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COMBATING FOREST MALARIA: A MAJOR CHALLENGE IN ELIMINATING MALARIA IN BANGLADESH

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ABSTRACT: Malaria is a major public health concern in tropical and subtropical areas including Bangladesh. The country has a long history of incurring high malaria morbidity and mortality in a heterogeneous transmission dynamics-demographical, spatial, and temporal. Elimination of malaria in Bangladesh remains a prerequisite for promoting better public health, especially in the malaria hotspots in its remote south-east and north-east border areas. The country boasts with the world's largest delta and lengthy monsoons sharing her border with India and Myanmar- additional two endemic countries for malaria in the SEA.With a significant progress in combating malaria in recent past, Bangladesh now envisages to eliminate the disease by 2030. A significant decline in malaria cases and deaths in its plain areas, however is intrigued with in-country as well as cross-border human movement to and from the forests in and around Chattogram Hill Tracts that reportedly works as a source of infections of the disease. This forest malaria remains a significant obstacle to the country's malaria elimination efforts.

Key Words: *Malaria situation, incidence, forest, elimination, Bangladesh*

INTRODUCTION

Malaria is a mosquito borne plasmodial infectious disease that causes significant loss to human lives and properties in the endemic areas in tropical and subtropical region including Bangladesh. In the region, Bangladesh ranks fourth in malaria prevalence behind India, Indonesia, and Myanmar. Historically, the country has had incurred high malaria morbidity and mortality in a heterogeneous transmission dynamics- demographical, spatial, and temporal in its 13 endemic districts with around 14 million population at risk (Karim *et al.*, 2019). Interestingly, the country has dramatically reduced malaria by > 93% from 2008 to 2020 (BRAC, 2020). Following a significant progress across its National Malaria Control Program between 2006 and 2015, Bangladesh now on the way to winning three time bound milestones for making its endemic districts malaria free under the National Malaria Elimination

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programme (Fig.1). But some stray events of sudden enhanced case morbidity in some areas on some occasions, especially in south-eastern part of the country claim for investigating malaria occurrences in an integrated and cross points approach. This would help better understand and track the threats, implications and challenges of eliminating malaria from better interventions in the ongoing elimination efforts. With this end, meta-analysis of malaria screening data, monitoring and/or follow-up reports are highly expected to explore malaria transmission dynamics, demographics, and the associations (risks) finally, to better guide the malaria elimination programme of the country.

Malaria occurrence in Bangladesh has had been a major public health concern for long until a striking fall of the disease burden in the country since after 2010s.: Bangladesh has been a malaria endemic country for long in south-east Asia as asserted by a recent past retrogressive analysis of various data on malaria situation in the country (Islam *et al.*, 2013). Around 34% of its population in thirteen endemic districts remain under malaria risk that contributed to a national malaria prevalence rate between 3.1% and 36% being caused mostly by *Plasmodium falciparum* while the number of reported death from malaria in Bangladesh in 2017 was 13 (Haque *et al.,* 2009, Alam *et al.,* 2010, WHO, 2018, Karim *et al.,* 2019, Kaler Kontho, 2019, 25 April). On seasonality of its transmission, malaria peaks during the wet and humid season of monsoon that largely lasts between May and October (Islam *et al.*, 2013).

In addition to offering suitable transmission bionomics for *P. vivax*, the geographical conditions of the country pose a potential risk for *P. knowlesi* malaria. While reported for some instances of antimalarial resistance, the prominence of lower socio-economic status, individual age factor, heterogeneous transmission between seasons, poor awareness on avoiding mosquito bites, and close proximity to untreated mosquito breeding places with water bodies and forest areas are identified as important risk factors for malaria in the country. But malaria in childhood, especially those under 5 years or pregnancy was not significantly associated as exposure-outcomes risk factors in malaria incidences (Haque *et al.,* 2009).

Keeping aside, relentless antimalarial efforts in Bangladesh has already passed the control phase to embark on the recent elimination goal. Despite a significant success in nationwide peacetime antimalarial campaign, the remote hilly and forested settings on south-east border areas of the country potentially pose hard challenges towards ensuring total elimination of the disease (Karim *et. al.*, 2010). The poor appreciation of the unique bionomics of the forest dwelling infected/infective anopheline mosquitoes and monitoring of the forest travellers with proper anti-mosquito bite measures seemingly adds to the complexities in fighting forest malaria in Bangladesh.

Epidemiologically, the forest travelling adult males in the country's population incur the highest malaria burden. This has added to the threats of sudden malaria outbreak both from local and regional contexts in the south-east Asia. Shifting malaria resources into the country's forested south-east part under an activated surveillance then appears to be the best choice. Strengthening 'test-treat-track' in malaria hotspots, especially for the forest travellers should lead the country's anti-malarial campaign. That treating malaria can offer drug resistance by the plasmodial species, insecticide resistance of the vector mosquitoes, and the issues of relapse, recrudescence, recurrence, or reintroduction, the much needed elimination interventions should be addressed comprehensively in an integrated way. A significant decline in malaria cases and deaths in its plain areas, however is intrigued with in-country as well as cross-border human movement to and from the hilly forests in and around Chattogram Hill Tracts (Figure-2).

MATERIAL AND METHODS

Considering the inquisitive issues in previous section, malaria situation in Bangladesh in relevant instances and settings depicted in literary sources- offline (books, papers, etc.) as well as online (Google scholar) in terms of malaria cases and their relationships (risks) were consulted and reviewed in some epidemiological viewpoints. In the discussion of the literature, at first, the national relevance and implications of malaria elimination in south-east Asia has been focused whilst transmission factors of malaria occurrences are intermingled within a greater cross border area of the three south-east Asian countries- India, Bangladesh, and Myanmar. So, beside unearthing the past instances of malaria occurrences with recurrent forms of epidemics, the impacts and influences of population displacement from the rapid environmental changes, like biological, ecological, social, and political on malaria transmission dynamics were revisited. This integrated approach helped uncover the challenges of eliminating malaria through reviewing and redrawing its transmission figure in the country in a comprehensive and meaningful way.

