



Devising a method towards development of early warning tool for detection of malaria outbreak

Preeti Verma, Soma Sarkar, Poonam Singh & Ramesh C. Dhiman

Environmental Epidemiology Division, ICMR-National Institute of Malaria Research, New Delhi, India

Received March 18, 2016

Background & objectives: Uncertainty often arises in differentiating seasonal variation from outbreaks of malaria. The present study was aimed to generalize the theoretical structure of sine curve for detecting an outbreak so that a tool for early warning of malaria may be developed.

Methods: A 'case/mean-ratio scale' system was devised for labelling the outbreak in respect of two diverse districts of Assam and Rajasthan. A curve-based method of analysis was developed for determining outbreak and using the properties of sine curve. It could be used as an early warning tool for *Plasmodium falciparum* malaria outbreaks.

Result: In the present method of analysis, the critical C_{\max} (peak value of sine curve) value of seasonally adjusted curve for *P. falciparum* malaria outbreak was 2.3 for Karbi Anglong and 2.2 for Jaisalmer districts. On case/mean-ratio scale, the C_{\max} value of malaria curve between C_{\max} and 3.5, the outbreak could be labelled as minor while >3.5 may be labelled as major. In epidemic years, with mean of case/mean ratio of ≥ 1.00 and root mean square (RMS) ≥ 1.504 of case/mean ratio, outbreaks can be predicted 1-2 months in advance.

Interpretation & conclusions: The present study showed that in *P. falciparum* cases in Karbi Anglong (Assam) and Jaisalmer (Rajasthan) districts, the rise in C_{\max} value of curve was always followed by rise in average/RMS or both and hence could be used as an early warning tool. The present method provides better detection of outbreaks than the conventional method of mean plus two standard deviation (mean+2 SD). The identified tools are simple and may be adopted for preparedness of malaria outbreaks.

Key words Case/mean ratio - early warning - malaria - outbreak - root mean square - sine curve - tool

Malaria is a public health problem of many tropical and subtropical countries. An estimated 216 million people are at risk¹ of malaria. After Africa, South East Asia is the second most affected area in the world where India has the highest malaria burden. In the early 1960s, malaria was on the verge of eradication in India, but in the 1970s, malaria situation reversed back²

with frequent outbreaks³⁻⁷. *Plasmodium falciparum* malaria outbreaks are frequent in different parts of India⁷ with varying intensities. As per the World Health Organization (WHO)⁸, an outbreak is defined as 'the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season.' The definition of disease

outbreak by the WHO is not explicit in defining the fine line between seasonal variation and malaria outbreak, and with 'excess' cases, often confusion arises while deciding the seasonal trend and outbreak⁹. The accurate determination of malaria outbreak requires a system of finding critical value of seasonal malaria cases beyond which it can be labelled as 'outbreak'. Being remote areas, lack of early preparedness for interventions is one of the major reasons for outbreaks, necessitating the need for early detection tool for outbreaks for early preparedness. For early detection of malaria outbreaks, there was an early warning system in the country dating back to 1921¹⁰ but not in use after 1946 due to changes in malaria-metric indices (such as spleen rate) and socio-economic and environmental conditions.

To overcome the problem, researchers have proposed various models of malaria transmission and detection of outbreaks^{11,12}. Malaria Early Warning Systems using rainfall, temperature and relative humidity¹³⁻¹⁶ have been developed by various researchers, but these are either constrained by accuracy or difficult to be used by public health specialists¹⁷⁻¹⁹. Therefore, there is a need to have a simple tool for the development of Malaria Early Warning System, which can be used by public health persons at district level^{20,21}. As it takes about 30-45 days in build-up of malaria vector population, picking up infection from infected person, development of parasite in vector and transmission to new host, it is prudent to identify the signal of impending outbreak before 1-2 months in advance.

Malaria outbreak situation varies from place to place due to varied endemicity, which depends on variation in mosquito infectivity rate and parasite load of a particular area²². In order to define such a situation on conceptual level, operational definition of the variable is required to be developed at 'Zero' origin scale. In absence of the distinct line between the seasonal rise and outbreak in hyperendemic areas such as Karbi Anglong (Assam, India), outbreaks go unnoticed leading to a high mortality. The present analysis proposes a 'case/mean-ratio scale' (0, C_{\max}) to detect and measure malaria outbreaks for early preparedness for control.

Material & Methods

Two diverse areas, one in northeastern part of India, Karbi Anglong district (Assam), and another in Thar Desert of India *i.e.*, Jaisalmer district (Rajasthan), which have *P. falciparum* malaria endemicity, were

identified for detailed analyses. Karbi Anglong district is characterized by humid climate with an average annual rainfall around 1646 mm, whereas Jaisalmer district has arid climate with an average rainfall around 172 mm. Monthly malaria (*P. falciparum*) data from 1993 to 2013 for Karbi Anglong were collected from the office of District Malaria Officer, Karbi Anglong at Diphu (Assam) and for Jaisalmer data from 1997 to 2007 were collected from the office of Chief Medical and Health officer at Jaisalmer (Rajasthan). The monthly *P. falciparum* cases were transformed using Equation 1²³. The number of cases of each month was divided by the average value of the dataset of that area. Equation 1,

$$\frac{x}{\frac{1}{n} \sum_{i=1}^n x_i}$$

where x is monthly observed cases, n is the number of months and $\sum_{i=1}^n x_i$ is the mean of total monthly observed cases.

Data analysis: We compared two outbreak theorems, (i) conventional mean+2 standard deviation (SD)²⁴, and (ii) proposed curve-based method of analysis for detecting *falciparum* malaria.

