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Burden of Malaria in India: Retrospective and Prospective View

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Abstract. In India, nine Anopheline vectors are involved in transmitting malaria in diverse geo-ecological paradigms. About 2 million confirmed malaria cases and 1,000 deaths are reported annually, although 15 million cases and 20,000 deaths are estimated by WHO South East Asia Regional Office. India contributes 77% of the total malaria in Southeast Asia. Multi-organ involvement/dysfunction is reported in both *Plasmodium falciparum* and *P. vivax* cases. Most of the malaria burden is borne by economically productive ages. The states inhabited by ethnic tribes are entrenched with stable malaria, particularly *P. falciparum* with growing drug resistance. The profound impact of complicated malaria in pregnancy includes anemia, abortions, low birth weight in neonates, still births, and maternal mortality. Retrospective analysis of burden of malaria showed that disability adjusted life years lost due to malaria were 1.86 million years. Cost–benefit analysis suggests that each Rupee invested by the National Malaria Control Program pays a rich dividend of 19.7 Rupees.

INTRODUCTION

Malaria imposes great socio-economic burden on humanity, and with six other diseases (diarrhea, HIV/AIDS, tuberculosis, measles, hepatitis B, and pneumonia), accounts for 85% of global infectious disease burden.[1,2] Malaria afflicts ~90 countries and territories in the tropical and subtropical regions, and almost one half of them are in Africa, South of Sahara. About 36% of the world population (i.e., 2020 million) is exposed to the risk of contracting malaria. The World Health Organization estimates 300-500 million malaria cases annually, with 90% of this burden being in Africa. In addition, the estimated annual mortality attributed to malaria ranges from 700,000 to 2.7 million globally and > 75% of them are African children and expectant mothers. Doubts have been expressed about reliability of these estimates because most of the hyper- and holoendemic countries, especially in Africa, lack credible diagnostic facilities and reporting systems.[3,4]

In the Southeastern Asian Region of WHO, of ~1.4 billion people living in 11 countries (land area, 8,466,600 km^2; i.e., 6% of global area), 1.2 billion are exposed to the risk of malaria, most of whom live in India.[5] However, Southeast Asia contributed to only 2.5 million cases to the global burden of malaria. Of this, India alone contributed 76% of the total cases. Taking into account clinical episodes, it has now been estimated with the help of epidemiologic models and geographical and demographic data that *Plasmodium falciparum* estimates outside Africa, especially in Southeast Asia, are 200% higher than reported by the World Health Organization (i.e., 118.94 million of global estimates of 515 million cases).[4] In addition to this, burden of *P. vivax* malaria in the world has been calculated at 71-80 million cases, of which Southeast Asia and Western pacific countries contributed 42 million cases.[6]

Health care and the Malaria Control Program in India. India has 29 states and 7 union territories. There are a number of well-structured National Disease Control/ Elimination Programs that are implemented by the state governments following national policies. There are three tiers of government-funded health care system throughout India (primary health care system having network of primary health centers and subcenters in rural areas, urban health centers, and urban health posts or dispensaries in the towns functional under municipal councils and corporations; district hospitals for secondary care; and medical colleges and hospitals for tertiary care). Among private health care providers, there are general practitioners and quacks besides hospitals and polyclinics that are professionally managed. Tertiary care hospitals are also operated by large public sector industrial units and a large private sector industry. An organized National Vector Borne Disease Control Program (NVBDCP) provides technical and operational guidelines to the state governments besides sharing one half the costs for the control of malaria, filariasis, Japanese encephalitis, leishmaniasis, and dengue/ Dengue Hemorrhagic Fever control in India. NVBDCP is implemented through the primary health care system with the assistance of multi-purpose workers at the grass roots level. In inaccessible areas, drug distribution centers (DDCs) and fever treatment depots (FTDs) are provided at the community level. Early detection and complete treatment, selective vector control, and behavioral change communication are the key components of current malaria control strategy of the NVBDCP. World Bank assisted Intensified Malaria Control Project (IMCP) has been launched recently in India. In the 1990s, Enhanced Malaria Control Project (EMCP) in 181 selected districts of the country was operational with the assistance of the World Bank. Another project supported by Global Fund for AIDS, Tubercolosis and Malaria (GFATM) is on the anvil under NVBDCP and would be launched in the districts hitherto not covered either under EMCP or IMCP.

Malaria incidence in India. In India, the epidemiology of malaria is complex because of geo-ecological diversity, multiethnicity, and wide distribution of nine anopheline vectors transmitting three Plasmodial species: *P. falciparum, P. vivax,* and *P. malariae*. *Anopheles culicifacies* is widely distributed and is the principal vector of rural malaria, *An. stephensi* is the primary urban vector, *An. fluviatilis* is a vector in the hills and foothills, and *An. minimus*, *An. nivipes*, *An. philippinensis,* and *An. dirus* are vectors in the northeast and *An. sundaicus* is restricted to Andaman and Car Nicobar islands. *An. annularis* and *An. varuna* are secondary vectors with wide distribution.

In 1947, when India became independent, 75 million malaria cases in a population of 330 million were estimated.[7] During the eradication era in the late 1950s and early 1960s,

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a spectacular achievement was witnessed on the malaria eradication front because malaria cases significantly declined to just 100,000 in 1964. However, reversal was experienced, and malaria staged a comeback. By 1976, malaria cases had touched the 6.4 million mark. A continued rise in *P. falciparum* was witnessed, and its proportion has gradually risen to nearly 50% in recent years (Figure 1).