RESULTS AND DISCUSSION

Various demographic cohorts can be defined based on malaria vulnerability in Bangladesh. In the late 1990s, the overall malaria prevalence in the thirteen endemic districts of the country accounted 3.1% with significantly higher incidence in children. Children under 4 years incurred 8.5% *P. falciparum* prevalence while those in 5-14 year age range counted 6.6%. Prevalence of *P. vivax* in males and females were 0.15% and 0.27% respectively in males and females. Prevalence of mixed infections in females was 0.15% whilst 0.21% in males. This was inconsistent with Haque *et al.* (2009) and Khan *et al.* (2023) that did not find malaria in childhood (especially those under 5 years) or pregnancy to be significantly associated with malaria occurence in the country. Anyway, from interventional points, though Bangladesh has posted significant account in insecticidal bed net coverage, it needs yet to extend malaria support to the country's remote and hard to reach areas including the forested CHTs (Khan *et al.,* 2023).

Malaria incidences in Bangladesh are heterogeneous (clustered) in demographic and spatiotemporal contexts: From vector specificity, *Anopheles baimi, An. philippinensis, An. sundaicus, An. minimus, An. aconitus, An. annularies, An. vagus*, *An. dirus, An. albimanus, An. karwari*, *An. maculatus*, *An. barbirostris*, *An. nigertimus*, and *An. vagus* are found to be prominent anopheline vector species in the country. Interestingly, all these anopheline species are common in India and Myanmar also (Bashar & Tuno, 2010; Dhiman *et al.,* 2018, WHO, 2012) (Table-1). Additionally, considering the porous border with India and Myanmar, Bangladesh potentially faces the threat of trans-border malaria transmission causing epidemics, especially in crisis or emergency situations. Hence, the population of Bangladesh can be divided into three categories, viz. high transmission with > 1 case per 1000 population for 2.1 million, low transmission with 0-1 case per 1000 population for 15.6 million, and malaria free with zero case for 147 million people based on the vulnerability to the risks for malaria transmission (Haque *et al.,* 2009, Noé *et al.*, 2018, Naher, 2021).

Again, on temporal trend, Bangladesh experiences wide fluctuations in malaria transmission with unstable annual case incidence and death rates. On seasonality, malaria peaks during the wet and humid season of monsoon that largely lasts across May to October (Islam *et al.*, 2013; Karim *et al.*, 2019; Maude *et al.,* 2008). Notably, systematic decline in the national malaria incidence figures between 2001 and 2006 was not found. In 2001-2006, a country wide routine surveillance of BRAC and ICDDR, B estimated 2.9 million cases of malaria in Bangladesh defined clinically and/or with RDT or Microscopy (Haque *et al.,* 2009). The study confiremed significant anti-malaria efforts to run in the years through 2001 to 2006 despite missing convincing data on the impacts of such control program. The study constituted a malaria map targeting the endemic areas of Bangladesh and found high malaria prevalence areas to be located along the north-eastern and south-eastern areas of the country. But the country's south-western, and central areas lie under low to moderate prevalence areas (Haque *et al.,* 2009). Interestingly, Maruf (2019) reports 228 malaria mortality in Bangladesh that in 2007. The figure plummeted to 13 in 2017 whilst in 2018, the malaria death was recorded as 7 out of 10523 confirmed cases.

To add, some areas, especially Rangamati and Bandarban near the international border on the country's north-east and south-east part experience high malaria incidence (Haque, 2009; Islam *et al.*, 2013, 2014; Maude, 2008). In following spatiotemporal aspect, Noé *et al.* (2018) found malaria to be highly seasonal and hypo-endemic in a number of geographical hotspots mainly in the hilly south eastern parts of the country that remained constant over 4 years (2013-2016). In another study, 1% annual rate of malaria with 85% of cases in the rainy months of May-October was found in rural Bandarban in 2011 (Khan *et al.,* 2011). On the other hand, the case and death incidences of malaria in Cox's Bazar has declined significantly since 2010 till 2017 despite various shortcomings (Prothom alo, 2017, 25 April). In the district in 2016, 1301 malaria cases with zero mortality were recorded by the office of Cox's Bazar civil surgeon while the death toll of the disease was 188 in 2005 followed by 34, 25, 60, 4, 1, 2 and 1 respectively in 2006, 2007, 2008, 2009, 2010, 2011, and 2012 in the district. The district also experienced no death case from the disease in 2013.

In the first three months of 2017, the case morbidity was 121. This success in reducing malaria incidence in Cox's Bazar can be attributed to large coverage of malaria control program from the use of long lasting insecticide treated nets (LLITNs) and rapid diagnosis with RDT being extended far into the remote areas of hilly and coastal part of the district. This later was done by deploying trained health workers with basic logistic support. Keeping aligned, Anderson *et al.* (2018) showed that in Bangladesh, the proportion of total malaria cases being managed by the private sector other than the NGOs adds 1-10% on top of public sector cases. In addition, subclinical and submicroscopic malaria infections contributes a significant malaria burden of Bangladesh while the infection reservoir misses malaria detection in routine surveillance.

Again, due partially to the chronic maintaining of heterogeneous incidence, a small proportion of the population at risk for malaria in the country suffers most malaria cases. An estimate of 11% of the population in the country's south-east part incurred 80% case incidence whilst 32% of the north-east part's population suffered 80% in 2013-2016 (Okell *et al.,* 2009, 2012, Shannon *et al.,* 2016). This went supportive to Woolhouse *et al.* (1997) that confirmed that the stable malaria hotspots in Bangladesh maintains 20 for 80%, i.e. 20% of the total population at risk suffer 80% of the malaria cases in malaria endemic zones. Corroborative of this figure, Anderson *et al.* (2011) layed out malaria incidence figures in some districts, like in Netrokona, 19 for 80% and in Rangamati, 21 for

80%. However, in north-east part of the country, stable malaria hotspots are identified in the plains to the south of Indian border and west of the Khasi hills.