Conventional mean+2 standard deviation: The method defined by Cullen *et al*²⁴ was attempted to detect outbreaks in Karbi Anglong and Jaisalmer districts. Mean and SD were calculated from transformed case/mean ratios.

Curve-based method of analysis: For curve-based method of analysis, Equation 2 was used. Equation 2,

$$\alpha = C_{\max} \sin \Theta$$

where α is case at any point of time in the curve and C_{\max} is peak value of the same curve with Θ equals to 90° , whereby C_{\max} can be calculated by mean+2 SD method²⁴, for outbreak, $\alpha > C_{\max}$.

For analyzing the curve, the following steps were used:

(i) Seasonal Adjustment: The seasonal adjustment of data was done in Microsoft Excel. The linear trend (C_t) of dataset was multiplied with its seasonal index. To obtain linear trend of dataset, the linear regression equation was calculated using chart and linear trend line option in Excel. To obtain seasonal index, each X value (*i.e.*, number of cases in any month) was divided by its trend value. The

obtained ratio was averaged monthly, and a seasonal index of 12 months was obtained. The seasonally adjusted (SA) value for month t can be expressed as follows:

$$SA_t = C_t \cdot SI$$

where C_t is linear regression trend value for month t and SI is the monthly seasonal index.

(ii) C_{\max} value of curve: mean+2 SD was calculated for SA data.

(iii) Root mean square (RMS): The RMS value of the SA curve was calculated using Equation 3. Equation 3,

$$C_{\max} / \sqrt{2}$$

Defining outbreak: Irrespective of data volume, a ratio scale can quantify the variable for better and efficient understanding. Mean is the single value which summarizes a set of data by identifying the centroid. Advantage of mean ratio transformation is to generalize the scale. 'Case/mean ratio' can be calculated using Equation 1.

This transformation system does not change the form of waveform (time series). In general, seasonal variations in *falciparum* malaria cases represent sinusoidal curve (full-wave rectifier)²⁵, and therefore, the equation of curve for seasonal variation should be as Equation 2.

In sine waveform, peaks are characterized by two factors: mean and RMS value. In a true sinusoidal waveform, the peak of curve is 1.414 *i.e.*, $\sqrt{2}$ times the RMS value. The RMS value of sine curve can be calculated using Equation 3.

The outbreak in such areas where seasonality of malaria cases follows sinusoidal waveform can be determined either by increase in mean value or increase in RMS value of the waveform. RMS value is 0.707 times the C_{\max} and mean of waveform is 1.0. Therefore, these two parameters can be used to pre-sense the outbreak.

Whenever, the mean of case mean ratio was >1 , RMS of case mean >1.5 gave the signal of an outbreak, and at the value of >2.2 , an outbreak occurred.

The comparative performance of the two methods, *i.e.* conventional mean+2 SD and curve-based method of analysis is given in Tables I and II, respectively.

Results

Sinusoidal seasonal fluctuations were observed in *falciparum* malaria cases of Karbi Anglong, Assam

(Fig. 1) and Jaisalmer (Fig. 2), Rajasthan, districts. The results of malaria curve analysis show that the C_{\max} (peak value of sinusoidal curve) value of SA case/mean ratio was 2.3 for Karbi Anglong and 2.2 for Jaisalmer districts. Therefore, any value >2.2 identifies an outbreak. Comparison between seasonal peak and outbreaks is shown in Fig. 3 for Karbi Anglong and Fig. 4 for Jaisalmer districts.

Using the conventional method of mean+2 SD, the outbreaks of *falciparum* malaria in Karbi Anglong district could be detected in 1999, 2008 and 2009 (Table I), while in Jaisalmer district, it could be detected in the years 1999, 2000, 2001, 2004, 2006 and 2007 (Table II). On the other hand, with curve-based method, malaria outbreak could be detected in 1994, 1999-2001 and 2006-2010 in Karbi Anglong district (Table III) and in 1999-2002 and 2006-2007 in Jaisalmer district (Table IV).

With conventional method, outbreaks were detected in the month of March to July and August-September in Karbi Anglong, whereas in Jaisalmer district, the outbreaks were detected in the months of January, February and June.

By the curve-based method of analysis, the outbreaks were detected in June/July in 1994, 2000-2001 and 2007 where C_{\max} value of time series curve was 2.3, 2.4, 2.5 and 2.4, respectively. According to case/mean ratio scale, these values indicated minor outbreaks. In 1999, 2006, 2009 and 2010, the C_{\max} values of curve were 3.8, 3.1, 3.5 and 3.2, respectively, indicating major outbreaks of *falciparum* malaria on case/mean ratio scale. In 2008, when C_{\max} value was 5.0, a severe outbreak was observed.

The RMS value of SA curve was 1.504 for Karbi Anglong and Jaisalmer districts. In Karbi Anglong district, with $RMS \geq 1.504$, both minor and major outbreaks could be predicted one month in advance. Moreover, during major outbreak years, the mean case/mean ratio value of 1.00 could predict the outbreak two months in advance (Table III). In Jaisalmer district, the outbreaks of May, which were minor, could be detected by mean of case/mean ratio ≥ 1 , whereas the outbreaks of June and July were detected by $RMS \geq 1.504$.

Discussion

Existing regression or other mathematical forecasting models forecasted the malaria transmission in Africa^{26,27} and in India²⁸⁻³⁰ in one month advance using climatic variables such as rainfall and temperature.