Distribution of malaria in different states of India. The annual parasite incidence (API) is a malariometric index to express malaria cases per thousand population. As per the NVBDCP incidence records, in most of India, the API was < 2, whereas 2–5 API was in scattered regions, and regions with > 5 API were scattered in the states of Rajasthan, Gujarat, Karnataka, Goa, Southern Madhya Pradesh, Chhattisgarh, Jharkhand, and Orissa and in northeastern states (Figure 2).

The proportion of *P. vivax* and *P. falciparum* varies in different parts of India. Although mostly indo-gangatic plains and northern hilly states, northwestern India and southern Tamil Nadu state have < 10% *P. falciparum*, and the rest are *P. vivax* infections; in the forested areas inhabited by ethnic tribes, the situation is reversed, and the *P. falciparum* proportion is 30–90%, and in the remaining areas, it is between 10% and 30% (Figure 3).

In India, malaria is contributed the most by Orissa state (Figure 4). Although Orissa has a population of 36.7 million (3.5%), it contributed 25% of a total of 1.5–2 million reported annual malaria cases, 39.5% of *P. falciparum* malaria, and 30% of deaths caused by malaria in India (Source NVBDCP, India). Similarly, in the other states inhabited by ethnic tribes mainly in the forest ecosystems, meso to hyperendemic conditions of malaria exist with the preponderance of *P. falciparum* to the extent of 90% or even more.

Annual blood examination rate. The National Vector Borne Disease Control Program prescribes that the annual blood examination rate (ABER) for malaria should be at least 10% on the presumption that 10% of the population in a year will have fever at one point in time. It is assumed that if all or most of the fever cases are examined for malaria, most of the incidence of malaria could be captured during fortnightly active surveillance. A look at the 2004 data (Figure 5) shows that the average ABER was 9% in India. In 14 of 29 states, however, it ranged from 1% to 8%, and in the remaining 15 states and union territories, ABER ranged from 10% to 40%.

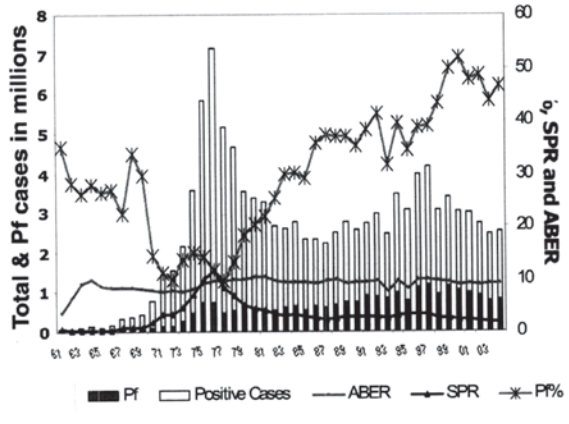


FIGURE 1. Trends of malaria incidence in India from 1960 to 2005. Nearing eradication in 1960s (< 100,000 cases) to resurgence in the mid-1970s (~6.4 million cases) and stabilizing trend to ~2 million cases in the 1990s. *P. falciparum* proportion has steadily risen to ~50% in the recent years, and the remaining incidence is of *P. vivax* and a small proportion of *P. malariae* (source: National Vector Borne Disease Control Program data). SPR, slide positivity rate; ABER, annual blood examination rate.

FIGURE 2. Distribution of malaria incidence in India according to annual parasite incidence in 2004 (data source: NVBDCP). Majority of India had < 2 cases per 1,000 population, 2–5 cases in some scattered regions, and > 5 cases per 1,000 population where ethnic tribes live and stable malaria conditions prevail.

Widespread problem of drug resistance. In India, chloroquine resistance in *P. falciparum* was first reported by Manjha in the Karbi Anglong District in 1973[8] and from Nowgaon in 1974 in the northeastern state of Assam. More cases were detected in the next 3-4 years in Assam, Arunachal Pradesh, Mizoram, and Nagaland. Although foci of resistance to chloroquine are present in the entire country, the problem is more pronounced in areas with intense *P. falciparum* transmission like the northeastern states and Orissa and in areas where there is intermixing of the population, such as project areas, including construction sites, in big metropolitan areas, and along international borders (Figure 6). In most of the studies, only late treatment failure to chloroquine has been observed, probably because of the semi-immune nature of the population.

The problem of drug resistance has also been studied using molecular markers. Molecular studies in 274 Indian Pf isolates detected *K76T* mutations in all patients who did not respond to chloroquine and 96% of cases who were cured with chloroquine, showing the lack of a correlation between the *K76T* mutation and clinical cure.[9] However, in this study, a significant association of the *K76T* mutation was observed with the *in vitro* response to chloroquine in *P. falciparum*. Alleles of the *PfMDR*1 gene showed a strong association but incomplete correlation with chloroquine resistance.[10]

FIGURE 3. *Plasmodium falciparum* proportion distribution in India. High proportion of *P. falciparum* up to 90% is seen in zones inhabited by ethnic tribes in forest ecosystems where stable malaria conditions occur.