Table 1. Malaria vectors in and around Bangladesh

Vector	**Location**					**Season**	
	India		Bangladesh		Myanmar (Western Part)	Wet (May-October)	Dry (Nov-Apr)
	East forested	West	Forested North-east	Forested South-east			
An. baimaii	√	√	√	√	√	---	---
An. philippinensis	√	√	√	√	√	---	√
An. sundaicus	√	√	√	√	√	√	√
An. minimus	√	√	√	√	√	√	√
An. aconitus	√	√	√	√	√	√	√
An. annularis	√	---	√	√	√	---	√
An. vagus	√	---	√	√	√	---	√
An. dirus	√	√	√	√	√	---	√
An. jeyporiensis	X	X	√	√	---	---	√
An. karwari	X	X	√	√	---	---	√
An. barbirostris	√	√	---	√	---	---	√
An. wilmori.	√	√	√	√	---	---	---
An. subpictus	√	√	√	√	---	---	---
An. culicifacies	X	√	√	√	√	√	---
An. stephensi	X	√	√	√	---	√	√
An fluviatilis	X	√	√	X	√	√	√

[√- Found, X- Not found, --- Data deficiency] (Adapted from Alam *et al.*, 2010; Bashar & Tuno, 2014)

Table 2. Malaria situation in mostly forested versus non-forested endemic districts of Bangladesh, 2010-2023

Indicators	**Endemic areas**	**Risk status**	**Prevalence, % in 2023**	**Decline to annual malaria case incidence (%) since 2010**	**Overall decline to annual malaria case incidence (%)**
	Khagrachari	High	3	55	
Mostly Forested areas	Rangamati	High	3	57	
	Bandarban	High	2.5	58	63
	Chattogram	Medium	< 1	71	
	Cox's Bazar	Medium	2.7	66	
	Sylhet	Low	< 1	70	
	Moulovi Bazar	Low	< 1	70	
	Sunamganj	Low	< 1	70	
Mostly non-forested areas	Hobiganj	Low	< 1	78	88
	Mymensing	Least	< 0.5	85	
	Netrokona	Least	< 0.1	85	
	Sherpur	No risk	≈ 00	99	
	Kurigram	No risk	≈ 00	99	

(Adapted from Alam *et al.*, 2016, Chang *et al.*, 2019, Haque *et al.*, 2009, 2010,2014, Islam *et al.*, 2013, Karim *et al.*, 2019, Khan *et al.*, 2023, Lu *et al.*, 2020, Maruf, 2019 April 25, Naher, 2021, Noe *et al.*, 2018 Prothomalo, 2017, April 25, Rosenberg & Maheswary, 1982)

The wet land of 'Tanguar Haor' in the study was defined as a malaria hotspot having occupational importance for the local people (Haroon & Kibria, 2017). Apart from, the malaria hotspots in both south-east and north-east areas are deemed to be backed by the transmission biasness among agricultural workers, seasonal forest travelers, and coal miners in and around the areas to drive imported and introduced cases there (NMEP, 2017). By the way, less stable malaria hotspots for any given period belong to the country's north-east area compared with its south-east part (Anderson *et al.,* 2011). An augment to spatial heterogeneity in malaria transmission and the resulting decline in the disease occurence over time should be the best explanation for a relatively unstable and lower malaria incidences in the north-eastern part of Bangladesh**.** With this, the demographic, environmental, and social characteristics of the population at risk in malaria prone areas can potentially complicate the estimates of epidemiological risk factors for malaria (Bannister-Tyrrell *et al.*, 2017).

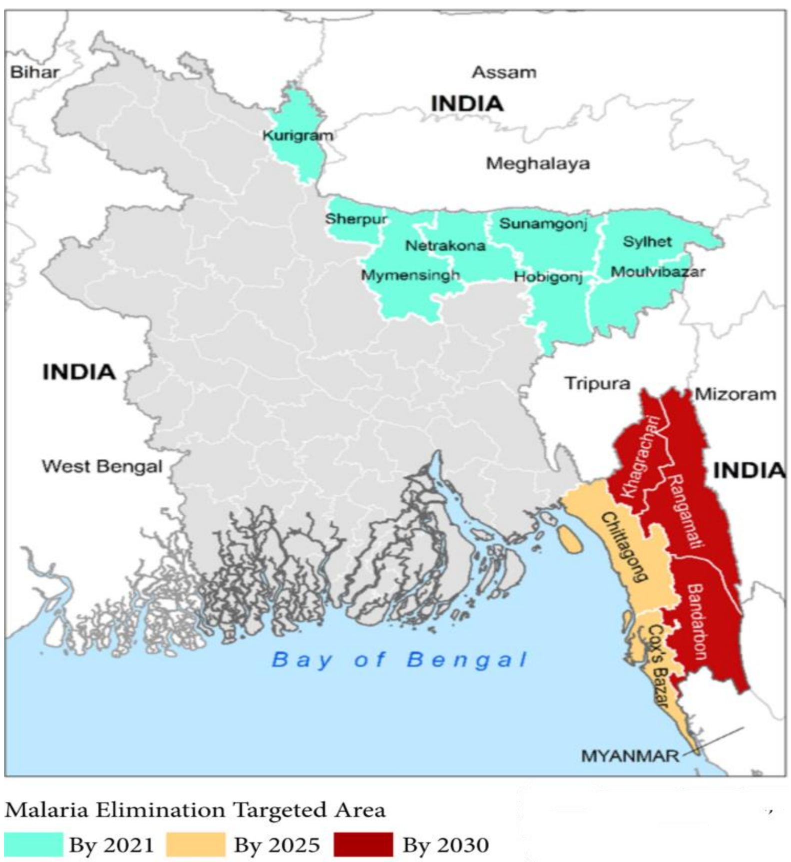

Fig.1. Areas of Bangladesh under elimination programme (Noé *et al.*, 2018)

On a separate note, geographic and seasonal relationships of malaria occurrences in Bangladesh are clustered similar to that in India, i.e., malaria remains concentrated in tribal, inaccessible, and hilly areas of the two countries (Anderson *et al.*, 2011, Wangdi *et al.*, 2016). Interestingly, such instances of the relative proportions of malaria burden among the population at risk reportedly suit in peacetime situations. A stray heterogeneity in malaria situation in Bangladesh is corroborated whist a high trend of seasonal variation, i.e. the temporal association in malaria incidences in the country is also documented (Ahmed *et al.,* 2013; Haque *et al.*, 2013; Khan *et al.,* 2011; Maude *et al.,* 2008). In a clear contrast, Anderson *et al.* (2011) did not find the north-east area of Bangladesh to be within high transmission season spanning between May and October. This could be because of a rapid decline in malaria incidence throughout the country, especially in the north-eastern part following 2010 (Islam *et al.*, 2013).