Table 1. *Plasmodium falciparum* malaria outbreak detection using mean±2 standard deviation in Karbi Anglong District (Assam)

| Year | January | February | March | April | May | June | July | August | September | October | November | December |
|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 1993 | 0.27 | 0.38 | 0.5 | 0.7 | 1 | 1.6 | 1.5 | 1.3 | 1 | 1.2 | 0.8 | 0.6 |
| 1994 | 0.3 | 0.4 | 0.5 | 1.06 | 1.6 | 2.3 | 2.3 | 1.4 | 0.8 | 0.7 | 0.6 | 0.4 |
| 1995 | 0.3 | 0.2 | 0.3 | 0.6 | 1.5 | 1.5 | 1.4 | 1 | 0.8 | 0.9 | 0.8 | 0.5 |
| 1996 | 0.3 | 0.3 | 0.5 | 0.7 | 1.3 | 2 | 1.9 | 1.5 | 0.9 | 0.8 | 0.7 | 0.5 |
| 1997 | 0.3 | 0.2 | 0.3 | 0.7 | 1 | 1.6 | 1.8 | 1 | 0.9 | 0.6 | 0.6 | 0.4 |
| 1998 | 0.2 | 0.2 | 0.3 | 0.5 | 1 | 1.5 | 1.3 | 1.1 | 1 | 1 | 0.9 | 0.6 |
| 1999 | 0.3 | 0.4 | 0.6 | 1.01 | 2.2 | 3.8 | 2.1 | 1.5 | 1.5 | 1.3 | 1.1 | 0.5 |
| 2000 | 0.3 | 0.3 | 0.5 | 0.8 | 1.5 | 2.1 | 2.4 | 1.6 | 1.1 | 1 | 0.9 | 0.6 |
| 2001 | 0.4 | 0.4 | 0.5 | 0.7 | 1.8 | 2.5 | 2.2 | 1.8 | 1.1 | 0.8 | 0.8 | 0.6 |
| 2002 | 0.3 | 0.3 | 0.5 | 0.7 | 1.7 | 2.2 | 1.8 | 1 | 0.7 | 0.5 | 0.5 | 0.4 |
| 2003 | 0.2 | 0.2 | 0.4 | 0.6 | 1.2 | 2 | 1.3 | 1 | 0.9 | 0.9 | 0.8 | 0.5 |
| 2004 | 0.3 | 0.4 | 0.5 | 0.9 | 1.4 | 2 | 1.3 | 1 | 0.8 | 0.7 | 0.5 | 0.4 |
| 2005 | 0.3 | 0.3 | 0.5 | 0.8 | 0.9 | 1.6 | 1.4 | 1.3 | 0.8 | 0.7 | 1 | 0.6 |
| 2006 | 0.40 | 0.3 | 0.7 | 1.2 | 2.3 | 3.1 | 2 | 0.9 | 0.6 | 0.7 | 0.7 | 0.6 |
| 2007 | 0.3 | 0.3 | 0.5 | 0.9 | 1.8 | 2.4 | 2.6 | 1.2 | 0.8 | 0.6 | 0.6 | 0.5 |
| 2008 | 0.4 | 0.3 | 0.5 | 1.1 | 2.8 | 5.0 | 3.4 | 1.7 | 0.9 | 0.8 | 0.8 | 0.4 |
| 2009 | 0.3 | 0.5 | 1.0 | 1.6 | 3.5 | 4.2 | 4.2 | 2.0 | 1.2 | 1.6 | 1.3 | 0.6 |
| 2010 | 0.3 | 0.4 | 0.9 | 1.2 | 2.2 | 3.2 | 2.5 | 1.8 | 1.1 | 0.7 | 0.7 | 0.4 |
| 2011 | 0.3 | 0.3 | 0.6 | 1 | 1.8 | 2 | 2.1 | 1.1 | 0.8 | 0.6 | 0.4 | 0.3 |
| 2012 | 0.2 | 0.3 | 0.4 | 0.5 | 0.8 | 1.2 | 1.2 | 1 | 0.8 | 0.4 | 0.3 | 0.1 |
| 2013 | 0.1 | 0.1 | 0.3 | 0.4 | 0.6 | 0.9 | 0.7 | 0.3 | 0.3 | 0.2 | 0.3 | 0.1 |
| Mean±SD | 0.29±0.07 | 0.31±0.09 | 0.51±0.18 | 0.84±0.29 | 1.62±0.70 | 2.32±1.02 | 1.97±0.79 | 1.26±0.39 | 0.90±0.24 | 0.80±0.31 | 0.72±0.25 | 0.46±0.15 |
| Mean±2 SD | 0.4 | 0.5 | 0.9 | 1.4 | 3.0 | 4.4 | 3.6 | 2.0 | 1.4 | 1.4 | 1.2 | 0.8 |

Source: Office of the District Malaria Officer, Karbi Anglong. Red blocks mark malaria outbreaks.

