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AN OVERVIEW WITH MATHEMATICAL MODELING IN PLASMODIUM FALCIPARUM MALARIA,INDIA

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Abstract

The purpose of malaria surveillance is to find out the trends and distribution of the disease for the purposes of planning, evaluation and early detection of epidemics. However, it is important to get a true estimate of malaria related morbidity and mortality in order to plan and project the resource requirements for its control. The WHO has estimated that malaria was responsible for 10.6 million cases and 15,000 deaths in India in 2006. These estimates are based on extrapolations from surveillance data with assumptions made on underreporting. Taking into consideration the highly focal distribution of malaria and the size of the country, the accurate estimation of the national malaria mortality and morbidity burdens is inherently very difficult. There are also very few studies on estimation of the malaria morbidity, mortality and burden of malaria in pregnancy in the country. The NVBDCP intends to arrive at better estimates of severe malaria cases and mortality by establishment of a sentinel surveillance system in all high endemic areas. Nongovernmental health care providers are also increasingly involved for reporting of malaria cases and deaths. Collaboration with research institutions is also enhanced for conducting studies to assess the true malaria burden in the country. Malaria outbreaks occur frequently in various parts of the country. Malaria in India is mostly unstable and the outbreaks are caused mostly by infection due to P. falciparum. The reasons for such outbreaks have been identified as improper surveillance and inadequate residual spray activities in rural areas, and antilarval measures in urban areas.

Key Words: Malaria, Mortality, Morbidity, Infection, P. Falciparum.

INTRODUTION

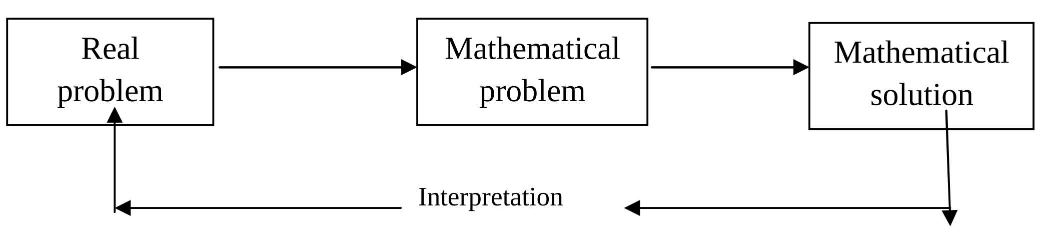
Mathematical modeling is the art of translating problems from an application area in to an tractable mathematical formulations whose theoretical and numerical analysis provides insight, answers and guidance use full for the originating application.

Mathematical modeling

- Is dispensable in many applications
- Is successful in many further applications
- Gives precision and direction for problem solution
- Enables a thorough understanding of the system modeled
- Prepares the way for better design as control of a system
- Allows the efficient use of modern computing capabilities

Learning about mathematical modeling is an important step from theoretical mathematical training to an application oriented mathematical expertise.

Mathematical modeling essentially consists of translating real world problems into mathematical problems, solving the mathematical problems and interpreting these solutions in the language of the real world.



The above figure explained that the real world problem in our teeth, dive into the mathematical ocean, swim there for some time and we come out to the surface with solution of the real world problem with us. Alternatively we may say that we soar high in to the mathematical atmosphere along with the problem, fly there for some time and come down to the earth with the solution.

In fact every branch of knowledge has two aspects, one of which is theoretical, mathematical, statistical, and computer based and other of which is empirical experimental and observational.

Classification of Mathematical Models

A math model is a mathematical description of a real world system or event. Models provide the user with concise descriptions of complicated non-linear systems. The model also provides a method for relating the process of infection of the individual to the process of infection of a population. The modeller must have as much empirical data as possible and the only way to get that data is to have someone in the field collecting. New knowledge in its correct place and correct emphasis, there by delineating critical areas that will need new research and maybe showing that older data was insufficient or incorrectly analyzed again showing needs for new work.

