Risk factors for malaria deaths in Jalpaiguri district, West Bengal, India, 2008.

By

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(MAE-FETP Scholar 2007-2008)

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CERTIFICATION

This is to certify that this dissertation, titled **'Risk factors for malaria deaths in Jalpaiguri district, West Bengal, India, 2008',** submitted by Dr. Jagannath Sarkar, in partial fulfillment of the requirements for the degree of Master of Applied Epidemiology, is the original work done by him.

Date 31.1.09

Director

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PREFACE

Malaria is public health problems in Jalpaiguri district, West Bengal, India. My dissertation work is on the study of risk factors for malaria deaths in Jalpaiguri district. We have taken cases whose who died due to malaria in the district and taking controls whose who are survivors from malaria (cure after treatment), age (± 5 years), sex and locality matched controls in our study. As the study identifies risk factors for malaria deaths, presenting with fever, similar in severity, we have presented their findings separately. We have also done a review of the literature on both the diseases and risk factors have provided them herein in the appendix.

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Risk factors for malarial deaths in Jalpaiguri, West Bengal, India, 2008.

Abstract

Introduction: Malaria is highly endemic in Jalpaiguri district of West Bengal. Despite additional inputs to the national anti-malaria programme in the district in 2007, malaria deaths continue to occur. We conducted a study to identify the risk factors for malaria deaths.

Methods: We conducted a matched case-control study. We defined a case as death of a patient with fever and microscopically confirmed plasmodium falciparum infection in a resident of Jalpaiguri, West Bengal and control as microscopically confirmed falciparum malaria cases cured after treatment in the district during 2007-2008. For each case, we recruited three age, sex and locality matched controls. We abstracted information about clinical and treatment details from records. We interviewed the relatives of cases and controls and collected information about knowledge about malaria, presence of bed nets and DDT spray in last year.

Results: A total 51 malarial deaths occurred during 2007-2008 (malaria death rate: 1.3/100,000). Death rates due to malaria were higher among males and children aged less than 5 years. Malarial deaths were significantly higher among patients who presented with complications [Adjusted Odds Ratio (AOR) = 4.1, 95% CI=1.6- 10), who were treated at private facility (AOR= 3.7, 95% CI= 5.1.2- 12), received treatment after 48 hours of fever onset (AOR= 13.6, 95% CI= 2.9- 64), received first line of

treatment AOR=13.3 (95% CI= 3.7- 47). Deaths were more likely to occur among houses which, did not own bed nets (AOR= 6.3, 95% CI= 1.9- 24), and households were not sprayed with DDT last year, AOR=9.2, (95% CI= 2.8- 31).

Recommendations: First, department of health needs to sustain the inputs provided in the district for early diagnosis and treatment. Second, medical officers at the peripheral health institutes need to be educated about prompt referral of malaria cases presenting with complications. Third, programme managers need to generate community awareness about malaria and need of seeking for prompt treatment. Fourth, strengthen the DDT spray operation. Fifth, educate the private practitioners about appropriate use of anti-malarial.

Risk factors for malarial deaths, Jalpaiguri, West Bengal, India, 2008.

Introduction:

In the South-East Asia Region of World Health Organization (WHO), an estimated 290 million people (80% of the region's population) are at risk for malaria. An estimated 247 million new cases occurred in 2006 with 881,000 deaths.[1] More than 90% of these cases were reported from five countries: India, Indonesia, Myanmar, Sri Lanka and Thailand. Effective malaria controls depends on (1) early diagnosis and prompt treatment of malaria cases (2) vector control and personal protection.[2-4] The main objectives of an anti-malarial treatment policy are to ensure rapid cure of the infection, reduce morbidity and mortality and prevent the progression of uncomplicated malaria into severe and potentially fatal disease. World Health Organization recommends that all uncomplicated plasmodium falciparum infections should be treated with an artemisinin-based combination therapy, and plasmodium vivax with chloroquine and primaquine (except where plasmodium vivax is resistant to chloroquine, when it should be treated with artemisinin based combination therapy and primaquine). Patients suffering from severe malaria presenting at the peripheral levels of the health system should be provided pre-referral treatment with quinine or artemisinin, and transferred to a health facility where full parenteral treatment and supportive care can be given.[1-4] The main objective of malaria vector control is to reduce significantly the incidence and prevalence of both parasite infection and clinical malaria. There are two main approaches to malaria prevention by mosquito control: the use of insecticide-treated

bed nets (ITBNs) and indoor residual spraying (IRS). These core interventions may be complemented, usually in specific locations, by other methods such as larval control or environmental management.1,

India accounts for 60% of the cases reported from the Southeast Asia region region.[1] Forty six percent of these cases were due to plasmodium falciparum.[3] Plasmodium falciparum is the malaria species occurring in endemic and forest areas and accounts for more than 95% of malaria deaths in the country.[3] The disease is highly endemic in Madhya Pradesh, Orissa, Andhra Pradesh, Assam, Gujarat, north-eastern states, Bihar and Maharashtra.

In West Bengal, malaria is endemic in Jalpaiguri, Coochbehar, Purulia and Kolkata districts.[7] These districts account for more than 90% of the state burden.[6] Jalpaiguri district, located in the northern part of the state had an average annual parasite incidence (API) of 17/1000 during 2007.[6] Eleven of 13 blocks of the district were high risk with an API of more than two.[6] Analysis of malaria surveillance data in the district during year 1992 and 2006 indicated perennial transmission of malaria with frequent outbreaks.[6] Two large outbreaks occurred in the district during 2003 and 2006. During the outbreak in 2003, 842,409 malaria cases and 149 deaths occurred. Forty percent of the cases were due to plasmodium falciparum.[7] Drug resistance studies conducted during 2004 documented chloroquine resistance among falciparum malaria. Entomological investigations pointed to anopheles dirus as the primary vector for malaria in the areas nearby forests and tea gardens. During the malaria outbreak in 2006, 61,796 malaria cases and 97 deaths occurred in the district.[6] Evaluation of malaria control activities in Alipurduar sub-division of the district, which reported 67

malaria deaths during 2006 outbreak, pointed to inadequate human resources (malaria laboratory technician, health assistants and medical officers) funds and logistics (for expenses of training and material). [4] About one-fourth of deaths occurred in tea garden and received treatment from the private sector. [6]

The department of health, Government of West Bengal, took several corrective measures to address these deficiencies by increasing inputs for early diagnosis (malaria laboratory technicians, rapid diagnostic kits), treatment (artemisinin based combination therapy), vector control (larvivorus fish cultivation) and personal protection (insecticide treated bed nets).[2,8] The staffs strength of malaria laboratory technicians in the district increased by 164% in 2007 compared to the sanctioned strength.[6] Artemisinin based combination therapy Sulfadoxin- pyremethamine and artemisinine (SPACT) was made available in all the block primary health centers. In high-risk areas, insecticide treated bed nets (ITBN) were also distributed to families that were below poverty line.[6]

Between 2006 and 2007, the number of reported deaths has reduced by 52%. However, malaria deaths continued to be reported in the district.[6] Hence, we conducted a study to identify risk factors for malaria deaths in the district. The objectives of our study were to (1) describe the malaria deaths by time, place and persons, (2) identify the risk factors associated with the malarial deaths.

Methods

Study population and study design: We conducted a matched case-control study in Jalpaiguri district, West Bengal. The projected population of the district in 2007 was 3,973,930.

Definition of cases and controls: We defined a malarial death (case) as death in fever case patients due to microscopically confirmed plasmodium falciparum infection in a resident of Jalpaiguri district during January 2007 and October 2008. We defined microscopically confirmed falciparum malaria case patients who were cured after treatment during January 2007- October 2008 as controls.

Recruitment of cases and controls: We recruited all malaria deaths that occurred between January 2007 and October 2008 in the district as cases. We collected the information about malaria deaths from the office of the Deputy Chief Medical Officer of Health-II. We line-listed plasmodium falciparum case patients that occurred during the study period in different health facilities of the district from malaria forms and malaria case register maintained in the block primary health centers (BPHC). We excluded all the malaria deaths from this line-list and selected three age ($\pm$ 5 years), sex and locality matched controls for each case.

Sample size: Assuming prevalence of exposures among controls as 20% (treatment from private sector), 95% confidence interval (CI), power of 80% and 3 controls per cases, the required sample size was 42 cases and 126 controls to detect an odds ratio of three. Considering non-response of 10%, we needed to recruit a minimum of 47 cases and 141 controls.