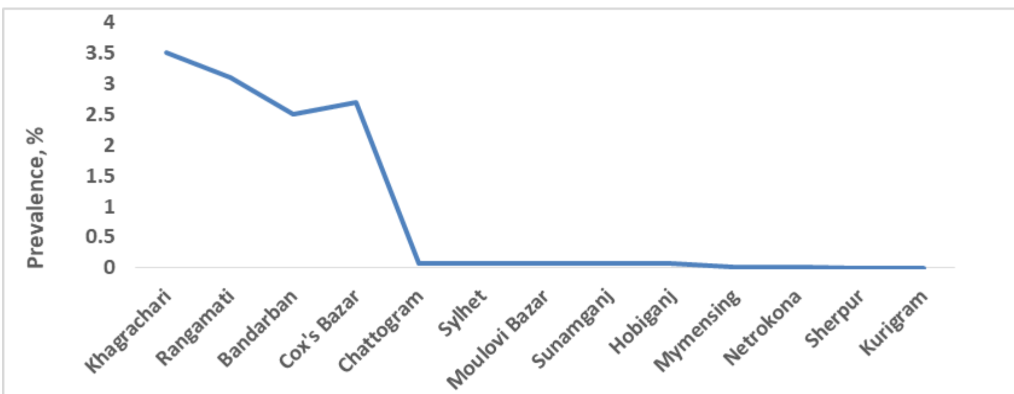

Fig.-2 Malaria prevalence (%) in endemic districts of Bangladesh in 2023

Chances of higher encounter with infective/infected anopheline mosquitoes along with compromised immunity and drug resistance leads the malaria risks (associations): On risk group perspectives, non-immune and semi immune pregnant women, young children, people with AIDS, immigrants as well as their children from endemic areas, international travelers from non-endemic areas, and forest travelers are the prominent risk groups in Bangladesh (Islam *et al.*, 2013; Karim *et al.*, 2019; Khan *et al.*, 2023; Noe *et al.*, 2018). Upon experiencing recurrent malaria outbreaks in recent past, the country seemingly requires to sustain steady malaria surveillances whilst the concerns of reintroduction, relapse, recrudescence, resurgence, drug resistance, insecticide resistance, and existence of reservoir with submicroscopic (asymptomatic) case incidences are quite relevant. A malaria outbreak in Netrokona district in 2005 was recorded with 1087 case morbidity and 14 case mortality. In 2004, a similar outbreak in Netrokona, Chattogram, and Cox's Bazar resulted in respectively 10, 25, and 168 deaths affecting correspondingly 2.2, 4.1, and 1.9 million people in the three districts. In Chattogram, during 998-2001, malaria mortality cases for complicated malaria and cerebral malaria cases stood 9.25% and 6.17% respectively (Hussain *et al.*, 2003).

Malaria risk factors in endemic areas have a link with the matter of public awareness and attitude in its treatment and necessary protection against mosquito bites and medicines (Haque *et al.*, 2010). In 2017, an increase of national malaria case incidences by 2000 to 29,000 compared with that in 2016 was found in Bangladesh in a joint survey of the National Malaria Elimination Program (NMEP) of Bangladesh and Bangladesh Rural Advancement Committee (BRAC, 2017). Interestingly, this was reflected with similar relationship in some hypo endemic unions of Bandarban of the CHTs (Ahmed *et al.,* 2013). This is argued that the south-east of the CHTs is densely forested, hilly, and elevated with several streams containing stable malaria hotspots and the proximity to water bodies and forests work as effective malaria risk factors in the region (Ahmed *et al.,* 2013; Bannister-Tyrrell *et al.*, 2017; Haque *et al.*, 2009; Shannon *et al.,* 2016).

Anyway, Cox's Bazar being one of the ten most endemic districts for malaria in Bangladesh should claim for a detail picture of malaria morbidity and mortality in the district for better understanding of malaria epidemiology the south-east part of the country. During 1995-1997, a retrospective malaria surveillance data analysis in the district, the total number of blood slides for microscopic tests of malaria exceeded the total number of clinical cases (suspects) of malaria whilst considering all the fever episodes for laboratory tests. This helped many of the blood slides not to fall into the early diagnosis and treatment practice for malaria patients then (Montanari *et al.*, 2001). The study also found a significant decline by half in positive predictive value of malaria incidences in Cox's Bazar in coherence with the falling trend of the overall malaria prevalence in 1995-1997.

Noticeably, the shifting trends in the clinical and laboratory (parasitological) malaria records in the district were consistent with the significant decline of malaria incidences though the reporting of the former were maintained separately at upazila health complex being collated and analyzed later at district level. An additional counts of blood slides could be the result of the local people's claim for testing their blood beside the traditional healers who used to refer their febrile patients to the governmental services for blood tests during the period of high nationwide malaria incidence. Khan *et al.* (2023) generated data from a single route of recording and reporting of malaria incidences that all the febrile patients or the malaria suspects in the Rohingya refugee camps in the country needed to undergo either RDT or Microscopy before being treated in the static health facilities in the camps. Overall malaria incidence in the camp was 0.16% most of which was significantly linked to forest travel. At this point, Maruf (2019, April 25) reported malaria in Cox's Bazar and other endemic districts of Bangladesh to be a concerning public health issue even in this decade. The report states that 18 million people of the endemic parts of Bangladesh lie under malaria threat with the potential risks of poor diagnosis, under reported case incidences, development of drug resistance, especially for Cox's bazar and its refugee settlements in a complex situation.

