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NEWS & VIEWS

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INTERVIEW

Dr Deepak Upadhyay,
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UPCOMING

Lecture Series on Infectious Diseases 2.0:
Lecture 11 by Professor Sunil Parikh,
Associate Professor of Epidemiology (Microbial Diseases) and of Infectious Diseases
Yale School of Public Health, USA

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Editorial

Dear Readers,

The MERA-India team brings you the thirty-sixth issue of our newsletter, "News & Views".

WHO recently published a photo story where they shared photographs of the tribal areas of Chhattisgarh and identified it as the state responsible for nearly 20% of the malaria burden in India. This alarming situation requires immediate attention and strategies to address the endemicity of malaria in Chhattisgarh.

In this month's lecture series, Professor Michael C Wimberly (Department of Geography and Environmental Sustainability, University of Oklahoma, USA) gave a talk on 'Mapping the effects of climate and urbanization on transmission of mosquito-borne diseases', with a focus on the effects of geographic patterns and climate variation on malaria outbreaks. The highlights from the informational lecture have been enclosed in this newsletter in the form of a summary.

The "Malaria Scientists to Watch" section encompasses an insightful and edifying interview with a talented clinician and malariologist, Dr Deepak Upadhyay, Professor in the Department of Community Medicine, at Rohilkhand Medical College and Hospital, Bareilly.

The "Research in Spotlight" section covers the summary of three malaria-relevant research articles. In the first article, Conrad *et al.*, reported the emergence of partial resistance to artemisinins in multiple geographic locations in Uganda, with increasing prevalence and regional spread over time. In another article, Balta *et al.* showed that the atovaquone-resistant malaria parasites failed to establish infection within mosquito vectors. In the third article, Lalmalsawma *et al.,* identified hotspots for targeted intervention in Mizoram using the Geographic Information System and its correlation with climate change trends.

Further, the "Malaria Through the Lens of Researchers" section showcases an image submitted for the MERA-India Image Competition 2022 by Ms. Pooja, PhD scholar, at the National Institute of Malaria Research (NIMR), Delhi.

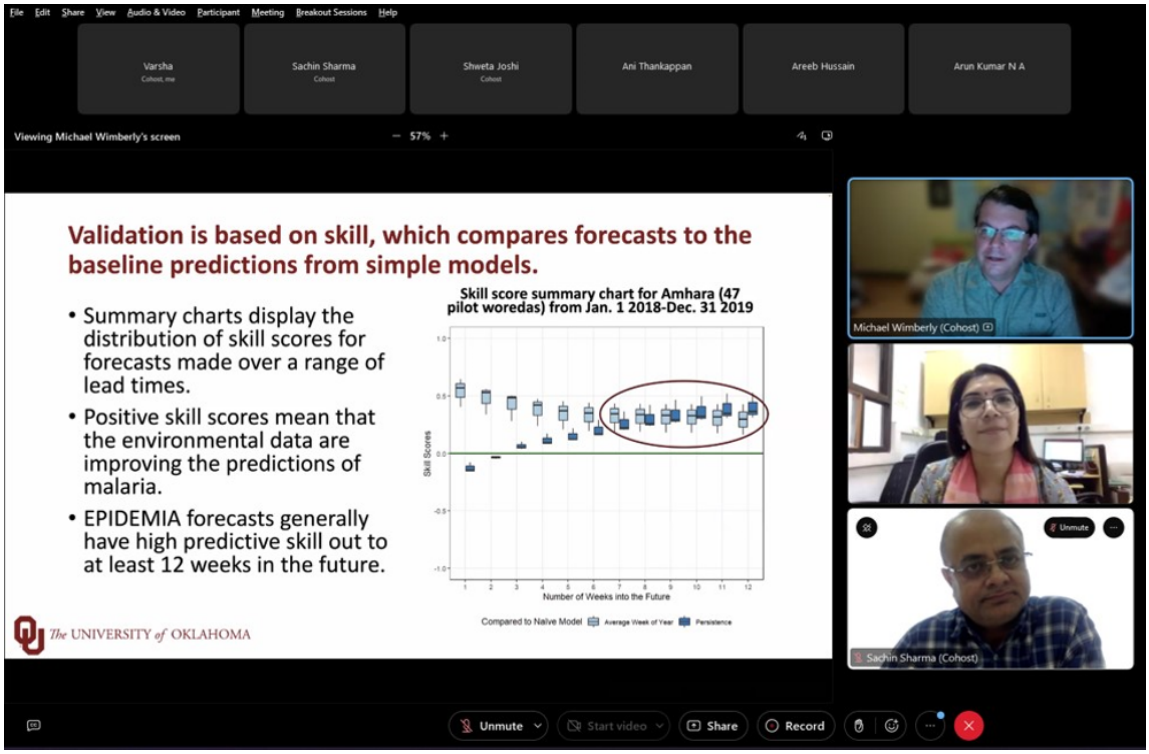
The "Upcoming Events" section comprises information on the 11th lecture in the Lecture Series on Infectious Diseases 2.0, to be given by Professor Sunil Parekh, Yale School of Public Health, USA.