Table II. *Plasmodium falciparum* malaria outbreak detection using mean+2 standard deviation in Jaisalmer District, (Rajasthan)

| Year | January | February | March | April | May | June | July | August | September | October | November | December |
|-----------|----------|----------|----------|----------|----------|----------|----------|----------|-----------|----------|----------|----------|
| 1997 | 0.3 | 0.2 | 0.3 | 0.7 | 1.0 | 1.6 | 1.8 | 1.0 | 0.9 | 0.7 | 0.7 | 0.5 |
| 1998 | 0.3 | 0.2 | 0.3 | 0.5 | 1.0 | 1.5 | 1.4 | 1.1 | 1.0 | 1.1 | 0.9 | 0.6 |
| 1999 | 0.3 | 0.4 | 0.6 | 1.0 | 2.3 | 3.9 | 2.2 | 1.6 | 1.6 | 1.3 | 1.1 | 0.5 |
| 2000 | 0.3 | 0.4 | 0.5 | 0.8 | 1.6 | 2.2 | 2.5 | 1.6 | 1.1 | 1.0 | 0.9 | 0.6 |
| 2001 | 0.4 | 0.4 | 0.6 | 0.7 | 1.8 | 2.6 | 2.2 | 1.8 | 1.2 | 0.8 | 0.8 | 0.6 |
| 2002 | 0.3 | 0.3 | 0.5 | 0.7 | 1.7 | 2.2 | 1.8 | 1.0 | 0.7 | 0.5 | 0.5 | 0.4 |
| 2003 | 0.2 | 0.3 | 0.4 | 0.6 | 1.3 | 2.0 | 1.4 | 1.0 | 0.9 | 0.9 | 0.9 | 0.5 |
| 2004 | 0.3 | 0.4 | 0.5 | 0.9 | 1.4 | 2.0 | 1.4 | 1.0 | 0.8 | 0.7 | 0.5 | 0.4 |
| 2005 | 0.3 | 0.3 | 0.5 | 0.8 | 0.9 | 1.6 | 1.4 | 1.3 | 0.9 | 0.7 | 1.0 | 0.6 |
| 2006 | 0.5 | 0.3 | 0.7 | 1.2 | 2.4 | 3.2 | 2.0 | 0.9 | 0.6 | 0.7 | 0.7 | 0.6 |
| 2007 | 0.3 | 0.4 | 0.5 | 0.9 | 1.8 | 2.5 | 2.7 | 1.2 | 0.8 | 0.6 | 0.6 | 0.5 |
| Mean±SD | 0.3±0.06 | 0.3±0.06 | 0.5±0.13 | 0.8±0.19 | 1.6±0.50 | 2.3±0.73 | 1.9±0.47 | 1.2±0.30 | 1.0±0.26 | 0.8±0.23 | 0.8±0.20 | 0.5±0.08 |
| Mean±2 SD | 0.4 | 0.4 | 0.8 | 1.2 | 2.6 | 3.8 | 2.8 | 1.8 | 1.5 | 1.3 | 1.2 | 0.7 |

Source: Office of Chief Medical and Health Officer, Jaisalmer. Red blocks mark malaria outbreaks.

Table III. *Plasmodium falciparum* malaria outbreak detection and early warning using curve based method in Karbi Anglong District (Assam) (1993-2013)

| Year | January | February | March | April | May | June | July | August | September | October | November | December |
|------|---------|----------|----------------|-------------------|------------------|------------------|------------------|--------|-----------|---------|----------|----------|
| 1993 | 0.27 | 0.38 | 0.5 | 0.7 | 1 | 1.6 | 1.5 | 1.3 | 1 | 1.2 | 0.8 | 0.6 |
| 1994 | 0.3 | 0.4 | 0.5 | 1.06 ⁺ | 1.6 [*] | 2.3 [§] | 2.3 | 1.4 | 0.8 | 0.7 | 0.6 | 0.4 |
| 1995 | 0.3 | 0.2 | 0.3 | 0.6 | 1.49 | 1.5 | 1.4 | 1 | 0.8 | 0.9 | 0.8 | 0.5 |
| 1996 | 0.3 | 0.3 | 0.5 | 0.7 | 1.3 | 2 | 1.9 | 1.5 | 0.9 | 0.8 | 0.7 | 0.5 |
| 1997 | 0.3 | 0.2 | 0.3 | 0.7 | 1 | 1.6 | 1.8 | 1 | 0.9 | 0.6 | 0.6 | 0.4 |
| 1998 | 0.2 | 0.2 | 0.3 | 0.5 | 1 | 1.5 | 1.3 | 1.1 | 1 | 1 | 0.9 | 0.6 |
| 1999 | 0.3 | 0.4 | 0.6 | 1.01 ⁺ | 2.2 [*] | 3.8 [§] | 2.1 | 1.5 | 1.5 | 1.3 | 1.1 | 0.5 |
| 2000 | 0.3 | 0.3 | 0.5 | 0.8 | 1.53 | 2.1 [*] | 2.4 [§] | 1.6 | 1.1 | 1 | 0.9 | 0.6 |
| 2001 | 0.4 | 0.4 | 0.5 | 0.7 | 1.8 [*] | 2.5 [§] | 2.2 | 1.8 | 1.1 | 0.8 | 0.8 | 0.6 |
| 2002 | 0.3 | 0.3 | 0.5 | 0.7 | 1.7 | 2.2 | 1.8 | 1 | 0.7 | 0.5 | 0.5 | 0.4 |
| 2003 | 0.2 | 0.2 | 0.4 | 0.6 | 1.2 | 2 | 1.3 | 1 | 0.9 | 0.9 | 0.8 | 0.5 |
| 2004 | 0.3 | 0.4 | 0.5 | 0.9 | 1.4 | 2 | 1.3 | 1 | 0.8 | 0.7 | 0.5 | 0.4 |
| 2005 | 0.3 | 0.3 | 0.5 | 0.8 | 0.9 | 1.6 | 1.4 | 1.3 | 0.8 | 0.7 | 1 | 0.6 |
| 2006 | 0.4 | 0.3 | 0.7 | 1.2 ⁺ | 2.3 [§] | 3.1 [§] | 2 | 0.9 | 0.6 | 0.7 | 0.7 | 0.6 |
| 2007 | 0.3 | 0.3 | 0.5 | 0.9 | 1.8 [*] | 2.4 [§] | 2.6 [§] | 1.2 | 0.8 | 0.6 | 0.6 | 0.5 |
| 2008 | 0.4 | 0.3 | 0.5 | 1.1 ⁺ | 2.8 [§] | 5 [§] | 3.4 | 1.7 | 0.9 | 0.8 | 0.8 | 0.4 |
| 2009 | 0.3 | 0.5 | 1 ⁺ | 1.6 [*] | 3.5 [§] | 4.2 [§] | 4.2 | 2 | 1.2 | 1.6 | 1.3 | 0.6 |
| 2010 | 0.3 | 0.4 | 0.9 | 1.2 ⁺ | 2.2 [*] | 3.2 [§] | 2.5 | 1.8 | 1.1 | 0.7 | 0.7 | 0.4 |
| 2011 | 0.3 | 0.3 | 0.6 | 1 | 1.8 | 2 | 2.1 | 1.1 | 0.8 | 0.6 | 0.4 | 0.3 |
| 2012 | 0.2 | 0.3 | 0.4 | 0.5 | 0.8 | 1.2 | 1.2 | 1 | 0.8 | 0.4 | 0.3 | 0.1 |
| 2013 | 0.1 | 0.1 | 0.3 | 0.4 | 0.6 | 0.9 | 0.7 | 0.3 | 0.3 | 0.2 | 0.3 | 0.1 |

