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Malaria transmission and disease burden in Assam: challenges and opportunities

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Abstract Malaria is major public health illness in Assam and 30–40% of the population is estimated to be at high-risk. Despite decades of attempted control interventions, malaria transmission is perennial and persistent in most parts of the state mostly transmitted by *Anopheles minimus*. Malaria outbreaks are returning associated with high rise in *Plasmodium falciparum* and attributable death cases. Therapeutic efficacy investigations for treatment of malaria revealed that chloroquine resistance was widespread for which artemisinin-based combination therapy (ACT) is being instituted in the control program. For data based on the preceding years, we briefly reviewed the available information on transmission dynamics, vector biology and control, drug policy, and discuss the challenges and opportunities for strengthening interventions for malaria control to help design situation specific strategies to check impending disease outbreaks with special reference to Assam. Under increased assistance from external agencies, we strongly advocate scaling up interventions based on mass distribution of long-lasting insecticidal nets (LLINs) for prevention and ACTs for treatment of drug-resistant malaria, and developing strong health delivery system in high-risk areas for meeting the complex emergencies and achieving transmission reduction.

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Introduction

Northeastern states of India (22°.4'–29°.31' N lat; 89°.48'–97°.25' E long) are malaria endemic and contribute 10–12% of cases and >20% of deaths annually (Dev et al. 2003). Assam is the major constituent state that alone accounts for 70% of the total population (30.56 million) contributing >50% of reported cases in the northeast. The region is endowed with rich biodiversity associated with heavy rainfall (2–3 meters) and malaria receptivity is high with estimated 30–40% population at high-risk (Dev et al. 2006a). Nearly 40% of the land area is under forest cover and large tracts are flood prone rendering them inaccessible. Malaria is major public health illness in the state reporting focal disease outbreaks characterized by high rise in cases and deaths attributable to *Plasmodium falciparum* (Prakash et al. 2000). The transmission of the causative parasites is perennial with peaks during April–September corresponding with months of rainfall. Given the terrain and ethnic heterogeneity, disease is unevenly distributed across the state with varying risk factors and intensities of malaria transmission maintained by *Anopheles minimus* in foothill villages and by *A. baimaii* (formerly species D of *A. dirus* species complex) in forested/forest fringe areas (Dev et al. 2004). With the countrywide launching of National Malaria Eradication Program in 1958, there was spectacular reduction in cases but unlike other parts of India, majority malaria units in Assam remained under

attack phase for DDT residual spraying (Sharma 1996). Since both vector species are still susceptible to DDT, it remains the insecticide of choice for vector control. However, despite decades of attempted control, malaria is a major impediment for socioeconomic development of the region. We report the retrospective analysis of malaria scenario, and briefly review the available information on transmission dynamics, vector biology and control, drug policy, and discuss the challenges and opportunities for strengthening interventions for malaria control with special reference to Assam.

Malaria transmission and attributable morbidity and mortality

There are 156 block level Primary Health Centres (PHCs) that have diagnostic facilities and serve as reporting units for malaria in Assam. The data retrieved from all sources for the past 10 years (1998–2008) are presented in Table 1 It may be noted that annual blood examination rate (ABER) for each year remained <10%, a primary cause of under-reporting due to poor disease surveillance. In these blood-smears, malaria parasite rate varied from 3.12–4.59%, majority of which were *P. falciparum* cases (58–69%). The annual parasite incidence (API) ranged from 2.02–4.91 per thousand population/year. Given the DDT spray coverage (>70% of target population) against malaria transmitting mosquito species, disease surveillance and treatment of cases, malaria transmission remained high, and as a result deaths due to malaria were common. All deaths were due to *P. falciparum* as confirmed by microscopic examination of blood-smear and/or rapid diagnostic test kit. Data analysis for 2007–2009 revealed that deaths were reported from all age groups of both sexes but were significantly higher in males ($p < 0.05$), and majority occurred in age group >15 years (Table 2).

Vector biology and control

Anopheles minimus is unequivocally proven as the major malaria vector in foothill areas of Assam valley (Dev et al. 2004). It is most abundant and widely prevalent for most part of the year. It is a typical indoor-resting species and have strong predilection for human host for blood feeding with peak biting activity during 01:00–04:00 hours. It breeds in slow-flowing seepage water streams which are innumerable in all foothill districts maintaining perennial transmission. *A. baimaii* is the only other vector species but of seasonal importance with distribution restricted to deep forest fringe areas (Prakash et al. 2001). *A. fluviatilis* mostly prevalent during winter months (January–March) has now been characterized merely a morphological and seasonal form of *A. minimus* (O.P. Singh, personal communication).