Quoting one ICDDR, B expert, the report also resolved that the risk of drug resistance among the Rohingyas in Bangladesh is high given their connections with geographic commonalties, new host experience, past history of treatment negligence, chances of substandard case diagnosis and treatment. It added also that the traditional rapid diagnosis and microscopy might fail to detect the resistant strain of malaria infections in greater south-east Asian countries. Such issue of lower sensitivity of both RDT and microscopy was corroborated by one recent study in equatorial Guinea that showed highest sensitivity of PCR technique in detecting malaria followed by RDT and Microscopy for 1274 blood samples of screening malaria (Berzosa *et al.*, 2018).

The forest travellers in Bangladesh incur the highest malaria burden adding to the threats of sudden malaria outbreak from in the south-east Asia. Suggestions for shifting malaria resources into its south-east forested part appears to be the best choice of malaria interventions. Strengthening 'test-treat-track' in malaria prone areas should also lead the malarial combating campaign of the country. On top, the climate of the country favours the fluctuation in malaria cases between years and seasons. Otherwise, mass coverage of LLINs and RDTs stands very useful preventive measures, irrespective of the demographics and settings- peacetime or crisis situation in the country (Karim *et al.*, 2019). Achievment 100% coverage of insecticidal bed nets in the south-east areas of Bangladesh stands a significant stride in Bangladesh malaria programme (Islam *et al.*, 2013), Haque *et al.*, 2014), and Alam *et al.*, 2016) whilst the artemisinin based combination therapies remained free of cost in the country.

The poor appreciation of the unique bionomics of the forest dwelling infected/infective anopheline mosquitoes and monitoring of the forest travellers with proper anti-mosquito bite measures seemingly adds to the complexities in fighting forest malaria in Bangladesh: The recent malaria screening data in the border lined Rohingya camps in the country shows extra-ordinarily highest incidence of forest linked cases while the incidence among those who used insecticidal mosquito nets accounted nil. Additionally, malaria control in Bangladesh's eastern forests has persistently been underperformed that evidently turns the forests into the major source of infections for countrywide malaria resurgence. In such, the interventions must be target oriented with regard to the ranges of malaria susceptibility of different demographic groups of the population at risk.

The vectorial capacity of various anopheline mosquitoes should also be considered for an effective vector control assay in the preventive segment of the elimination efforts. In all respects, this requires proper coordination among all stakeholders under the country's malaria elimination programme. On a separate note, the recent malaria screening data in the Rohingya camps in the country shows extra-ordinarily highest incidence of forest linked cases while the incidence among those who used insecticidal mosquito nets accounted nil (Khan *et al.*, 2023). The CHTs shelters diverse species of both vectors (forest mosquitoes) and the nonhuman reservoir hosts (monkeys) to work as a source of infections of the disease (Figure-1). This stands as a big threat to the country's efforts for winning SDG-3 to eliminate malaria by 2030.

This has been supported by a number of studies. Epidemiologically, the forest travelling adult males in the country's population incur the highest malaria burden. This has added to the threats of sudden malaria outbreak both from local and regional contexts in the south-east Asia. Shifting malaria resources into the country's forested south-east part under an activated surveillance then appears to be the best choice. Strengthening 'test-treat-track' in malaria hotspots, especially for the forest travellers should lead the country's anti-malarial campaign. That treating malaria can offer drug resistance by the plasmodial species, insecticide resistance of the vector mosquitoes, and the issues of relapse, recrudescence, recurrence, or reintroduction, the much needed elimination interventions should be addressed comprehensively in an integrated way (Rosenberg & Maheswary 1982; Khan *et al.,* 2023). The prevalence of malaria in Bangladesh has decreased since the Global Fund to Fight AIDS, Tuberculosis and Malaria started to support its National Malaria Control Program (NMCP) in 2007. The country's last districts targeted for elimination border India and Myanmar that incurs *Plasmodium falciparum* infections resistant to artemisinin (key drugs used in artemisinin-based combination therapies).

The remote forest dominating areas in the districts pose several challenges for prevention, detection, and treatment of malaria. Complicity in monitoring emergence of artemisinin resistance, detecting parasite reservoirs, changes in vectorial roles of mosquitoes, and insecticide resistance along with the host factors emerged with the advent of hundreds of thousands of Rohingyas have already added to the challenges of conducting the final phase of eliminating malaria in Bangladesh. This is highly supported from Khan, *et al.* (2023) that found significantly highest malaria test positivity rate (TPR, 13.60%) among the Rohingya male adults aged 15-60 years who had traveled to the nearby forests from their camps in Bangladesh in the previous two months. Efforts to reduce malaria in a population neighboring forests, therefore are suggested to be targeted at the forest goers irrespective of age, sex, or any other demographic stratifications. This also conforms the malaria situation in many other refugee settings in malaria endemic countries (Sullivan, 2000; Rowland & Nosten, 2001). Such emergency settings are afflicted further with the implications of human movement to the forests on the crisis ridden border areas that offer unique vector bionomics and diversity to worsen malaria situation (Pindolia *et al.*, 2013). At this point there should stem a self explanatory statement of resolution in the country's malaria a situation that needs to be understood properly with a view to forging due interventions in eliminating malaria in proper time and contexts.

Despite our recent progress towards malaria elimination success, winning fight against forest malaria stands key to the ultimate victory in the battle: It is obvious that malaria control in Bangladesh's eastern forests has persistently been under performed that apparently turns the forests into the major source of infections for countrywide malaria resurgence (Rosenberg *et al.*, 1982). But, on the back of a significant progress in combating malaria in recent past, Bangladesh now envisages to eliminate (three consecutive years of zero indigenous *P. falciparum* infections) the disease by 2030.

