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MALARIA: CURRENT SCENARIO AND RARE COMPLICATIONS

According to the World Malaria Report 2021 (World Malaria Report 2021, Geneva, World Health Organization 2021.), India represents 3% of the global malaria burden. Despite being the highest malaria burden country of the South East Asia Region, India showed a reduction in reported malaria cases of 49% and deaths of 50.5% compared with 2017. Worldwide, in 2020, there were an estimated 241 million malaria cases and 6,27,000 deaths due to malaria. In 2020, there were 14 million more malaria cases and 69,000 more deaths than in 2019. Two-thirds of these deaths were attributed to disruption during the COVID-19 pandemic. The WHO African Region remains one of the hardest hit malaria areas with 95% of all malaria cases and 96% of all malaria deaths.

This Year's Report at a Glance

Emergence of partial resistance to artemisinin in the WHO African Region. Recent evidence of the independent emergence of artemisinin and partial resistance in the WHO African Region is of great global concern.

WHO recommendation on the use of the RTS, S/AS01 malaria vaccine

Data from the pilot introductions have shown that the vaccine has a favorable safety profile; significantly reduces severe, life-threatening malaria; and can be delivered effectively in real-life childhood vaccination settings, even during a pandemic. On 6 October 2021, WHO recommended that the RTS,S malaria vaccine be used for the prevention of *Plasmodium falciparum* malaria in children living in regions with moderate to high transmission.

Trends in the Burden of Malaria

Twenty-nine countries accounted for 96% of malaria cases globally, and six countries—Nigeria (27%), the Democratic Republic of the Congo (12%), Uganda (5%), Mozambique (4%), Angola (3.4%) and Burkina Faso (3.4%)—accounted for about 55% of all cases globally.

The WHO South East Asia Region accounted for about 2% of the burden of malaria cases globally. Malaria cases reduced by 78%, from 23 million in 2000 to about 5 million in 2020. Malaria case incidence in this region reduced by 83%, from about 18 cases per 1000 population at risk in 2000 to about three cases in 2020. India accounted for 83% of cases in the region. Sri Lanka was certified malaria free in 2016 and remains malaria free.

Malaria Deaths

In the WHO South East Asia Region, malaria deaths reduced by 75%, from about 35,000 in 2000 to 9,000 in 2020. India accounted for about 82% of all malaria deaths in the WHO South East Asia Region.

Severe Malaria

Severe malaria is multi-syndromic and often manifests as cerebral malaria, severe malaria anemia and respiratory distress. Mortality is high if severe malaria is not promptly and effectively managed. The distribution of severe malaria syndromes varies by age across transmission intensities, influenced mainly by changes in community-level immunity patterns.

High Burden to High Impact (HBHI) Approach

Between 2019 and 2020, all HBHI countries except India reported increases in cases and deaths (and in India, the rate of reduction decreased compared with pre-pandemic years). Overall, malaria cases in HBHI countries increased from 150 million cases and 3,90,000 deaths in 2015, to 154 million cases and 3,98,000 deaths by 2019, and to 163 million cases and 4,44,600 deaths in 2020.

Investments in Malaria Programs and Research

The Bill & Melinda Gates Foundation has been another major player, investing US$ 1.8 billion (25% of all malaria R&D funding) between 2007 and 2018, and supporting the clinical development of key innovations such as the RTS, S vaccine.

Progress towards the Global Technical Strategy (GTS) Milestones of 2020

Forty countries (43%) that were malaria endemic in 2015 achieved the GTS mortality milestone for 2020, with 32 of them reporting zero malaria cases.

The WHO South East Asia Region met the GTS 2020 milestones for both mortality and morbidity. All countries in the region except Bhutan and Indonesia reduced case incidence and mortality by 40% or more.

Biological Threats

Deletions in the parasite's *pfhrp2* and *pfhrp3* (*pfhrp2/3*) genes renders parasites undetectable by Rapid Diagnostic Tests (RDTs) that are based on histidine-rich protein 2 (HRP2).

Alternative RDT options (e.g. based on detection of the parasite's lactate dehydrogenase) are limited; in particular, there are currently no WHO-prequalified non-HRP2 combination tests that can detect and distinguish between *P. falciparum* and *P. vivax*.

Parasite Resistance to Antimalarial Drugs

Antimalarial drug efficacy is monitored through therapeutic efficacy studies (TES), which track clinical and parasitological outcomes among patients receiving antimalarial treatment.