These vector species are susceptible to DDT residual spraying but are less amenable to control due to species specific behavioral characteristics. Systematic monitoring of vector density revealed that *A. minimus* avoided resting indoors for 10–12 weeks postspraying permitting extra-domiciliary transmission related to forest related livelihood (unpublished observ.). Situational analyzes of the high-risk districts revealed that interventions based on DDT spray operations were poorly applied, and for some years second round of spray was not done (Prasad 2009). Community refusal rates for indoor spraying were >50% amounting to low coverage so much so that there was no correlation between DDT used and malaria transmission intensities for the period observed (Table 1). *A. baimaii* is a jungle pool breeder and rests outdoors avoiding direct contact with sprayed surfaces rendering control interventions ineffective (Prakash et al. 1997). The relative abundance of *A. fluviatilis* during winter months may be due to lack of DDT spraying of which two rounds are usually undertaken during March–August corresponding to peak transmission period.

Given the scenario, we strongly advocate alternative interventions that are community-based and environmental friendly such as insecticide-treated nets (ITNs)/ long-lasting insecticidal nets (LLINs) as personal protection against these vector species that are highly anthropophilic and difficult to control. ITNs/LLINs are widely accepted by the communities and proven to be effective in the control of malaria transmitting mosquitoes in Assam (Dev 2009). What is important is targeting interventions in right place and right time to check transmission in the face of rapid urbanization, population migration and changing ecology for effective mosquito vector control.

Malaria outbreaks and containment practices

Most districts in Assam share an international or inter-state border (Fig. 1). This population is estimated between 30 and 40% and categorized high-risk for malaria and prone to focal disease outbreaks. Retrospective analysis of data

Table 1 Malaria transmission intensities and vector control interventions in Assam, northeast India (1998–2008)*

Year	Population in millions (% pop affected)**	No. and (%) of blood-smears			% of positive blood-smears with *Plasmodium falciparum*	Annual parasite incidence (No. of confirmed cases/1,000 population	DDT data				No. of death cases
							Targeted population (% coverage)		Quantity used in kg		
		Examined (% of population checked)	Positive for malaria parasite (%)	Positive for *Plasmodium falciparum* **(%)**			Ist spray	2nd spray	Ist	2nd	
1998	26.12	2441084 (9.34)	94645 (3.87)	54769 (2.24)	57.86	3.61	14658872 (79.67)	Not done	877904	0	34
1999	26.63	2872859 (10.78)	131048 (4.56)	83064 (2.89)	63.38	4.91	15436286 (81.86)	6031876 (76.90)	1081477	363830	111
2000	26.90	2215375 (8.23)	84915 (3.83)	52116 (2.35)	61.37	3.15	14592590 (79.30)	6967822 (61.89)	937238	339453	43
2001	27.32 (39)	2432620 (8.90)	95142 (3.91)	58951 (2.48)	61.97	3.48	15645797 (77.02)	Not done	917766	0	122
2002	27.73 (23)	2325105 (8.32)	89601 (3.85)	55825 (2.40)	62.30	3.21	14008712 (70.80)	5838094 (70.63)	823537	292956	72
2003	27.85 (17)	2133820 (7.66)	76570 (3.85)	48647 (2.27)	63.53	2.74	14144089 (77.45)	7071625 (90.00)	802885	378449	53
2004	28.73 (13)	1853560 (6.45)	58134 (3.13)	41400 (2.23)	71.21	2.02	11842156 (81.00)	Not done	748801	0	52
2005	29.00 (31)	2050261 (7.06)	67885 (3.31)	45453 (2.21)	66.95	3.34	12964867 (78.00)	Not done	797253	0	113
2006	29.32 (33)	2743092 (9.35)	126178 (4.59)	82546 (3.00)	65.42	4.30	12534987 (74.00)	12820065 (91.42)	756540	1381905	304
2007	29.65 (30.71)	2399836 (8.09)	94853 (3.12)	65542 (2.73)	69.09	3.19	13365385 (81.72)	10929778 (75.21)	840431	575991	152
2008	30.59	2687756 (8.62)	83939 (3.12)	58124 (2.20)	69.30	2.74	8427442 (79.00)	7696344 (78.00)	495373	428912	86

