

REVIEW

An epidemiological overview of malaria in Bangladesh



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Summary Bangladesh is one of the four major malaria-endemic countries in South-East Asia having approximately 34% of its population at risk of malaria. This paper aims at providing an overview of the malaria situation in this country. Relevant information was retrieved from published articles and reports in PubMed and Google Scholar.

Malaria in Bangladesh is concentrated in 13 districts with a prevalence ranging between 3.1% and 36%, and is mostly caused by *Plasmodium falciparum*. Geographical conditions pose a potential risk for *Plasmodium knowlesi* malaria. Resistance to a number of drugs previously recommended for treatment has been reported. Low socio-economic status, poor schooling and close proximity to water bodies and forest areas comprise important risk factors.

Despite the significant steps in Long Lasting Insecticide Net (LLIN)/Insecticide Treated Net (ITN) coverage in Bangladesh, there are still many challenges including the extension of malaria support to the remote areas of Bangladesh, where malaria prevalence is higher, and further improvements in the field of referral system and treatment.

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Introduction

Genetic research suggests that human malarial parasites might have originated some 2–3 million years ago, although some studies propose a later appearance of malarial pathogens in human populations, perhaps 10,000 years back.^{1,2} Since then, malaria has established itself as a major cause of morbidity and mortality globally. The recent World Health Organization (WHO) estimates showed that 106 countries were malaria-endemic in 2010, and more than 3.3 billion people worldwide were likely to get a malarial infection that year.^{1,3} The global malaria trends show a decline in the percentage of population exposed, at least up to 1994, but the total number of people at risk for malaria has never declined since 1900.^{1,3}

The burden of malaria is significant in South-East Asia, which follows Africa in terms of reported malaria cases; almost 70% of a total of 1.8 billion people living in this region are at risk of malaria.^{1,3} All the countries in the area except the Maldives are malaria endemic. Cases of malaria in South-East Asia account for approximately 15% of the global toll and 38,000 people died from malaria in 2010.³ In addition, these numbers may be even higher because existing surveillance systems suffer from substantial under-reporting.⁴ Conversely, signs of reduction have been observed in both malaria cases and deaths over the last years as depicted in Fig. 1.⁵

Bangladesh is one of the four major malaria endemic countries in the region with approximately 34% of its population at risk of malaria.^{3,6} Given the high burden of malaria in Bangladesh and the lack of recent comprehensive epidemiological reviews, in the current paper we try to describe the dynamics of malaria transmission in Bangladesh, explain trends and suggest measures for a better response.

Methods

Relevant information was retrieved from published articles and reports. Electronic databases (PubMed and Google Scholar) were searched using the terms: "Malaria" combined with "Bangladesh" (last search: February 07, 2012).

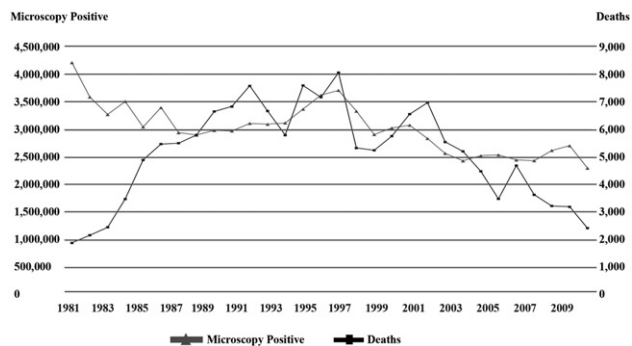


Figure 1 Malaria microscopy positive cases and deaths in South-East Asia, 1981–2010.