We hope that you will find this issue engaging and fascinating. Please write to us for any feedback or suggestions regarding the newsletter's content at meranewsletter@gmail.com.

With best wishes,
MERA-India team

ICMR-NIMR & MERA-India Activity

Lecture Series on Infectious Diseases 2.0: Lecture 09 by Professor Michael C Wimberly



Dr Michael C Wimberly is a Professor in the Department of Geography and Environmental Sustainability at the University of Oklahoma and the head of the EcoGRAPH research group. His research combines ecological models with Earth observation data to address scientific questions and create practical applications in the fields of public health and natural resource management. Dr Wimberly builds upon the results of this research to create software that applies geospatial data and analysis methods for decision support. He has explored the effects of land use and climate on vector-borne disease transmission in a variety of systems, including tick-borne pathogens in the southeastern U.S., epidemic malaria in the highlands of Ethiopia, West Nile virus in the U.S., and urban malaria in India. Dr Manju Rahi, Scientist-F, ICMR, and Principal Investigator, MERA-India, welcomed Dr Michael C Wimberly, and Dr Sachin Sharma, Chief Consultant, MERA-India, introduced him to the audience.

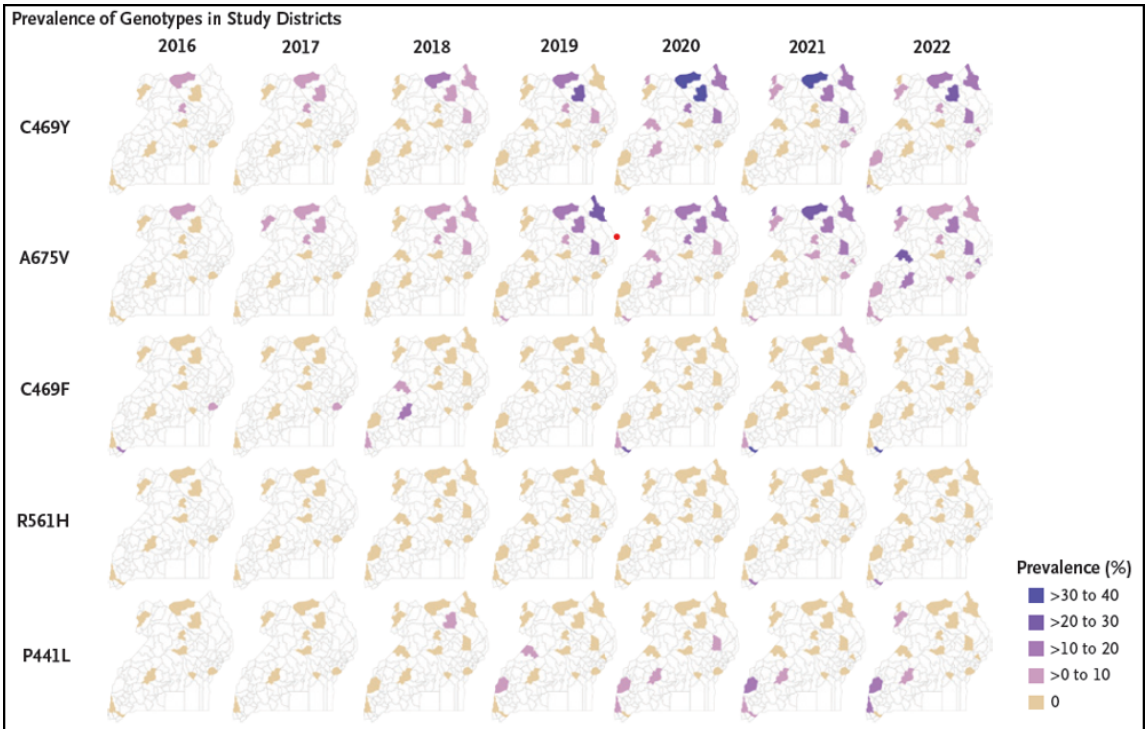
Professor Wimberly gave a talk on ‘Mapping the effects of climate and urbanization on transmission of mosquito-borne diseases’. At the beginning of the lecture, he gave an outline focusing on the environmental determinants of malaria in Ethiopia and the development of an application for malaria early warnings. Professor Wimberly talked about the hurdles in the progress toward improved malaria control and elimination including the increasing human population, widespread poverty in malaria-endemic countries, drug and insecticide resistance, and most importantly climate and land use change that can influence