In the WHO African Region, the first-line treatments for *P. falciparum* include artemether–lumefantrine (AL), artesunate–amodiaquine (AS–AQ), artesunate–pyronaridine (AS–PY) and dihydroartemisinin–piperaquine (DHA–PPQ).

In the WHO South East Asia Region, first-line treatments for *P. falciparum* include AL, AS–AQ, AS–PY, artesunate plus sulfadoxine–pyrimethamine (AS+SP) and DHA-PPQ.

Vector Resistance to Insecticides

Globally, resistance to pyrethroids—the primary insecticide class currently used in Insecticide-treated mosquito Net (ITNs)—is widespread, being detected in at least one malaria vector in 68% of the sites for which data were available. Resistance to organochlorines was reported in 64% of the sites. Resistance to carbamates and organophosphates was less prevalent, being detected in 34% and 28% of the sites that reported monitoring data, respectively.

Rare Complications of *Falciparum* Malaria in Adults

"Rare Complications" have been reported in the literature among the adult malaria cases:
Post-malarial Neurological Syndrome (PMS),[1] Bil foot drop,[2] Acute hemorrhagic leukoencephalitis (AHLE/Hurst's disease),[3] strokes with neuro-deficits (bleed, cortical/cerebral venous thrombosis)[4], Post-cerebral malaria residual neuro-deficits,[5] psychosis, neurosis, parkinsonism, encephalopathy, tremors, ataxia, frontal lobe syndrome,[6] spinal cord disorders & polyneuropathy, bilateral optic neuritis and Guillain–Barre syndrome.

Complications in abdomen (spleen/liver/pancreas) include: Splenic abscess/infarction & rupture,[7] bowel ischemia,[8] cholestatic jaundice, malaria hepatitis and pancreatitis.[9]

Malaria co-infections include: Dengue & Malaria, Malaria & Salmonella, Malaria & Leishmaniasis, Malaria & Hepatitis B/E.

Cardiovascular system complications of malaria include: Symmetric peripheral gangrene, pericardial effusion,[10] myocarditis,[11] global, left ventricular hypokinesia and refractory hypotension.

Hematological complications of malaria include: Disseminated intravascular coagulation with purpura fulminans,[12] hemophagocytic lymphohistiocytosis (HLH).[13]

Eye complications of malaria include: Retinal hemorrhage, malarial retinopathy.[14]

Acute cortical necrosis is a rare renal complication.

Acute lung injury—Acute Respiratory Distress Syndrome (ARDS) is a well-recognized rare complication seen in severe malaria cases.

The miscellaneous complications include: Toxic shock syndrome, rhabdomyolysis, pyrexia of unknown origin (fever >1 year), cervical lymphadenopathy.

Rare Complications Reported in *P. vivax* and *P. ovale* Malaria Cases

Occurrence of intracerebral bleed, right hemiparesis and seizures[4] and spontaneous chronic subdural hematoma following *P. vivax* malaria are rare associations.[5]

The rare abdominal complications include: Splenic rupture during acute malaria mostly in non-immune adults of *P. vivax*, *Plasmodium ovale* (*P. ovale*) infections. Splenic abscess in *P. vivax* malaria with secondary *Escherichia coli* infection has been reported.[7]

Only three cases of malarial hepatitis caused by *P. vivax* have been reported in the world.

Myocarditis complicating *P. vivax* malaria is an extremely rare complication.[11]

Hemophagocytic lymphohistiocytosis (HLH) is a rare but potentially fatal association with *P. vivax* malaria.[13]

Rare renal complications include *P. ovale* infection complicated with jaundice, thrombocytopenia, hypotension and acute renal failure.[15]

P. vivax and hepatitis E co-infection is a rare cause of malarial jaundice.[16]

Rare toxic shock syndrome can occur in *P. vivax* malaria which presents with clinical pictures of toxic shock, DIC, marked thrombocytopenia, oliguric renal failure, and pulmonary edema.

Retinal hemorrhage: In *P. vivax* infection,[17] retinal hemorrhage is very rare; only five cases have been reported in the literature.

CONCLUSION

There has been an increase in incidence of malaria and its systemic complications in the last 20 years. Clinicians in general should be aware of rare complications of such an infection. There are no reliable markers to diagnose these complications. Clinical suspicion is important in identifying such complications.

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