Results

Malaria endemicity in Bangladesh

More than 10 million people of Bangladesh are at high risk for malaria.³ The steady rise of the prevalence of malaria in Bangladesh has partly been attributed to the 1985 ban on use of dichlorodiphenyltrichloroethane (DDT), to the discontinuation of malaria eradication program and to the large-scale population movements during the war of independence.^{7,8} Malaria is not epidemic in the general population of Bangladesh.^{9,10} However, certain areas of the country are more affected. Most of the malaria cases in Bangladesh (95–98%) originate from 13 Eastern and South-Eastern districts with overall weighted prevalence rates ranging from 3.10 to 3.97%.^{3,6,7,11–14} The Chittagong Hill Tracts (CHT) area in particular is hyperendemic with a prevalence of 11% or even higher.^{11,15–18} Among the three Hill Tract districts (Khagrachari, Rangamati, and Bandarban), an extremely high prevalence (36%) has been recorded in a sub-district of Bandarban.¹⁶ A total of 55,873 probable and confirmed malarial cases have been reported in Bangladesh in 2010.^{3,19} The trend of malaria in Bangladesh since 1990 is summarized in Fig. 2.³ The spread of the parasite can be explained by the Bangladesh's borders in the East and North-East with India and in the South with Myanmar, where malaria prevalence is much higher. As a matter of fact, Indian areas in that region have an Annual Parasite Incidence (API) of more than 5, while approximately 50% of the population in Myanmar is at high risk for contracting malaria.^{3,20}

Major malarial parasites in Bangladesh

Malaria in Bangladesh is mostly caused by *Plasmodium falciparum* with estimates ranging between 54% and 93%.^{3,6,7,11,17,21,22} However, the lowest figures had been observed almost a decade ago, which indicates an increasing trend in malaria cases from *Plasmodium falciparum*.^{3,22} This upwards shift has been attributed to human residence in forest areas, which explains why malaria is hyperendemic in

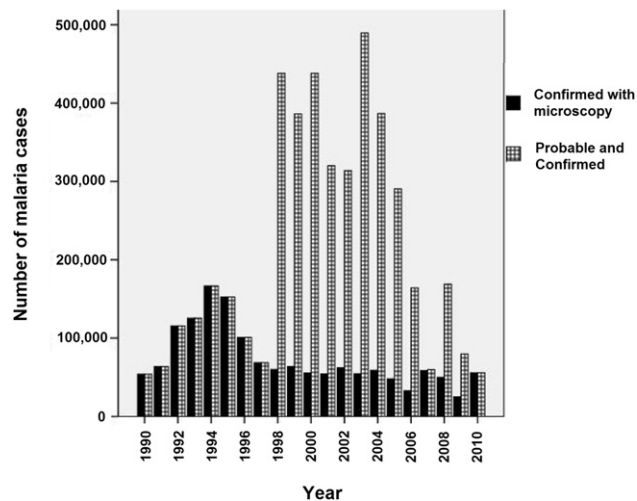


Figure 2 Malaria trend in Bangladesh, 1990–2010.

CHT.³ *Plasmodium vivax* causes now less than 20% of all malarial cases in Bangladesh.^{16,21,22} Mixed infections of *P. falciparum* and *P. vivax*, and cases with *Plasmodium malariae* have also been identified.^{11,16,21–24} The first infection with *Plasmodium ovale* was reported in 2010, which now accounts approximately for 1.6% of all malaria cases in Bangladesh.^{21,25} Recently, *Plasmodium knowlesi* has been suggested as the fifth malarial pathogen in humans, based on tests of human cases and archived blood.^{26–29} Though *P. knowlesi* has not been found in Bangladesh, which could possibly be due to difficulties in distinguishing it from *P. malariae* and in identifying it by microscopy, this new malaria parasite is of great public health concern because it can cause severe and fatal malaria.^{26,27,29,30} Myanmar, a smaller part of India and a significant part of Bangladesh have been mapped within the geographic distribution of *Anopheles leucosphyrus*, the main vector for *P. knowlesi*. Moreover, several Macaque species including usual hosts of *P. knowlesi* have their habitats in Bangladesh. *Macaca fascicularis*, one of the critically endangered Macaque species, is known to live in the wild in extreme southeastern areas of the country.^{21,27}

Malaria vectors in Bangladesh

Out of 41 dominant malaria vector species globally, 34 have been reportedly found in Bangladesh. Among these, *Anopheles (An) dirus*, *An. minimus*, *An. philippinensis*, and *An. sundaicus* are deemed as major malaria vectors in Bangladesh.^{3,6,13,25,31,32} *An. vagus* has also been incriminated as important vector in some studies.^{6,33,34} Other species in Bangladesh implicated in malaria transmission include *An. karwari*, *An. maculatus*, *An. barbirostris*, *An. nigerrimus*, *An. aconitus*, *An. annularis* and *An. baimaii*.^{6,35–37}