S	Susceptible
I	Infectious
E	Exposed(infected)
R	Recovered(immune)
M	Mother(maternal immunity)

All resources are limited, therefore another need for a concise model is for correct placement of those limited recourses to minimize human suffering from this disease. The well tuned model will allow better evaluation of the impact of new strategies for controlling the disease learning more quickly what works and what doesn't therefore, the waste of valuable resources is minimized.

TERMS OF DIFFERENT CLASSICAL MODEL TYPES

There are many types of mathematical models of disease SI, SIS, SIR, SIRS, SEIR, SEIRS and MSEIRS just to mention a few.

M Model

This aspect of the model deals with the temporary immunity that a mother can pass on to her offspring via the placenta.

SI Model

This model indicates that all individuals in a class are susceptible to the disease and after being exposed the individual is infectious. This assumes that there is no incubation period and no recovery i.e. you stay infectious.

SIS Model

This model is similar to the SI model but the individual will not stay infectious instead he (she) will recover from the disease but will not acquire any immunity and renter the susceptible group.

SIR Model

Again this model will use the base of SI model but the individual will recover from the infection and gain immunity to the disease.

SIRS Model

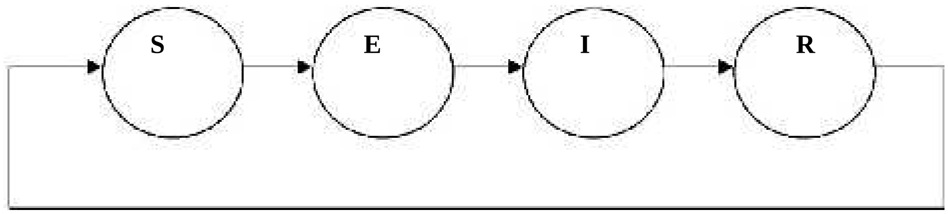
This model will follow the SIR model except that the immunity gained is only temporary and after a small period of time the individual will again enter the susceptible category.

SEIR Model

In this model a person is susceptible to the infection and later exposed. There is a lag time between exposure and when you become infectious, but with time you recover and have immunity.

SEIRS Model

This model is the same as the SEIR model but the immunity is only temporary phenomena.
Hence the flow of the disease will follow the SEIRS model



Models of Mathematical Approach

Here, we discuss about some models with mathematical approaches are,

- SIR Model
- Another SIR Model
- SIRS Model
- TIME DEPENDENT IMMUNITY (TDI) Model
- TEMPORARY IMMUNES (Extended Models)
- SUPER INFECTION Model

SIR Model

The classical SIR model by definition only has three classes if individuals
S - *susceptibles*,
I - *infecteds* and
R - *partial immunes*.

The assumptions associated with this model are, all who come into contact with the disease may contract the disease, those who contract the disease are at first severely symptomatic and later they either die or become mildly symptomatic and then they enter the *partial immunes* where they cannot be re infected as long as their immunity lasts.

Malaria in India

The largest population at risk of malaria, 1,320 million people, now lives in the South-Eastern WHO Region. India is one of 11 countries in that region with nearly 980 million people at risk. According to WHO's estimated number of cases, India also has the largest number of malaria cases occurring outside of Africa. India's official statistics suggest that **P. falciparum** accounts for about 50% of the clinical cases in India.

India has a long history of attacking malaria. Organized control programmes started in the 1940s used DDT to control mosquitoes. The programmes were originally very successful and brought malaria in India near elimination by 1961. Since that time, malaria has become re established in India. As hopes for eradication dim, India has redirected resources to keeping the disease under control. The re emergence of malaria has been accompanied by a steady rise in the percentage of **P. falciparum** among all malaria cases.

The resurgence of malaria throughout the world and the rising death toll have drawn the attention of the international community. WHO, the World Bank and several charitable organizations launched in 1998 the Roll Back Malaria Partnership (RBM), a global initiative that coordinates actions against malaria. The mission of the RBM Partner ship has more recently been outlined in its Global Malaria Action Plan .
Some of the major goals of the Partnership are

1. Reduce global malaria cases from 2000 levels by 50% in 2010 and by 75% in 2015
2. Reduce global malaria deaths from 2000 levels by 50% in 2010, and to near zero by 2015
3. Eliminate malaria in 8-10 countries by 2015 and eventually
4. Achieve eradication of malaria worldwide.