Data collection: We abstracted the information about demographic details, clinical features and treatment details of cases from 'malaria death investigation form' available for every malarial death. As per the guidelines of the National Anti-Malaria Programme, Medical Officers have to conduct an investigation of all malarial deaths that occur in their jurisdiction within two weeks. This form is filled on the basis of the hospital records as well as interview of the relatives. This form contains information of the demographic details, date of onset, results of the laboratory investigations, clinical information and treatment details. For controls, we abstracted demographic, clinical and treatment details from hospital admission records and malaria case register. We interviewed the close relatives/ neighbors of cases and controls to collect information of their knowledge, attitude, practice and health seeking behavior during fever episode, about malaria, personal protection and vector control measures. We used a pre-tested structured questionnaire to abstract the information from records as well as through interview the relatives/ neighbor of study subjects.

Data analysis: We calculated age and sex-specific malaria death rates per 100,000 population using the projected population for 2007 as denominator. We described the distribution of malaria deaths by months. We plotted map for the malaria deaths rates per 100,000 populations by community development blocks. We conducted univariate analysis and calculated matched odds ratio (MOR) and their 95% confidence intervals (CI) to identify factors associated with malarial deaths. We included all the variables

with p value <0.2 on univariate analysis in the conditional logistic regression model. We analyzed the data using Epi-info 2006.

Human subject protection: The institutional ethics committee of the National Institute of Epidemiology, Chennai approved the study protocol. We obtained written informed consent from the relatives of cases and controls before interviews.

Results

Descriptive epidemiology: In Jalpaiguri district, 51 malaria deaths were reported from January 2007 to October 2008 with a death rate of 1.3 per 100,000. Malaria death rates were higher among males (1.5 per 100,000) and children under five years of age (2.3 per 100,000 populations) (Table-1). Malaria deaths occurred throughout the year with peak during May and July (Fig. 1). Malaria deaths were reported from 11 out of 13 blocks (Fig. 2).

Analytic epidemiology:

Univariate analysis: Malaria deaths were more likely to have been admitted with complications (e.g., unconsciousness, seizures, coma, diarrhea, pulmonary edema or neurological abnormalities), (MOR= 6, 95% CI= 2.5-13), to have been treated the private sector (MOR= 17, 95% CI, 5.1- 56), and to have received anti-malarial treatment delayed (> 48 hours after fever onset), (MOR= 19, 95% CI= 2.1- 170). Malarial deaths were more likely to have received first line of drug (MOR=6, 95% CI= 2.6- 15), to have been treated in primary level facilities (MOR= 3, 95% CI=1.4- 5.4) and live in houses without bed nets (MOR= 6, 95% CI= 2.3- 14). Absence of visits by health workers in last year (MOR= 9, 95% CI= 2.3- 32) and absence of DDT spraying

in the house in the last year were also significantly associated with malarial death (MOR=3, 95% CI= 1.3- 5) (Table-2).

Conditional logistic regression analysis: Variables significantly associated with malarial deaths were delayed presentation with severe malaria [Adjusted Odds Ratio (AOR)= 4.1, 95% CI=1.6- 21)], management in the private sector (AOR= 3.7, 95% CI=1.2 - 12), delayed anti-malaria treatment (AOR= 13.6, 95% CI= 2.9- 64), use of chloroquine (AOR=13.3, 95% CI= 3.7- 47), absence of bed nets in the house (AOR= 6.3, 95% CI= 1.9- 24) and absence of DDT spraying of households (AOR=9.2, 95% CI= 2.9- 31). (Table- 3)

Discussion

Despite additional inputs to the national anti-malaria programme in the district, malarial deaths continued to occur, though the number of deaths has decreased since 2007.[6] We identified several factors associated with malarial deaths including presence of complications at the time of admission, treatment delay, treatment at private sector, use of only first line anti-malarials, absence of DDT spraying and absence of bed nets. The findings of the study would help the programme managers in designing interventions to reduce the malaria mortality.

Once diagnosed as malaria, either on a clinical or parasitological basis, the patient should be treated early with safe and effective anti-malarial drugs, preferably within 24 hours of the onset of symptoms.[5] Inadequate and delayed treatment of uncomplicated malaria, especially in the non-immune patient could result in progression to severe

malaria, which is associated with a high case fatality rate. In Jalpaiguri, delay in starting the anti-malarial treatment 48 hrs. after fever onset was significantly associated with mortality among falciparum malaria cases. Deaths among patients who presented with complications of malaria also suggest a delay in starting the treatment.

Use of appropriate anti-malarial drug is a key pre-requisite of malaria control and for reducing mortality due to malaria.[3-5] In view of the rapidly growing resistance of Plasmodium falciparum to conventional monotherapies in many malaria endemic regions,[5,7] National anti-malarial treatment policies should aim to offer anti-malarial that are highly effective. The main determinant of policy change is the therapeutic efficacy and the consequent effectiveness of the anti-malarial in use. A combination therapy is recommended instead of mono-therapy.[7, 8, 10] The rationale for combining antimalarials with different modes of action are two folds: (1) the combination is more effective and (2) a mutant parasite that is resistant to one of the drugs arises de novo during the course of the infection, the parasite will be killed by the other drug.[10] This mutual protection is thought to prevent or delay the emergence of resistance.[2,3] Artemisinin based combination therapies (ACT) have been reported highly efficacious than mono-therapy and is recommended regimen in endemic regions.[1,8,10] A study conducted in Rwanda showed that the supply of artemisinin based combination therapy in subsidiary price to the patient reduced 40% of malaria deaths.[7] Considering large number of malarial deaths in the district in earlier years, Artemisinin based combination therapy [(Sulfadoxin-Pyremethamine (SP)-Artemisinin] were made

available in the block primary health centers. In the present study, case fatality was significantly higher among the falciparum malaria cases who received only chloroquine as the first line of treatment. No systematic studies have been undertaken to evaluate the therapeutic efficacy of chloroquine against Pf infection since 2005 in the district. However, in view of these findings, such studies are necessary to evaluate the therapeutic efficacy of chloroquine.

As much as 30% of the population in the district reside in tea gardens and receive treatment from the tea garden clinics.[13] In Jalpaiguri, malaria death was four times higher among those patients who received treatment from private facilities. Apart from severity of illness, time before starting the treatment, private practitioners' knowledge about correct use of combination therapy could also affect the outcome of plasmodium falciparum malaria cases. It is therefore necessary to educate the private providers in the area about the correct use of anti-malarial drugs. This would not only reduce the case fatality but would also prevent development of resistance to the anti-malarial drugs for plasmodium falciparum malaria.

Not having at least one bed net in the house was found to be a significant predictor of malaria mortality in our study. Use of bed nets is an important measure for prevention of malaria and is one of the strategies of World Health Organization's roll-back malaria programme.[7] A study in Ethiopia reported that 60% of malaria cases and 50% death rates were decreased due to supply and use of two bed nets per family during 2005 and 2007.[11,12] In order to reduce the transmission of malaria in Jalpaiguri, insecticide

treated bed nets were distributed to below poverty line families residing in high-risk area. However, the evaluation of national anti- malaria programme indicated that only 5% of the population and 21% of the below poverty line families covered by the bed nets in high-risk areas. The evaluation of DDT spray activities also indicated that the quantity and quality of spray operations in the district were inadequate.[6] It is therefore necessary to increase the supply of bed nets in the area as well as increase the coverage of DDT spray operations in the district.

Our study had three limitations. First, we relied on available records to collect information about clinical and treatment details from cases and controls instead of prospectively recruiting study subjects and collecting the clinical and treatment details from them. In order to address this limitation, we validated the information about severity of study subjects by interviewing the respondents. Second, it is possible that respondents' knowledge about malaria as well information about DDT spray in the house might have been influenced by the clinical outcome of study subject. We tried to crosscheck the information about DDT spray by interviewing the neighboring houses. Third, we considered presence of at least one bed net as a proxy for use of bed nets in the house. We did not collect information about adequacy of bed nets per household as well as proper use.

In conclusion, malaria deaths continue to occur in Jalpaiguri district despite of additional inputs to the anti-malaria programme in the district. Our study identified several factors pertaining to treatment, vector control and personal protection that

were related to malarial deaths. Based on these findings, we propose number of recommendations to reduce malaria deaths in the district. First, the department of health needs to sustain the inputs provided in the district in terms of rapid diagnostic kits, second line of anti-malarial drugs and funds. It is also necessary to increase the coverage of bed nets by distribution to BPL families; Second, medical officers at the peripheral health institutes need to be educated about early referral of malaria cases presenting with complications. Third, programme managers need to generate community awareness about malaria and need of seeking for prompt treatment. Fourth, ensure regular DDT spray maintaining quality and quantity in high-risk areas. Fifth, educate the private practitioners about management of severe malaria as well as use of appropriate anti-malarials.