⁺Mean of case/mean ratio ≥ 1 ; ^{*}RMS of case/mean ≥ 1.5 ; [§]Outbreak. RMS, root mean square

Table IV. *Plasmodium falciparum* malaria outbreak detection and early warning using curve based method in Jaisalmer District (Rajasthan) (1997-2007)

| Year | January | February | March | April | May | June | July | August | September | October | November | December |
|------|---------|----------|-------|------------------|------------------|------------------|------------------|--------|-----------|---------|----------|----------|
| 1997 | 0.3 | 0.2 | 0.3 | 0.7 | 1.0 | 1.6 | 1.8 | 1.0 | 0.9 | 0.7 | 0.7 | 0.5 |
| 1998 | 0.3 | 0.2 | 0.3 | 0.5 | 1.0 | 1.5 | 1.4 | 1.1 | 1.0 | 1.1 | 0.9 | 0.6 |
| 1999 | 0.3 | 0.4 | 0.6 | 1.0 ⁺ | 2.3 [§] | 3.9 [§] | 2.2 | 1.6 | 1.6 | 1.3 | 1.1 | 0.5 |
| 2000 | 0.3 | 0.4 | 0.5 | 0.8 | 1.6 [*] | 2.2 [§] | 2.5 [§] | 1.6 | 1.1 | 1.0 | 0.9 | 0.6 |
| 2001 | 0.4 | 0.4 | 0.6 | 0.7 | 1.8 [*] | 2.6 [§] | 2.2 | 1.8 | 1.2 | 0.8 | 0.8 | 0.6 |
| 2002 | 0.3 | 0.3 | 0.5 | 0.7 | 1.7 [*] | 2.2 [§] | 1.8 | 1.0 | 0.7 | 0.5 | 0.5 | 0.4 |
| 2003 | 0.2 | 0.3 | 0.4 | 0.6 | 1.3 | 2.0 | 1.4 | 1.0 | 0.9 | 0.9 | 0.9 | 0.5 |
| 2004 | 0.3 | 0.4 | 0.5 | 0.9 | 1.4 | 2.0 | 1.4 | 1.0 | 0.8 | 0.7 | 0.5 | 0.4 |
| 2005 | 0.3 | 0.3 | 0.5 | 0.8 | 0.9 | 1.6 | 1.4 | 1.3 | 0.9 | 0.7 | 1.0 | 0.6 |
| 2006 | 0.5 | 0.3 | 0.7 | 1.2 ⁺ | 2.4 [§] | 3.2 [§] | 2.0 | 0.9 | 0.6 | 0.7 | 0.7 | 0.6 |
| 2007 | 0.3 | 0.4 | 0.5 | 0.9 | 1.8 [*] | 2.5 [§] | 2.7 [§] | 1.2 | 0.8 | 0.6 | 0.6 | 0.5 |

⁺Mean of case/mean ratio ≥ 1 ; ^{*}RMS of case/mean ≥ 1.5 ; [§]Outbreak. RMS, root mean square