Bangladesh's malaria elimination efforts are spearheaded by its National Malaria Elimination Program (NMEP) in collaboration with an NGO consortium under BRAC (an NGO). The NMEP seeks for preventing re-introduction of malaria in once declared malaria free areas and emergence of artemisinin resistant plasmodial strains, which has already been reported to the east of the CHTs in Myanmar, the greater Mekong sub region, and westward in India. Anyway, to support the national elimination program, Bangladesh has invested in advanced research towards addressing the threats of emerging drug and insecticide resistance. This is based on the need for evidence-based data to guide an epidemiological program successfully. A major advance in this case, has been the clinical clearance of parasites from patients from forested hills after they start ACT treatment (the gold standard to measure ART-R). Interestingly, a recent *in vitro* culture adaptation of local parasites showed ART-

R to develop a comprehensive model for monitoring drug resistance in Bangladesh and other malaria-endemic countries (Nima *et. al.*, 2022).

Besides, the detection of spread of insecticide resistance (Alam *et. al.*, 2016) has offered guidance of spatial and temporal dimensions of vector interventions and empowered malaria programme with more target oriented strategies to purge transmission 'hotspots' before securing the elimination goals. This along with others has helped Bangladesh make significant strides into reducing both case morbidity and mortality. Nonetheless, the country should recognize both expected and unexpected elimination barriers. Considering the vector bionomics in malaria transmission, climate appears to be correlated to the increased annual parasite incidence (API) as seen in 2019 (*Nima et al.*, 2022). Climate mitigation, accordingly might have mixed effects shown in some modeling studies (Carlson *et al.*, 2022). Given this all, the theme of the World Malaria Day (Apr 25) of the year- 2023 arguably stands**-** "*Time to deliver zero malaria: invest, innovate, implement"*. But proper investment for strategic implementation programme needs proper research and development aspect under well focused surveillance with effective interventions for cutting the 'long-lusting' malaria transmission pathways. In this case, as mentioned, Bangladesh is experiencing consistently chronic dominance of forest origin malaria cases across its malaria hotspots that has been a major elimination threat (Rosenberg & Maheswary, 1982) (Table-2).

Plasmodium falciparum dominates other infections of malaria in Bangladesh: As noticed in many studies, *P. falciparum* in Bangladesh dominates over *P. vivax* case incidence. In the five south-eastern districts- Chittagong, Rangamati, Khagrachari, Bandarban, and Cox's Bazar, the average weighted prevalence rate to the beginning of 21st century was 6.0% while 0.40% in the rest eight north-eastern districts (Attlmayr *et al.,* 2006, BRAC & ICDDR, B, 2006, Faiz *et al.,* 2002). *P. vivax* was found in ten districts with the prevalence 0.13 to 1.2%. Prevalence of *P. falciparum* in eleven endemic districts including Cox's Bazar varied from 0.13% to 15.07%. The weighted prevalence of *P. falciparum, P. vivax*, and mixed infections of *P. falciparum* and *P. vivax* were estimated as 3.58%, 0.21%, and 0.18% respectively. But the proportion of *P. falciparum* was 90% while 5% for *P. vivax* and 5% for mixed infections in the thirteen endemic districts. Besides, prevalence of *P. falciparum* in males and females were 3.96% and 3.98% respectively.

Notably, malaria status in Chattogram seems to be poorly reported. Rahman *et al.* (2010) found *P. malariae* with typical band form trophozoites, schizonts containing 4-6 merozoites, a parasitemia of 3 per 1000 red cells, and occasional gametocytes in a malaria patient in July 2008 in the district. Following microscopy, a rapid PfHRP2-based antigen test gave *P. falciparum* negative and polymerase chain reaction performed on the same blood sample confirmed the infection as *Plasmodium malariae* malaria. The study also claimed to uncover the rare case of a PCR-confirmed mono-infection of *P. Malariae.* Such PCR-confirmed *P. malariae* infection was the first ever reported case in Bangladesh.

On treatment context, the first line malaria treatment in Bangladesh includes artemether-lumefantrine for falciparum malaria whilst chloroquine-primaquine combinations for vivax malaria. Evidence of antimalarial drug resistance to chloroquine and salphadoxine-pyrimethamine in the country was recorded between 1995 and 1998. In addition, resistance to chloroquine, mefloquine and sulfadoxine was recorded in 2004 and 2005. Such drug resistance was developed by *P. falciparum* infections (Islam *et al.*, 2013). On the matter of plasmodial resistance to drugs, several reports on the development of antimalarial resistance by *P. falciparum* species caused Attlmayr *et al.* (2006) to run a trial of an in-vitro drug susceptibility test for the deadly parasites in south-eastern Bangladesh. A combination of sulfadoxine and pyrimethamine with quinine was found to give a better treatment privilege in dealing with malaria in the areas where risk of drug resistance by *P. falciparum* reported high. Thus, until 2010, an approximate 34% of the country's population remained under malaria risk that contributed to a national malaria prevalence rate between 3.1% and 36% caused mostly by *P. falciparum*.

Reinforcingly, malaria elimination in Bangladesh depends on cutting its transmission from the reservoirs of mainly falciparum infections, especially those of forest origin: Bangladesh, with the world's largest delta and lengthy monsoons shares her border India and Myanmar- two malaria endemic countries and ranks fourth in malaria prevalence behind India, Indonesia, and Myanmar. The country is on the way to winning its national malaria elimination goal by 2030. Relentless antimalarial efforts in Bangladesh has already passed the control phase to embark on the recent elimination goal. Bosting of a significant success in nationwide peacetime antimalarial campaign, the population in the forest areas on the border areas of the country's CHTs evidently pose complex challenges towards ensuring total elimination of malaria.

