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Factors Influencing on Transmission of Malaria in India: Application of Negative Binomial Regression Model

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Abstract-*Malaria is the life threatening parasite disease which has different effect on different regions. The aim of this study is impact of climatic and non-climatic factors such as annual average rainfall, minimum temperature, maximum temperature, humidity, percentage of migrants and forest cover growth rate as predictors on the number of annual malaria cases occurred in India. The information about malaria cases of India from 1990 to 2015 were collected from National Vector Borne Diseases Control Board (NVBDC), Government of India. Spearman's correlation has been shows relation between the malaria cases and all other variables and Negative Binomial (NB) Regression model is used to estimate the relation between malaria cases and all the variables. Study concludes annual average rainfall is positively correlated with malaria cases while remaining variables shown negative correlation. Negative Binomial Regression shows impact of percentage of migrants more than the other variables on the transmission of malaria.*

Keywords- *Malaria, Transmission, climatic factors, Forest cover, Spearman's Correlation, Negative Binomial Regression etc*

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I. INTRODUCTION

Malaria is a life threatening parasite disease which has different effect on different regions. Mainly to the developing countries, malaria is still being severed public health issue. It is caused by primarily four parasites of Plasmodium species i.e. P. Vivax, P. Ovale, P. Malariae and P. Falciparum. According from WHO (2015), it is estimated that 262 million cases and 8,39,000 deaths occurred in the year 2000. But malaria cases and deaths got declined by 18% and 48% respectively from the year 2000 to 2015 i.e. 214 million cases and 4,38,000 deaths in the year 2015. Of this African region, South East Asia region and Eastern Mediterranean region reported 90%, 7% and 2% malaria deaths respectively in the year 2015.

India's contribution of the malaria cases to the South East Asia region is 58%. One fifth of the India's population lives in high transmission areas and more than half of the population lives in the low transmission areas (World Malaria report, 2014). P. Falciparum and P. Vivax are the most common parasites in India and these two parasites are unevenly distributed across the country (Sharma et al., 2006). According to WHO 2016, India accounted for half of the global total of estimated malaria deaths due to P. Vivax parasite.

Malaria is mainly considered as a sensitive disease to climatic changes. The climatic factors like rainfall, temperature and humidity are the main reasons behind the transmission of malaria because these factors influence parasite life cycle in vectors (Gubler et al., 2001). Non climatic factors like population density, population movement and deforestation have also caused for malaria transmission.

In the development of life span of the malaria parasites, temperature variable leads very crucial rule. A change of only 1^0 C temperatures in the range of 18^0 C-26^0 C that can add a week of life span and some temperature not less than 18^0 C or 19^0 C can keep malaria parasites alive for a month (Jepson et al., 1947). It was reported that humidity > 60% and temperature 20^0 C- 30^0 C are optimal for Anopheles to live long enough to attain and spread the parasite (McMicheal et al., 1995).

Many studies have been carried out in India and also globally to know the relationship between climatic variables (such as humidity, rainfall, minimum and maximum temperature) and malaria cases. The study carried in Assam, in which polynomial regression model have been developed to reveal the impact of climatic variables on transmission of malaria and it was resulted that main population, rainfall, humidity and temperature plays key role in predicting the malaria cases (Saikia et al., 2015). Another study in Uttaranchal revealed that rainfall and malaria cases have highest significant positive correlation when lag of one-month was considered (Devi et al., 2006) but in Madhya Pradesh it was completely reverse i.e., insignificant negative correlation (Singh et al., 2002).

In Delhi, same climatic variables used as predictors to forecast the malaria cases and fitted ARIMA (0, 1, 1) (0, 1, 0) model well that could explain the 72.5 % variability in the time series data (Jan 2006- Dec 2013). For the transmission of malaria, rainfall and relative humidity were found significant predictors (Kumar et al., 2014). The study carried out in Arunachal Pradesh revealed that temperature and rainfall were most influencing factors for high transmission of malaria incidence using Principle Component Analysis and Hotelling's T^2 statistics (Upadhyayalu et al., 2015).

Not only Climatic variables influence for the transmission of malaria but also there is share of some major non-climatic variables such has Population Density, Population movement or Migration, Urbanization and Deforestation in the transmission of malaria. Migration is the one of the factor contributing re-emergence of malaria. The relationship between the livestock development along with agricultural practices and transmission of vector borne diseases was studied. Changing the environment, deforestation for the agricultural practices and introducing the imperfect irrigation scheme leads to increment in the risk of acquiring malaria in the migrants. (Service, 1991).