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Table 1: Malarial deaths by age and sex, Jalpaiguri, West Bengal, India, January 2007- October 2008.

Demographic characteristics		Malaria deaths	2007 population	Death rates (per 100,000 population)
Age group	< 5 year	10	431,992	2.3
	5-14 year	18	1,059,117	1.7
	15-29 year	11	1,065,175	1.0
	30-49 year	6	998,483	0.6
	50 year +	6	419,163	1.4
Sex	Male	31	2,046,504	1.5
	Female	20	1,927,436	1.0
Total		**51**	**3,973,930**	**1.3**

Table-2. Frequency of selected exposures among cases and controls, Jalpaiguri, West Bengal, India, 2007-2008 (univariate analysis).

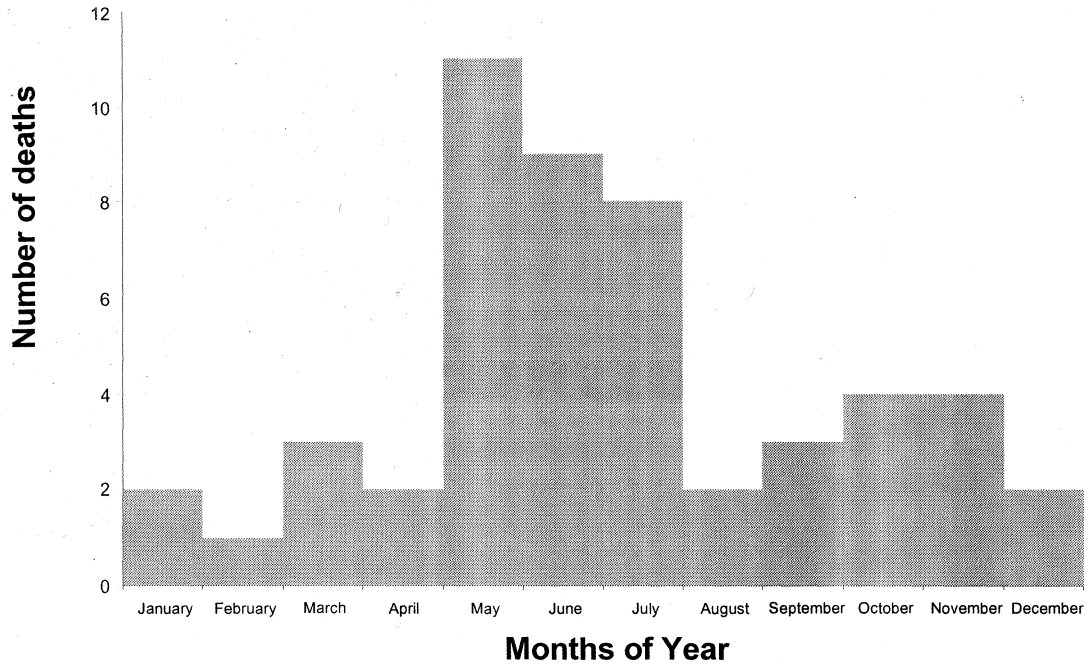
	Exposure variables	Cases (n=51)		Controls (n=153)		MOR	95% C.I
		#	%	#	%		
Socio-demographic characters	Below poverty level	47	92	148	97	0.8	0.3- 2
	Illiterate	43	84	132	86	0.8	0.3- 2
	Daily wage workers	24	47	59	39	1.7	0.8- 4
Treatment received	Presented with severe malaria	46	90	77	50	6	2.5- 13
	Treated at private facility	25	49	11	7	17	5.1- 56
	Treatment started after 48 hrs. of fever onset	11	22	15	10	19	2.1- 171
	Received first line of treatment	44	86	73	48	6	2.6- 15
	Treated at primary level	40	78	82	54	3	1.4- 5
Knowledge	House hold not sprayed with DDT last year	26	51	42	27	3	1.3- 5
	Did not own a bed net	40	78	63	41	6	2.4-14
	No house visit by health workers last year	21	41	25	16	9	2.3- 32
	Mosquito bite can cause malaria	1	2	15	10	0.2	0.03- 1
	Mosquito bite any time of day	31	61	124	81	0.4	0.2- 0.8
	Malaria is curable	2	4	5	3	1	0.2- 6
	Malaria causes anemia	29	57	91	59	0.9	0.4-2

Any fever may be fatal in not treated early	49	96	139	91	0.5	0.1- 2
Blood test necessary when fever	2	4	10	6	0.5	0.1- 2
Malaria affects children	3	6	27	18	0.3	0.1- 1
Malaria affects pregnant women	3	6	2	1	4	0.7- 27
Insecticide treated bed nets prevent malaria	5	10	10	6	2	0.5- 5
Insecticide treated bed nets cost worthy	3	6	8	5	1	0.3- 4

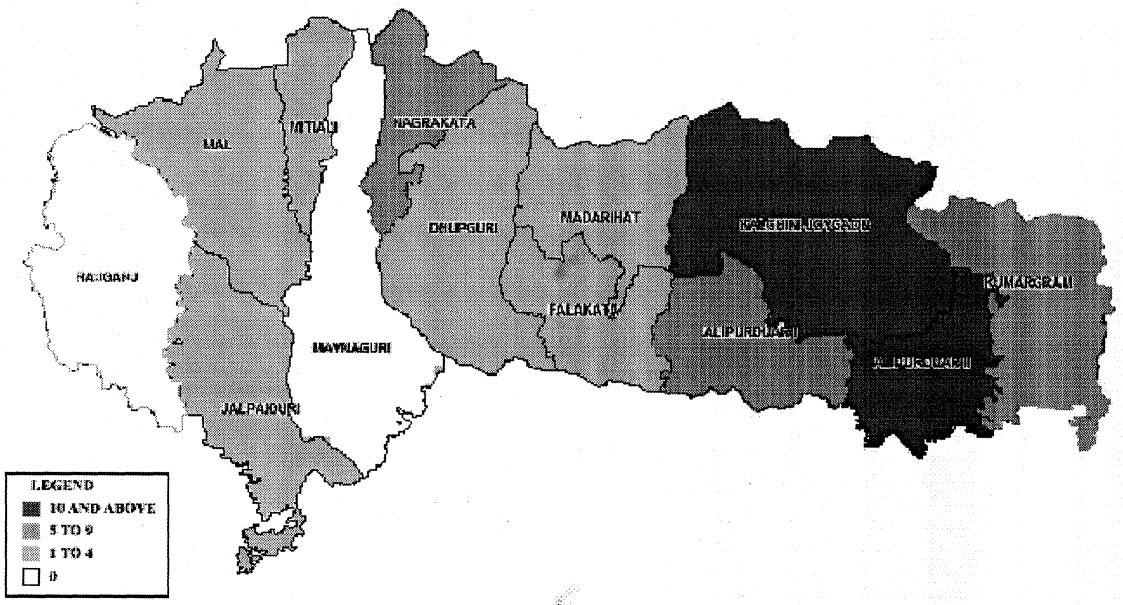
Table-3. Conditional logistic regression analysis showing selected exposures associated with malarial deaths, Jalpaiguri, West Bengal, India, 2008

Exposure variables	Odds Ratio	95% CI
Patients presented with severe malaria	4.1	1.6- 10.
Patients treated at private facility	3.7	1.2- 12
Treatment delayed ≥ 48 hours	13.6	2.9- 64
Received first line of treatment	13.3	3.7- 47
Owned bed net to use	6.3	1.9- 24
House hold not sprayed with DDT	9.2	2.8- 31

Graph I. Malarial deaths by months, Jalpaiguri, West Bengal, India, 2007- 2008.



Graph 2, Malaria death rates (per 100,000 population) by block, Jalpaiguri, West Bengal, India 2007-2008



Malaria – a review

Historical aspects Malaria was linked with poisonous vapors of swamps or stagnant water on the ground since time immemorial. This probable relationship was so firmly established that it gave the two most frequently used names to the disease mal'aria, later shortened to one word malaria, and paludisme. The term malaria (from the Italian mala "bad" and aria "air") was used by the Italians to describe the cause of intermittent fevers associated with exposure to marsh air or miasma. The word was introduced to English by Horace Walpole, who wrote in 1740 about a "horrid thing called mal'aria, that comes to Rome every summer and kills one." The term malaria, without the apostrophe, evolved into the name of the disease only in the 20th century. Up to that point the various intermittent fevers had been called jungle fever, marsh fever, paludal fever, or swamp fever.

