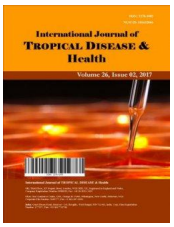

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Nine Years of Malaria Cases in Bangladesh: A Time Series Analysis

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Authors' contributions

This work was carried out in collaboration between all authors. Author MSIL designed the study, performed statistical analysis and wrote the first draft of manuscript. Author MK performed the analysis and editing the manuscript. Author SN wrote the protocol of study and involved in editing the manuscript. Author MAI reviewed and finalized the manuscript. Author MBHP involved in data acquisition and management of literature review. Author MAS made the graph, figure and conducted spatial analysis. All authors read and approved the final manuscript.

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ABSTRACT

Aims: Bangladesh, a malaria endemic country in South East Asia Region, has successfully decreased malaria over the years through the adoption of different strategies. Still, this is un-notified and no systematic malaria trend analysis has been done. Hence this study assesses the malaria trend through different dimension with consideration of various anti-malarial programmes.
Study Design and Methodology: Secondary data from National Malaria Elimination Program (NMEP) and BRAC were used to analysis the trend of malaria cases and time series of the data were done to complement the analysis. A comparison of different regions through spatial distribution was also fitted out to determine the present scenario of malaria in Bangladesh.

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Results: The annual malaria incidence declined from 7.77 per 1000 population in 2008 to 1.58 per 1000 population in 2016 [R^2=0.712, *P*-value=0.004, 95% CI:-1.04, -0.29]. Both *P. falciparum and P. vivax* decreased by 75% and 77% respectively since 2008 though *P. vivax is still* slightly increased after major shuffling in 2014. Severe malaria gradually decreased by 78% from 2008 to 2016 [R^2=0.779, *P*-value=0.002, 95% CI:- 480.9, -170.7].
A different scenario was found through stratification as malaria infection steadily decreased in both low [R^2=0.83, *P*-value=0.0001, 95% CI:-5.98, -4.87] and medium [R^2=0.29, *P*-value=0.0001, 95% CI:-5.82, - 2.82] endemic districts but the same rate of decrease of malaria infection did not happen in Chittagong Hill Tracts. The study showed that malaria prevalence was higher in males (57.86%) than females (42.13%) and older age group of 15 years and above (59.3%) more than in other younger age groups.
Conclusion: Though malaria infection has sharply declined in all endemic districts except Chittagong Hill Tracts, a sustained intensified strategy is required in all endemic districts to achieve malaria elimination within 2030.

Keywords: Chittagong Hill Tracts; malaria; endemic; elimination.

1. INTRODUCTION

Malaria is a protozoan disease caused by parasites of the genus *Plasmodium*. It is one of the leading causes of illness and death in the world. In 2015, there were an estimated 212 million malaria cases and 429,000 malaria deaths worldwide, with 92% of deaths were recorded in WHO African Region, followed by the WHO South–East Asian Regions (6%) and then the WHO Eastern Mediterranean Region (2%) [1]. Malaria is concentrated in the world's poor countries mostly Africa and South East Asia, where pregnant women and under 5 years of age are at greater risk of malaria infection [2].

Bangladesh is a malaria endemic country in South–East Asian Region where the disease is endemic in 13 out of 64 districts under North–East and South–East regions that share border with India and Myanmar. Since 2008, Malaria Control Programme in Bangladesh got a momentum after securing funding from The Global Fund (GF) Round 6 proposal whose goal was "to reduce malaria specific morbidity and mortality by 50% in 2012 from the baseline year 2005". This project has shifted its strategy from control to elimination of malaria after nine years of widespread systematic implementation in three stratified regions (i) high – Chittagong Hill Tracts (CHT) (ii) medium - Cox's Bazar and (iii) other low endemic areas under different Round of proposals.

Malaria positivity decreased from 84,690 in 2008 to 27,737 in 2016 resulting very few cases happened in a year in low endemic areas. Now malaria infection mostly occur in rural areas which is close proximity to hard to reach areas and/or to fringe or deep forest under Chittagong Hill Tracts (CHT) and Cox's Bazar districts. This reduction of malaria encourages National Malaria Programme to develop a far-reaching National Malaria Strategic Plan (2017-2021) [Unpublished data, National Malaria Elimination Programme, DGHS, Bangladesh, 2017] in view of Global Technical Strategy for Malaria (2016-2030) [3]. The three CHT districts -Khagrachari, Rangamati Bandarban–with high malaria endemicity still remain major causes of malaria morbidity and mortality in Bangladesh.

In 2007, the overall malaria prevalence rate was 3.1% with Khagrachari district (15.25%) being most prevalence area followed by Bandarban (10.97%) and then Rangamati district (7.42%). Among the nine low endemic areas, the prevalence rate was high in Hobiganj district (1.74%) [4]. In 2013, the prevalence of malaria reduced to 0.9 per 1000 population with Bandarban having the highest prevalence district (6.7 per 1000 population) [5]. Then Bangladesh got an unusual experience of malaria case infection in 2014 which was more than double that of 2013 malaria cases. This unusual increase in malaria cases also occurred in Northeastern districts of India that close to Bangladesh, where malaria cases were almost double in 2014 than that of 2013 [6].