Seasonality of malaria in Bangladesh

Appropriate understanding of seasonal patterns is important, especially in terms of strategic preparedness and resource allocation. Malaria peaks during the monsoon in Bangladesh (between May and October) with the highest incidence being in June/July, which might extend up to September, and the lowest being in November.^{6,15,25,38}

Diagnosis of malaria

Microscopic examination has long been recommended as the gold standard for the diagnosis of malaria.³⁹ Yet, other diagnostic methodologies have appeared including the Rapid Diagnostic Test (RDT), which has shown superior properties in identifying symptomatic malaria cases with low parasitaemia over microscopic examination. Nested Polymerase Chain Reaction (PCR) is also a very accurate malaria diagnostic.⁴⁰ These tools might not be suitable or affordable in resource-poor settings like Bangladesh but modified tests can be promising alternatives.⁴¹ Blood slide analysis is no longer used to document malarial fever episodes in Bangladesh but only to support early diagnosis and prompt treatment.⁴² The positive predictive value of earlier approaches to malaria diagnosis in Bangladesh including simple clinical and epidemiological criteria has been proved to be very low (32%) and much lower for

P. vivax (14%), findings that suggested the incorporation of laboratory procedures for confirmatory diagnosis.⁴³ Indeed, locally available commercial RDTs were highly sensitive (94.6%) and specific (88.5%) in diagnosing falciparum cases.^{6,39} Immuno-Chromatographic Test (ICT) has shown sensitivity and specificity of 93.22% and 94.87%, respectively, for antigen detection and 89.83% and 87.17%, respectively, for antibody detection.⁴⁴ "Pigments in peripheral leucocytes" were proved to be superior over "conventional routine malaria microscopy", "prolonged microscopy", "dipstick antigen capture assay (Para Sight TM-F test)" and "routine microscopy repeated at 12 h interval" at initial evaluation of cerebral malaria at a tertiary level hospital in Bangladesh, while another study suggested the use of dipstick test as the best option in the initial assessment of falciparum malaria.^{45,46}

Predictors of mortality in severe malaria

Several prognostic factors have been associated with higher mortality among severe malaria cases in Bangladesh. These include multi-organ manifestations, in-hospital complications, and laboratory variables e.g. high parasite count, low blood glucose level, and raised Cerebrospinal Fluid (CSF) protein levels.⁴⁷ Increasing values on the 5-point Coma Acidosis Malaria score (CAM), which is based on cerebral malaria and acidosis (base deficit), have also been independently related with higher mortality.⁴⁸

Drugs for malaria treatment

Nationally, artemether–lumefantrine is used as first-line treatment for falciparum malaria, and doxy cycline + quinine, and tetracycline + quinine combinations are provided in case of treatment failure in malaria patients with *P. falciparum*. Artemether and quinine are used for the treatment of severe malaria, while chloroquine–primaquine combination (14-day therapy) is administered for vivax malaria.³ Quinine-cotrimoxazole-tetracycline triple drug therapy has been found in 1995 in Bangladesh to significantly reduce deaths among patients with cerebral malaria.⁴⁹ Historically, chloroquine became ineffective in 2001 and a combination of quinine and sulfadoxine-pyrimethamine has been suggested as first-line therapy for better outcomes.⁵⁰ The effectiveness of artemether in the treatment of cerebral malaria in adult patients in Bangladesh was similar to that of parenteral quinine as evidenced by a randomized controlled trial conducted in 2001.⁵¹ In a later study (2005), Coartem (artemether–lumefantrine) and a combination of mefloquine–artesunate showed effectiveness and the research group recommended Artemisinin Combination Therapy (ACT).⁵² Artesunate was well tolerated and reduced mortality in patients with severe falciparum malaria when compared with quinine in an open-label randomized controlled trial in 2005.⁵³ Artemether–lumefantrine combination has been introduced officially in Bangladesh as the first line regimen for treating uncomplicated falciparum malaria in 2005 and has been found highly synergistic in clinical field isolates.⁵⁴ Later, in 2007, azithromycin–dihydroartemisinin combination gave promises for the treatment of falciparum malaria. At