Although the available data on sulfadoxine-pyrimethamine (SP) resistance is limited, it seems that efficacy for this drug is within acceptable limits, except in limited areas such as the Indo-Myanmar border in Arunachal Pradesh and some parts of Assam and West Bengal.[11,12] In one study, of 40 clinical isolates, 87.5% had dihydrofolate reductase and 15% had dihydropteroate synthase mutations.[13] Parasites carrying double or single mutants also showed increased minimum inhibitory concentration values for both pyrimethamine and sulfadoxine.

Only limited reports of chloroquine resistance in *P. vivax*

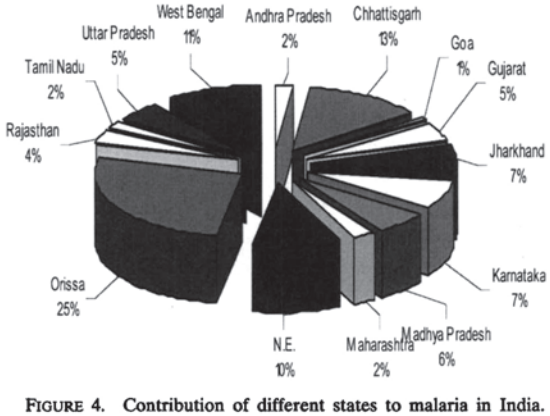


FIGURE 4. Contribution of different states to malaria in India. Orissa, Chhattisgarh, West Bengal, Jharkhand, and Karnataka contributed the most.

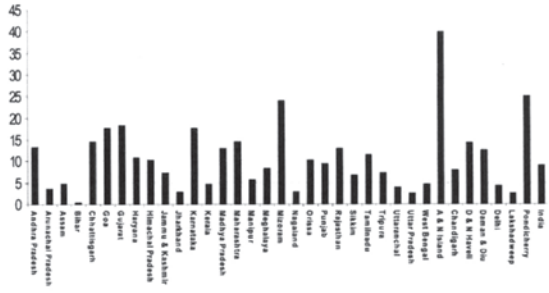


FIGURE 5. Annual blood examination rates (ABERs) for detection of malaria in different states of India in 2004. Ten percent is considered adequate to reflect a true picture of malaria, but there are some highly endemic states where ABER is much less than the norm. Even the national average was 9% (source: NVBDCP, India).

malaria are available from India. Two cases from Mumbai did not respond to a full dose of chloroquine (1,500 mg) and peripheral smear continued to be positive despite adequate blood concentration of drug.[14] Similarly, there is another case report from Mathura (U.P.) of nonresponse to standard dose of chloroquine as confirmed by repeated blood examination.[15] Recently 16% RI and 6.7%, RII resistance in *P. vivax* was reported in a study conducted in 75 patients in Bihar.[16] In addition, multi-drug resistance has also been reported.[17] Contrary to these reports, in a study in West Bengal and Orissa during 1998–2001, 100% cure rates by Day 7 in 480 *P. vivax* malaria patients were observed.[18] Incidentally, these areas, where *P. vivax* is still sensitive to chloroquine, have high drug pressure and chloroquine resistance in *P. falciparum*. Similar

FIGURE 6. Areas shown in gray (triangles and patches) where chloroquine resistance in *P. falciparum* has been confirmed, qualifying for use of the second-line drug SP (source: Data from National Vector Borne Diseases Control Program, India).

findings were confirmed in a therapeutic efficacy study with chloroquine in vivax malaria in Gautam Budh Nagar (Uttar Pradesh) in the north, Navi Mumbai (Maharashtra) in the west, and Chennai (Tamil Nadu) in south India in 287 patients in 2002. The curative efficacy of chloroquine was 100% in these patients with vivax malaria. Rapid parasite and fever clearance was observed in all cases, and the drug was well tolerated.[19] From the data available thus far, it is evident that the problem of drug resistance in *P. vivax* is not of major concern; however, one needs to be vigilant because *P. vivax* produces a relapsing type of infection and is a predominant species in India.

Based on the results of 28-day *in vivo* studies until 2001 and therapeutic studies from 2002 onward conducted by the NVB-DCP and research institutes including the National Institute of Malaria Research, the drug policy has been revised in 241 primary health centers (PHCs) of 71 districts in 20 states of India (Figure 6).

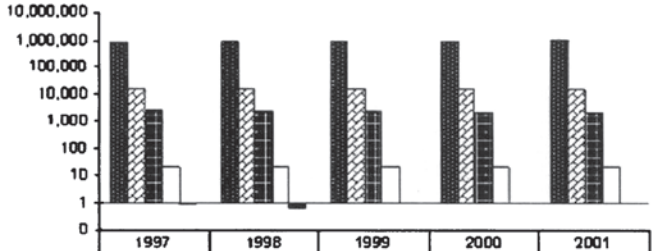
The salient features of the national drug policy that has been modified and approved in January 2007 by the NVB-DCP are as follows:

1. All efforts should be made to confirm the diagnosis of malaria. If it is not possible, chloroquine in full therapeutic dose of 25 mg/kg body weight over 3 days should be given to all cases of clinical malaria including confirmed cases at all levels, irrespective of high- or low-risk malaria status of district/block. In high-risk areas, in addition to chloroquine, primaquine (single dose) should be given. Practice of presumptive treatment with 600 mg chloroquine will be discontinued.
2. Change of drug from chloroquine (first line of treatment) to artesunate plus sulfadoxine-pyrimethamine (ACT) combination therapy (second line of treatment) will be done at the treatment failure of > 10%. The change will be done in PHCs with drug resistance and clusters of blocks around that PHC.
3. Mefloquine is available in the country and is only to be provided to patients with the prescription of medical practitioners supported by a laboratory report showing asexual stages of *P. falciparum* in the peripheral smear.
4. Artemisinin derivatives may only be used in injectable form for the treatment of severe and complicated *P. falciparum* malaria in adults. Use of oral forms of these derivatives (for monotherapy) is not recommended.
5. Chemoprophylaxis is recommended for 1) pregnant women in high-risk areas and 2) travelers, including service personnel, who temporarily go on duty to high malarious areas. In chloroquine-sensitive areas, chloroquine is given weekly, but in chloroquine-resistant areas, chloroquine should be supplemented by daily proguanil.
6. For treatment of vivax malaria, treatment with 1500 mg chloroquine over 3 days and Primaquine 0.25 mg/kg for 14 days (under medical supervision) is recommended.

Malaria prevalence according to age and sex in India. Most of the point prevalence studies in India have been carried out for outbreak/epidemic investigations. There is very limited information on age- and sex-specific seasonal prevalence of malaria in different paradigms in the country. In the available studies, age and sex classification used is arbitrary.[20–26] The burden is generally higher in men than women in all age groups. Children in the states of Assam,[20–22] Arunachal Pradesh,[23] and Rajasthan[24] had a higher incidence of malaria than adults, whereas in the indo-gangatic plains, the situation was reversed.[25,26]

Incidence gap. In 1990, it was estimated that, of a population of 843.7 million in India, 75, 240, and 500 million people were, respectively, at high, moderate, and low risk of contracting malaria. The situation has not changed much since then except for the population growth in each risk category.[27] It is now well accepted that the reported incidence of malaria at the national level on the basis of surveillance carried out in the primary health care system at best reflects a trend and not the true burden of malaria. In the 1990s, the reported malaria incidence in India was ~1.5–2.6 million cases and 666–1000 deaths/yr whereas the estimated incidence by WHO was 15 million malaria cases with 19,500–20,000 deaths/yr (WHO SEARO website) (Figure 7).

A comparison of malaria incidence reported during routine surveillance under the primary health care system with that of parallel longitudinal studies carried out in some states of India showed that a huge gap of 68% to 98% existed between the reported and true incidence of malaria (Table 1).[28–32] Reasons attributed to this gap are inadequacies in surveillance and examination and underreporting of malaria cases.



	1997	1998	1999	2000	2001
Population in malarious area	884,719	907,297	929,192	973,146	1,006,845
Estimated cases	15,000	15,000	15,000	15,000	15,000
Reported cases	2,660	2,223	2,285	2,019	1,972
Estimated deaths	19.5	19.5	20	20	20
Reported deaths	0.879	0.666	1.057	0.946	0.938

FIGURE 7. World Health Organization estimates that India has 15 million cases of malaria with 19,500–20,000 deaths annually vs. ~2 million cases and 1,000 deaths reported (WHO SEARO website).

TABLE 1

Malaria incidence gap between routine surveillance and parallel longitudinal surveys/point prevalence studies carried out in Uttar Pradesh (now Uttaranchal), Haryana and Orissa state of India

Area	Data source	Cases	SPR	SFR	Percent gap	Ref.
Kichha PHC						
Nainital	RS	76	4.7	NA	95	Sharma and others 1983[32]
(Uttaranchal)	LS	1,784	22.1	NA		
Kharkhode						
PHC	RS	183	12.6	5.5	97.4	Sharma and others 1983[32]
(Haryana)	LS	7,117	43.2	30.46		
Gadarpur						
PHC	RS	49	5.27	1.61	98.1	Malhotra and others 1985[31]
(Uttaranchal)	LS	2,623	58.66	34.58		
Bisra PHC						
Rourkela	RS	8	7.6	3.8	68.0	Ghosh and others 1989[29]
(Orissa)	PP	25	26.3	15.8		

SPR, slide positive rate; SfR, slide falciparum rate.

Underreporting of malaria because of misdiagnosis has been observed in Gujarat, where re-examination of blood smears in nine PHCs revealed that 6.7% of them had been misdiagnosed. As a result, 1,262 malaria cases went undetected and unreported. Consequently, the API of malaria should have been 9.0 instead of the 5.9 reported.[33] How reliable was the clinical diagnosis alone for the treatment of malaria was shown in a hospital-based study. Although there were 24% malaria cases on the basis of clinical judgment alone, the cases were actually 52% when microscopic diagnosis was done, showing a gap of 28%.[34] In a recent study conducted in Ahmedabad in Gujarat state, it was estimated that there were on average 25,465 malaria cases/yr versus 4,119 cases reported and at least 22 malaria deaths/million population versus 0.3/million reported.[35] Thus, there existed glaring gaps between the reported and true burden of malaria in India.