The epidemiology of malaria in Bangladesh is highly complex. All four species of human plasmodium are present but the vast majority of malaria cases are caused by *Plasmodium falciparum*. Most of the rest are caused by *Plasmodium vivax*. The epidemiology of the disease varies from location to location and from one population to another population. Intense malaria transmission is largely restricted to hilly, forested and forest fringe areas of the

Chittagong Hill Tracts. The most efficient vectors are *Anopheles dirus* and *Anopheles minimus* where the former can survive in high dense forest in CHT and the latter also primarily forest-based but can survive in less densely shaded forest, forest fringes and part of bamboo thickets. The success of malaria reduction in Bangladesh has been largely overlooked and a trend analysis of malaria cases had not been studied. This study was undertaken to determine whether there was any significant effect in malaria endemic areas considering the strategies implemented over the years that opened a new window in Bangladesh towards malaria elimination.

2. METHODS AND MATERIALS

Secondary data from NMEP and BRAC were used to analyze the trend of malaria cases from 2008-2016 with consideration of various anti-malarial activities. A district-wise monthly surveillance data (2008- 2016) was obtained from BRAC to get the effectiveness of programme across the malaria region. The blood examination rate which is based on blood slide examination per 100 population, was collected through programmatic data reporting system. Annual Parasite Index (API), a unique measurement of malaria severity, was also calculated from confirmed malaria per 1000 population. Mid-year of district populations were used to compute these rates derived from the national census (2005 & 2011) and with consideration of population growth. A time series of the data was done to analyze the trend using centered moving average. Data was entered and analyzed by SPSS v 16.

3. RESULTS

During the study period (2008–2016), a total of 3,376,333 blood films and 1,6,73,808 RDT were done for malaria diagnosis of which 156,627 (4.63%) microscopically and 280,949 (16.7%) RDT were positive with mean malaria cases of 48,619 in Bangladesh. During the study period (2008-2016), malaria positivity decreased by 32% [R^2=0.51, *P*-value=0.031] while annual blood examination rate remained almost unchanged from 3.087 in 2008 to 3.274 in 2016 (Table 1) (Fig. 1). Annual Parasite Index (API) also declined from 7.77 in 2008 to 1.58 in 2016 [R^2=0.71, *P*-value =0.004, 95% CI: -1.04, -0.29] (Table 1).

The study shows there was significant annual decline in malaria incidence over the years with a high peak in 2014. Malaria incidence continued to fall till 2013 (32% as of 2008) and then it suddenly increased in 2014 before decreasing in the following two years 2015 and 2016. Both *P. falciparum and P. vivax* also decreased by 75% and 77% respectively from 2008 to 2016 (Table 1). Since 2008, *Plasmodium falciparum* declined steadily [R^2=0.86, *P*-value=0.003] while *P. vivax* showed the fluctuation, increased after the year 2013 which is not significant (Fig. 2).

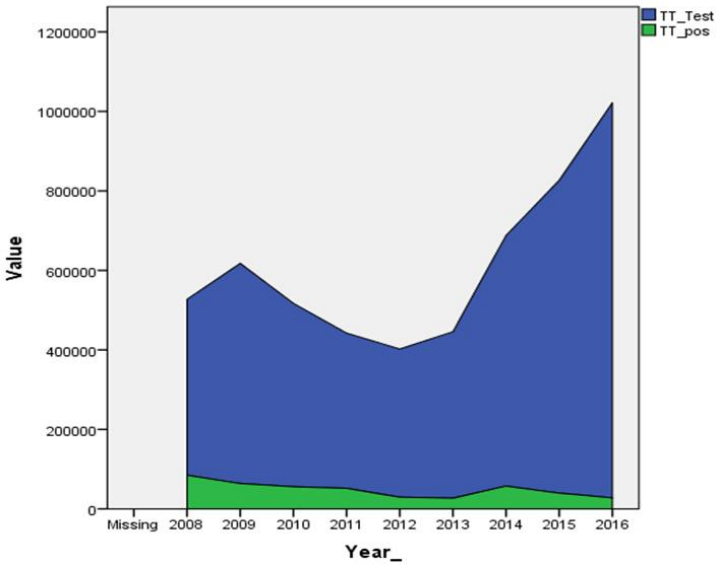


Fig. 1. Malaria blood slide examination and malaria positivity in Bangladesh (2008-2016)