To add, the poor appreciation of the unique bionomics of the forest dwelling infected/infective anopheline mosquitoes and monitoring of the forest travellers seemingly adds to the difficulties in fighting forest malaria in Bangladesh (Khan *et al.*, 2023; Noe *et al.*, 2018; Rosenberg & Maheswary, 1982). To this end, the recent malaria screening data in Rohingya camps in the country shows extra-ordinarily highest incidence of forest linked cases while the incidence among those who used insecticidal mosquito nets accounted nil (Khan *et al.*, 2023). Moreover, tracking malaria in the country's eastern forests has persistently been underperformed that causes its forests to remain as the major source of infections for a countrywide malaria resurgence.

Besides, offering suitable transmission bionomics for *P. falciparum* and *P. vivax*, the geographical conditions of the country pose a potential risk for *P. knowlesi* malaria. In addition to a few concerns of antimalarial resistance, individual age factor, the prominence of lower socio-economic status, heterogeneous transmission between seasons, close proximity to untreated mosquito breeding places with water bodies and forest areas, and poor awareness on avoiding mosquito bites are identified as important risk factors for malaria in the country (Alam *et al.*, 2010; Islam *et al.*, 2013, Karim *et al.*, 2019, *Noe et at.*, 2018). Proper malaria interventions are repeatedly suggested for dense forests and/or vegetation on the border areas in the south-east and north-east part of Bangladesh to interrupt spreads and importation of forest malaria as a part of Bangladesh's national malaria elimination targets (Chang, 2019). Cheng also found frequent mixing of local and imported infections of malaria occurs in the low transmission areas in the country's south-west part through movement of infected people between different regions.

Not withstandingly, Bangladesh keeps steady pace of success towards malaria elimination by 2030: Dealing with malaria and its implications in Bangladesh illuminated hitherto, the national malaria elimination program of the country, NMEP, (2017) has fixed a distinct set of priorities: reducing malaria incidence in four districts (3 hill-tract districts and the Cox's Bazar), malaria treatment for higher risk groups, devolving the threats of emerging more complicated malaria upon the emergence of the Rohingya refugee crisis, strengthening the present malaria surveillance system, ensuring zero case morbidity in 'non-endemic' districts, engaging the private organizations in malaria response, garnering political engagement to combating malaria, and building the capacity of health service providers to win the challenges in malaria elimination program in Bangladesh. This supports Maruf (April 25, 2019) that showed a decline in malaria case and death incidences in the country by 88% and 95% respectively in 2018 compared with that in 2008. Additionally, as reported in the Prothomalo (2017, April 25) decline in malaria occurence in Cox's Bazar is quite impressive. But the progress in malaria elimination in the country since 2015 seemingly remains inconsisted as explored already. Interestingly, the spread of malaria within country is largely clustered in Bangladesh (Noé *et al.*, 2018).

The rural areas in the country during 2013-2016 experienced clustered clinical malaria cases in place and time that the hotspots acted not as sources of spread yet remained stable across the whole period. The same study found the malaria endemic areas of Bangladesh to account for 2.62 malaria cases per

1000 population between 2013 and 2016. This meant for marking the country as a very low transmission for malaria under the guidelines of WHO (2017) being supported by Naher (2019) aslo. By contrast, Haque *et al.* (2009) and Naher (2021) showed population of high transmission risk for > 1 case per 1000 population among other two categories: low (0-1 case per 1000 population) and malaria free (nil case) in Bangladesh. Anyway, Khan *et al.* (2023) and Lu *et al.* (2020) showed consistency to claim zero active case morbidity among children under 15 years of age in the Rohingya population in Bangladesh.

Nevertheless, depicting a complete picture of malaria heterogeneity- both temporal and spatial in Bangladesh seems difficult for lack of adequate data. This goes with Haque *et al.* (2014) that advocated for proper identification of malaria heterogeneity in Bangladesh for proper interventions in targeted areas in combating the disease successfully. On a separate note, the prevalence of malaria in Bangladesh has decreased since after 2010 whilst the Global Fund to Fight AIDS, Tuberculosis and Malaria started to support its National Malaria Control Program (NMCP) in 2007. The country's three CHT districts for malaria elimination by 2030 border India and Myanmar that incurs artemisinin (key drugs used in artemisinin-based combination therapies) resistant *Plasmodium falciparum* infections. These remote forest dominating areas pose discernible challenges for prevention, detection, and treatment of malaria.

Interestingly, Hu *et al.* (2016) found clear seasonal heterogeneity in malaria incidences in five closely situated villages on the China-Myanmar border area wherase, the villages with lower malaria incidence experienced erratic temporal distribution of cases compared to that with higher case incidence. Similar findings found from Zhang *et al.* (2014) who confirmed a declining or weaning seasonal peak with reduction in malaria incidence from 2004 to 2012 in China. This apparently indicates a heterogeneity in malaria occurrence on demographic and spatiotemporal stratifications of the country like that in Bangladesh. To this end, climate appears to be correlated to the increased annual parasite incidence in terms of the vector bionomics in malaria transmission in Bangladesh (Nima *et al.,* 2022).

Climate change mitigation, in place then might have mixed effects shown in some modeling studies (Carlson *et al.* 2022). Given this, the theme, "*Time to deliver zero malaria: invest, innovate, implement*" of the World Malaria Day of the year, 2023 (Apr 25) arguably guides Bangladesh in approaching towards elimination. The failure to follow the theme could result from unstably higher temporal and spatial variations in malaria distribution in the country. The studies of Haque *et al.* (2014) that analyzed malaria hotspots in Bangladesh to describe malaria prevalence in the endemic districts of the country between 2008 and 2012, and Anderson *et al.* (2020) that used malaria hotspots stability maps for the first time in Bangladesh demonstrated both temporal and spatial malaria incidence scenario in the country.