* Source, State Health Directorate of Assam

** % population reporting high rise in cases and attributable deaths

Table 2 Distribution of malaria-attributable death cases by age and gender during 2007–2009 in Assam, northeast India*

Age-group (yrs)	0–4		5–9		9–14		≥15		Total cases	
Year	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
2007	13	08	07	12	11	12	55	34	86	66
2008**	11	10	06	03	04	06	32	14	53	33
2009**	09	04	04	04	04	04	22	08	39	20
Total**	33	22	17	19	19	22	109	56	178	119

*Source, State Health Directorate of Assam

**Number of death cases were significantly higher in males (P = <0.05) of which majority were in >15 age group (P = <0.001)

for the years (1991–2008) revealed that every 3–4 years there was unusual rise in *P. falciparum* cases and malaria deaths mostly along bordering population groups (Fig. 2). For the districts investigated for disease outbreaks during 1988–2006, it was observed that in the affected population, *A. minimus* was the predominant vector species incriminated by dissection and demonstration of the sporozoites (Table 3). In 2006, 304 confirmed deaths were recorded in Assam, the highest in last 15 years. All border districts were adversely affected, of which Lakhimpur (sharing an inter-state border with Arunachal Pradesh) reported 82 deaths, highest in the state. Deaths were reported from all age groups (excluding <1 year) of both sexes, most of which were attributed to late reporting. Among the deceased, majority (44%) died the same day of hospital admission, 39% died within 2 days, 14% within 3 days, and the remaining in ≥3 days of hospital care (Source, Chief Medical and Health Officer, Civil Hospital, Lakhimpur). As per hospital records, during outbreak period