Table 1. Malaria cases in Bangladesh from 2008-2016

Year	Blood slide examination	RDT testing	Total test	Blood slide positive	RDT positive	Total positive	Pf	Pv	Mixed	Severe malaria	Population	API	Annual blood examination rate (%)
2008	336505	106001	442506	50004	34686	84690	69606	14409	675	3042	10900000	7.770	3.087
2009	397148	156639	553787	25203	38670	63873	56912	6853	108	3287	11118000	5.745	3.572
2010	308326	152936	461262	20519	35354	55873	52012	3824	37	2726	11340360	4.927	2.719
2011	270253	120172	390425	20231	31564	51795	49105	2580	110	3095	16286155	3.180	1.659
2012	253887	118919	372806	9901	19617	29518	27644	1699	175	1457	16525561	1.786	1.536
2013	290496	128259	418755	7303	19588	26891	25815	983	93	1155	16768487	1.604	1.732
2014	418519	211662	630181	13628	43852	57480	41261	3348	12871	2063	17014984	3.378	2.460
2015	527659	259171	786830	6621	33098	39719	26525	4011	9183	1023	17265104	2.301	3.056
2016	573540	420049	993589	3217	24520	27737	17318	3306	7113	670	17518901	1.583	3.274
	3376333	1673808	5050141	156627	280949	437576	366198	41013	30365	18518	134737552		

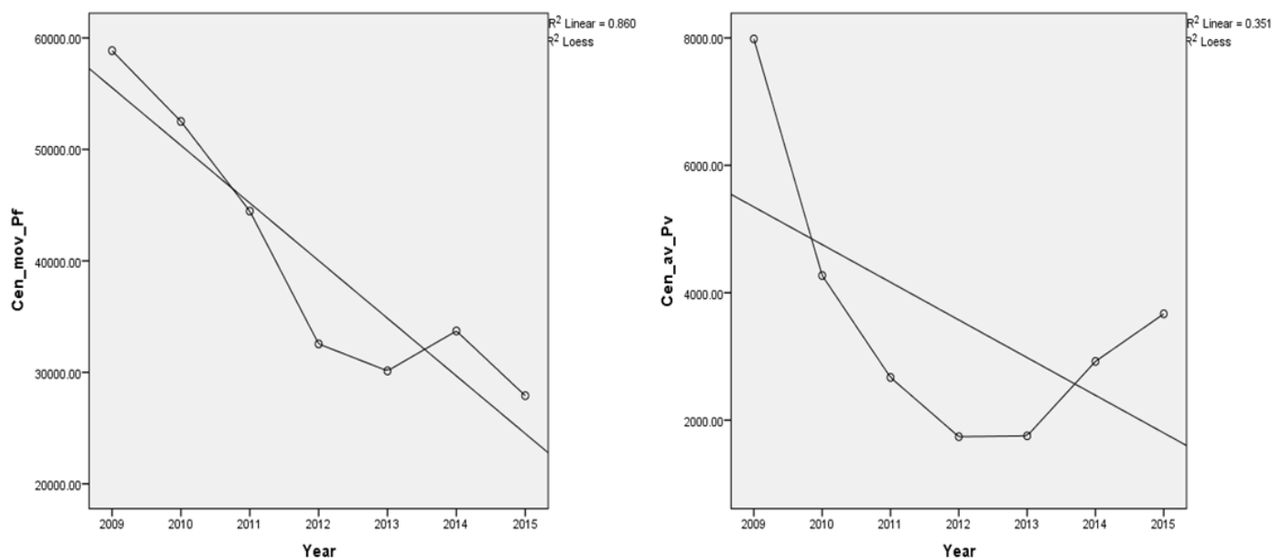


Fig. 2. Trend of *P. falciparum* and *P. vivax* malaria in Bangladesh (2008-2016)

The result of the study also shows that malaria prevalence was higher in males than females. Overall, 57.8% of malaria infected patients were male and 42.2% were female (Fig. 3). Malaria prevalence was higher in age group 15 years and above (59.3%) and least among those aged <I years (1%) (Fig. 4).

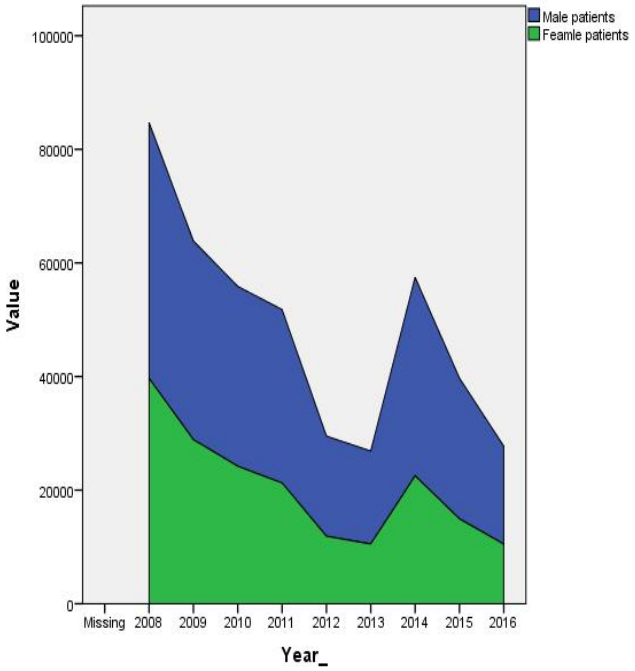


Fig. 3. Distribution of sex group (2008-2016)