mosquitoes and malaria transmission. Many of the environmental factors influencing malaria can be monitored by Earth-observing satellites. These Earth-observing satellites can monitor environmental change by measuring reflected, emitted, and backscattered radiation and explore their associations with malaria transmission. He discussed how the geographic distribution of wetlands was associated with regional patterns of malaria cases in Ethiopia and how the wetlands were a better predictor of malaria distribution than other environmental variables including climate (temperature and precipitation) and elevation.

Based on these findings, Professor Wimberly's team developed the Epidemic Prognosis Incorporating Disease and Environmental Monitoring for Integrated Assessment (EPIDEMIA) software tool that supports the implementation of malaria forecasting in Ethiopia by using environmental data collected by NASA Earth-observing satellites. Currently, they are working on improving software engineering to enhance usability, streamline implementation, and extend the approach to different diseases and novel geographic settings. The lecture was followed by an interactive question and answer session wherein the attendees raised their doubts and Professor Wimberly provided insightful responses to all the queries. The session concluded with a vote of thanks from Dr Sharma to the speaker and the attendees.

Research in Spotlight

Melissa D. Conrad *et al.*, *N Engl J Med* 2023. Evolution of Partial Resistance to Artemisinins in Malaria Parasites in Uganda.



Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2211803

Initially a cause for concern only in Southeast Asia, the establishment of partial resistance to artemisinins has recently been recognized as a growing challenge in East Africa. This form of partial resistance, characterized by delayed parasite clearance following treatment, is primarily driven by genetic mutations within the kelch protein K13 (PfK13). There is a scarcity of long-term data pertaining to the development and dissemination of artemisinin resistance in Africa.