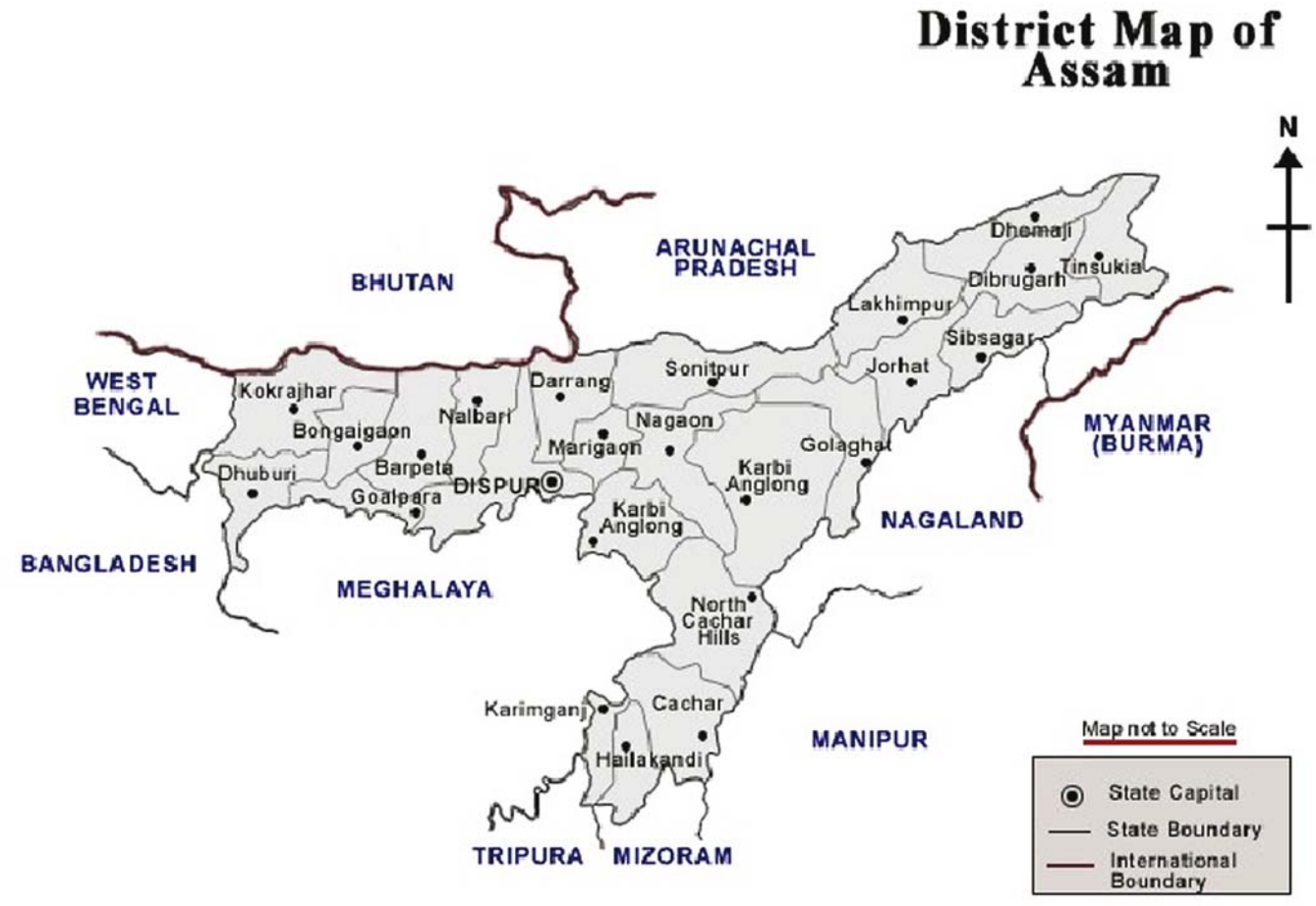

Fig. 1 A sketch map of Assam showing geographical proximity to Bhutan, Bangaldesh and Myanmar

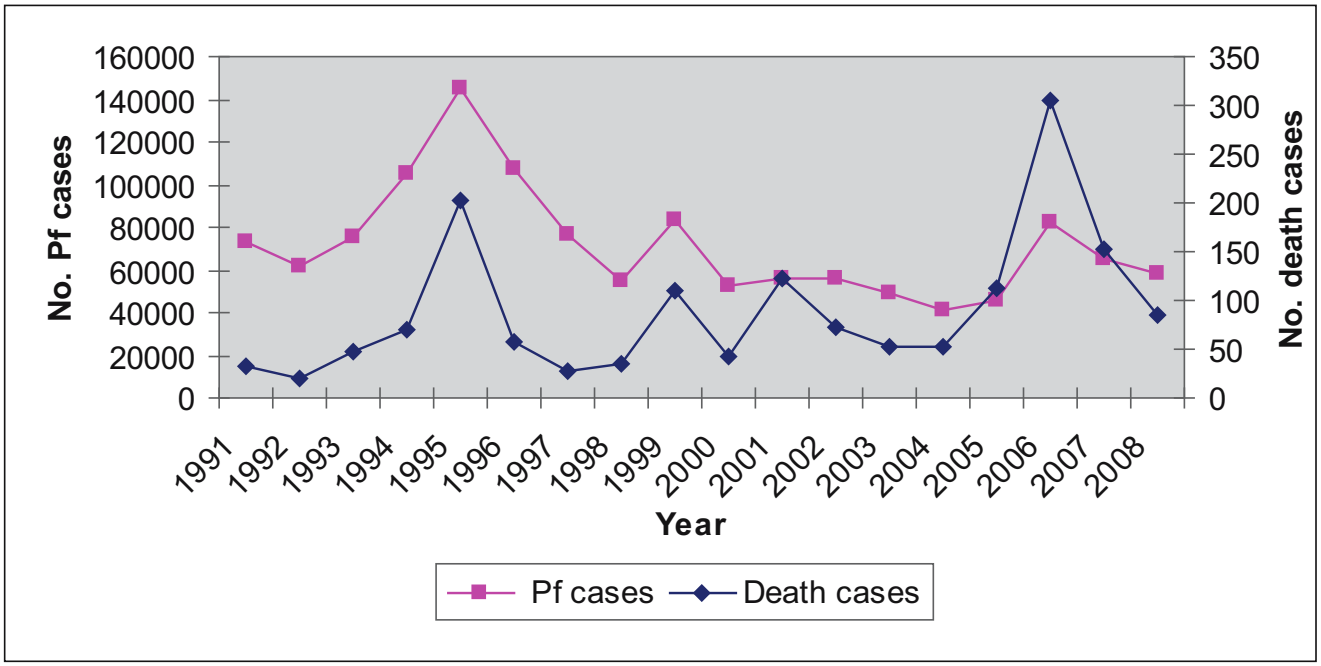

Fig. 2 Malaria-attributable morbidity due to *Plasmodium falciparum* cases and deaths in Assam during 1991–2008 (Source, State Health Directorate of Assam)

(April–June 2006), of total admissions in the hospital, 85% were due to malaria with severe complications that included hepatic jaundice, renal failure and cerebral involvement in decreasing order. The actual death toll is always high as this does not include fever-related deaths lacking blood-smear examination report.