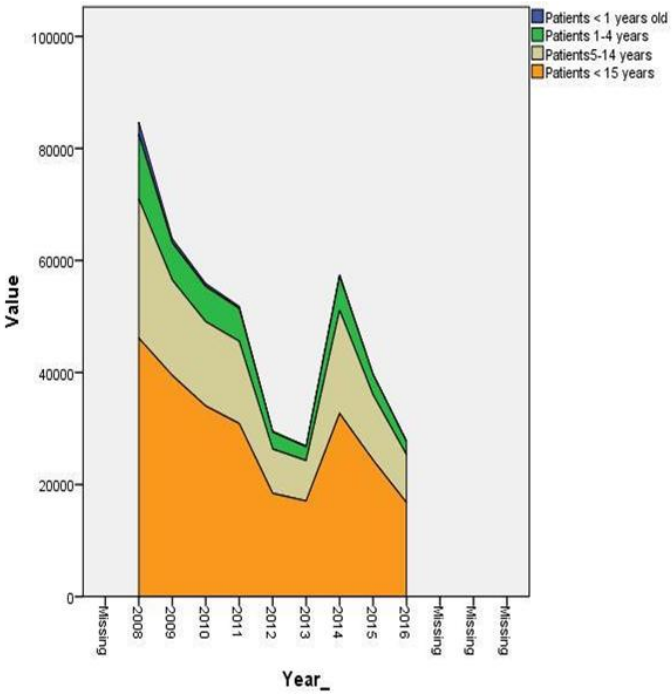


Fig. 4. Distribution of age group (2008-2016)

Severe malaria also gradually decreased during the years (2008-2016) [R^2=0.78, *P*-value =0.002, 95% CI: -480.9, -170.7] being 78% lower in 2016 in relation to 2008 (Table 1) (Fig. 5).

Malaria case fatality rate also fell by 38% from 1.8 per 1,000 cases in 2008 to 0.69 per 1000 cases in 2016, reflecting a major improvement in access to early diagnosis and appropriate treatment in Bangladesh. However, there was steep rise in malaria case fatality from 0.56 per 1000 cases in 2013 to 0.78 per 1000 cases in 2014 cases due to malaria upsurge in Bangladesh.

3.1 Malaria at Different Region Base

When the malaria endemic areas were stratified and a strategic analysis was conducted at region base, it was evident that there was more relative decline in malaria incidence [R^2=0.83, *P*-value=0.0001, 95% CI: -5.98, -4.87] in low endemic districts than in medium endemic district [R^2=0.29, *P*-value=0.0001, 95% CI: -5.82, -2.82] but not much decrease in CHT districts (Fig. 6). For the low and medium endemic districts, malaria incidence decreased in a similar pattern in the first five years (2008-2013) of study period but thereafter, the decrease continued only in low

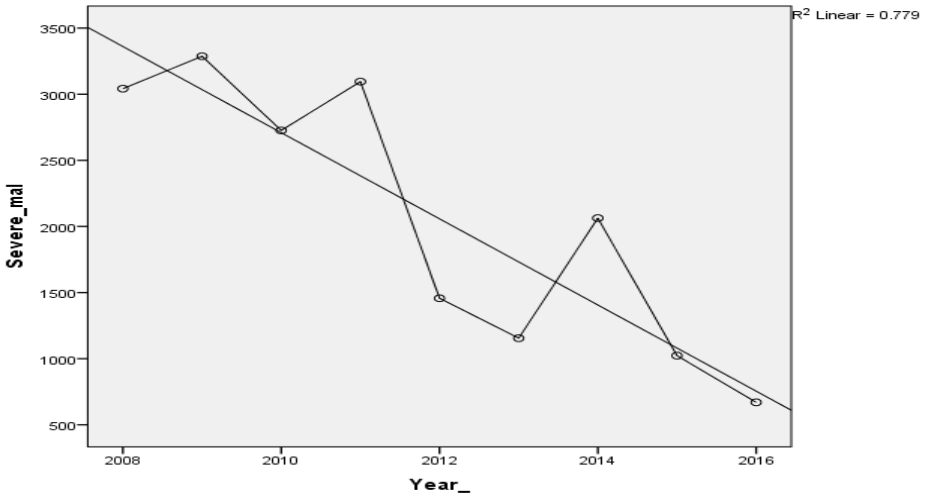
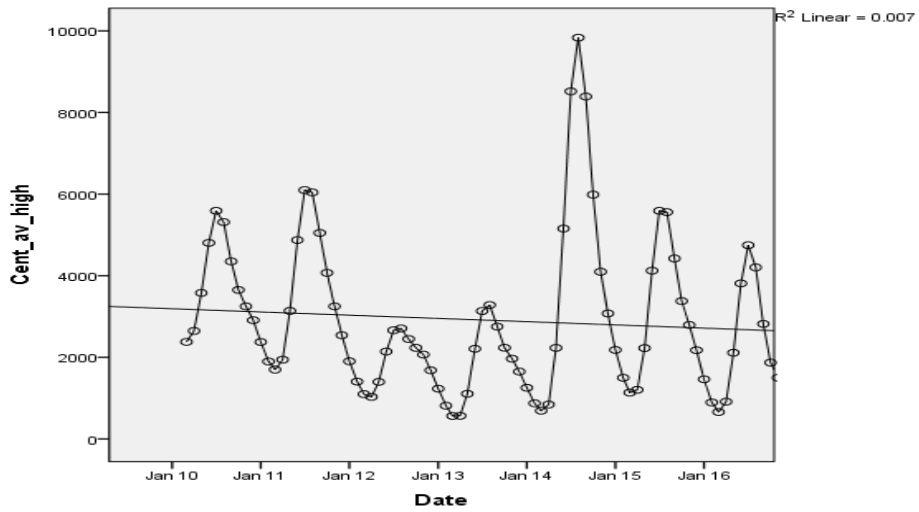
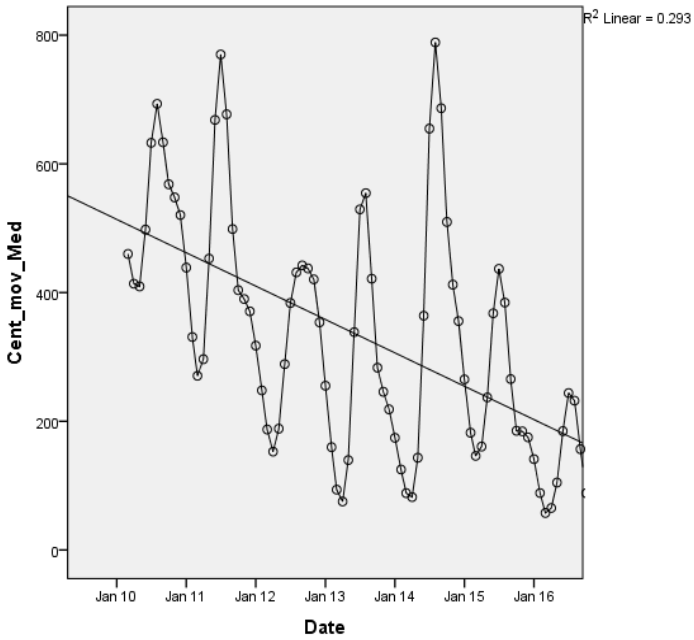