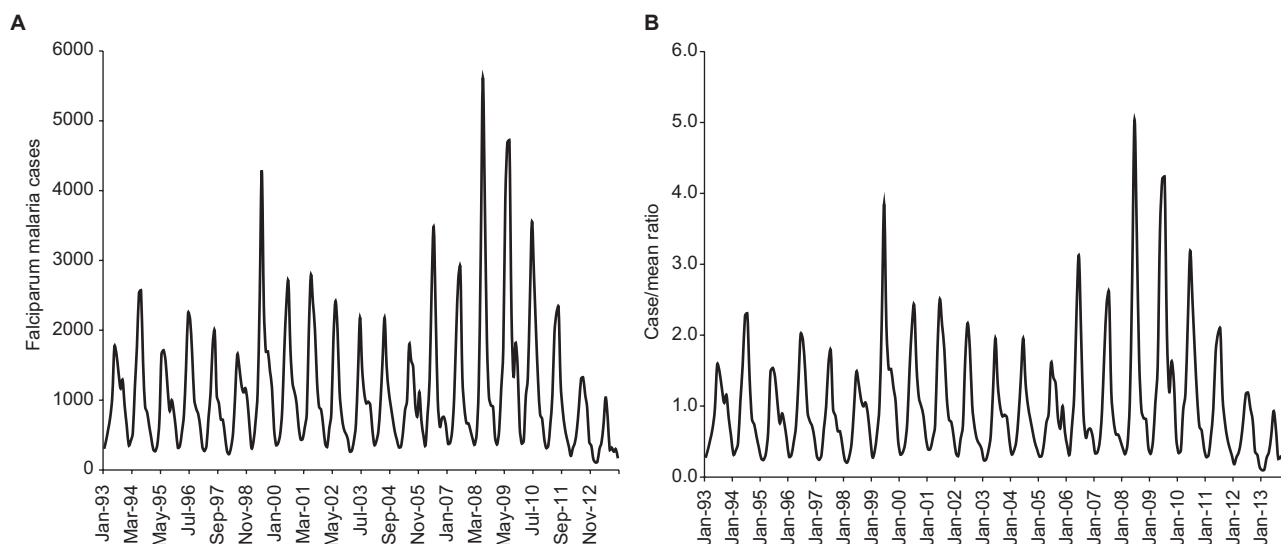


Fig. 1. (A) Seasonal fluctuations in *Plasmodium falciparum* cases in Karbi Anglong, Assam (1993-2013). (B) Seasonal fluctuation in *Plasmodium falciparum* malaria after case/mean ratio transformation in Karbi Anglong, Assam (1993-2013). The graph shows no change in the structure of curve after transformation of data but brings the data on a measurable scale.

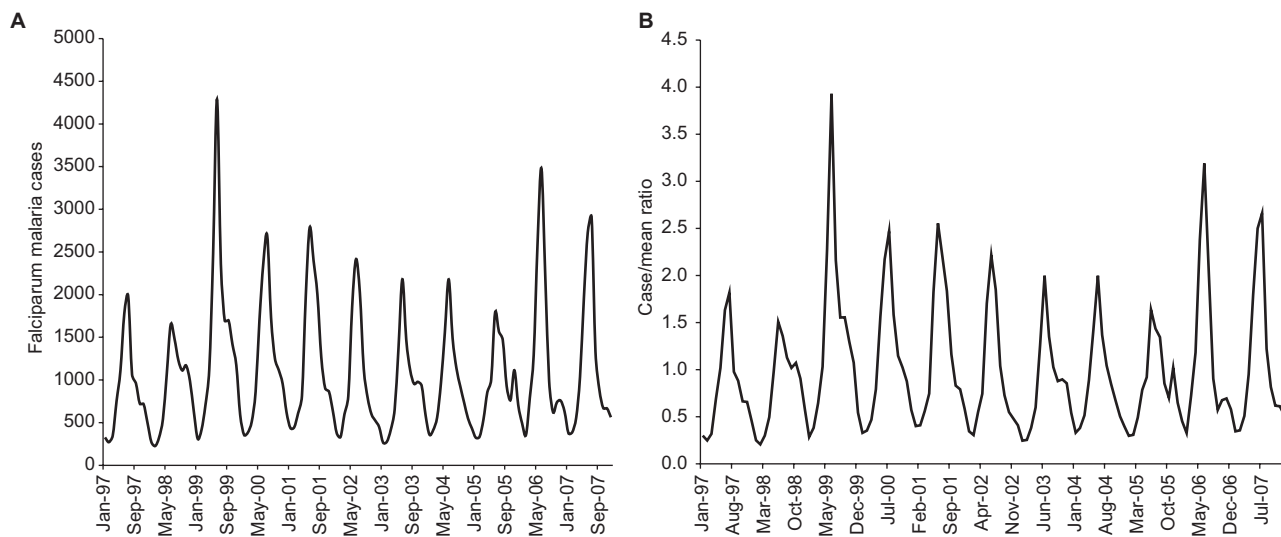


Fig. 2. (A) Seasonal fluctuations in *Plasmodium falciparum* cases in Jaisalmer (1997-2007). (B) Seasonal fluctuation in *Plasmodium falciparum* malaria after case/mean ratio transformation in Jaisalmer (1997-2007). The graph shows no change in the structure of curve after transformation of data but brings the data on a measurable scale.

India has diversified climatic characteristics; therefore, implementation of climate-based model for the whole country is not possible. In this regard, the presented model has successfully identified the outbreaks in two climatically contrast regions *i.e.*, Karbi Anglong and Jaisalmer districts. The proposed method differentiated between seasonality and outbreak using a single variable *i.e.*, malaria cases. With the devised method, all the minor and major outbreaks could be detected, which were undetectable using conventional method²⁴. In Karbi Anglong district, RMS value of ≥ 1.504 could

detect an outbreak one month before in all the outbreak years. Similarly, in Jaisalmer district, the outbreaks which occurred in the month of June were consistently detected by increase in $RMS \geq 1.5$ one month in advance.