approximately the same time, quinine with a single dose of sulfadoxine–pyrimethamine has been recommended in the absence of ACT.^{55,56} In 2008, researchers found the similar effectiveness of both supervised and non-supervised artemether–lumefantrine in patients with uncomplicated falciparum malaria in Bangladesh.⁵⁷ N-acetylcysteine, though hypothesized to be beneficial in treating severe malaria as an adjunct to artesunate therapy, showed no effect in a randomized, double-blinded, placebo-controlled trial in 2009 involving patients from Thailand and Bangladesh.⁵⁸ In 2010, researchers found that azithromycin–artesunate could be an efficacious and well-tolerated option for uncomplicated falciparum malaria in Bangladesh.⁵⁹ Rectal artesunate reduces the risk of death and permanent disability in people with severe malaria who could not take anti-malarial drugs orally according to a 2009 multi-country randomized controlled trial that included Bangladesh.^{60,61} A combination of dihydroartemisinin and piperazine has been found to be effective in three Asian countries but with few serious adverse effects.⁶² Apart from pharmaceutical agents, medicinal plants have been used for centuries, especially by the indigenous tribal population in the malaria endemic areas of Bangladesh.^{63–69} Previous research has suggested that a number of naturally occurring flavonoids, richly available in plant sources, have been successful even in chloroquine-resistant cases.⁶⁷ Fish and shellfishes have also been reported to be used, as indigenous treatments.⁷⁰

Historical data on resistance to anti-malarial drugs

Drug resistance has attracted medical attention in South-East Asia since 1962, when the first case of resistance to chloroquine was reported in Thailand. Evidence of resistance to chloroquine and sulfadoxine–pyrimethamine in Bangladesh has been reported as early as in 1970 and 1985, respectively.^{5,11,12,71} Resistance to mefloquine has also been recorded. Between 1995 and 1998, a research group found significant resistance to chloroquine among Bangladeshi emigrants to Kuwait.⁷² In a later study of 2003, a substantial percentage of its participants responded (66%) well to chloroquine, but in other studies published in the same year, higher rates of resistance to Chloroquine (84%) and Mefloquine (61%) were recorded.^{22,73,74} Significant failure rates have been observed for the combined therapy of chloroquine and sulfadoxine–pyrimethamine in 1998, 2004, and 2005.^{52,75,76} Another study in 2006 found remarkable failure rates among patients treated with pyrimethamine.⁵⁵ An *in-vitro* study the same year reconfirmed the existence of resistant strains to chloroquine and suggested a combination of sulfadoxine–pyrimethamine with quinine for uncomplicated falciparum malaria.⁷⁷ The Ministry of Health and Family Welfare changed in 2004 the national policy on the treatment of uncomplicated malaria and switched to the effective ACT.⁷⁸ Treatment by unqualified individuals and self treatment by taking medications directly from the drug shops have been reported in 40% of the people from a malaria endemic area in 2009, behaviors and practices that have likely contributed to the large-scale resistance to anti-malarial drugs.¹¹ Quite alarmingly, another publication in 2009 reported a significant decrease in artemisinin

susceptibility.⁷⁹ A 2010 study found a higher prevalence of sulfadoxine–pyrimethamine resistant alleles in *P. falciparum* in Bangladesh.⁸⁰ Finally, while chloroquine–primaquine combination has been in use since 2004, a recent study of 2011 recorded a failure rate of 57.8% in patients receiving this regimen.⁸¹

High-risk groups, treatment seeking behavior and risk factors

Several population groups are vulnerable to malaria including young children, non-immune and semi-immune pregnant women, people with Human Immunodeficiency Virus (HIV) infection, international travelers from non-endemic areas, and immigrants from endemic areas and their children.³ Recent research reported that the prevalence of malaria among pregnant women attending antenatal checkup was close to 4% in the South-East regions of Bangladesh.⁸² The incidence of malaria has been higher in young adults and men were at greater risk than women.^{4,16,83,84}