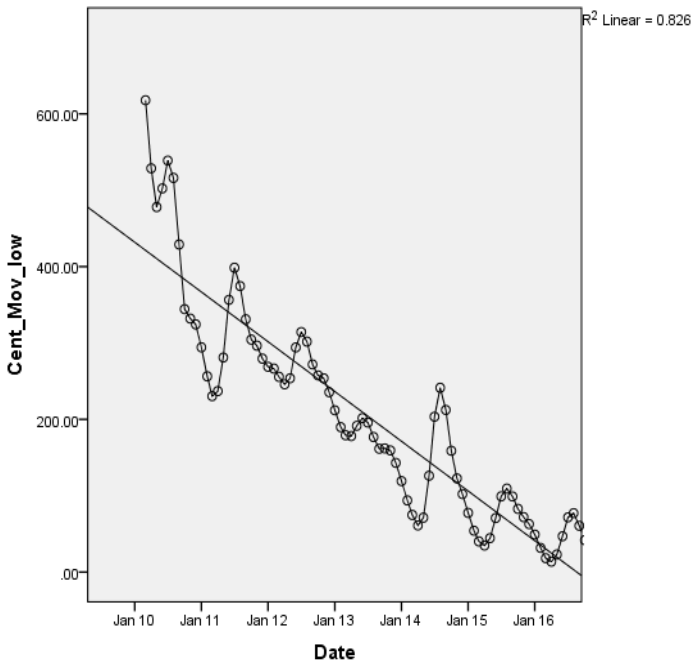
Fig. 5. Trend of severe malaria in Bangladesh (2008-2016) (With moving average)



a) Chittagong Hill Tracts



b) Cox's Bazar district



c) Low endemic districts

Fig. 6. Malaria trend in a) CHT, b) Cox's Bazar and c) low endemic districts (W ith moving average)

endemic districts (Fig. 6).Thus, malaria was still more prominent in CHT districts (API: 12.56) and several preventable measures, in terms of both epidemiological and entomological activities, are needed to mitigate it.

3.2 Spatial Distribution at Region Base

The Figs. 7-9 shows that malaria incidence at different geographical base - CHT (high endemic districts), Sylhet (low endemic districts) and Cox's Bazar (medium endemic district) – had been decreased during the study period.