Current scenario

Malaria is widespread, and in true sense a global disease occurring more than 100 countries. Almost half of which are in sub- Saharan Africa, more than 2.4 billion of the world's population are still at risk. The incidence of malaria worldwide is estimated to be 300-500 million clinical cases each year, with about 90 percent of these occurring in sub-Saharan Africa and mostly caused by P.Falciparum. Reported malaria death is 1.1 to 2.7 million people world wide each year, of which about 1 million are children under

the age of 5 years in these areas. These childhood deaths resulting mainly from cerebral malaria and anemia constitute nearly 25 percent of child mortality in Africa. Fatality rates of 10-30 percent have been reported among children referred to hospital with severe malaria. However. These rates are even higher in rural and remote areas where patients have restricted access to adequate treatment. Malaria also contributes indirectly to illness and deaths from respiratory infections, diarrheas disease and malnutrition. Deaths from malaria in countries outside sub-Saharan Africa occur principally in non-immune people who become ill with P. falciparum. Urban and periurban malaria are on the increase in south Asia and in many areas oh Africa. Military conflicts and civil unrest, along with unfavorable ecological changes, have greatly contributed to malaria epidemics, as a large number of unprotected, non-immune and physically weakened refugees move into malarias areas. Such population movements contribute to new malaria outbreaks and make epidemic prone situation more explosive.The WHO estimates for the mortality and burden of disease in terms of Daly's lost due to malaria during 2002 in different regions.Malaria remains a serious public health problem in south east Asia region with nearly 290 million people estimated to be at risk. Although the reported morbidity and mortality showed a declining trend, the proportion of p.falciparum cases has increased significantly over the past many years. Now constitute nearly 50 percent of all reported malaria cases. India accounts for 77 percent of the regional total, while 54 percent of all deaths

are reported from Myanmar. the disease is on increase in Myanmar and Nepal. Maldives remain malaria free. Malaria is on decline trend in Bhutan, DPR Korea. Indonesia, India, Srilanka and Thailand. Due to shortage of laboratory facilities to confirm malaria cases and weak surveillance system, under reporting of malaria cases and deaths is one of the major challenges in SEAR. Against the 2.4 million cases reported in 2003, nearly 20 million cases were estimated to have occurred during the same period. The number of deaths estimated was 80,000 compared to 4500 reported during 2003. an increase in drug resistance was observed in Bangladesh, Indonesia, Thailand and Myanmar. As a result they have revised their national policy of malaria treatment and adopted artemisinin- based combination therapy (ACT) to treat drug resistant P.falciparum Thailand introduced ACT nation wide, while India initiated it in some areas as pilot project.The coverage of indoor residual spraying with insecticides (IRS) remains low (42 per cent). Insecticide treated bed nets have been introduced in almost all SEAR countries to supplement IRS efforts, but the coverage remains extremely low.In India, with the implementation of modified plan of operation (MPO) in 1977, the upsurge of malaria cases dropped down from 6.74 million cases in 1976 to 2.1 million cases in 1984. Since then, the epidemiological situation did not show any great improvement. It seemed to have reached a plateau which was causing concern. Since 1997, there is a consistently declining malaria trend in the annual malaria incidence in the country. During 2005 about 1.8 million

cases were reported with 940 deaths.Malaria has been a serious problem in north eastern states mainly due to topography and climatic conditions being congenial for perennial malaria transmission; prevalence of malaria vectors particularly An. minimus, An. Fluviatalis and An. Dirus, predominance of P. falciparum as well as prevalence of chloroquine resistant P. falciparum in some areas. The major epidemic areas in India are in the north – eastern states, Orissa, Assam, West Bengal Rajasthan, marjoram, Meghalaya, Karnataka, Madhya Pradesh and Jharkhand report the largest number of deaths.

With World Malaria Day, April 25, 2008, the international community—led by UN Secretary-General Ban Ki-moon—throws its weight behind an ambitious campaign to expand access to a comprehensive set of malaria-control interventions in sub-Saharan Africa with the aim of ending malaria deaths on the continent in the near future. The first wave of the effort will be to fund and deliver about 250 million long-lasting insecticide-treated bed nets to achieve universal access for malaria endemic populations by Dec 31, 2010. This goal applies not only to pregnant women and children aged less than 5 years, as previous efforts sometimes have, but to all people at risk of malaria. Although we will lead with bed nets, near-zero mortality can only be achieved with a comprehensive approach that includes targeted spraying of insecticides, provision of effective medicines, and expanded delivery through community health workers and other means. We must make these efforts simultaneously. The world has seen ambitious plans

before that have fallen far short of achieving their goals—the 2005 Abuja target of 60% of people in sub-Saharan Africa using essential malaria control interventions, to name just one. So why is this effort any different? We now have clear instances of country-level success in sub-Saharan Africa, mounting political will, expanded resources, and more effective approaches than ever before. Together, these factors make aggressive new goals achievable. Last month, WHO reported that cases of malaria in Rwanda decreased by 64% and deaths by 66% between 2005 and 2007 among children aged less than 5 years. 2 Ethiopia, meanwhile, saw reductions of 51% in deaths and 60% in cases in the same age group. 3 These remarkable outcomes were achieved through expanded access to malaria control, primarily long-lasting insecticide-treated bed nets and artemisinin-based combination therapies. 4 But how did these programmes work? And why should we expect these successes to translate to a continent-wide scale-up in the next 32 months? The case of Ethiopia is especially informative, because this is the first time such significant achievements have been recorded over such a large geographical area in sub-Saharan Africa. In the face of widespread skepticism,

Comment on insecticide treated bed nets for malaria prevention:

Ethiopia managed to distribute more than 20 million bed nets—two for every household in malaria-prone areas—largely through a vast network of community health workers established to strengthen the routine health

system. The achievement of these results in just 3 years proves that malaria control can be quickly and effectively scaled up. Combining bed nets with rapidly expanding access to artemisinin-based combinations and diagnostics, Ethiopia's scale-up model deserves careful study and dissemination. Although multiple factors have contributed to success in Ethiopia, there are arguably four main contributing components: 1. a catalytic moment, 2. demand for universal coverage, 3. pragmatic donor response, and 4. innovative problem-solving. In 2003, Ethiopia experienced its worst malaria epidemic on record. Despite warning signs, the country found itself ill-equipped to deal with the crisis. The number of malaria cases rose from 6 million to about 12 million, with an estimated 100000 child deaths. The epidemic spurred the government to rethink its approach. Recognizing that successful malaria control needed adequate scale, Ethiopia made a bold proposal in early 2005: it would achieve universal coverage with long-lasting insecticide-treated bed nets by distributing 20 million in 3 years in the hope of reducing malaria-related deaths by 50%. Rather than making do with the money available, Ethiopia made a compelling case for the money it needed. The required US$160 million was almost three times the previous national malaria-control budget; and some people viewed this request as unrealistic. Donors responded not just to the urgent need, but also to committed leadership and a sound plan grounded in the technical realities of the disease. Additional resources totalling over $200 million were made available by a consortium of partners including the

Global Fund to Fight AIDS, Tuberculosis and Malaria, the World Bank Booster Program for Malaria Control, the UK Department for International Development, the Dutch Government, the Carter Center, and others Ethiopia took advantage of flexibility built into both Global Fund and World Bank processes to frontload funding. Rather than disbursing its grants over 5 years, the country drew down on the pledged funds to finance its ambitious bed net distribution programme in 1–2 years. Procurement of intervention is often a rate-limiting factor, but Ethiopia negotiated reduced fees with and outsourced much of the purchasing of bed nets to UNICEF to increase speed and coordination. Most of the monies flowed directly to UNICEF, so funds did not have to be disbursed first from the Global Fund to the government and then back to a procurement agent. At the same time, significant investments were made by the government and partners to build in-country procurement capacity for the post scale-up phase. These decisions expedited the delivery of bed nets by 21 months or more. Now is the moment to aim for results like those in Ethiopia and Rwanda throughout Africa. With the successful replenishments of the Global Fund and the World Bank's International Development Association, as well as the prospect of increased resources from the US, UK, and other G8 governments, malaria-endemic countries should no longer limit their aspirations to small-scale, incremental progress. Ethiopia proves that large-scale success is achievable in a short time. Donors must also be willing to assume greater risk by encouraging and funding ambitious programmes

while showing increased flexibility in their processes and procedures. And both parties must plan early for the maintenance and eventual elimination phases so that donor support does not flag as malaria deaths are reduced. The pieces are increasingly in place to achieve the Secretary General's vision for universal coverage and make rapid gains toward ending malaria deaths in Africa. With one child dying every 30 s from malaria in Africa, we have not a moment to lose. Corbis

Bednet demonstration in Ambowuha, Ethiopia 1406 www.thelancet.com **Vol 371 April 26, 2008**

