of 39.8% (14.1-65.5), $p = 0.002$.

CONCLUSIONS: On the basis of this review, anti-malarial treatment success was high (92.9%) and standard regimens showed good efficacy against Plasmodium falciparum (98.1%) and P. vivax (94.7%) infections in Ethiopia, but associated with high rates of adverse drug reactions (ADRs). However, these ADRs were not serious enough to discontinue anti-malarial treatment. The results of this study suggest that the current anti-malarial medications are effective and safe; however, greater priority should be placed on the discovery of new anti-malarial drugs to achieve successful outcomes as resistance seems inevitable since cases of anti-malarial drug resistance have been reported from other areas of the world.

KEYWORDS: Adverse drug reactions; Artemether–lumefantrine; Chloroquine; Efficacy; Ethiopia; Malaria; Plasmodium falciparum; Plasmodium vivax; Safety; Treatment

Low and heterogeneous prevalence of glucose-6-phosphate dehydrogenase deficiency in different settings in Ethiopia using phenotyping and genotyping approaches

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Background: 8-Aminoquinolines such as primaquine clear mature Plasmodium falciparum gametocytes that are responsible for transmission from human to mosquitoes and bring radical cure in Plasmodium vivax by clearing dormant liver stages. Deployment of primaquine is thus of relevance for malaria elimination efforts but challenged by the widespread prevalence of glucose-6-phosphate dehydrogenase deficiency (G6PDd) in endemic countries since primaquine in G6PDd individuals may lead to acute haemolysis. In this study, the prevalence of G6PDd was investigated in different settings in Ethiopia using phenotyping and genotyping approaches. **Methods:** Community and school based cross-sectional surveys were conducted from October to December 2016 in four administrative regions (Gambela, Benishangul Gumuz, Oromia, and Amhara) in Ethiopia. Finger prick blood samples were collected for G6PD enzyme activity using the CareStart™ G6PD screening test and genotyping of 36 selected single nucleotide polymorphisms (SNPs) located in the G6PD gene and its flanking regions.
Results: Overall, the prevalence of phenotypic G6PDd was 1.4% (22/1609). For the first time in the Ethiopian population, the African variant (A−) was detected in 3.5% (7/199) of the limited set of genotyped samples, which were all phenotypically normal. Interestingly, all of these individuals had a variation at the rs2515904 locus. Strong geographical variation was observed for both phenotypic and genotypic G6PDd; three-quarters of the phenotypically G6PDd individuals were detected in Gambela. **Conclusion:** A very low prevalence of G6PDd was detected in the present study populations. The presence of the A− variant alongside other G6PD mutants and the patchy distribution of G6PDd indicate that larger studies specifically designed to unravel the distribution of G6PDd at small geographical scale may be needed to tailor malaria elimination efforts in Ethiopia to the local context.

Keywords: Radical cure, P. vivax, G6PD, 8-Aminoquinoline, Haemolysis

Ultrasensitive rapid tests detected four-fold more asymptomatic reservoirs than microscopy in Ethiopia

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Abstract

Background: Following exposure to an infectious mosquito bite, individuals could be clinical or sub-clinical. Those with clinical manifestation usually seek malaria diagnosis for resolution of their symptoms while the latter will remain apparently healthy. Indeed, the diagnosis of asymptomatic individuals is not straight forward. As the global public health objectives for malaria evolve from malaria control towards malaria elimination, there is increasing interest in the significance of asymptomatic infections and the optimal diagnostic test to identify them.

Method: We conducted a cross-sectional study of asymptomatic individuals (n=562) to determine epidemiological characteristics associated with asymptomatic malaria. Participants were tested by RDTs (CareStartTM, SD Bioline, and Alere uRDT), LAMP, and quantitative reverse transcription (RT)-PCR to determine malaria positivity. Hemoglobin values were recorded, and anemia was defined as a binary variable according to WHO guidelines. Prevalence ratios were calculated univariately using 2X2 tables and binomial regressions with a log link.