Burden of complicated malaria. In India, reports suggested that mortality in complicated *P. falciparum* malaria in Vellore in the southern state of Tamil Nadu was 7.9%, whereas in Jabalpur (Madhya Pradesh) and Rourkela (Orissa), it was 25.6% and 30%, respectively.[36,37] In Jabalpur Medical College, 1,783 patients were admitted with complicated *P. falciparum* infection, of which 152 (8.5%) had cerebral malaria.[37] Of these, 39 (25.6%) died, and most of them were in the 16- to 40-year age group. Mortality was significantly higher in patients with hyperparasitemia and hypoglycemia. Delayed diagnosis and comatose condition were the main determinants of death. In a tertiary care industrial hospital at Rourkela, a comparative analysis revealed that the total number of patients admitted with complicated malaria significantly increased from 14.4% (62/431) in 1995–1997 to 23.7% (236/996) in 2000–2002. Similarly, cases of acute renal failures doubled from 22.5% (83/369) to 44.2% (117/265), and deaths in patients without renal involvement also increased from 12.8% (47/369) to 16.3% (119/731) (Ispat General Hospital, Rourkela, unpublished data). A general shift in the clinical profile in patients with complicated malaria has been observed, and multiple organ dysfunction/failure is becoming a common feature. For example, in a tertiary care hospital in Cuttack, only 10.9% (96/879) of cases admitted were without complications, whereas 382 (43.5%) had cerebral, renal, or hepatic involvement, 298 (33.9%) had cerebral malaria with either renal or hepatic involvement, 103 (11.7%) had multi-organ failure, and 138 of 783 (17.6%) died from malaria (BK Das, personal communication).

Complications caused by the hitherto considered benign species *P. vivax* have been reported from Bikaner, India[38] as from elsewhere in recent years.[39–41] It was observed that 72 of the 440 patients with microscopically and polymerase chain reaction–confirmed monoinfection of *P. vivax* had severe manifestations, which included jaundice (33; 45.8%), severe anemia (11; 15.3%), respiratory distress with acidosis (8; 11.1%), acute renal failure (7; 9.7%), cerebral dysfunction with multiple convulsions (6; 8.6%), abnormal bleeding (6; 8.3%), shock (hypotension; 5; 6.9%), pulmonary edema (3; 4.2%), and hemoglobinuria (3; 4.2%).[38] Many combinations of severe manifestations were observed in 35 of the 72 *P. vivax* cases followed. In 12 pregnant women with *P. vivax* infection, there were 2 abortions, 2 still births, and 4 preterm deliveries.

Burden of malaria in pregnancy in India. It is well known that pregnant women constitute an important risk group for malaria infection, particularly in hyper- and holoendemic situations. The well-known effects include effectiveness of placental barrier, parasite sequestration in placenta, suboptimal nutrition of the fetus, congenital malaria, intrauterine growth retardation, low birth weight, premature interruption of pregnancy, infant mortality, and maternal death.[42–44] It may be the cause of cerebral malaria and severe anemia. In low transmission areas, maternal mortality is ~1%, whereas in Africa it could be between 84 and 2,000 per 100,000 live births (0.00084–2%).[45]

In southeast Asia, malaria is a serious burden in pregnancy, with a spectrum of ill effects as shown by Slide Positive Rate (1.1–58%; N = 45–365), parasitemia (1–70%; N = 55,365), cerebral malaria (7–76%; N = 45–365), anemia (8.6–90%; N = 45–365), maternal mortality (7–66.6%; N = 45–365), placental malaria (18–29%; N = 256,365), abortions (2–11%; N = 45–365), intrauterine fetal development impairment (2–31%; N = 45–322), stillbirth (2–13%, N = 45–365), preterm (4.2–60%; N = 45–322), and low birth weight (5.4–89%; N = 55–365).[46]

In northwestern India, in a hospital-based study in Bikaner,[43] it was found that the mortality rate in 45 pregnant women with *P. falciparum* infection was highly significant (37.8%) compared with non-pregnant women with *P. falciparum* infection (14.81%) at $P < 0.001$. Similarly, the incidence of cerebral malaria (75.55%), severe anemia (< 5 g%; 20%), hepatic failure (13.3%), and renal failure (20%) was significantly higher in pregnant women than non-pregnant women at 32.92%, 4.11%, 9.05%, and 6.17%, respectively.

From central India, it has been reported that pregnant women (N = 365) suffer significantly more from both *P. vivax* (N = 121) and *P. falciparum* (N = 244) malaria than non-pregnant women (N = 150).[47] The weight of neonates born to infected mothers was 300–350 g less on average than neonates born to non-infected mothers (N = 1762). The weights continued to be significantly lower until 6 months, affecting the growth of babies in infancy. It was found that rates of malaria infection reduced from the first to third pregnancy. The mean parasitemia in pregnant women suffering from *P. vivax* ($P < 0.05$) or *P. falciparum* ($P < 0.0001$) malaria was much higher than non-pregnant malaria-infected women. Similarly, women with *P. falciparum* infection were significantly more anemic than the non-infected pregnant women ($P < 0.0001$) or infected non-pregnant women ($P < 0.001$). The pregnant women with *P. falciparum* malaria were significantly more anemic than those suffering from *P. vivax* infection. Of the 244 pregnant women who had *P. falciparum* infection, 3(1.22%) died, whereas in another 3, abortions were recorded, and 2 others had still births. Only one still birth and abortion each were recorded in *P. vivax*–infected women who were primigravidae. Among non-infected women, however, one abortion (in a primagravida) and one still birth (in a multigravida) were recorded.