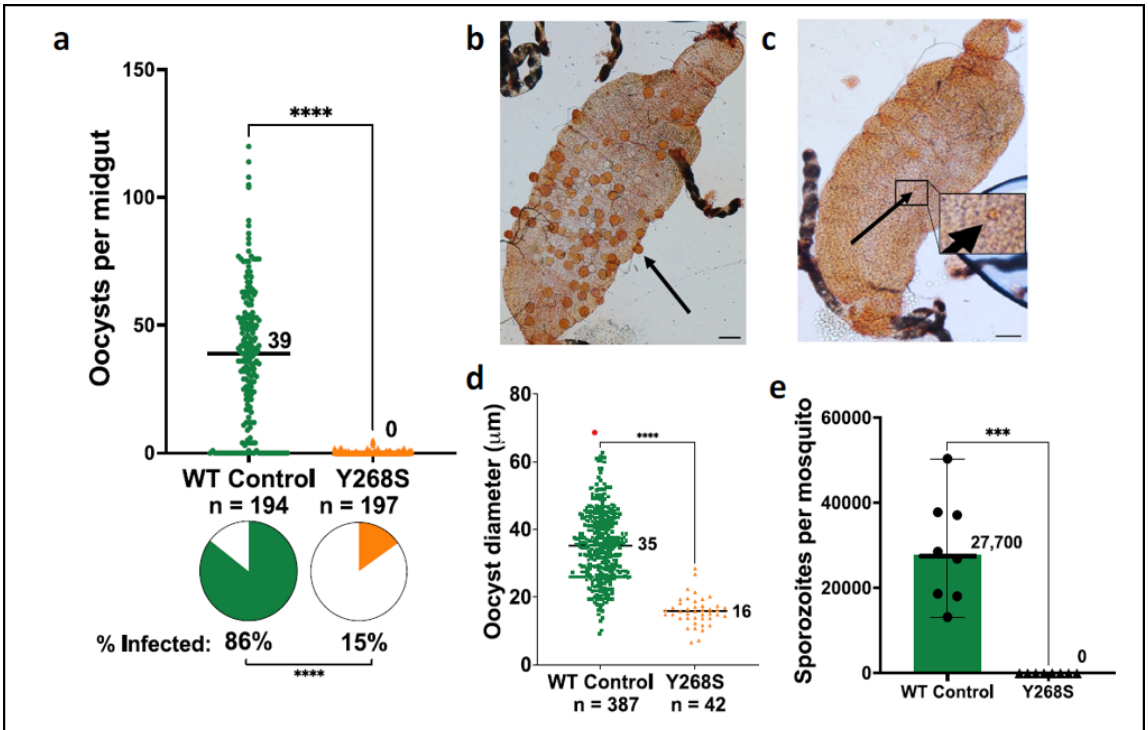
The study by Conrad *et al.* carried out in Uganda between 2016 and 2022 observed the emergence and spread of partial resistance in the malaria-causing agent, *Plasmodium falciparum*, against combination therapy based on artemisinin. The study included an annual surveillance programme that covered 10–16 surveillance sites and focused on Ugandan cases of uncomplicated malaria. The scientists meticulously observed the emergence and spread of this resistance by using genetic sequencing of the PfK13 gene and molecular analysis to investigate genetic relatedness.

In 11 of the 16 districts under surveillance, the prevalence of parasites carrying confirmed or putative resistance markers was higher than 20% as of 2021–2022. Notably, in 2016–2017, mutations such as PfK13 469Y and 675V first surfaced in far northern Uganda. From there, they spread throughout a large portion of northern Uganda, where their prevalence rates

ranged from 10% to 54%. In addition, the 469F mutation became more prevalent, reaching a prevalence of 38% to 40% in one district in southwest Uganda in 2021–2022. First discovered in southeastern Uganda in 2021, the 561H mutation—which had previously been documented in Rwanda—had a prevalence of 23% by 2022. In addition, the 441L mutation started to become common in 2022, with prevalence rates in three regions in western Uganda ranging from 12% to 23%.

These mutant parasites originated locally and have no relation to those found in Southeast Asia. It was discovered that resistance mostly emerged in regions with unstable malaria transmission or where effective malaria management tactics had been abandoned. The study's findings demonstrate the critical need for continuing surveillance initiatives and the creation of plans to stop the spread of artemisinin resistance across Uganda and East Africa. The effectiveness of essential antimalarial drugs is declining in this region, necessitating immediate attention and action.

Victoria A. Balta *et al.*, *Nat Commun* (2023). Clinically relevant atovaquone-resistant human malaria parasites fail to transmit by mosquito.



Source: https://www.nature.com/articles/s41467-023-42030-x

Long-acting injectable medications like atovaquone have the potential to act as a "chemical vaccine" for malaria, combining the effectiveness of drugs with the durability of vaccines. However, the emergence and transmission of drug-resistant parasites pose a significant concern. Previous laboratory studies have suggested that atovaquone-resistant parasites

have disadvantages in mosquitoes, but the lack of data on clinically relevant *Plasmodium falciparum* strains has hindered the integration of these findings into drug development decisions.