Stratification based on API for the period 2004–2008, revealed that the increase in districts reporting API >10 was at the expense of low endemic districts (API <1) due to sudden spurt of *P. falciparum* associated with death cases, whereas districts reporting moderate endemicity were stable with little variation (Fig. 3). The common denominator was that the affected population groups were located along borders where healthcare access was poor and distant. These villages were inaccessible and communities were poorly informed of disease prevention and control. Disease surveillance was scarce resulting in build up of gametocyte reservoir and vector density amounting to increased risk of malaria. In such complex emergencies, it is advisable to strengthen interventions by focal DDT spray operations, impregnation of community-owned mosquito nets, early diagnosis and treatment.

Table 3 Relative abundance of *Anopheles minimus,* sporozoite infectivity, mosquito biting and entomological inoculation rates (EIRs), and prevalence of malaria in districts of Assam reporting focal disease outbreaks, northeast (India)*

District	Location	Study period	Daytime resting collections per person hour	Mean biting/ rate/person/ night (MBR)	No. mosquitoes dissected (sporozoite rate)	EIR (MBR × sporozoite rate) per person/night	% positivity in clinical cases of malaria	
							Plasmodium falciparum	*P. vivax*
Kamrup	Sonapur	Jun–Oct 1988	07.00	14.00	332 (0.033)	0.46	17.0	11.0
Sonitpur	Rangapara	Jul–Sep 1992	02.00	13.00	142 (0.042)	0.55	42.8	10.2
Darrang	Tangla	Aug–Sep 1992	11.00	20.00	382 (0.031)	0.62	48.0	8.1
Golaghat	Bokakhat	May–Jul 1994	05.35	12.25	303 (0.010)	0.12	6.2	22.8
Goalpara	Agia	Apr–May 1995	0.95	18.75	105 (0.029)	0.54	34.5	13.4
Morigaon	Nellie	Jul–Aug 1999	02.87	23.00	130 (0.031)	0.71	39.4	4.1
Lakhimpur	Boginadi	Apr–Jun 2006	07.00	34.00	No data	–	18.9	10.6

*Source, Dev et al. 2004

Drug policy and changing transmission profiles

Ever since inception of control program in 1950s, chloroquine has been the drug of choice for treatment of both *P. falciparum* and *P. vivax* cases. It is in 1973 that resistance to chloroquine for treatment of *P. falciparum* was first documented in Karbi Anglong district of Assam (Sehgal et al. 1973). Since then drug-resistant foci have multiplied and spread widely in most parts of India resulting in steady increase in proportions of *P. falciparum* from 13% in 1978 to presently 50% of those reported in India (Sharma 1996, 2000; Mohapatra et al. 2003). Development and spread of drug-resistance is a major challenge and is responsible for increased morbidity and mortality in northeastern states. Periodic assessment of therapeutic efficacy in malaria endemic districts led to change of drug policy for treatment of drug-resistant malaria (Table 4). Consequent to research inputs, it was in 2004 that there was switch from chloroquine (CQ) to sulfadoxine-pyrimethamine (SP) as first-line of therapy in select districts with documented chloroquine resistance (Source, State Health Directorate). In 1990s, the development of artemisinin derivative, i.e. alpha-beta arteether and its clinical assessment as monotherapy raised new hopes to control drug-resistant malaria. It was evaluated to be fast acting schizontocidal drug that was convenient for treatment of severe and complicated *P. falciparum* cases (Asthana et al. 2001). Beginning 2007, NVBDCP adopted artemisinin-based therapy by combining SP (that was already in use) with artesunate for treatment of every confirmed case of *P. falciparum* in high-risk districts that have been declared chloroquine-resistant. Therapeutic assessment of this combination in different malaria endemic pockets resulted in rapid parasite clearance, and was concluded to be safe and effective for treatment of *P. falciparum* malaria (Dev et al. 2009).