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The Clinton Foundation, is optimistic about the benefits of subsidized ACTs for children. She says that in the first month, 40% of customers seeking treatment for children under 5 years bought subsidized ACTs. She is also impressed by the rapid manner in which stores have stocked the drug. "After 1 month, half the stores were carrying the product, so access has been increased in a short time." The stores also seem to be selling the drugs at a reduced price, according to the initial findings. So the subsidy is reaching the target audience. The investigators found that the average price paid by consumers in the duka la dawa baridis was 20 times less than the standard price paid in private pharmacies in the commercial capital Dar Es Salaam. And, contrary to expectation, consumers in the Maswa district, where the price was not on the ACT packaging, paid less than customers in

the Kongwa district. So what effect has this all had on malaria cases and deaths? Anecdotally, Temba Nazar says he has seen a reduction in admissions for malaria at Kongwa's District Hospital this year compared with last year. But the pilot is not assessing malaria morbidity or mortality in the intervention districts, so the effect of the subsidy on these outcomes may become apparent only when the country's next Demographic and Health Survey takes place in 2009–10. Andrea Bosman, medical officer at WHO's Global Malaria Programme, says that the preliminary results are encouraging, especially because other experiences to introduce subsidized ACTs into the private sector have taken a much longer time to work. There are some "very nice and positive findings", he told The Lancet. He thinks that the involvement of an international agency and the preexistence of a network of accredited drug dispensaries might explain part of the early success being seen in Tanzania. But whether the findings could be replicated in diff erent settings is unclear. "In other countries drug distribution can be difficult. It can be a bit of a jungle", he says.

Going global

Tanzania is not the only sub-Saharan African country assessing an ACT subsidy. The Medicines for Malaria Venture is currently running a pilot in Uganda and the World Bank is exploring the possibility of starting one in Zambia. But Tanzania's pilot, which is due to finish at the end of 2008, is further down the line. With second quarter results due out soon, all eyes are on the country to provide the first results to inform a global subsidy.

Meanwhile the plans for the global scheme, called the Affordable Medicines Facility-malaria (AMFm), are moving ahead. Observers say the AMFm could be officially launched at the end of April, when the board of the Global Fund to Fight AIDS, Tuberculosis and Malaria meet. However, Bosman thinks that the facility will not start-up properly before 2010. "Large amounts of money need to be pledged and there needs to be commitment to sustain the subsidy before launching the whole thing", he says. In July last year, the Roll Back Malaria Partnership announced that the resources required for the global subsidy fund would be around $250 million yearly from 2009 onwards.

Bosman thinks that progress with the AMFm has been disappointingly slow so far. "For an initiative that was meant to buy time and save lives things are happening very slowly. Since 2004 people have been pushing interest in this area. But still 4 years down the line and the initiative is not yet up and running." He adds that the lack of progress is especially worrying since tolerance tartemisinin has already been detected along the Thai/Cambodia border. "With malaria there is no possible replacement of artemisinin until 2016. And that's if all the drugs in the pipe line make it through. If we lose artemisinin we lose our ability to fight a major killer." He says that some donors seem to have an all-or-nothing approach to the AMFm but he thinks that middle ground needs to be sought. "Even when subsidy is launched, countries will not be able to enter the subsidy all at once, so there will be a phased roll-out." In the meantime, Tanzania is moving forward with plans to

launch an ACT subsidy nationwide for children under 5 years, with fi nancial support from the Global Fund. The government also plans to distribute over 5 million long lasting insecticide-treated bed nets to children under 5 years this year, with the help of UNICEF. For Minister Mwakyusa the goal with all the country's antimalarial eff orts is clear. He wants Tanzania to one day be malaria-free. "Some people think eradicating malaria is ambitious but we have to have that target. We should be talking about eradicating the disease—that is my philosophy. "The AU [African Union] conference of health ministers decided on eradication and we need to coordinate with other countries in the continent. Mosquitoes don't need visas to cross borders. If we can coordinate, we can wipe it out." Udani Samarasekera "We should be talking about eradicating the disease—that is my philosophy." Sala Lewis US received financial assistance from the Bill & Melinda Gates Foundation to visit Tanzania Special Report www.thelancet.com Vol 371 April 26, 2008 1405 The repackaged ACTs are then sold to a pharmaceutical wholesaler at around 95% less than the prices offered by the manufacturer. The wholesaler distributes the drugs through its usual channels to regional wholesalers or directly to private drug shops. The partners hoped that a subsidy high up in the distribution chain would result in reduced prices for consumers. But those implementing the pilot knew that even if the subsidy worked, it would not automatically mean that those seeking treatment for malaria in the private sector would purchase low-cost ACTs instead of the more familiar SP or other ineff

ective drugs. Encouraging behavior change had to be a big part of the project.

Convincing consumers

Standing in the pediatric ward at Kongwa District Hospital, Temba Nazar, the doctor in charge, says that there is a lot of ignorance about malaria among the population. "People don't know the first signs of malaria. They may try local traditional medicine or paracetamol for a fever first." Like Morogoro Regional Hospital, Kongwa's pediatric ward is full of children with malaria, accompanied by their watchful mothers. The Clinton Foundation and the Tanzanian Government enlisted the help of non-profit organization Population Services International (PSI) to get the message about ACTs across to people. PSI has experience with successful health-promotion work in Tanzania using methods such as radio broadcasts, mobile video, and cultural shows. In the rural village of Pandambili, in the Kongwa district, hundreds of people have gathered outside the local schoolhouse following a loud speaker broadcast by a PSI van. A row of drummers are lined up in front of the school. People are jostling around to get a good position and one man is even standing on his bicycle to get a view over the crowds. The drumming starts and barefoot performers take centre stage, singing and dancing. Their songs encourage patients to seek prompt treatment, to use the low cost combination therapy available at private drug shops, and to complete the recommended dose. Cultural shows, like the one in Pandambili, seem to be having the desired effect. In areas where their

promotional activities have taken place, the sale of ACTs from private drug shops has been higher than in areas without them. 26-year-old Happy Jeremiah works in a duka la dawa baridi in Kongwa town, where bright green and white murals adorn the walls of shops and advertise the fact that Alu is available in outlets like hers. Jeremiah studied nursing and hopes to work in the local hospital one day but for now her charge is the small shop from 7 am to 9 pm, Monday to Sunday. Standing behind the glass counter she says that "business is going good nowadays". The shop started selling ACTs as part of the pilot in mid- October last year. Jeremiah went on a 1-day training course for shopkeepers on the diagnosis and treatment of malaria, run by the TFDA as part of the pilot study. People that work in duka la dawa baridis are supposed to have a year of health training but unlike Jeremiah, many do not, making the TDFA training an important part of the project. Jeremiah says that most of the time the customers come into the store and know what they want. They often ask for SP because it is cheaper but she advises them that Alu is more eff ective. There have been "no complaints from customers so far", she says.

Encouraging results

The work of shopkeepers like Jeremiah seems to be paying off .The preliminary 1-month findings from the pilot show that the recommendation of shopkeepers was the most frequently cited reason by consumers for purchasing subsided ACTs. However, the advice of shopkeepers may only be reaching adults. It seems that caregivers are less likely to seek

treatment for children in private outlets than if they are seeking treatment for themselves or another adult. “Last month, we sold 60 adult courses. The adult course sells more than drugs for children”, says Jeremiah. This trend could be because parents may prefer to send their children to the hospital to receive professional care, especially since health care is free for children under 5 years of age. Lorrayne Ward, who has been working on the pilot in Tanzania for Sala LewisHappy Jeremiah works in a privately owned drug shop (duka la dawa baridi) in the Kongwa district 1404 www.thelancet.com Vol 371 April 26, 2008

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Which hit the country twice a year and turn dirt tracks into muddy lanes, the journey to the nearest health centre can be even more arduous. These barriers mean that about 15 million Tanzanians self-treat their malaria and seek treatment for their illness at local over-the-counter drug shops, known as duka la dawa baridis. At these privately owned shops people have been used to buying the cheap antimalarial sulfadoxinepyrimethamine (SP). However, in 2006, Tanzania, like most malaria endemic countries in sub-Saharan Africa, switched its first-line malaria treatment from SP to ACT because of a dramatic rise in resistance to older therapies such as SP. But making the transition to ACTs was not a simple move, since the drugs, which cost US$8–10, are ten times more expensive than SP and only available with a prescription. This situation left the millions of Tanzanians seeking treatment in the private sector, most of who live on less than $2 a

day, without access to effective, high quality treatment. "We had a short honeymoon with SP", says Mwakyusa. "With 18 million episodes of malaria in my country a year, if I had to buy ACTs my entire budget would go." For the minister, a former co-chair of the Global ACT Subsidy Taskforce, the way forward was clear: malaria drugs had to be subsidized.