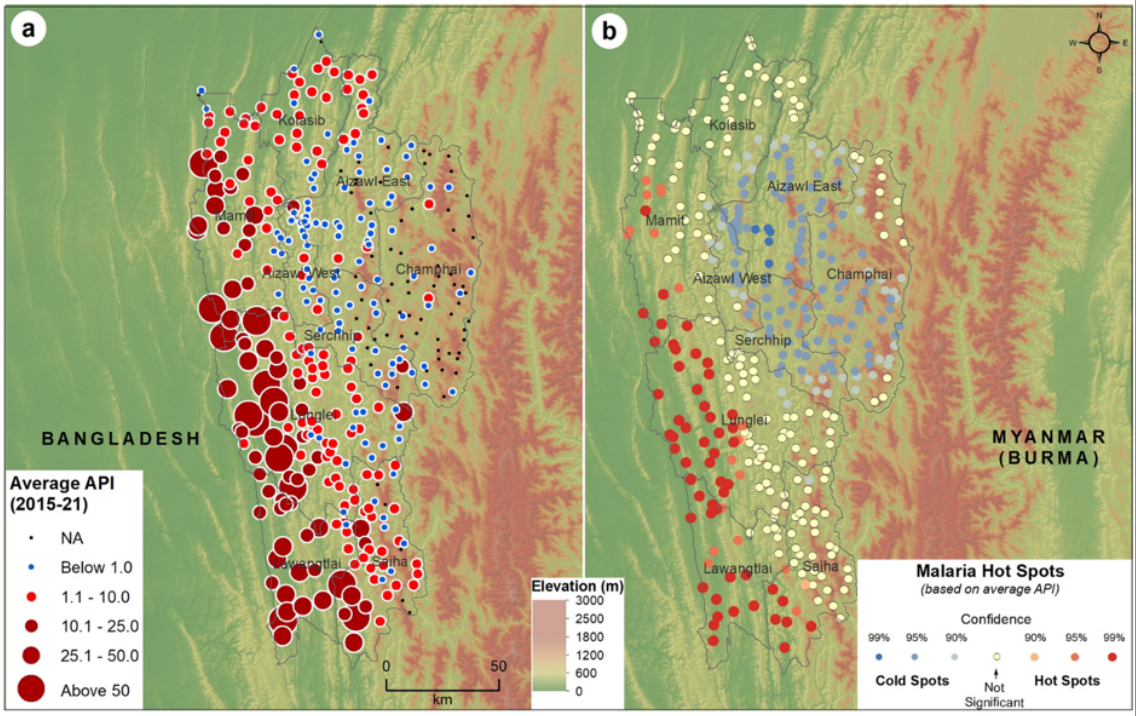
In this paper, Balta VA *et al.* investigated the ability of atovaquone-resistant strains of human malaria parasites to transmit from humans to mosquitoes with the aim of understanding the transmission potential of drug-resistant malaria strains, which has crucial implications for malaria control efforts.

The malaria parasites acquire atovaquone resistance due to the Y268S mutation in cytochrome b. The resistant strains were produced *in vitro*, and molecular and phenotypic characterization were used to confirm resistance. The laboratory-bred mosquitoes were fed on the blood of infected individuals. Mosquitoes were then dissected at different time points, and various parameters related to the parasite's development and prevalence were assessed.

The results of the study indicated that the atovaquone-resistant malaria parasites failed to establish infection within mosquito vectors. The prevalence of these resistant strains in mosquitoes was significantly lower compared to the wild-type (non-resistant) strains. Additionally, the midgut of the mosquito was impaired, which prevented the formation of resistant parasites and prevented transmission.

Several factors were found to contribute to the reduced transmissibility of atovaquone-resistant malaria parasites. Firstly, the replication ability of these strains within the mosquito midgut was impaired, leading to a lower number of oocysts. Furthermore, the parasites' overall fitness within the mosquito vector appeared to be impacted by the resistance mutations in the cytochrome b gene. These results emphasize the importance of drug resistance in controlling the dynamics of malaria transmission.

Lalmalsawma P. *et al.*, *Sci Rep* 2023. Malaria hotspots and climate change trends in the hyper-endemic malaria settings of Mizoram along the India–Bangladesh borders.



Source: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0287667

Malaria remains a significant public health concern in Northeast India region, and understanding its relationship with environmental factors is crucial for effective control and prevention measures. In this study, Lalmalsawma *et al.* investigated the dynamics of malaria and its correlation with climate change trends in the state of Mizoram, located in Northeast India along the border with Bangladesh.

The research was conducted over several years, utilizing data from 1996 to 2019, to analyze the trends and hotspots of malaria incidence. The study adopted a comprehensive approach, combining climate data, topography, land-use patterns, and epidemiological data to provide a holistic understanding of malaria dynamics in the region.

One of the key findings of the study was the identification of malaria hotspots in Mizoram, particularly along the India–Bangladesh borders. These hotspots were characterized by consistently high malaria incidence. The research attributed the persistence of these hotspots to various factors, including climate conditions, topography, land-use changes, and human activities. Climatic variables, such as temperature and rainfall patterns, played a significant role in influencing the transmission of malaria in the region.