The RBM Partnership provides financial and logistical support to many countries, including India. As the country with the largest population at risk from malaria, India's success in control and elimination of malaria is a key component of the RBM plans. India has recently experienced significant economic growth, becoming the second fastest growing major economy in 2008. The economic achievements of India have lead to significant reduction in poverty, thereby positioning India well for reducing the burden of malaria. In the period 1999-2010, India administered a number of control programs and made significant progress in managing malaria.

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Incidence of Malaria in India

Year	Total cases	*P. falciparum*	Deaths
1947	75 million		8,00,000
1961	49151		--
1965	99667		--
1976	6.47 million	0.75 million	59
1984	2.18 million	0.65 million	247
1985	1.86 million	0.54 million	213
1986	1.79 million	0.64 million	323
1987	1.66 million	0.62 million	188
1988	1.85 million	0.68 million	209
1989	2.05 million	0.76 million	268
1990	2.02 million	0.75 million	353
1991	2.12 million	0.92 million	421
1992	2.13 million	0.88 million	422
1993	2.21 million	0.85 million	354
1994	2.51 million	0.99 million	1122
1995	2.93 million	1.14 million	1151
1996	3.04 million	1.18 million	1010
1997	2.66 million	1.01 million	879
1998	2.22 million	1.03 million	664
1999	2.28 million	1.14 million	1048
2000	2.03 million	1.05 million	932
2001	2.09 million	1.01 million	1005
2002	1.84 million	0.90 million	973
2003	1.87 million	0.86 million	1006
2004	1.92 million	0.89 million	949
2005	1.82 million	0.81 million	963
2006	1.79 million	0.84 million	1707
2007	1.51 million	0.74 million	1311
2008	1.53 million	0.77 million	1055
2009	1.56 million	0.84 million	1144
2010	1.59 million	0.83 million	1018

India's Plasmodium Falciparum Malria

P. falciparum and half by **P. vivax**. The other two kinds contribute little to the cases of malaria in India. **P. falciparum** causes fewer of the cases in India, but it has a shorter average incubation period in the mosquito vector, which accelerates the transmission, and it causes the highest morbidity and mortality. A trend of concern shows that the proportion of the incidence (number of clinical cases) due to **P. falciparum** has been rising from about 30-35 % in 1984 to about 50% in 2008. Presumably, this trend is due to the ability of **P. falciparum** to evolve into strains, resistant to the classical single drug therapies.

In 2009 alone India had 1.56 million cases of malaria, 0.84 million of them were caused by **P. falciparum**. Official statistics reports that malaria cases in 2009 resulted in 1144 deaths. In 2010 alone India had 1.59 million cases of malaria, 0.83 million