Mortality attributable to malaria and gaps. In India, malaria is one of the most important causes of direct or indirect infant, child, and adult mortality. In pre-independent India, the death toll caused by malaria was estimated at 1 million during normal years and 2 million during epidemic years.[7] Malaria mortality steeply declined after the National Malaria Eradication Program was launched in 1958. The National Program reported 879, 666, 1,057, 946, and 938 deaths caused by complicated *P. falciparum* malaria from 1997 to 2001, showing a specific malaria mortality ratio (SMMR) of 0.30–0.48 in these years, which was one of the lowest in the world. However, as per the WHO SEARO, 19,500–20,000 deaths occurred annually in India. Other than these sources, there are scanty reports on deaths caused by malaria that are primarily based on outbreak or epidemic studies.[25,48–54] Age-, sex-, and cause-specific deaths are most extensively covered in the Government of India report on the basis of Medical Certification of Cause of Death (MCCD).[55] The most recent available report is for 1998, during which there were 4,481 certified malarial deaths reported from various categories of hospitals in rural and urban areas of India. Significantly, in this report, only 14.9% of the total registered deaths were medically certified and to which a specific cause of death was attributed. A simple conversion to 100% certification would mean that the deaths caused by malaria could be 49,796, assuming that the malarial deaths were uniformly distributed in the remaining 85.1% of the sample (Table 2). During the same year, only 666 deaths were reported by the National Vector Borne Disease Control Program; hence, these estimates were incomparable. It may be further noted that the MCCD-1998 report[55] contained death statistics from only 15 states and union territories of a total of 29 states and 7 union territories. Certified death data from many malaria endemic states such as Uttar Pradesh, Bihar, Assam, West Bengal and Tamil Nadu were not available. Had there been reporting of deaths from these states, the malarial deaths would have been much more than the estimated 49,796. Hence, available data on deaths are incomplete, and there seems to be a large gap between reported and actual deaths caused by malaria in India.

TABLE 2

Estimates of deaths caused by malaria in 15 states and Union Territories (UT) in India based on report on medically certified deaths in 1998[55]

State no.	State/UT	Proportion of deaths medically certified to total reported deaths (a)	No. of certified deaths attributable to malaria (b)	Total no. of estimated deaths caused by malaria* (c) = b × 100/a
1	Pondicherry	53.5	8	15
2	Nagaland	4	7	175
3	Manipur	32.7	10	31
4	Meghalaya	15.6	37	237
5	Haryana	10.5	80	762
6	Goa	89.9	87	97
7	Gujarat	4	95	2,375
8	Arunachal Pradesh	69.5	119	171
9	Andhra Pradesh	6.6	165	2,500
10	Delhi	58.5	212	362
11	Rajasthan	12.8	245	1,914
12	Maharashtra	33.6	326	970
13	Karnataka	13.8	407	2,949
14	Madhya Pradesh	4.9	890	18,163
15	Orissa	9.4	1,793	19,074
	Total India	14.9	4,481	49,796

* Assuming malarial deaths were uniformly distributed in the entire sample of deaths from all causes.

Age and sex distribution of malaria mortality. Age-sex distribution of malaria deaths shows that, in general, malaria mortality across all ages was comparatively higher in males than in females (Figure 8). This mortality gap in sex widens after the age of 25 years.[55] Overall, the number of deaths in males was 2,827 (63.1%) compared with 1,654 (36.9%) in females, with a male: female ratio of 1:0.56. Unlike in Africa, where most of the deaths are reported in infants and children, it is seen that in India, malarial deaths increased up to the age of 44 years in both sexes and declined thereafter. Although the deaths in infants and children < 14 years of age accounted for 20.6%, in older ages (15–54 years), they accounted for 56.1%, and the rest 23.3%, were in those > 55 years of age. Hence, most of the burden of malarial mortality was borne by the economically productive ages.

Burden of malaria in terms of disability-adjusted life years lost in India: a preliminary estimate. In 1993, the Harvard School of Public Health in collaboration with World Bank

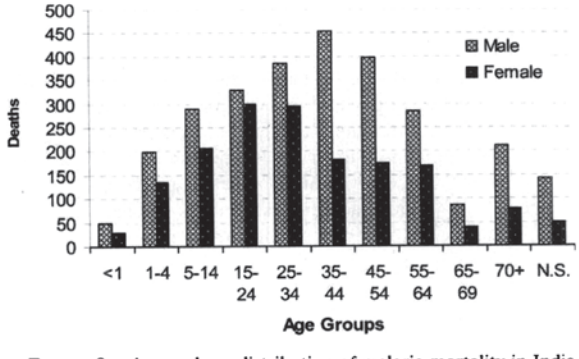


FIGURE 8. Age and sex distribution of malaria mortality in India in 1998.[28] The deaths are more in men than women across all ages, whereas middle productive ages in general have much higher mortality than children. (N.S. = age not specified).

and WHO assessed the Global Burden of Disease (GBD).[2] The GBD study introduced a new metric—the (DALY)—to quantify the burden of disease. One DALY means 1 lost year of healthy life on account of disease and is a common currency for disease morbidity and mortality expressed in time. This concept has gained importance in the past decade. WHO undertook the GBD study of 135 major causes for 2002 and estimated DALYs for each cause in different regions and countries.[56]

We computed DALYs lost because of malaria in India for 1997. Deaths caused by malaria were estimated at 71,396 based on MCCD-1997 report.[57] Deaths were proportionately distributed according to age and sex based on the MCCD data. From a population census of the India-1991 report,[58] the mid-year population was calculated and assigned to different ages of both sexes. The incidence of malaria was taken as per the WHO estimates of 15 million. Disability weights estimated in the GBD 2000 study for episodes (0.172–0.211), anemia (0.012–0.013), and neurologic sequelae (0.581) were used. Duration of an episode of malaria was taken as 7 days. DALYs were estimated using a GBD template with age weighting and discounting. The total DALYs lost because of malaria were 1.86 million years. Among females, DALYs lost were 0.786 million versus 1.074 million in males (Figure 9). The maximum DALYs lost (53.25%) were in the middle productive ages from 15 to 44 years of age, followed by children < 14 years of age (27.68%), and 19% in those > 45 years of age (Figure 10).