Implementation of the revised drug policy resulted in drastic reduction in cases as evidenced in the Sonapur Primary Health Centre (Dimoria block) of Kamrup district of Assam (Table 5). Data from 2004–2008 revealed that SP therapy in 2004 resulted in appreciable reduction in *P. falciparum* cases in 2005 but that was not sustainable resulting in 2-fold rise in the following year. However, introduction of artesunate + sulfadoxine-pyrimethamine (AS + SP) artemisinin-based combination therapy (ACT) in 2007 amounted to notable reduction in case incidences over 2 year study period. The transmission profile of malaria had changed noticeably indicating declining trends of *P. falciparum* (Fig. 4). Similarly, other recommended ACTs that included artesunate + mefloquine (AS + MQ), artemether + lumefantrine (AL) and dihydroartemisinin + piperaquine (DHA + PQP) that were subject to assessment in northeast reported cure rate >95%, and were concluded to be safe and effective as alternate drugs (Neena Valecha, personal communication). Newer ACTs such as artesunate + pyronaridine (AS + PRN), and potent molecules (acridones) offer a powerful approach to address the gaps and weaknesses in the existing armamentarium of the combination therapies available at present (Ramharter et al. 2008; Kelly et al. 2009). We strongly advocate rolling out ACT for every single case of *P. falciparum* to avert impending disease outbreaks, and help contain spread of drug-resistant malaria. Based on research inputs, ACTs have been adopted by the NVBDCP for all districts of Assam beginning 2009.

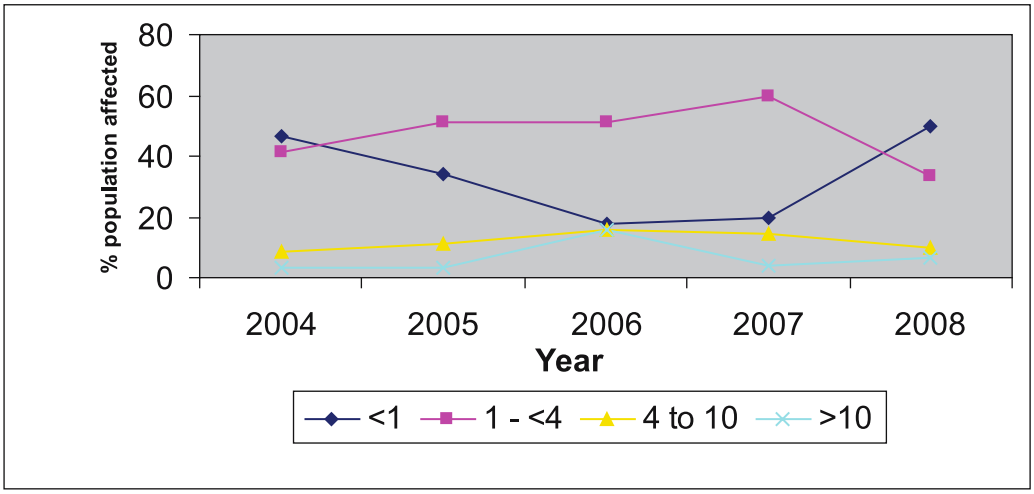

Fig. 3 Malaria stratification based on parasite incidence per thousand population/year for districts of Assam during 2004–2008

Table 4 Therapeutic efficacy of antimalarials for treatment of *Plasmodium falciparum* malaria in northeast India

Antimalarial treatment	District (state)	Study period	No. and (%) of subjects parasitemic on follow up day of						
			Day 0	Day 2	Day 3	Day 7	Day 14	Day 21	Day 28
CQ[1]	Kamrup and Nalbari (Assam)	2000–02	144 (100)	23 (15.9)	17 (11.8)	5 (3.5)	11 (7.6)	9 (6.3)	3 (2.1)
CQ/SP[2]	Kamrup and Nalbari (Assam)	2000–02	34 (100)	4 (11.8)	2 (5.9)	1 (2.9)	1 (2.9)	0 (0)	0 (0)
SP[3]	Kamrup (Assam)	2004	54 (100)	28 (50.9)	4 (7.3)	0 (0)	1 (1.8)	4 (7.3)	4 (7.3)
Alpha/beta arteether	Kamrup and Darrang (Assam)	1995–96	41 (100)	6 (14.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Kamrup and Darrang (Assam)	2005	60 (100)	50 (83)	23 (38)	3 (5)	0 (0)	0 (0)	3 (5)
AS + SP[4]	Darrang (Assam)	2005	51 (100)	No data	0 (0)	0 (0)	0 (0)	0 (0)	3 (5.9)
	Nalbari (Assam)	2006	53 (100)	No data	1 (1.9)	0 (0)	0 (0)	4 (7.5)	2 (3.8)
	West Garo Hills (Meghalaya)	2007	54 (100)	No data	0 (0)	0 (0)	1 (1.8)	2 (3.7)	0 (0)
AL[5]	Kamrup (Assam)	2007	53 (100)	10 (18.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