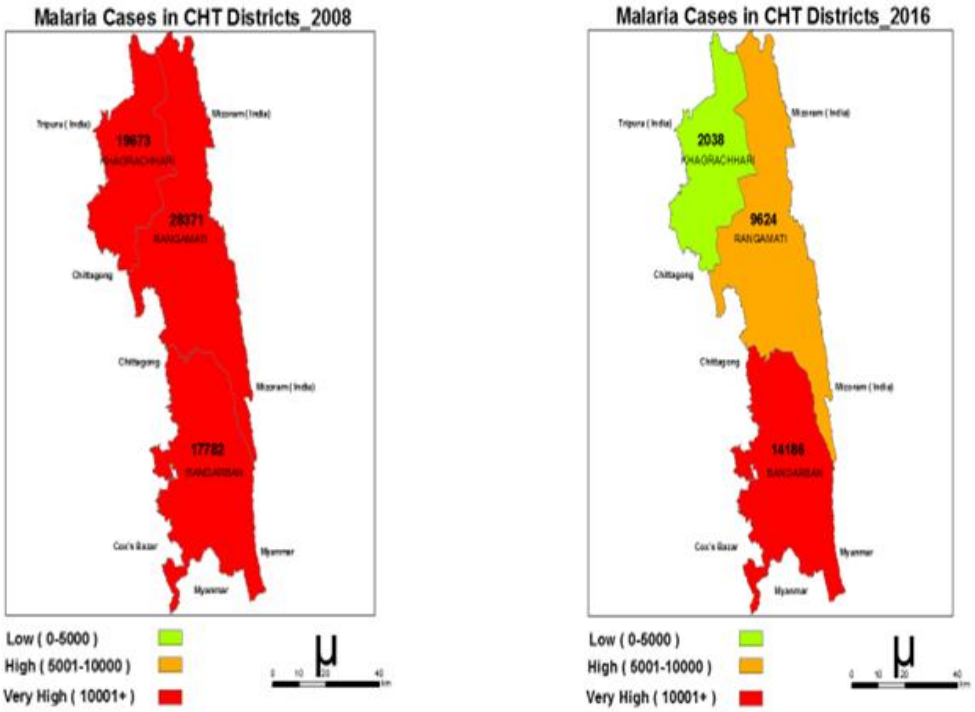


Fig. 7. Malaria cases in CHT districts in 2008 and in 2016

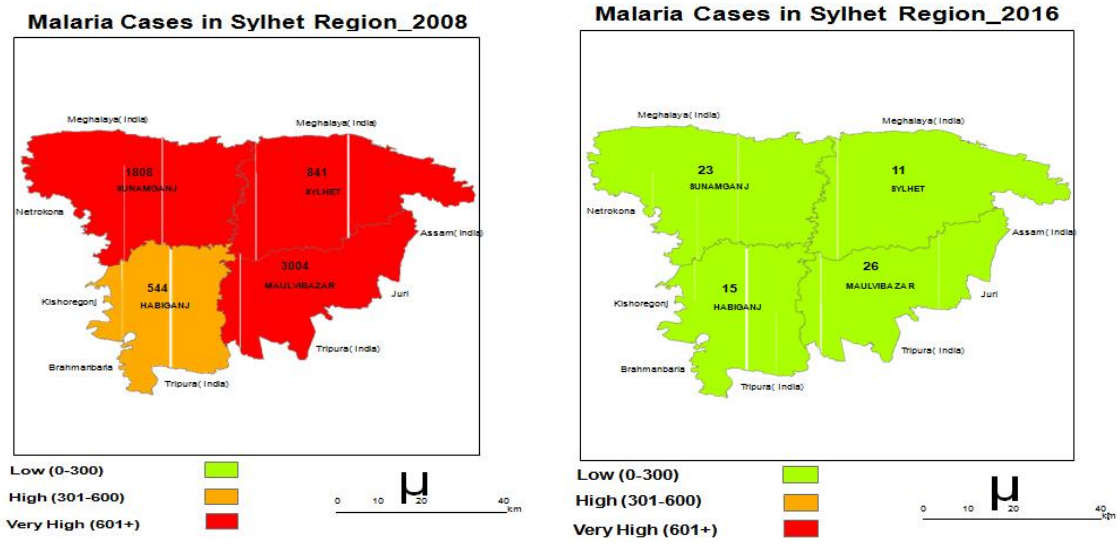


Fig. 8. Malaria cases in Sylhet division (Sylhet, Moulvi bazar, Sunamganj and Hobignaj districts) in 2008 and in 2016