Most of the *P. falciparum* hotspots in Bangladesh are located within south-east area while those of *P. vivax*, are located in north-east area (Haque *et al.*, 2009). Anyway, these study data set until Anderson *et al.* (2020) was unable, otherwise to define the spatial and temporal species level hotspots analyses. The scarcity of malaria data for the remote and forest-travel linked population in the country's south-east area appears as a big challenge to explore the relevant literature in a critical way, especially until unfolding the study of Khan *et al.* (2023). Complicity in monitoring emergence of artemisinin resistance, detecting parasite reservoirs, changes in vectorial roles of mosquitoes, and insecticide resistance are yet to be resolved. Besides, host factors with the advent of hundreds of thousands of Rohingyas have already added to the challenges of conducting the final phase of eliminating malaria in the country. To support this, Khan *et al.* (2023) estimated significantly highest malaria test positivity rate (13.60%) among the Rohingyas with forest travel history.

Fighting malaria in a population neighboring forests then lies on targeted interventions at the forest goers irrespective of demographic stratifications. This also conforms malaria situations in many refugee settings in malaria prone countries (Sullivan, 2000; Rowland & Nosten, 2001). Thus, malaria burden in the south-east area of Bangladesh could be aggravated with the advent of refugee crisis that the country's peacetime experience in combating malaria draws new thoughts and ideas or operational rethinking adjusted for the new incumbent, socio-political, demographical, environmental, and cultural contexts. This definitely offers a novel challenge in the country's anti-malarial efforts (Cousins, Lu *et al.,* 2020; Spiegel *et al.*, 2010; United Nations Office for the Coordination of Humanitarian Affairs, UNOCHA, 2019).

At this point, we can claim ourselves to be closer to malaria elimination success being conditional first of winning fight against forest malaria. It is also a much agreed view to generate proper temporal and spatial resolution database on malaria incidences in population at risk to ensure success in set targets in eliminating the disease. Worth to note, Bangladesh's malaria elimination efforts are orchestrated by a consortium of National Malaria Elimination Program (NMEP) and BRAC (an NGO). The NMEP gaurds off re-introduction of malaria in areas declared as free of malaria earlier. It also offset emergence of artemisinin resistant plasmodial strains reported already to the east of the CHTs, the greater Mekong sub region, and westward in India. To accelerate this, Bangladesh has invested in advanced research on emerging drug and insecticide resistance. Some evidence-based data then can guide an epidemiological program successfully. A major advancement- the clinical clearance of parasites from patients from forested hills after they start ACT treatment, in this case, has happened (Nima *et. al.*, 2022). Further, to develop a comprehensive model for monitoring drug resistance in their *in vitro* culture adaptation of local parasites, Nima *et al.* showed ART-R in Bangladesh and other malaria-endemic countries. Additionally, spread of insecticide resistance detection (Alam *et. al.*, 2016) has offered us guidance of spatial and temporal dimensions of vector interventions. This has empowered malaria actions of the country with more target oriented strategies to undo transmission 'hotspots' for securing elimination goals. This evidently joined others depicted above and helped Bangladesh snatch significant marks in reducing malaria burden under NMEP.

CONCLUSION AND RECOMMENDATIONS

The demographical, biological, environmental, and interventional factors and their implications in malaria situation in Bangladesh is explored in this meta-analysis of relevant data. The country has had maintained a few stable hotspots and transmission paths of malaria despite showing significant decline to case fatality and morbidity in recent past, especially since after 2010. The country yet needs to recognize both expected and unexpected obstacles in total elimination of the disease. Strengthening mobilization of malaria investment should also be considered. With this, proper investment in strategic implementation program rests on proper research and development in an effectively working surveillance and interventions to cut the pathways in chronic malaria transmission. To this end, Bangladesh experiences dominance of forest linked malaria cases across its malaria hotspots in and around the CHTs as a major elimination threat. Finding a suitable vectorial breeding ground in the forests, the forest malaria in the country poses a significant threat to lthe elimination assays on local and national scales. Accordingly, the resource management for the ultimate goal of malaria elimination in Bangladesh should focus more on the following issues:

Conducting regular epidemiological monitoring and tracking of malaria incidences among individuals visiting forested areas in the country. For this strengthening surveillance systems by prompt and early detection of forest linked malaria and the sub-clinical and low-density infections is imperative. Initiatives for preventing, controlling, testing, treating, and tracking the proportion of population who used to move/visit to forests for various businesses will definitely help reduce spread of forest malaria .

Promoting case detection and checking for the emergence of *P. falciparum* strains resistant to artemisinin and tracking their spread in peace time and emergency situations. Prevention of the spread of artemisinin resistance in the CHTs over the next few years could give a significant result. Mobilizing malaria resources in forests along with controlling human movement in and around trans-border areas should be a priority intervention in fighting malaria in Bangladesh.

Enhancing community engagement program like education campaigns on bed nets and mosquito repellents to foster a sense of ownership and responsibility among the populations at risk.

5. Bolstering entomological control for *Anopheles* vector as a key component in the elimination efforts. Individual and community awareness for treating the vectors' breeding places, using effective mosquito repellents and insecticides, and mass usage of bed nets then should be the integral component in malaria surveillance.

Striking enhanced investment in research, development, and innovation in antimalarial actions including studies on mosquito bionomics, drug resistance patterns and habitat preferences aimed at better tailoring of malaria interventions with maximum effectiveness. Cutting-edge technologies of genetic modification of mosquitoes in malaria transmission cycles in malaria hotspots can also be funded. Facilitating the mobilization of malaria resources in malaria risk areas in CHT districts by building more roads, clinics, schools, industries, and other infrastructure there to further accelerate the elimination efforts.

Executing collaborative malaria surveillance program till the achievement of the malaria elimination goals in national and regional contexts. In this regard, acknowledging the Global Strategic Techniques for Malaria, GTSM (2016-2030) to ensure zero malaria transmission risk for any part of Bangladesh and its trans-border areas from building of human reservoir or reconstruction of new transmission routs there.

Last not least, Bangladesh should weigh high these challenges and implications of eliminating malaria by 2030. Despite showing a stellar progress in anti-malaria efforts in the near past, stray malaria outbreaks in clustered spots of forest rish areas are not uncommon. A proper appreciation of the recommendations made above then needs more investment, more innovation, and the shared participation of the stakeholders- government as well as NGOs for making a malaria-free Bangladesh by 2030.

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