Setting up the subsidy

When, early in 2007, the Clinton Foundation contacted the ministries of health in several sub-Saharan African countries about starting malaria work in their country, Tanzania saw an opportunity to work on the problem of private sector access to ACTs. By May that year, the government and the Clinton Foundation, with a grant from the Bill & Melinda Gates Foundation, had begun the groundwork for the pilot ACT subsidy. In the study, two districts— Kongwa and Maswa—would receive subsidized drugs, a package of social communication interventions, and approval from the Tanzania Food and Drug Authority (TFDA) to sell the drugs over-the-counter. The third district, Shinyanga Rural, would serve as a control. To set up the subsidy, the Clinton Foundation first procured the recommended ACT for the country— artemether-lumefantrine, or Alu as it is known in Tanzania—from manufacturer Novartis at a reduced public sector price (around $1). Then, before being sold to a wholesaler, the drugs are placed into packaging that has been specially designed for Tanzania and includes a user-friendly instruction sheet in the native language, Swahili. A suggested retail price is printed on the packs for the Kongwa district, but

the price is left off the packs for the Maswa district to see what effect a stated price has on the final amount paid by consumers.

The packaging for the over-the-counter ACTs was specially designed for the pilot Ambassador Gertrude Mongella arrived late to meet journalists at UNICEF's offices in Dar Es Salaam because of the notoriously bad traffic in the country's commercial capital. But neither the city's congested roads nor her brightly coloured African dress could distract the audience from her message about malaria. She says that people need to look at the issue from a gender perspective. To deal with malaria in children "you need to deal with the mother", she explained. "Survival of child is related to the actions of mother, so the mother needs to be part and parcel of the game. If mother dies then the child's survival is reduced." Sadly, Mongella admits that too many mothers are dying in Tanzania and the country is not on track to meet the Millennium Development Goal to reduce maternal deaths by two-thirds by 2015. "Maternal deaths are still high", she says. "We are not away from that." Mongella, who is president of the Pan-African Parliament, is a well known and respected politician and advocate of women's rights and maternal health in her native Tanzania and throughout Africa. She says that the "delays" that are commonly associated with maternal deaths can be applied to malaria. For example, she says that a mother may delay the decision to seek health care because she has so much work to do. "A mother says she will have to wait to get medicine. She has to feed her children

or may be she thinks that her fever will go away. When the mother finally makes the decision to go to the health facility then services are not there, another delay." Mongella, who is also a member of parliament in Tanzania, thinks that malaria needs to be taken more seriously at the political level. "If we had to lose votes if children were dying things would be different, things would change", she says. "If we could lose our constituency if mothers died it would completely change the whole picture in this country." But as well as politicians being held accountable for preventable deaths, Mongella believes it is also "up to the individual ". She said that patients have a responsibility to take malaria drugs. "With malaria we should also make it an individual issue—same as HIV/AIDS. Wear a condom, use a bed net." But she added that health concepts need to be easily digested for people so that they can understand why they need to taken certain precautions. People need "to have ownership of the disease", she said Today, like most days, there are too many admissions and mothers and children from different families have to share their woes together in a single bed along with the graying mosquito net that hangs above it. Stuck on a wall near the entrance to the ward, a small, inconspicuous piece of white paper tells of a pattern of admissions that keeps repeating itself year in, year out, at the hospital. Written on it, in blue felt pen, are the top ten diseases on the paediatric ward in 2007. Malaria is number one on the list. This ranking is unsurprising in a country where malaria is the main reason for health facility admissions nationwide. In some respects the children on

ward number six are lucky. Their mothers have got them to the hospital and if their malaria has been caught early, their treatment has a high chance of being successful. But for millions of Tanzanians the journey to a hospital or health facility is not an easy one, and more often than not, is a trip that is never made. “If you fall sick and meet a doctor, it is a luxury in my country”, explains David Mwakyusa, Minister of Health and Social Welfare in Tanzania. “80% of people live in rural areas.” But now there is hope that access to effective malaria drugs might be improved for those living far from any professional health care. A pilot project running in three rural districts in the country is looking at providing the fi rst-line treatment—artemisinin based combination therapy (ACT)— at a low cost over-the counter in private drug shops that are common in villages in Tanzania, with some promising preliminary results. The findings from the study are not only eagerly awaited by the Government of Tanzania and the partners involved, the global malaria community is also watching the pilot closely because the information from it will feed into plans to launch a global fund to subsidise ACTs. The idea for a global subsidy was first mooted in 2004 in a report— Saving lives, buying time—by the US Institute of Medicine. The authors recommended a subsidy fund to increase access to ACTs in the private sector and limit the use of artemisinin monotherapies, which rapidly lead to the development of resistance. But governments and policy makers were concerned about rolling out ACT subsidies globally, without

seeing what would happen in countries first. Tanzania was an ideal initial test bed for a subsidized.

The problem with malaria

Tanzania has the third largest malaria burden in the world, after Nigeria and its conflict-afflicted neighbor, the Democratic Republic of Congo. Over 90% of the population (37 million people) are at risk of malaria. There are around 20 million clinical cases of the disease per year, resulting in 100 000 deaths—80% of which are in children under 5 years of age. In the geographically diverse east African country, which is home to Mount Kilimanjaro and Lake Victoria, over half the population lives more than 5 km from a health facility and the distance to a hospital can be more than 26 km for people living in rural areas. If a person is unlucky enough to fall ill during the rainy seasons

Drug subsidy could help Tanzania tackle malaria

In Tanzania, millions of people seek treatment for malaria through the private sector. But most cannot afford effective medicines. Now a pilot study is testing whether a drug subsidy scheme could help these patients, with some positive preliminary results. Udani Samarasekera reports. Over 60% of children seen in health facilities in Tanzania are diagnosed with malaria "If you fall sick and meet a doctor, it is a luxury in my country."- Sala Lewis

Sala Lewis Development and Evaluation of Long-Lasting Insecticide-Treated Nets

Insecticide-treated bed nets are advocated for the control and prevention of malaria in sub-Saharan Africa. However, widespread implementation of ITNs has been hampered by the need for frequent retreatment with insecticide. Several companies have developed long-lasting nets that theoretically retain effective concentrations of insecticide after long-term use and repeated washings. CDC has been active in developing new long-lasting treatment technologies as well as evaluating candidate long-lasting ITNs in the laboratory and the field.

Diagnosis

Overview

Malaria must be recognized promptly in order to treat the patient in time and to prevent further spread of infection in the community. Malaria should be considered a potential medical emergency and should be treated accordingly. Delay in diagnosis and treatment is a leading cause of death in malaria patients in the United States. Malaria can be suspected based on the patient's symptoms and the physical findings at examination. However, for a definitive diagnosis to be made, laboratory tests must demonstrate the malaria parasites or their components

Diagnosis of malaria can be difficult:

Where malaria is not endemic any more (such as the United States), health care providers are not familiar with the disease. Clinicians seeing a malaria patient may forget to consider malaria among the potential diagnoses and not order the needed diagnostic tests. Laboratories may lack experience with malaria and fail to detect parasites when examining blood smears under the microscope.

In some areas, malaria transmission is so intense that a large proportion of the population is infected but not made ill by the parasites. Such carriers have developed just enough immunity to protect them from malarial illness but not from malarial infection. In that situation, finding malaria parasites in an ill person does not necessarily mean that the illness is caused by the parasites.

In many malaria-endemic countries, lack of resources is a major barrier to reliable and timely diagnosis. Health personnel are under trained, under equipped and underpaid. They often face excessive patient loads, and must divide their attention between malaria and other equally severe infectious diseases such as pneumonia, diarrhea, tuberculosis and HIV/AIDS.

Clinical Diagnosis

is based on the patient's symptoms and on physical findings at examination.