Socio-economic burden of malaria in India. Malaria obviously has a devastating socio-economic impact on affected countries, the majority of which are developing, poor, and located in the tropics. Such is the effect that the cost of control measures is worthwhile, considering the disability, mortality, economic loss and industrial inefficiency the afflicted population and the country faces.[59] A treatise written by Sinton[7] on "what malaria costs India" stated that the problem of the very existence in many parts of India was in fact the problem of malaria in the 1930s. In those days, it constituted one of the most important causes of economic misfortune, engendering poverty, lowering the physical and intellectual standards of the nation, and hampering prosperity and economic progress in every way. This was not only true for India but for all the malarious countries in the world.

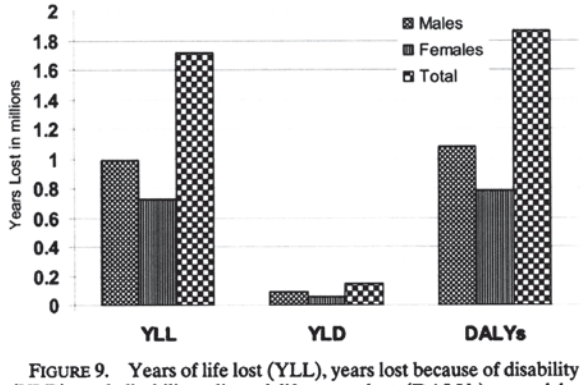


FIGURE 9. Years of life lost (YLL), years lost because of disability (YLD), and disability-adjusted life years lost (DALYs) caused by malaria in both sexes in 1997 in India.

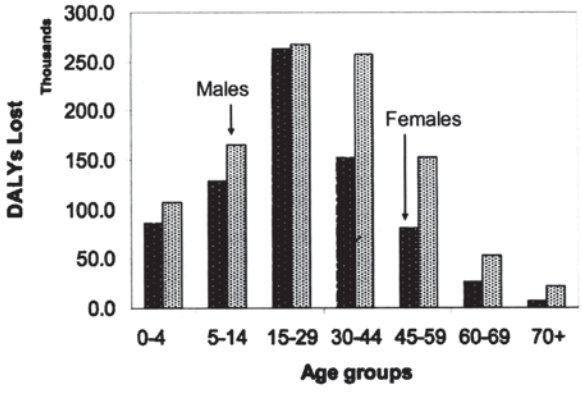


FIGURE 10. DALYs lost according to age and sex in India in 1997.

Efforts were made to calculate the economic burden of malaria as early as 1933 using evidence that there were 100 million cases of malaria annually, and of these, one third were in adults (33 million).[60] The adults of productive age earned on an average of 7.5 Rupees per month at that time. Furthermore, it was worked out that actual working days lost per man per year were ~15 days because of the disability during primary attacks, relapses, and re-infections. However, based on the financial loss in the community in terms of lost wages, Sinton[7] calculated a total loss of Rupees 1237 lacs (£10 million at the then prevailing exchange rates, and ~ US$27.49 million). Because of sublevel performance as a result of 10–25% loss of efficiency, there would be an additional loss of 29.7 crores (£22 million equivalent to US$62 million at current prices) when computed at a 10% loss. Together, the loss would be Rupess 42 crores at 1935 currency conversion level (£32 million equivalent to ~US$93.3 million at current prices). This loss does not include cost of medical attendance, loss to agriculture, mining, industry, and other fields. Had estimates for these losses also been computed, the figure would have been much higher.

Similarly, Kondrachine and Trigg estimated that the annual direct and indirect cost of malaria in Africa was US$800 million in 1987 and US$1,800 million in 1995.[61] They opined that, outside Africa, the economic impact is equally high. In South America, the days of work lost because of malaria have been shown to vary from 1.5 to 14.3, with an average loss of income estimated to be 13.2% of the minimum salary, ranging between 7% and 75.8%. In Asia, studies in Nepal have shown that *P. falciparum* and *P. vivax* are responsible for 10 and 5 days total disability and 2.5 and 1 days of partial disability, respectively. Monitory loss because of malaria per case was between US$3.7 and US$35.8. For the control of disease alone, the WHO Action Plan for malaria control (1995–2000) estimated that ~US$28 million/yr of external investment in malaria control was needed in Africa. Outside Africa, malaria control programs cost an estimated US$175–350 million a year.

The prevalence of malaria and economic loss was studied in the iron ore mines in the Sundargarh district of Orissa.[62] It was calculated that Rupees 11,04,841 (US$24,282 at current prices) were lost in three mines because of malaria in 1988. Individually average annual loss or expenditure per patient per episode was Rupees 178.38 ($3.9) in case of laborers,

Rupees 77.93 (US$1.71) for regular mine employees, and Rupees 228.51 (US$5.02) for businessmen. In other words, poor casual labor was the worst hit by malaria in these mines. In a more recent study carried out in Gujarat state,[63] it was estimated that, per malaria episode, monitory loss in the urban area was Rupees 393.59 ($8.65) compared with Rupees 157.59 ($3.46) in rural areas, which was less than one half spent in the urban area.