[1]CQ = chloroquine, [2]CQ/SP = sequential therapy with sulfadoxine-pyrimethamine for chloroquine resistant cases, [3]SP = sulfadoxine-pyrimethamine
[4]AS + SP = artesunate + sulfadoxine-pyrimethamine, [5]AL = artemether + lumefantrine

Challenges and opportunities

There are many operational constraints specific to northeast India that amount to intolerable disease burden due to malaria. Amongst shortfalls that permit persistent transmission of malaria is the manpower attrition at various levels of operation (Source, State Health Directorate). There are existing vacancies for district level functionaries amounting to poor/delayed reporting and lack of much needed supervision (Prasad 2009). Disease surveillance at present can be best described as fragmentary inclusive of misdiagnosis and poor record keeping which should be robust for timely institution of intervention measures. True incidence of malaria is estimated to be manifold due to much larger private sector for which there is no existing mechanism for data collation. There are many more cases which had the least opportunity for blood-smear examination and treatment due to geographical remoteness and inaccessibility. Worst is the large asymptomatic reservoir in the endemic communities estimated to be in the range of 8–33% that are poorly addressed (Dev et al. 2006b). The adherence to national drug policy for treatment of cases should be enforced for government and private sector alike with increased regulation. There is need to implement a comprehensive and innovative approach for training of NGOs, private vendors, private clinics for accredited services to increase the strength and reach of the government program. Health infrastructure in the periphery remains inadequate for treatment of severe and complicated cases of malaria. Community participation for enhanced compliance for indoor residual spray operations and seeking treatment should be the guiding principle. The entomological component, the crucial epidemiological determinant for monitoring vector density and supervision of control intervention, is non-existent. A culture of performance, accountability and transparency should be established. Northeast shares lengthy borders with neighboring countries of Bhutan, Myanmar and Bangladesh that are equally malaria endemic. These borders are porous with high levels of human traffic which demands well

Table 5 Changing transmission profiles of malaria in the Sonapur Primary Health Centre (Dimoria block) of Kamrup district of Assam, northeast India

Year	Population	No. blood-smears examined (ABER)**	Positive for malaria parasite (%)	Positive for *Plasmodium falciparum*	% of positive blood-smears with *Plasmodium falciparum*	Annual parasite incidence (No. of confirmed cases/1,000 population)
2004*	146859	25420 (17.3)	2173 (8.54)	2006	92.31	14.79
2005	153460	22121 (14.4)	1313 (5.93)	960	73.11	8.55
2006	155721	35582 (22.8)	2551 (7.16)	1815	71.14	16.38
2007*	166491	29307 (17.6)	2152 (7.34)	1145	53	12.90
2008	166579	33925 (20.4)	584 (1.72)	279	48	3.50

*Sulfadoxine-pyrimethamine (SP) and artesunate + sulfadoxine-pyrimethamine (AS + SP) were implemented in 2004 and 2007 respectively for treatment of *Plasmodium falciparum* cases

**ABER denotes annual blood-smear examination rate (% population checked for malaria parasite)

supervised coordinated spray operations, and screening and treatment at entry points. Population migration across borders is one imminent threat that continues to thwart the control efforts. Unauthorized colonies have come up in erstwhile forest reserve areas where control measures are not instituted resulting in fulminating disease outbreaks and unattended parasite reservoir. Ethnic conflicts in some areas continue to plague the program resulting in uninterrupted malaria transmission. The surge of counterfeit drugs in southeast Asia (Dondorp et al. 2004; Newton et al. 2008), high refusal rates to indoor residual spraying (Prasad 2009), the slackness of workforce and treatment seeking behavior and compliance are some major challenges that need to be addressed (Dev et al. 2006b).

Enhanced allocation of resources under Global Fund against Aids, Tuberculosis and Malaria (GFATM), National