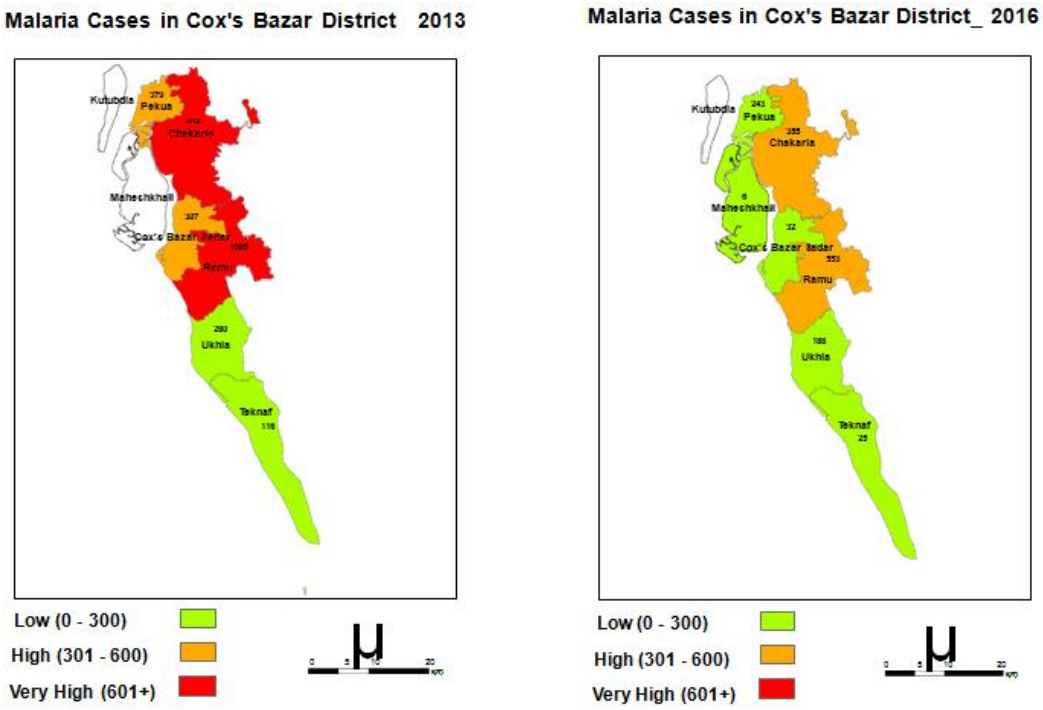


Fig. 9. Malaria cases in Cox's Bazar district in 2013 and in 2016

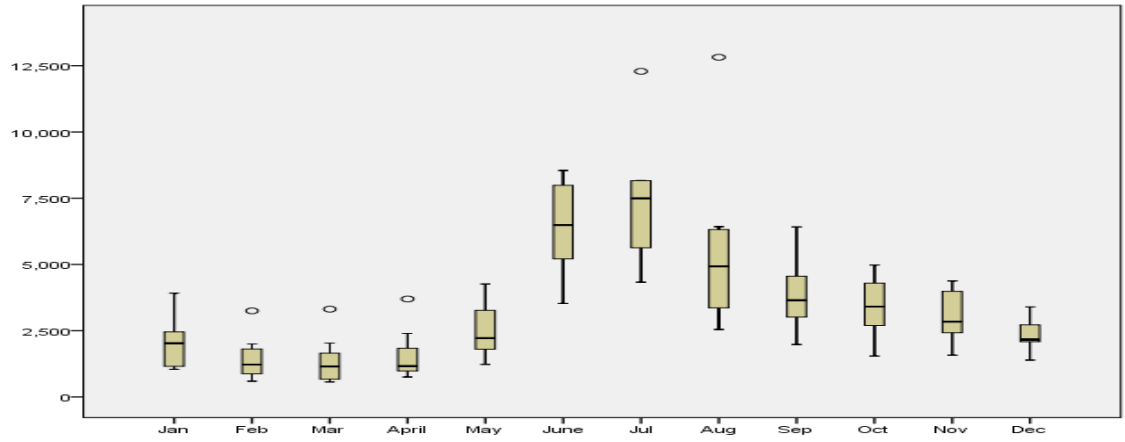


Fig. 10. Seasonal variability of malaria cases in Bangladesh (2010-2016)

3.3 Seasonal Variability

A seasonal variability of malaria infection is observed in Bangladesh. The highest peak of this seasonal disease along the years was observed during June-July, showing almost 200% increase in the incidence as compared to the annual mean. The minimum malaria incidence was observed during February-March, which was 40% less than the mean annual incidence (Fig. 10).

4. DISCUSSION

Malaria is a major public health problem in terms of morbidity and mortality in Bangladesh. Since 2008, burden of malaria cases has reduced over the years after availability of grant from the Global Fund. The result of our study revealed that during the last nine years, a fluctuating trend of malaria cases was observed in malaria endemic areas especially in high and medium endemic districts with a minimum number of

malaria cases reported in 2013 indicating that these endemic districts bear 84% of total malaria cases and is full of dense and fringe hill and deep forest areas which may be influential in vector breeding during the rainy season in Bangladesh. However, there was steep increase of malaria cases from 2013 to 2014 which was also visible in both CHT and Cox's Bazar districts. The primary cause of this outbreak was likely prolonged intermittent rainfall with insufficient heavy downpours to flush out vector-breeding sites in CHT and Cox's Bazar districts. Rainfall plays an important role in malaria epidemiology because water not only provides the medium for the aquatic stages of the mosquito's life but also increases the relative humidity and thereby the longevity of the adult mosquitoes [7]. The impact of rainfall on the transmission of malaria is very complicated, varying with the circumstances of a particular geographic region and depending on the local habits of mosquitoes. Rains may prove beneficial to mosquito breeding if it is moderate, but may destroy breeding sites and flush out the mosquito larvae when it is excessive [7]. This finding is consistent with what was reported in Mpumalanga Province, South Africa, in 2005-06 where 30% more malaria cases were recorded than average malaria incidence [8,9]. This finding was also similar to what was reported in Northern Indian states where the three Indian states (Meghalaya, Mizoram and Tripura), close to Bangladesh, had almost double malaria cases than that of 2013 [6].