Malaria outbreaks generally occur due to unexpected rainfall, resistance in vector and parasite towards insecticide and drugs, respectively^{30,31}, migration, inadequate intervention, *etc.* The statistical method of mean+2 SD for detecting outbreak could

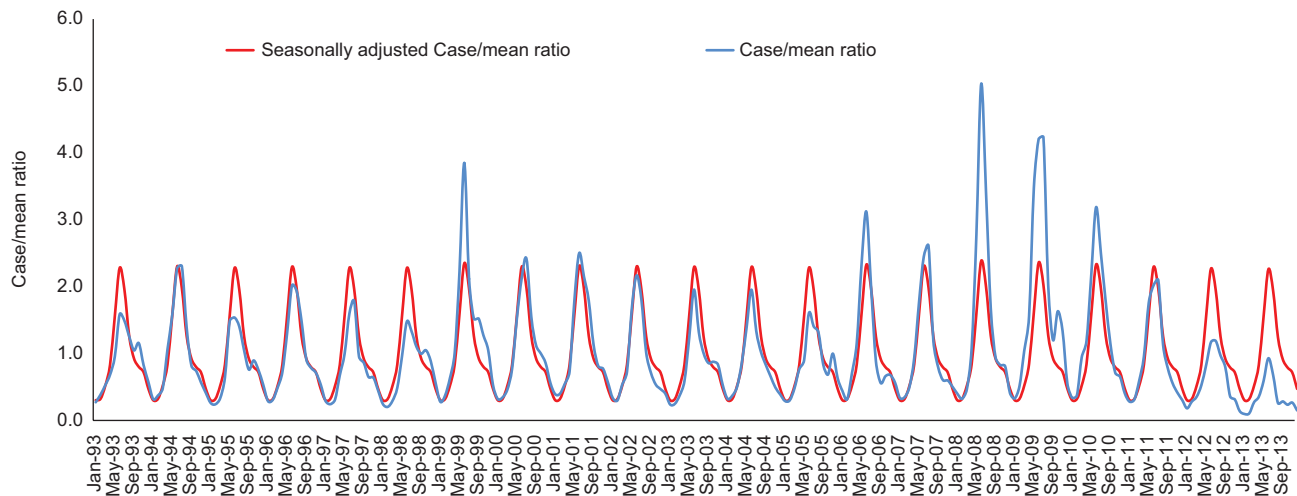


Fig. 3. Seasonally adjusted case/mean ratio of *Plasmodium falciparum* in Karbi Anglong, Assam (1993-2013).

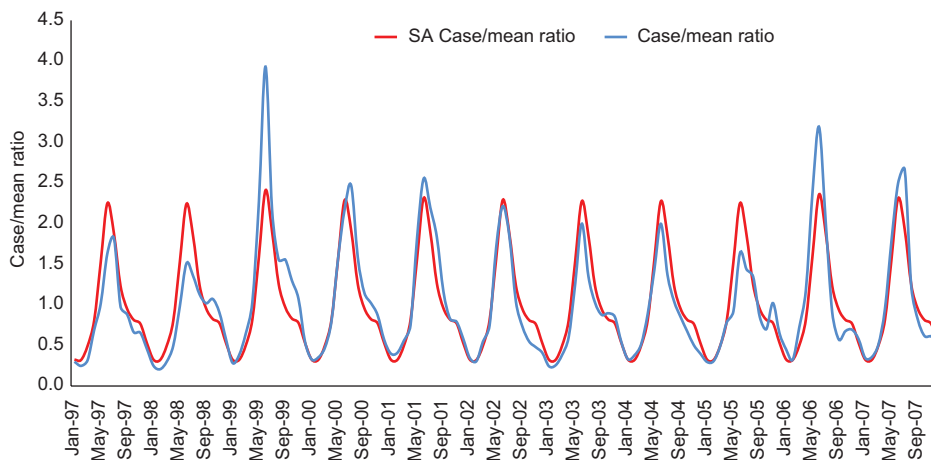


Fig. 4. Seasonally adjusted case/mean ratio of *Plasmodium falciparum* in Jaisalmer district, Rajasthan (1997-2007).

detect major outbreaks in Karbi Anglong district but not the minor outbreaks. Further, with the standard method of mean+2 SD, outbreaks could be detected in the month of September, October and November in Karbi Anglong district which was close to normal as per the present method. In Jaisalmer district, using mean+2 SD method, the outbreaks could be detected in the months of January, February and June. The proposed model for detecting malaria outbreak using properties of sine curve successfully detected both major and minor outbreaks. In the present study, the C_{max} value of >2.2 was the cut-off for differentiating seasonality and outbreak. With the C_{max} value from 2.2 to 3.5, the outbreak could be labelled as minor one, while with $>3.5 C_{max}$, the outbreak can be considered as the major one.

The proposed method provided early warning of malaria outbreak 1-2 months in advance in all the identified years with the exception of 2007 where it turned out to be only seasonal which might be due to the introduction of alternative drug regimen. Being varied geography in India, the findings of this study are limited to similar geographic areas of Assam and Thar Desert. Since *P. vivax* parasite has the tendency to relapse, it was not considered for analysis in the present study. The proposed method can be attempted in differentiating seasonal variation (C_{max}) and outbreak ($>C_{max}$) in similar geographic areas such as Karbi Anglong and outbreak-prone areas of Rajasthan and Gujarat.

Acknowledgment

Authors acknowledge Department of Science and Technology, New Delhi for financial support.

Conflicts of Interest: None.