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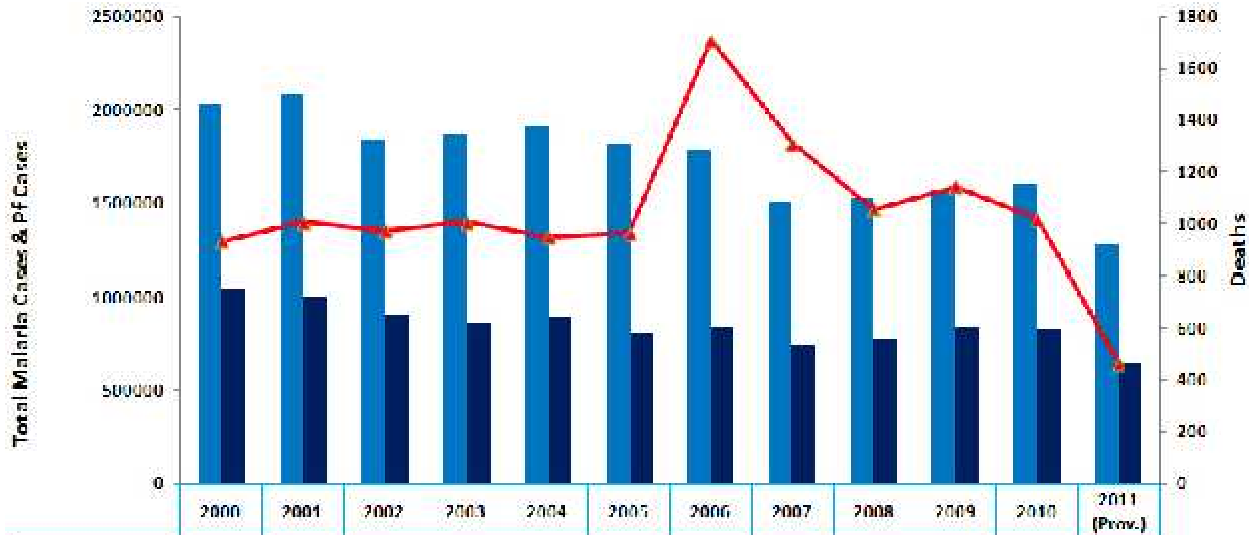
of them were caused by **P. falciparum**. Official statistics reports that malaria cases in 2010 resulted in 1018 deaths. Since **P. falciparum** is responsible for most deaths from malaria in India, the above data give a crude case-fatality proportion (CFP) of **P. Falciparum** cases of 0.0013

TOTAL MALARIA CASES ,P. FALCIPARUM MALARIA AND DEATH



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011 (Prov.)
Total Malaria Cases	2031790	2085484	1841229	1869403	1915363	1816569	1785129	1508927	1526210	1563574	1599986	1279381
Pf Cases	1047218	1005236	897446	857101	890152	805077	840360	741076	775523	839877	834364	643495
Deaths	932	1005	973	1006	949	963	1707	1311	1055	1144	1018	463

Fitting the Ross Modelto India's Malaria Incidence

India collects regular statistics of malaria incidence. Most of the data provides the total number of clinical cases per year, the number of clinical cases of **P. falciparum** per year.

Although differential equation modeling of malaria now has a long history and to date many models have been developed to account for the various simplifying assumptions in the Ross models.

Here we fit model

$$\frac{dy}{dt} = r\,(p_m - y(t))\,I(t) - d\,y(t) \quad ....(1)$$

$$\frac{dc}{dt} = \beta\,(p(t) - c(t) - I(t))\,y(t) - (v + \mu)\,c(t)$$

$$\frac{dI}{dt} = v\,c(t) - (\lambda\,p(t) + \mu)\,I(t) \quad ....(2)$$

to India's incidence of plasmodium falciparum and use that fit to make projections equations,

$$\frac{dp}{dt} = a\,p(t)\left(1 - \frac{p(t)}{k}\right) \quad ....(3)$$

for the human population does not depend on variables in the main diseases of models (1) and (2) and it may fitted to data separately .India collects census statistics of the population every 10 years, and we use census data for 1961-2001 to estimate parameters in (3).

The fit of the solution of equation (3) to the data is described in and the estimates of the parameters are shown in below Table. The sum of squares error (SSE) of the fit is 13.4.

List of Fitted Parameters With Values and Confidence Intervals

PARAMETERS	ESTIMATED VALUE
a	0.02555203
k	4235.46
b	16.9923
r	0.017989
ζ	0.00626284
η	0.0391625

Since the total mosquito population is not known, even approximately, we rescale the mosquito population to the proportion of infected mosquitoes. with,

$$y(t) = \frac{Y(t)}{P_m}$$

The model (1) and (2) may be rewritten in the following form,

$$\frac{dc}{dt} = \beta (p(t) - c(t) - I(t)) y(t) - (v + \mu) c(t)$$

$$\frac{dI}{dt} = v\, c(t) - (\lambda p(t) + \mu) I(t)$$

$$\frac{dy}{dt} = r(p_m - y(t)) I(t) - d\, y(t)$$

..........................(4)

where, the new parameter

$$b = \beta p_m$$

This reduces the number of parameter by one. The human classes are not rescaled, since they must be compared to data.