Climate change trends were also a focal point of the study. It was observed that the region had experienced changes in temperature and rainfall, which, in turn, impacted the malaria transmission patterns. The research highlighted that rising temperatures and altered

precipitation patterns could potentially expand the geographical range of malaria, making previously non-endemic areas more susceptible to the disease.

The study emphasized the importance of adapting malaria control strategies to the changing climate conditions in Mizoram. Such adaptations could include the modification of intervention programs, changes in mosquito breeding site management, and the development of early warning systems that can predict malaria outbreaks based on climate data.

In conclusion, the research sheds light on the complex interplay between malaria transmission and climate change trends in the hyper-endemic settings of Mizoram, India, particularly along the India–Bangladesh borders. Identifying malaria hotspots and understanding the climate-related factors contributing to its persistence are critical steps toward the development of more effective and targeted control and prevention measures in the face of evolving environmental conditions. This study underscores the importance of proactive measures to mitigate the impact of climate change on malaria dynamics in the region.

Malaria Scientist to Watch:
An interview with Dr Deepak Upadhyay

Dr Deepak Upadhyay
Professor,
Department of Community Medicine,
Rohilkhand Medical College and Hospital, Bareilly

1. As a clinician, what inspired you to embark on research endeavors in the field of malaria?

As a clinician, my decision to embark on research endeavors in the field of malaria was inspired by several compelling factors. First and foremost, my experiences working directly with patients affected by malaria brought to light, the profound and devastating impact this disease has on individuals, families, and communities, particularly in regions with high malaria prevalence *i.e.* endemic blocks of Bareilly. Witnessing the suffering and loss of life first-hand served as a powerful motivation to seek solutions beyond clinical treatment alone. In addition, collaboration with apex organization MERA-India, other researchers, and the opportunity to engage in interdisciplinary projects is both professionally rewarding and personally fulfilling.

2. Can you discuss the importance of early diagnosis and prompt treatment in malaria control, and how is this emphasized in public health programs?

Early diagnosis and prompt treatment are cornerstone strategies in the control of malaria, playing a crucial role in reducing the burden of this devastating disease. Early diagnosis & treatment strategy in malaria control under National Center for Vector Borne Diseases Control can be helpful in

a. Preventing Severe Complications: Timely diagnosis and treatment can prevent this progression, potentially saving lives.

b. Interrupting Transmission: Rapid diagnosis and treatment not only save individual lives but also interrupt the transmission cycle of the disease. When infected individuals are treated promptly, they become less likely to serve as reservoirs for the malaria parasite, reducing the risk of transmission to others through mosquito vectors.

c. Reducing Economic Burden: Malaria takes a heavy toll on economies by causing illness, reducing productivity, and increasing healthcare costs. Early diagnosis and treatment help minimize the economic burden by reducing the duration of illness and the need for extensive medical care.

d. Preventing Drug Resistance: Delayed or incomplete treatment can contribute to the development of drug-resistant malaria parasites. This underscores the importance of promptly treating individuals to reduce the risk of drug-resistant strains emerging and spreading.

e. Education and Awareness: Early diagnosis of malaria in the vicinity gives an opportunity to educate other members of the community about other aspects of malaria like symptoms of malaria, the importance of seeking medical care, and adhering to treatment.

3. What is the role of partnerships and collaboration between healthcare institutions, government agencies, and non-governmental organizations in addressing malaria from a public health perspective?

Partnerships and collaboration among healthcare institutions, government agencies, and non-governmental organizations play a pivotal role in addressing malaria from a public health perspective. Here are several key roles these partnerships fulfill:

a. Resource Pooling

b. Increased Reach

c. Expertise and Research

d. Advocacy and Public Awareness

e. Data Collection and Surveillance

f. Policy Development and Implementation

g. Capacity Building

h. Emergency Response

i. Funding and Donor Coordination

j. Sustainability

In summary, by leveraging each entity's strengths and resources, these collaborations create a more comprehensive and effective approach to combat this disease, ultimately working towards the goal of malaria control and, eventually, its eradication.

4. In your opinion, what are the most significant gaps or areas that need improvement in malaria control and prevention in your region?