References

- World Health Organization. *World Malaria Report 2017*. Geneva : WHO; 2017.
- Kumar A, Valecha N, Jain T, Dash AP. Burden of malaria in India: Retrospective and prospective view. *Am J Trop Med Hyg* 2007; 77 : 69-78.
- Singh RK, Dhiman RC, Das MK. Situation analysis of malaria in Godda district of Jharkhand during malaria epidemic. *J Commun Dis* 2011; 43 : 135-42.
- Das NG, Talukdar PK, Das SC. Epidemiological and entomological aspects of malaria in forest-fringed villages of Sonitpur district, Assam. *J Vector Borne Dis* 2004; 41 : 5-9.
- Prakash A, Mohapatra PK, Bhattacharyya DR, Doloi P, Mahanta J. Changing malaria endemicity - A village based study in Sonitpur, Assam. *J Commun Dis* 1997; 29 : 175-8.
- Dhiman RC, Pillai CR, Subbarao SK. Investigation of malaria outbreak in Bahraich district, Uttar Pradesh. *Indian J Med Res* 2001; 113 : 186-91.
- Sharma R. Epidemiological investigation of malaria outbreak in village Santej, district Gandhi Nagar (Gujarat). *Indian J Prev Soc Med* 2006; 37 : 125-32.
- World Health Organization. *Disease outbreaks*. Available from: http://www.searo.who.int/topics/disease_outbreaks/en/, accessed on September 30, 2017.
- Shiff CJ, Stoyanov C, Choobwe C, Kamanga A, Mukonka VM. Measuring malaria by passive case detection: A new perspective based on Zambian experience. *Malar J* 2013; 12 : 120.
- Gill CA. The role of meteorology in malaria. *Indian J Med Res* 1921; 8 : 633-93.
- Gatton M, Hogarth W, Saul A, Dayananda P. A model for predicting the transmission rate of malaria from serological data. *J Math Biol* 1996; 34 : 878-88.
- World Health Organization. *Using climate to predict infectious disease outbreaks: A review*. Geneva: WHO; 2004.
- Connor SJ, Thomson MC, Flasse SP, Perryman AH. Environmental information systems in malaria risk mapping and epidemic forecasting. *Disasters* 1998; 22 : 39-56.
- Craig MH, Snow RW, le Sueur D. A climate-based distribution model of malaria transmission in Sub-Saharan Africa. *Parasitol Today* 1999; 15 : 105-11.
- Holy M, Schmidt G, Schröder W. Potential malaria outbreak in Germany due to climate warming: Risk modelling based on temperature measurements and regional climate models. *Environ Sci Pollut Res Int* 2011; 18 : 428-35.
- Githeko AK, Ogallo L, Lemnge M, Okia M, Ototo EN. Development and validation of climate and ecosystem-based early malaria epidemic prediction models in East Africa. *Malar J* 2014; 13 : 329.
- Lowe R, Chirombo J, Tompkins AM. Relative importance of climatic, geographic and socio-economic determinants of malaria in Malawi. *Malar J* 2013; 12 : 416.
- McKelvie WR, Haghdoost AA, Raeisi A. Defining and detecting malaria epidemics in South-East Iran. *Malar J* 2012; 11 : 81.
- World Health Organization. *Malaria early warning systems, a framework for field research in Africa: Concepts, indicators and partners*. WHO/CDS/RBM/2001.32. Geneva: WHO; 2001.
- World Health Organization. *Prevention and control of malaria epidemics Part II*. Geneva: WHO; 2003.
- Grover-Kopec E, Kawano M, Klaver RW, Blumenthal B, Ceccato P, Connor SJ, *et al.* An online operational rainfall-monitoring resource for epidemic malaria early warning systems in Africa. *Malar J* 2005; 4 : 6.
- Kweka EJ, Mahande AM, Nkya WM, Assenga C, Lyatuu EE, Nyale E, *et al.* Vector species composition and malaria infectivity rates in Mkuzi, Muheza district, North-Eastern Tanzania. *Tanzan J Health Res* 2008; 10 : 46-9.
- Merigó JM, Guillén M, Sarabia JM. A generalization of the variance by using the ordered weighted average. In: Fernández-Izquierdo MÁ, Muñoz-Torres MJ, León R, editors. *Modeling and simulation in engineering, economics, and management. Lecture notes in business information processing*. Berlin, Heidelberg: Springer; 2013.
- Cullen JR, Chitprarop U, Doberstyn EB, Sombatwattanangkul K. An epidemiological early warning system for malaria control in Northern Thailand. *Bull World Health Organ* 1984; 62 : 107-14.
- Hii YL, Zhu H, Ng N, Ng LC, Rocklöv J. Forecast of dengue incidence using temperature and rainfall. *PLoS Negl Trop Dis* 2012; 6 : e1908.
- Gomez-Elipse A, Otero A, van Herp M, Aguirre-Jaime A. Forecasting malaria incidence based on monthly case reports and environmental factors in Karuzi, Burundi, 1997-2003. *Malar J* 2007; 6 : 129.
- Teklehaimanot HD, Schwatz J, Teklehaimanot A, Lipsitch M. Alert threshold algorithms and malaria epidemic detection. *Emerg Infect Dis* 2004; 10 : 1220-6.
- Chatterjee C, Sarkar RR. Multi-step polynomial regression method to model and forecast malaria incidence. *PLoS One* 2009; 4 : e4726.
- Laneri K, Bhadra A, Ionides EL, Bouma M, Dhiman RC, Yadav RS, *et al.* Forcing versus feedback: Epidemic malaria and monsoon rains in Northwest India. *PLoS Comput Biol* 2010; 6 : e1000898.
- Roy SB, Sarkar RR, Sinha S. Theoretical investigation of malaria prevalence in two Indian cities using the response surface method. *Malar J* 2011; 10 : 301.
- Dhiman RC, Sharma SK, Pillai CR, Subbarao SK. Investigation of outbreak of malaria in tribal area of Visakhapatnam, Andhra Pradesh. *Curr Sci* 2001b; 80 : 781-5.

Reprint requests: Dr Ramesh C. Dhiman, Environmental Epidemiology Division, ICMR-National Institute of Malaria Research, Dwarka, New Delhi 110 077, India
e-mail: r.c.dhiman@gmail.com