Presumptive malaria

The first symptoms of malaria (most often fever, chills, sweats, headaches, muscle pains, nausea and vomiting) are often not specific and are also found in other diseases (such as the "flu" and common viral infections). Likewise, the physical findings are often not specific (elevated temperature, perspiration, tiredness).In severe malaria (caused by Plasmodium falciparum), clinical findings (confusion, coma, neurological focal signs, severe anemia, respiratory difficulties) are more striking and may increase the suspicion index for malaria. Probable malaria-Presumptive malaria, test positive for RDT

Confirmed malaria

Presumptive malaria microscopically confirmed by presence of malaria parasites

Severe Malaria Severe malaria occurs when P. falciparum infections are complicated by serious organ failures or abnormalities in the patient's blood or metabolism. The manifestations of severe malaria include: Cerebral

malaria, with abnormal behavior, impairment of consciousness, seizures, coma, or other neurological abnormalities Severe anemia due to hemolysis (destruction of the red blood cells) Hemoglobinuria (hemoglobin in the urine) due to hemolytic Pulmonary edema (fluid buildup in the lungs) or acute respiratory distress syndrome (ARDS), which may occur even after the parasite counts have decreased in response to treatment Abnormalities in blood coagulation and thrombocytopenia (decrease in blood platelets) Cardiovascular collapse and shock Other manifestations that should raise concern are:Acute kidney failure. Hyperparasitemia, where more than 5% of the red blood cells are infected by malaria parasites Metabolic acidosis (excessive acidity in the blood and tissue fluids), often in association with hypoglycemia Hypoglycemia (low blood glucose). Hypoglycaemia may also occur in pregnant women with uncomplicated malaria, or after treatment with quinine. Severe malaria occurs most often in persons who have no immunity to malaria or whose immunity has decreased. These include all residents of areas with low or no malaria transmission, and young children and pregnant women in areas with high transmission. In all areas, severe malaria is a medical emergency and should be treated urgently and aggressively. Thus, in most cases the early clinical findings in malaria are not typical and need to be confirmed by a laboratory test.

"Presumptive Treatment"

In highly endemic areas (particularly in Africa), the great prevalence of asymptomatic infections and lack of resources (such as microscopes and trained microscopists) have led peripheral health facilities to use "presumptive treatment". Patients who suffer from a fever that does not have any obvious cause are presumed to have malaria and are treated for that disease, based only on clinical suspicion, and without the benefit of laboratory confirmation. This practice is dictated by practical considerations and allows the treatment of a potentially fatal disease. But it also leads frequently to incorrect diagnoses and unnecessary use of antimalarial drugs. This results in additional expenses and increases the risk of selecting for drug-resistant parasites

Microscopic Diagnosis:

Malaria parasites can be identified by examining under the microscope a drop of the patient's blood, spread out as a "blood smear" on a microscope slide. Prior to examination, the specimen is stained (most often with the Giemsa stain) to give to the parasites a distinctive appearance. This technique remains the gold standard for laboratory confirmation of malaria. However, it depends on the quality of the reagents, of the microscope, and on the experience of the laboratorian.

Alternate methods for laboratory diagnosis include:

Antigen Detection

Various test kits are available to detect antigens derived from malaria parasites. Such immunologic ("immunochromatographic") tests most often use a dipstick or cassette format, and provide results in 2-15 minutes. These "Rapid Diagnostic Tests" (RDTs) offer a useful alternative to microscopy in situations where reliable microscopic diagnosis is not available. Malaria RDTs are currently used in some clinical settings and programs. However, before malaria RDTs can be widely adopted, several issues remain to be addressed, including improving their accuracy; lowering their cost; and ensuring their adequate performance under adverse field conditions. The World Health Organization's Regional Office for the Western Pacific (WHO/WPRO) provides technical information, including a list of commercially available malaria RDTs, at http://www.wpro.who.int/rdt/

On June 13, 2007, the U.S. Food and Drug Administration (FDA) approved the first RDT for use in the United States. This RDT is approved for use by hospital and commercial laboratories, not by individual clinicians or by patients themselves. It is recommended that all RDTs are followed-up with microscopy to confirm the results and if positive, to quantify the proportion of red blood cells that are infected. The use of this RDT may decrease the amount of time that it takes to determine that a patient is infected with malaria.

Pathogen:

Malaria is caused by genus plasmodium, a parasite, in human is caused by four distinct species of the malaria parasite: P. vivax, P falciparum, P. ovale and P. malariae. In India about 70 percent of the infection are reported due to P. vivax and 25 to 30 percent are due to P. falciparum, 4-8 percent due to mixed and less than one percent due to P. malariae.

Vector and host

The vectors of malaria are the female anophilene mosquitoes, out of about 45 species of anopheline mosquitoes in India, only a few are regarded as the vectors of primary importance. These are : an. Culicifacies, An. Stephensai, An.fluviatalis, An. Minimus, An. Dirus, An. Philippinenssis, An. Sundaicus and An. maculatus. However, in the jalpaiguri district, an entomological survey done in 2003, found an. Culicifacies, An. Stephensai and An. Dirus are the main vectors of transmitting malaria. It has been seen that malaria occurrence was high in the residence of nearby forests where An. Dirus vectors inhabitant and due to their peculiar habit of biting day time in popular area and go back to the forest at night, they are resistant to DDT spray. So the nearby forest area malaria could not be controlled by preventive measures..

Pathogenesis: When malaria by the bite from an infected female anopheles mosquito to a human, it begins to grow at the liver parenchyma cells and subsequently invades the red blood cells of the general circulation

of blood. The malaria then spreads systemically via the haematogenous routes and the infected human develops various systemic symptoms. However, partial immunity from prior exposures might alter the response to infection in endemic areas. The pathogenesis of this disease is vasculitis caused by the proliferation of organisms in blood, veins and capillaries. The main organs affected were the heart, the lungs, the brain, G.I Tract and the kidney.

Clinical features

Clinical symptoms occur 12 to 18 days (incubation period varies according to species) after the bite of an infected anophiline mosquito . The onset is usually sudden and is characterized by paroxysms which corresponds to the development of the parasites in the red blood cells. the peak of the fever coincide with the release into the blood stream of successive broods of merozoites. The typical attack comprises three distinct stages : the cold stage, the hot stage and sweating stage. Theses are followed by an afebrile period in which the patient feels greatly relieved. cold stage: the onset is with lassitude, headache, nausea and chilly sensation followed in an hour or so by rigors. the temperature rise rapidly to 39-41.C. headache is often severe and commonly there is vomiting. The early part of the stage, skin feels cold; later it becomes hot. Parasites are usually demonstrable in the blood. The pulse is rapid and may be week. This stage lasts for 15 minute to one hour.

Hot stage: the patient feels burning hot and cast off his clothes. The skin is hot and dry to touch. Headache is intense effect of transmission setting and mixed species infections on clinical measures of malaria in Malawi. conclusions: Our study suggests that the interaction of Plasmodium co-infecting species can have protective effects against some clinical outcomes of malaria but that this is dependent on the seasonality and intensity of malaria transmission. Chloroquine (CHQ) is a cheap, relatively well tolerated drug initially developed for the treatment of malaria in the 1930s. CHQ has, however, since accrued aplethora of uses in the treatment and amelioration of several other diseases and conditions because of its lysosomotropic properties. It also has characteristic

physiological and systemic effects. This review gives an overview of the history and pharmacology of CHQ, and progresses to consider some of the mechanisms that may underlie its biochemical and physiological effects. Additionally, an overview of some of the novel uses of CHQ in the treatment of viral infections and cancer are presented. The antimalarial mechanisms of CHQ were not discussed in this review. The message is that CHQ, despite its well documented toxicity and adverse side effects may have important future uses that are associated with its lysosomotropic and immunomodulatory mechanisms. The possibility exists therefore that CHQ might be re-introduced into regular malaria treatment. Impact of intermittent preventive treatment with sulphadoxine-pyrimethamine targeting the transmission season on the incidence of clinical malaria in

children in Mali. conclusions: Two malaria intermittent treatments targeting the peak transmission season reduced the annual incidence rate of clinical malaria by 42.5% in an area with intense seasonal transmission. This simple strategy is likely to be one of the most effectives in reducing malaria burden in such areas. In-hospital morbidity and mortality due to severe malarial anemia in western Kenya. Transfusion did not lower mortality rates. In areas of high malaria transmission, children below 3 years are a high-risk group for malaria, anemia, blood transfusion, and mortality

Laboratory investigations

Identification of malaria parasite infection causing malaria could be done by five methods: First, identification of a malaria parasite may be achieved by microscopic examination after staining with Giemsa stains, identification of malaria infection is easy and could be done in every microscopic centre. Secondly, malarial infection can be done by molecular biology based method based on polymerase chain reaction (PCR) amplification of malarial DNA. However, this too is not commonly available except at reference laboratories. Thirdly, malarial detection can be done by serological tests, detecting malaria specific antibody which could be found only after 14 days after the primary infection..forthly by antigen detection with rapid diagnostic test kit. fifth way is to identify some specific pigments of parasites peripheral leucocytes. tertiary hospital in Bangladesh. Clinical diagnosis of cerebral malaria was done by WHO criteria. The tests were conventional

routine malaria microscopy; prolonged microscopy; dipstick antigen capture assay (Para Sight TM-F test); pigments in peripheral leucocytes and routine microscopy repeated at 12 hours interval. First four tests were done at 0 hours of hospital admission and repeat routine microscopy was added at 12 hours interval. Diagnostic capability of the test was 64%, 65%, 69%, 27% and 63% respectively. None of the tests except pigments in peripheral leucocytes was superior at initial evaluation. Only the dipstick test added 5% more diagnostic possibility compared with routine microscopy as standard. Stratification of diagnostic capability in different ways improved diagnosis 15% and 11% in smear negative cases by dipstick and prolonged microscopy respectively. It was increased by 50% (5/10 patients) with dipstick test in the smear negative patients with history of anti-malarial prior to hospital admission. WMR08-news-summary.doc 1