In terms of behavioral patterns, previous studies revealed that almost one-third of malaria patients in Bangladesh did not seek any therapy and about 12% of them practiced self-treatment, while a significant proportion of people consulted unqualified village doctors.^{11,17,84} Proximity to healthcare facilities run by malaria control programs and drug vendors have been associated with the choice of treatment.¹³

Low socioeconomic status and poor level of education were closely related to insufficient knowledge of Bangladeshi on malaria transmission, prevention and treatment.¹¹ Several risk factors for malaria have been proposed including proximity to water bodies, changes in land use, drug resistance, malaria control programs, environmental changes and climatic factors, number of bed nets, altitude and household density, ethnicity, and proximity to forests.^{9,14–18,85–91}

Complications of severe malaria

Cerebral malaria, serious anemia, malarial hepatitis, and malarial retinopathy (especially in falciparum malaria) were the most common complications seen in Bangladeshi patients with severe disease.^{22,47,92,93} The mortality rates among complicated malaria and cerebral malaria cases in Bangladeshi were 9.25% and 6.17%, respectively.²² Symmetrical upper motor neuron lesion and meningeal irritation and/or meningism have been reported as the most frequently observed neurological findings in cerebral malaria patients.⁹² Finally, in a clinical trial conducted in Bangladesh during 2003–2007, hyponatremia occurred in a substantial number of adults with severe malaria and was paradoxically associated with lower mortality.⁹³

Major malaria outbreaks in Bangladesh

A malaria outbreak in 2005 at Netrakona district resulted in 1087 cases and took away 14 lives. Outbreaks in 2004 at Chittagong, Netrakona, and Cox's Bazar affected 4.1, 2.2 and 1.9 million people, and caused 25, 10 and 168 deaths, respectively. Around 16,000 clinical cases with 177 deaths have been reported in an outbreak in 2002 at the areas of Bandarban, Rangmati, and Khagrachari.⁵

Malaria intervention policies and strategies

Indoor Residual Spray and DDT are not in use as intervention. The national policy of distributing Long Lasting Insecticide Net (LLIN)/Insecticide Treated Net (ITN) to all age groups free of charge has been adopted in 2008. In 2000, the country promoted the use of diagnostic tests for patients of all ages. Bangladesh has also adopted the strategy of using RDTs at community level and providing ACT free of charge for all ages in 2007. Two cross-sectional surveys, conducted in 2008 and 2011, found that LLIN/ITN coverage has reached more than 80% for under-5 children and pregnant women in the high-endemic districts.⁹⁴ The optimal prevention goal of a malaria vaccine has not been achieved yet.⁹⁵ However, a randomized, controlled, double-blinded phase-III trial reported a 50.4% efficacy after 14 months of the first dose of a vaccine.⁹⁶

Major issues and challenges

Major challenges include extending malaria support to the remote areas of Bangladesh, where malaria prevalence is higher, and capacity building at all levels of healthcare facilities. Improvements in the field of referral system and treating severe cases immediately are mandated. Further increase in LLINs/ITNs coverage is crucial while spread of malaria along the border areas with Myanmar and India pose a significant challenge.^{15,97,98}

Conclusions

Malaria in Bangladesh is concentrated in areas along the South-Eastern border of the country. While Bangladesh managed to extend its coverage of RDTs and LLINs/ITNs to significant levels, cross-border malaria and drug resistance to commonly used anti-malarial drugs comprise a major challenge in controlling the disease. Potential for *P. knowlesi* infection is another serious issue. Success in neighbouring countries can point the way to significantly reducing the malaria burden and endemicity. For instance, Maldives has been malaria free since 1984,^{3,99} which became possible through continuous entomological and parasitological surveillance. Community-based approaches were very effective in reducing malaria burden in countries like India, Sri Lanka, Ethiopia, Indonesia and Ghana. Incorporation of such practices, if examined and found feasible in Bangladesh, might be of utmost significance in a successful progression in accord with the Millennium Development Goal (MDG) target.

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Conflict of interest statement

We declare that we do not have any financial or personal conflict of interest.

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