Results: Compared to reference qRT-PCR, LAMP had the highest sensitivity: 92.6% (95% CI: 86.4 – 96.5) followed by uRDT Alere™ Malaria: 33.9% (95% CI: 25.5 – 43.1), CareStart™ Malaria: 14.1% (95% CI: 8.4 – 21.5), microscopy: 7.3% (95% CI: 2.7– 15.3) and SD Bioline: 5.0% (1.8 – 10.5). For *P. falciparum* specimens only, the sensitivity for uRDT Alere™ Malaria was 50.0% (95% CI: 38.8 – 61.3) and SD Bioline was 7.3% (95% CI: 2.7 – 15.3), respectively. Based on multivariate regression analysis with qRT-PCR as the gold standard,for every 3.2% increase in the prevalence of asymptomatic malaria, hemoglobin decreased by one gram per deciliter [PR 0.968 (0.940 – 0.997); p=0.032].

Conclusions: uRDT Alere™ Malaria has superior sensitivity to rapid diagnostic tests and microscopy in detecting asymptomatic malaria, with LAMP superior still. Ultrasensitive diagnostics paint a more accurate picture of both epidemiological and clinical factors linked to asymptomatic malaria required for elimination

The relative contribution of symptomatic and asymptomatic Plasmodium vivax and Plasmodium falciparum infections to the infectious reservoir in a low-endemic setting in Ethiopia

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ABSTRACT

Background: The majority of *P. vivax* and *P. falciparum* infections in low-endemic settings are asymptomatic. The relative contribution to the infectious reservoir of these infections, often of low-parasite-density, compared to clinical malaria cases, is currently unknown but important for malaria elimination strategies.

Methods: We assessed infectivity of passively-recruited symptomatic malaria patients (n=41) and community-recruited asymptomatic individuals with microscopy- (n=41) and PCR-detected infections (n=82) using membrane feeding assays with *Anopheles arabiensis* mosquitoes in Adama, Ethiopia. Malaria incidence and prevalence data was used to estimate the contributions of these populations to the infectious reservoir.

Results: Overall, 34.9% (29/83) of *P. vivax* and 15.1% (8/53) *P. falciparum* infected individuals infected ≥1 mosquitoes. Mosquito infection rates were strongly correlated with asexual parasite density for *P. vivax* ($\rho = 0.63$; $P < .001$) but not for *P. falciparum* ($\rho = 0.06$; $P = .770$). *P. vivax* symptomatic infections were more infectious to mosquitoes (infecting 46.5% of mosquitoes, 307/660) compared to asymptomatic microscopy-detected (infecting 12.0% of mosquitoes, 80/667; $P = .005$) and PCR-detected infections (infecting 0.8% of mosquitoes, 6/744; $P < .001$). Adjusting for population prevalence, symptomatic, asymptomatic microscopy- and PCR-detected infections were responsible for 8.0%, 76.2% and 15.8% of the infectious reservoir for *P. vivax*, respectively. For *P. falciparum*, mosquito infections were sparser and also predominantly from asymptomatic infections.

Conclusions: In this low-endemic setting aiming for malaria elimination, asymptomatic infections are highly prevalent and responsible for the majority of onward mosquito infections. The early identification and treatment of asymptomatic infections might thus accelerate elimination efforts.

Key words: malaria, infectiousness, reservoir, submicroscopic, elimination

Prevalence of *Pfcrt* and *Pfmdr1* alleles among asymptomatic *Plasmodium falciparum* malaria cases in different transmission settings in Ethiopia