The study shows that the burden of malaria decreased with deceasing rate of *Plasmodium falciparum* where the prevalence of *P. falciparum*, *P. vivax* and mixed infection in the country were observed to be 84%, 9% and 7% respectively, higher than what was reported in Ethiopia [9,10]. However, our data contrasted with the findings of another Ethiopian study in Jimma town which reported *P. falciparum, P. vivax* and mixed infection accounted for 26.4% 71.4% and 2.4% respectively [11]. This difference may be because the Ethiopian study was conducted in urban areas while the study in Bangladesh was conducted in rural areas. *Plasmodium vivax* initially declined steadily but reversed and increased slightly after 2013, indicating a paradigm shift, similar to the report of another Ethiopian study [9]. This may be happened as *P. vivax* parasites can remain dormant in the liver for several months and even up to a year or more. When these dormant parasites reactivate they can cause relapses of febrile illness [12]. These relapse cases were evident in Bangladesh, especially in low endemic areas. A study in Papua New Guine reported relapse cause approximately four out of every five *P. vivax* infection [13]. The study also shows that severe malaria declined significantly, especially in CHT and Cox' Bazar districts. This report is also consistent with the study of MRG (Malaria Research Group) of Bangladesh which was a hospital-based study conducted in 2012 [14]. This reduction of malaria cases from 2008 coincides with the increased availability of the new effective drug regimen ACT for the treatment of *P. falciparum* malaria at national and sub-national levels [15,16]. Other possible reasons for malaria reduction during this period (2008-2016) might be due to the increased LLIN distribution at community level with a view to 100% population coverage in line with 1.8 population per one LLIN in CHT and Cox's Bazar districts and hotspot-based LLIN distribution in other low endemic districts [16,17]. Though there has been aggressive LLIN distribution in CHT and Cox's Bazar districts, still malaria infection is high in CHT areas which require a more comprehensive malaria strategy to neutralize malaria infection in CHT districts.

Our study shows that malaria was more prevalent among males than females probably because male were more engaged in outdoor activities than females [18,19]. However, this scenario is not universal like in Chittagong Hill Tracts where both male and female tribal people work together in the field of Jhumma [20], but not the case with forest goers and bamboo cutters. Regarding the age group, the older age group of 15 years and above had the highest prevalence of malaria parasitaemia while the youngest age group of 1–4 years had the lowest, a finding that is in accord with what was reported from studies in Ethiopia [10,18]. However, there is a discrepancy between our findings and that of another South Ethiopian study in Wolaita zone which reported higher blood slide positivity rate in children aged 5-14 years [11]. The pre dominance of malaria infection in adult population of Bangladesh may be associated to the relative proportion of the adult population and the growing younger generation shift in Bangladesh .The current findings is an important implication that these age groups need due attention with regard to malaria intervention, particularly prevention and control measures taken by malaria programme in Bangladesh.

The low cases of malaria infection in low endemic areas including Chittagong districts is the result of pre-elimination strategy taken by National Malaria Programme in 2012. The programme has extended this strategy in North-East Sylhet division which has brought a successful result in Bangladesh. Although Chittagong did not experience with high burden of malaria cases, there were often fatal cases in the area probably because of ecological and epidemiological similarities with Cox's Bazar and CHT districts. It is apparent, therefore that Bangladesh still needs a comprehensive community based surveillance network which will reduce malaria mortality at expected level towards malaria elimination in 2030.

In this study, annual malaria occurrence was observed to have a seasonal variability with one peak season, June-July where malaria cases was more than double than mean malaria infection. Subsequently, Feb-March was the lowest malaria infection period in which 40% less malaria infection than mean malaria infection. The study coincided with another study in India where malaria peak season occurred from June to September [21] and slightly varied from the pattern in Sudan, where malaria cases are higher during July–November, strongly influenced by average monthly rainfall, especially in the rainy season [22]. Seasonal variation was also observed in Wolaita zone in Southern Ethiopia where two peak seasons occurred: the first one occurred between September to November and the second one ranges from April to June [11].

In this study, malaria occurrence might be under-estimated as we used secondary data from NMEP and BRAC though there was a credible evidence from the series of trend analyses which would provide a future reference. A more detailed entomological and epidemiological study and analysis would give a complete picture that will propel the country towards malaria elimination in 2030.

5. CONCLUSION

To conclude, we found, malaria substantially decreased in 13 endemic districts especially in medium and low endemic districts due to scaling up and rolling out of various strategies. Still we have a lot of concern regarding CHT districts where infection of malaria is a great agony for the people, and the effectiveness of program in neighboring Indian States cannot be ruled out. However, management of *Plasmodium vivax* is also a matter of apprehension for National Malaria Elimination Programme. Therefore the strategy the country has taken needs to be sustained and intensified in CHT districts to propel the country towards malaria elimination in 2030.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The data used in our analysis were center base aggregate programmatic data of NMEP and BRAC. These were routinely collected data from 2008 to 2016 by MIS department. No intervention done under this study. Thus, the ethical consideration was deemed to be inapplicable to the quantitative data.

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We thank the officials from NMEP and BRAC field office prepared the data and provided us for our study. We acknowledged their hard work for collecting the data and quality check-up over the years. A web based database prepared by NMEP is also very helpful for our study. We also express our gratitude to the Global Fund for funding the project that has a great deal of assistance to develop malaria surveillance in Bangladesh.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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