In Bareilly region, malaria control and prevention have made substantial progress in recent years, but several significant gaps including access to health care services, vector control, quality assurance of rapid diagnostic testing by Accredited Social Health Activists (ASHA), Climate Change and Environmental Factors, Effective data collection and surveillance systems, Integration of Services, Conflict, and Humanitarian Settings, Political Will and Leadership. Out of these 2 most important gaps in my point of view are:

a. Access to Healthcare Services: In Bareilly, previous Primary Health Centres (PHCs) have been upgraded to Community Health Centres (CHCs) due to population under coverage but still no PHC has been constructed. Moreover, these CHCs still lack manpower as well as infrastructure as per the Indian Public Health Standards. Due to increased urbanization, services being provided as per rural requirement needs to be changed.

b. Community Education and Awareness: Raising awareness about malaria, its symptoms, and preventive measures is crucial. Misconceptions, stigma, and low health literacy can hinder prevention efforts. Misconception about susceptibility is the major behavioral factor in the utilization of services in national programs.

Additionally, it's crucial to tailor interventions to the specific needs and conditions of each malaria-endemic region, as the challenges can vary significantly from one location to another.

5. In your view, how does MERA-India contribute to India's endeavors in achieving its malaria elimination goals?

MERA India's establishment was a significant and transformative step towards advancing efforts to eliminate malaria in India. MERA India has contributed in several crucial ways:

a. Research and Development

b. Data Collection and Analysis: MERA India has streamlined and coordinated data collection and analysis efforts, ensuring the availability of accurate and up-to-date information about malaria cases, transmission patterns, and trends.

c. Capacity Building: This includes training researchers, healthcare professionals, and community health workers to enhance their skills and knowledge.

d. Collaboration and Partnerships

e. Policy Development

f. Advocacy and Resource Mobilization

g. Coordination of Efforts

h. International Collaboration

In conclusion, MERA India serves as a vital catalyst in the pursuit of malaria elimination. Through research, data-driven decision-making, capacity building, and collaborative efforts, such an agency can help India develop and implement comprehensive strategies to combat and eventually eliminate malaria.

Malaria Through the Lens of Researchers

In the present edition, we are showcasing another shortlisted entry from the MERA-India Image Competition 2022, which has been submitted by Ms. Pooja, a PhD scholar representing the National Institute of Malaria Research (NIMR) in Dwarka, Delhi.

Image title: “Using Thermal Imager Infrared Cameras in Malaria Surveillance”

A brief description of the image is as follows:

Set up for malaria screening through Rapid diagnostic tests and fever surveillance during COVID-19 using thermal imager infrared cameras as a new and safe technique for screening of large population. This picture was taken during a survey of the project entitled ‘Transmission of malaria during a pilgrimage walk in western Rajasthan’ in arid regions of district Jaisalmer. The use of thermal scanners and RDT enhances the prospect of malaria screening on a large scale.

Upcoming Event

Lecture Series on Infectious Diseases 2.0: Lecture 11 by Professor Sunil Parekh

The 11th lecture in the ICMR-NIMR and MERA-India "Lecture Series on Infectious Diseases 2.0," will be delivered by Professor Sunil Parikh from the Yale School of Public Health, USA. The research interest of Professor Parikh is translational studies on malaria in sub-Saharan Africa. His research focuses on several aspects of malaria: early host immune responses to infection, human genetics, and treatment. Professor Parikh has projects in a number of African states, such as Uganda, Burkina Faso, and Nigeria. He obtained his Doctor of Medicine degree at Johns Hopkins University School of Medicine and completed residency training with Beth Israel Deaconess Medical Center. He joined the University of California, San Francisco (UCSF) faculty after completing his residency in infectious diseases at UC San Francisco, followed by a Master's degree in public health from UC Berkeley. He recently joined the Department of Epidemiology of Microbial Diseases at the Yale School of Public Health.

More information on the lecture will be made available through the ICMR-NIMR and MERA-India's official website (https://meraindia.org.in/) and social media accounts. Be sure to keep an eye out on these platforms to stay informed about this event. We look forward to your participation in this upcoming session.

To receive regular updates about the events being organized by MERA-India, please subscribe at https://www.meraindia.org.in/event_sub.

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