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*Equal contribution

Abstract

Background: In Ethiopia, *P. falciparum* and *P. vivax* are co-endemic, and Artemether-Lumefantrine (AL) and chloroquine are the first line treatment for uncomplicated cases, respectively. Ethiopia is one of the successful countries in its fight against malaria; currently of the 60% populations that leave in malaria prone areas, only 6.4% are in high transmission settings. Recently, compelling evidences are emerging that showed selections in *Pfmdr1* genes are implicated in susceptibility change to the Artemisinin combination therapy in Africa. Also more drug resistance was reported in asymptomatic infection that corroborate the evidence from experimental model which demonstrated that under low transmission settings within host competition favors the establishment of drug resistance. Thus, this study aimed to assess the prevalence of *Pfcrt*-K76T and *Pfmdr1*-N86Y among asymptomatic malaria cases under different malaria transmission settings. **Materials and methods**: Community based cross-sectional surveys were conducted from October to December, 2016 in Gambella and Benishangul-Gumuz regions and from July to November, 2017 in Oromia region of Ethiopia. Dried blood spot samples (DBS) were collected from figure pricks. A total of 183 18srRNA-nPCR confirmed asymptomatic *P. falciparum* cases samples were genotyped for *Pfcrt*-K76T and *Pfmdr1*-N86Y codons using PCR-RFLP techniques. **Results and discussion**: The Pfcrt-K76T and *Pfmdr1*-N86Y codons were successfully genotyped for 166 samples. The distribution of *Pfcrt*-76T mutant haplotypes were higher in Adama (96.67%) and Harar (90.0%) compared to the prevalence detected in Gambella (32.08%) and Benishangul-Gumuz (47.83%) areas. Overall, while mixed haplotype of *Pfcrt*-76K/T was detected in only 13 (8%) samples; the *Pfmdr*1-86N wild type was fixed in Harar and Adama areas with similar higher proportions in Gambella (90.38%) and Benishangul-Gumuz (77.27%). **Conclusion**: After over two decades of the introduction of AL in Ethiopia, *Pfcrt*-76 K wild type was not significantly selected but *Pfmdr1*-86N wild type was selected for across the study sites. As this type selection has been implicated with the AL drug tolerance in sub-Saharan Africa, we recommend the assessment of other Pfmdr1 codons and country wide assessment.

Key words: Asymptomatic malaria, *Pfmdr1*, Artemether-Lumefantrine, *P. falciparum*, Ethiopia

Contrasting transmission dynamics and genetic clustering of co-endemic *Plasmodium falciparum* and *Plasmodium vivax* infections in a low-transmission area of Ethiopia

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Abstract

Background: The distribution of malaria infections is heterogeneous in space and time, especially in low endemic settings. Understanding malaria transmission patterns and approaches to identify pockets of transmission may accelerate elimination efforts.

Methods: In Adama district, Ethiopia *P. falciparum* and *P. vivax* malaria patients (n=18), household members and immediate neighbors (n=498) were examined by rapid diagnostic test, quantitative PCR (qPCR) and genotyping of 26 *P. falciparum* neutral microsatellite markers. A similar number of controls without malaria infection (n=18) and neighbors (n=453) were examined. Evidence for geographic clustering of infections and genetic relatedness were assessed for *P. falciparum* and *P. vivax* separately.

Results: In addition to the clinical patients, 46 *P. falciparum*, 16 *P. vivax* and 10 mixed asymptomatic infections were detected in the community by RDT. Family members who lived in households of clinical *P. falciparum* patients were more likely to have qPCR detected infections (20.7%, 12/58) than individuals in control households (9.5%, 41/433; OR, 2.5, 95% CI 1.2 – 5.1; $P = .012$). Whilst there was no evident clustering of *P. vivax* cases in households of clinical malaria cases ($P = .837$) whilst individuals who lived in households with ≥1 RDT-confirmed *P. vivax* infection (both symptomatic and asymptomatic) were more likely to have qPCR detected infection (25.0%, 17/68) compared to individuals in households without RDT-detected infections (11.8%, 94/795; OR, 2.5; 95% CI, 1.4–4.5; $P < .0045$). Infections detected in the same household showed stronger evidence for genetic relatedness compared to infections detected between households. Interestingly, there was strong evidence for genetic relatedness among clinical infections.

Conclusion: The use of conventional diagnostics, supported by a detailed genotyping approach, provide evidence for a strong relatedness of infections within households and suggest that genetically related parasites are responsible for clinical *P. falciparum* infections recruited during the short study period. These findings may support a rational approach to reactive case detection strategies, as currently deployed in Ethiopia.

Key words: Clustering, Asymptomatic malaria, Malaria elimination, Reactive case detection, Parasite genotyping