World Malaria Report 2008

10 September 2008, There were an estimated 247 million cases of malaria and 881 000 deaths from the disease in 2006, mostly among children in Africa, making it one of the world's leading killers. Yet the "World Malaria Report 2008" provides strong evidence that a renewed global assault on malaria, underway since the turn of the millennium, has been accelerating in the last few years. The report documents the significant progress, early successes, and biggest challenges as of 2006. The report draws on reporting by countries, and on household surveys, to chart the global fight against malaria. Worldwide funding for malaria control increased sharply

between 2004 and 2006. The largest increase, and the biggest overall spending, was in Africa, the region, most affected by the disease. At least US$ 688 million was spent there to combat the disease in 2006. Funds came foremost from the governments of affected countries and from the Global Fund to fight AIDS, Tuberculosis and Malaria. Funding growth reflects a growing global commitment to fight malaria and growing commitment to use the best up-to-date methods of malaria control, namely: long-lasting insecticidal nets (LLINs), a relatively new treatment known as arteminisin-based combination therapy (ACT), indoor residual spraying (IRS) of homes with insecticides, and the provision of preventive medicines to pregnant women. One of the most striking signs of progress has been a sharp increase in the distribution of insecticide-treated nets (ITNs) in Africa, especially LLINs, which are effective for three years. In 2006, the number of LLINs distributed in the region grew to 36 million, accounting for 70% of all nets provided. Of 647 million people at risk in Africa, the portion covered by ITNs rose from 3% in 2001 to 26% in 2006 and an estimated 39% in 2007. (One net is required for every two people). Household surveys in 19 African countries confirmed a similar picture: on average 34% of households owned a mosquito net. (However net ownership varied widely: from 6% in Côte d'Ivoire to 65% in Niger).

Usage was lower, however, according to the surveys: only 23% of young children and 27% of pregnant women slept under an ITN. Despite the progress, coverage of nets and all other interventions are substantially

below the 80% target established by World Health Assembly to be achieved by 2010. The slow introduction of the newer ACT medicines has been of particular concern. Household surveys found that on average 38% of African children under 5 years of age who had a fever got some antimalarial drug in 2006. Yet despite a big increase in the supply of ACTs to public health services in 2006, only 3% of sick children were given this more effective medicine. This was a major, and not-well-understood, shortcoming. The report documents several early success stories in which stepped up control measures led to a sharp decline in malaria. The most persuasive evidence comes from three African countries and one part of a country with relatively small populations and good surveillance. Eritrea, Rwanda, Sao Tome and Principe, and Zanzibar (a part of the United Republic of Tanzania) each reported declines of 50% or more in reported WMR08-news-summary.doc 2 malaria cases and deaths between 2000 and 2006 or 2007, following high coverage of control activities. Outside of Africa, 22 countries also reported a drop of 50% or more in malaria cases and deaths between 2000 and 2006. The report's estimate of 247 million cases and 881 000 deaths in 2006 are considerably lower than the estimates contained in the first World Malaria Report, published in 2005. The earlier report estimated 350–500 million cases and more than one million deaths in 2004. However the change is due primarily to a refinement of calculation methods, especially for Asia. It is not known if global cases and deaths actually declined between 2004 and 2006.

Both reports used the same method for estimating the number of cases and deaths for most countries in Africa. Because national surveillance systems there are generally too weak there, estimates were made on the basis of long-term climate data from satellites and several field studies of malaria rates. Estimates for other parts of the world (and a few countries in Africa) were made in the earlier report on the basis of historical data on the malaria risk in different areas. However this method was found to produce overestimations in some countries, because it often did not take into account important changes such as deforestation and the introduction of malaria medicines, which have reduced incidence. The current report estimates the number of cases outside Africa on the basis of surveillance data reported by countries to WHO. The data was adjusted for incomplete reporting, and for the portion of the population thought to have used private health facilities or who did not seek treatment, and were therefore not counted in national statistics. WHO's estimate of the number of malaria cases that occurred in 2006, 247 million cases, is bracketed with a wide uncertainty range, of 189 to 327 million cases. The estimate of 881 000 deaths, has an uncertainty range from 610 000 to 1 212 000. (The estimates in the earlier report were bracketed by similar uncertainty ranges). WHO's goal is reduce those uncertainty brackets as estimation methods improve. This is not an academic exercise but reflects a need to know where to concentrate resources and to determine what is working, or not, and suggest possible explanations. The current report critically reviews

progress in the fight against the disease in 109 endemic countries, in five areas: 1. Malaria trends at the national, regional and global levels 2. National policies 3. Progress made by countries in implementing control measures, and current gaps 4. Funding for malaria control 5. Recent evidence of the impact of malaria control programmes. The conclusions are intended to stimulate improvements and make national malaria control programmes more effective. Using 2000 as a base year, the goal of the Roll Back Malaria partnership is a 50% reduction in malaria by 2010 and a 75% reduction by 2015. Half the world's population – 3.3 billion people – are at risk of malaria (1.2 billion of them are considered at high risk: they live mainly in Africa or South-East Asia). Of the 247 million estimated cases of malaria in 2006, 86% were in the African region. Over WMR08-news-summary.doc 3 half of these cases were in just five countries: Nigeria, Democratic Republic of the Congo, Ethiopia, United Republic of Tanzania and Kenya. Children, especially in Africa, bear the brunt of the disease. Of the estimated 881 000 malaria deaths in 2006, 91% were in Africa and 85% were among children under 5 years of age. 2005 and 2006 saw a sharp increase in the distribution of insecticide-treated nets, which are recommended for all people at risk, and especially young children and pregnant women. WHO guidelines call for their distribution free or at a highly subsidized price. One net is needed for every two people. There has been a clear shift towards longlasting insecticidal nets (LLINs), since 2005. Eight countries in Africa have completed nationwide distribution of LLINs.

Ethiopia (2005–2006) and Zambia (2006–2007) targeted all households. Togo (2004), Niger (2005–2006), Rwanda (2006), Kenya (2006), Sierra Leone (2006) and Mali (2007) distributed nets for young children and pregnant women. Outside Africa, nets are distributed, but to smaller portions of the population, in the South-East Asia and the Western Pacific regions. Countries reported more than 100 million people protected in 2006 by indoor insecticide spraying of homes, including 70 million in India and 22 million in Africa. Outside Africa, coverage of more than 20% of the population at risk was restricted to Bhutan and Suriname. This method is, however, the main method of control of disease-carrying mosquitoes in WHO's European region, with the greatest number of homes treated in Azerbaijan, Tajikistan and Turkey. An average of 18% of pregnant women received antimalarial medicine as a preventive treatment, according to surveys in 16 African countries. The practice has been shown to increase birth weight and survival of children. The systematic use of intermittent preventive treatment in pregnancy (IPT) is restricted to Africa. Despite the relatively

low coverage, 33 of 45 countries had adopted it as part of national policy by the end of 2006.In 2007, the World Health Assembly urged countries to switch to artemisinin-based combination therapy (ACT) and discourage or ban the use of older, less effective antimalarial drugs. By the end of 2006, ACT was the first-line treatment in 66 countries. By June 2008, all but four countries and territories in the world had adopted ACT as their first-line

treatment. The move has been helped by a 2001 agreement between WHO and the pharmaceutical company, Novartis, in which the company agreed to provide one ACT, artemether-lumefantrine, at cost to public health services. A large increase in the distribution of ACTs started in 2006. The number of doses supplied to public health services rose from 6 million in 2005 to 49 million in 2006, most of it to Africa. According to national reporting, only 16 million rapid diagnostic tests were delivered in 2006, of which 11 million were for countries in Africa. Tests can play an important role in ensuring that fevers are correctly diagnosed and treated, and in helping to track the impact of control measures.

WHO has identified four phases on the path to malaria elimination. By July 2008, the 109 countries and territories affected by malaria were classified as follows: control (80), pre-elimination (12), elimination (11), and the prevention of reintroduction (6). In January 2007, the United Arab Emirates was the first formerly endemic country since the 1980s to be certified malaria-free by WHO.