We used mathematica to fit the above model to India's incidence of malaria for the years 1984 – 2010 and we used ND solve to solve the differential equation model (4) numerically and non linear model fit to perform the fitting and estimate parameters. To begin, we estimate and fix certain parameters.

The mosquito life span is taken to be about 29 days (0.07945). A human life span for India is estimated to be 65 years. our model (3) estimates India's population in 1983 to be 714.277 million people.

Hence, the value of disease reproductive number with the parameter is $R_0 = 1.00732$. since the model parameter are estimated from the nearly endemic phase of malaria, rather than from the moment it invaded.

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Malaria Control Programs

In 1998 the United Nations and the World Bank joined the WHO to launch **Roll Back Malaria Partnership (RBM)**, which is an ambitious campaign to reduce the malaria burden by 50% by year 2010. RBM provided logistical support and financial assistance to multiple malaria affected countries, including India. With partial funding from the World Bank, India launched the Enhanced Malaria Control Project (EMCP) in October 1997. The project selectively targeted 100 districts within 8 states, deemed most high risk to malaria and accounting for about 70% of the **P. falciparum** incidence in the country in 1997.

The EMCP reduced the **P. falciparum** cases in the targeted areas from about 0.72 million in 1997 to about 0.41 million in 2004, while the national incidence of **P. falciparum** malaria was reduced from 0.99 million cases in 1997 to 0.89 million cases in 2004, largely due to efforts in the EMCP districts.

In response to rising incidence in malaria, and particularly malaria caused by **P. falciparum**, India adopted new approaches to malaria control, renaming the National Malaria Eradication Program (NMEP) into National Anti Malaria Programme (NAMP) in 1999. The basic components of the program are,

1. Early detection and prompt treatment of malaria. Due to growing wide spread resistance of **P. falciparum** to conventional single drug treatments, such as chloroquine, the country implemented combination therapies in 2006.
2. Selective mosquito control. As part of novel mosquito control strategies, India began to move away from conventional insecticides (such as DDT) to more environmentally friendly ones. Furthermore the wide spread spraying was replaced by more targeted spraying of high risk areas. More recently satellite remote sensing technologies are beginning to be used for locating habitats of the vector. Mosquito larval control is implemented through larvivorous fish and biolarvicides.
3. Medicated mosquito net program. The program incorporated increase use of insecticide treated bed nets (ITNs) through local production, marketing and distribution.
4. Strengthening institutions. New approaches were taken toward social development by training of staff, disseminating malaria information, and improving management and information systems.

After the funding for the EMCP expired, the World Bank provided new funding in assistance of the Enhanced Vector Borne Disease Control Project (EVBDCP) in 2005. More recently, in 2008, the World Bank allocated to India additional funding to help reduce malaria to 50% from its 1996 peak by 2010. In 2006, India also received financial assistance from the Global Fund which funded the Intensified Malaria Control Project (IMCP) . All these programs have helped India to intensify the malaria control measures and to stay on a steady path of malaria reduction in the period 1999-2010.

Conclusion

By fitting the India malaria data from 1984 to 2010 in mathematical modeling of Sir Ronald Ross model, we have the result of the disease reproductive number $R_o > 1$.

Malaria is a disease that is constantly changing. The parasite and the vector are adapting to the treatments use in the past. As global warming occurs new areas will become endemic requiring change to confront the new conditions. Therefore, a model that accurately predicts what results new treatments will produce would be an invaluable tool for the proper allocation of resources.

A major problem with all models is that the model is not real time. Data used within a model must always be historical data and conditions could have changed from the time the data was gathered and the time the data is used.

Malaria is a complex disease, and mathematical modelling has been instrumental in understanding and combating the disease. Early models of Ross informed public health policy. Nowadays, mathematical modelling is a powerful tool that plays an important role in investigations of alternative control strategies that can support malaria eradication.