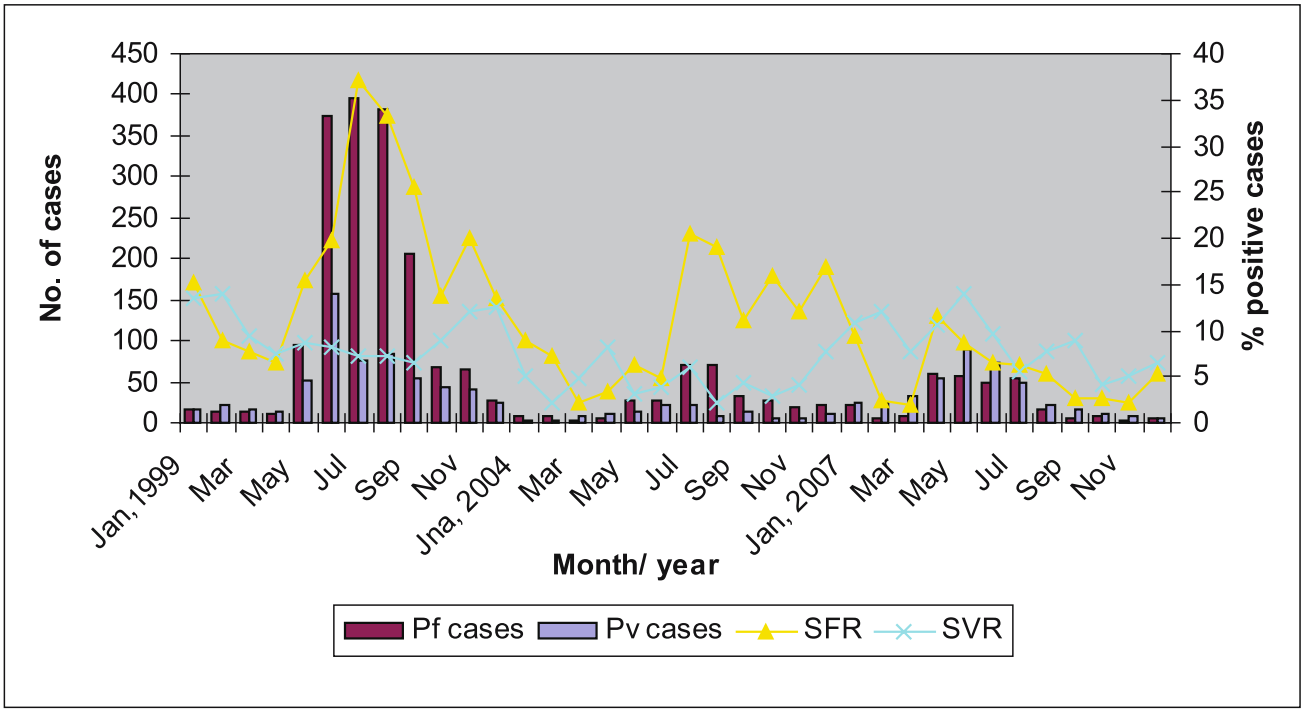

Fig. 4 Declining trends of malaria transmission in the Sonapur Primary Health Centre (Dimoria block) of Kamrup district of Assam consequent to change in drug treatment policy from chloroquine to sulfadoxine-pyrimethamine in 2004, and to ACT (artesunate + sulfadoxine-pyrimethamine) in 2007 (representative year 1999 when chloroquine was in force for treatment of *Plasmodium falciparum*) Pv = *Plasmodium vivax,* Pf = *P. falciparum,* SFR = % smear positive for *P. falciparum,* SVR = % smear positive for *P. vivax*.

Rural Health Mission (NRHM) and donors alike offer the opportunity for strengthening the healthcare services in the resource-poor settings to meet the malaria challenge. The strengthening of human resource and provision of logistic requirements on account of antimalarials (ACTs), diagnostics (RDKs) and preventive measures (ITNs/ LLINs) have resulted in substantial reduction in malaria transmission formerly intractable (Dev et al. 2008; Dev 2009). The challenge now is to ensure the sustained supply of these commodities and scale-up the interventions in reaching the population groups those are most in need. Public private partnership should be sought to meet the demand and supply at affordable prices. Political commitment for the continued support to the control program is of paramount importance failing which the gains of the preceding years may be lost. There is opportunity for coordinated action between agencies viz. defense, industry, public and private sector alike to keep malaria at bay helping restore confidence in the affected communities and boosting economic development.

Looking forward: Malaria map is shrinking so much so that as many 39 countries are contemplating malaria elimination (Greenwood 2008; Feachem and the Malaria Elimination Group 2009). Given the malaria endemicity in the northeast, concerted efforts should be made to achieve low levels of transmission prioritizing high-risk areas. We strongly advocate judicious mix of technologies that are feasible, sustainable and environment friendly based on understanding of local disease epidemiology (Beier et al. 2008). What is tantamount to economic development is the strong health delivery system to reach the outreach population groups (Whitty et al. 2008; Mendis et al. 2009). Research component should be strengthened for providing inputs to the control program updating with the new technologies for effective control. The political will for increased allocation of resources in the northeast will yield rich dividend in reducing the levels of transmission and building equitable healthcare services.

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