In 1994, Shiv Lal and others estimated that, if there were no control activities and malaria was allowed to transmit from the 1947 level, there would have been an expenditure of Rupees 76,600 million (US$1,670 million) for medication, medical advise, hospitalization, and absenteeism. Even if the estimates of the Malaria Research Center, Delhi (now NIMR; 25 million cases/yr)[64] were taken into account for calculation of economic loss, the cost would have been Rupees 68,600 million (US$1,508 million) versus expenditures of Rupees 3,467.9 million (US$76.2 million) for control. Thus, the net savings due to malaria control was estimated at Rupees 65,132.1 million (US$1,431 million). These authors inferred that every Rupee invested in malaria control has produced a direct return of Rupees 19.70. The estimated man-days saved were 1,328.75 million per year.

DISCUSSION

In the 1950s and early 1960s, a major global initiative of WHO to eradicate malaria also brought malaria under firm control in India and almost on the verge of eradication, but a reverse followed in the mid-1960s until the mid-1970s; the disease staged a comeback with vengeance. In the 1980s, new malaria ecotypes developed from environmental and developmental impact and were followed by outbreaks and epidemics in the 1990s.[20–22,24–27] There are vast lands inhabited by ethnic tribes in Madhya Pradesh, Chattisgarh, Jharkhand, Orissa, and the entire northeastern region, where malaria has remained deeply entrenched, *P. falciparum* preponderance is persistent, and asymptomatic burden in these areas is not known. The emergence of resistance to chloroquine in *P. falciparum* in many pockets of the country and reports of reducing sensitivity in *P. vivax* are major causes of concern.[14–17] In some areas in the northeastern region, even foci of multidrug–resistant *P. falciparum* have been found. Alternate therapies such as mefloquine and artemisnin derivatives or combination therapies are expensive, and since they have been selectively introduced in the control program, would require constant monitoring for their judicious use and to observe emergence of resistance against them.

The changing clinical manifestations with multi-organ involvement in *P. falciparum*, emerging trends of complications in *P. vivax* malaria, and burden of malaria in pregnancy are other important issues that merit attention and formulation of suitable intervention strategies. Historically, *P. vivax* has been suspected to impose a significant burden of mortality, resulting from its interaction with other diseases and conditions.[6] The malaria-specific mortality gap needs to be bridged. While the reported number of deaths is ~1,000, the actual mortality caused by malaria is many folds higher. Even the MCCD report, which covers both rural and urban areas, extensively suffers from serious limitations because of nonreporting of mortality by some key malaria-affected states and also because of the overall incomplete medical certification of deaths and attribution of specific cause of death.[55]

Health planners and administrators need estimates of the true burden of malaria for allocation of much needed resources for interventions. The current reported incidence of ~2 million/yr in India at best reflects a trend, and given the gaps identified in various studies, the actual incidence is definitely far more than presently known. The reasons attributed to such a gap are deficiencies in coverage, collection, and examination of blood smears and reporting systems.[27,29–31,33,34] Moreover, in India, the government health sector, which provides free or highly subsidized health care, caters to the needs of 20% of the population, mainly in rural areas, whereas the rest of the population seeks health care in the private sector as their first point of contact, where the bulk of malaria is generally treated empirically.[65,66] The clinically treated cases never or rarely find place in the official statistics. This gap needs to be bridged to build burden estimates. Coupled with this, there is the likelihood of a sizable population acting as asymptomatic carriers of plasmodial infection, particularly in malarious areas inhabited by ethnic tribes in India, where meso- to hyperendemic conditions exist. In such areas, inaccessibility and insurgency seem to be major causes of deficient routine surveillance services. In many such remote places, DDCs have been opened in India, where malaria is symptomatically treated by trained community volunteers without accounting for the treated cases. Similar doubts have been expressed about the validity of estimates available for Africa because of inadequate detection and reporting and general inadequacies in the surveillance in malarious countries of Africa. The known and missing incidence of malaria in affected countries has been compared with the ears of hippopotamus, which are visible above water, whereas the bulk lies unseen underneath.[3] This statement may also apply to many parts of India.

The true incidence of morbidity and mortality are of paramount importance in the estimation of DALYs lost. In the absence of true burden estimates, we computed DALYs lost for India using WHO projections and mortality estimations on the basis of MCCD data. Although our DALY estimates are conservative, they are much higher at 1.86 million years lost compared with WHO estimates of 0.844 million years for 2002.[56] India, therefore, must initiate burden estimation studies based on primary incidence and prevalence data to highlight the actual malaria burden in the country.

Malaria is well known for its debilitating, demoralizing, and impoverishing consequences, and therefore, estimation of its true burden and control is central to addressing these issues, with the final aim of lifting the human resource above the poverty line. The poor may find it hard to deal with persistent malaria problem, as coping with the disease is economically disastrous for the communities living on the edge. The estimated 20-fold returns on expenditure makes a strong case for adequate investment in malaria control in India. A good investment in malaria control not only makes public health sense but also economic sense in the present era of economic liberalization in India. Firm malaria control is imperative for human resource development, which in turn is imperative for equitable and sustained economic growth.

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