While population movement alone isn't itself a hazard factor for expanded malaria transmissions, a few elements may make migrants and the nearby populace is powerless against malaria disease. This incorporates 'push and pull' factors that urge individuals to go into and out of malaria endemic territories, for example, rural development and infrastructure, deforestation for logging and financial cultivating, political developments and natural disasters (Jitthai, 2013).

Deforestation itself a one of the leading non-climatic factor which has got impact on the transmission of malaria. Deforestation happened because of agriculture activities, industrial developments and urbanization. Still studies claimed that deforestation can increase the burden of malaria diseases due to lack of planning (Saxena et al., 2014 and Vittor et al., 2006), other claimed that deforestation can reduce the risk of malaria diseases by well-planned urbanization or genuine agricultural activities (de Castro et al., 2006).

The present study considers the climatic and non-climatic factors such as annual average rainfall, minimum temperature, maximum temperature, humidity, percentage of migrants and forest cover growth rate as predictors for number of annual malaria cases occurred in India. The rest of the paper is structured as follows:First section briefs about the introduction and relevant studies on these factors, section 2 discusses about Data Source and Methodology used, section 3 focuses on results and discussionand last section concludes the study.

II. DATA SOURCE AND METHODOLOGY

This paper aims to study the influence of climatic and non-climatic factors on transmission of malaria disease in India. Study considered annual average rainfall, humidity, minimum and maximum temperature as a climatic factors and population density, migration and deforestation as a non-climatic factors. The information about malaria cases of India from 1990 to 2015 is collected from National Vector Borne Diseases Control Board (NVBDC), Government of India. The data related to annual average rainfall, minimum and maximum temperature is extracted from Open Government Data (OGD) platform India. But data for Humidity is collected from National Climatic Data Centre (NCDC) official website.

Population of India and total migration decadal data have been collected from Census of India. Data interpolated the decadal data into annual data using Newton's Gregory backward interpolation formula. Population density per square kilometre has been calculated as population divided by the geographical area of India and percentage of migration is also calculated as total migrants divided by total population. All India level forest cover estimates from 1990 to 2015 have been collected from OGD platform India. We have calculated growth rate of the forest cover using simple arithmetic growth model, here negative growth rate indicates deforestation. Spearman's correlation coefficient has been calculated to know the significant relation between malaria cases and all other independent variables.

Finally negative binomial regression model used because of over-dispersion (i.e. variance > mean) present in the dependent variable i.e. malaria cases and also it is used to estimate the relation between malaria cases, and all the variables Deviance have been calculated for the measurement of model fit.

2.1 Negative Binomial Regression Model:

Negative binomial regression is model for count variables; usually for over-dispersed count response variables. The Poisson regression model can be generalized by introducing an unobserved heterogeneity term for observation i. Thus, the individuals are assumed to differ randomly in a manner that is not fully accounted for the observed covariates. This is formulated as

$$E(Y_i \mid X_i, \tau_i) = \mu_i \tau_i = \exp(x_i' \beta + \varepsilon_i)$$

Where the unobserved heterogeneity term $\tau_i = e^{\varepsilon_i}$ is independent of the vector of regressors x_i .Then the distribution of y_i conditional of x_i and τ_i is Poisson with conditional mean and conditional variance $\mu_i \tau_i$.

$$f(y_i \mid x_i, \tau_i) = \frac{e^{-\mu_i \tau_i} (\mu_i \tau_i)^{y_i}}{y_i!}, \; y_i = 0,1,2,...$$

Let $g(\tau_i)$ be the probability density function of τ_i. Then the distribution $f(y_i \mid x_i)$ is obtained by integrating $f(y_i \mid x_i, \tau_i)$ with respect to τ_i.

$$f(y_i \mid x_i) = \int_0^\infty f(y_i \mid x_i, \tau_i) \; g(\tau_i) d\tau_i$$

An analytical solution to this integral exists when τ_i is assumed to follow a gamma distribution. This solution is the Negative binomial distribution. When model contains a constant term, it is necessary to assume that $E(e^{\varepsilon_i}) = E(\tau_i) = 1$ in order to identify the mean of the distribution. Thus it is assumed that τ_i follows a $g(\theta, \theta)$ distribution with $E(\tau_i) = 1 \, and \; \text{var}(\tau_i) = 1/\theta$. Where $g(\tau_i) = \frac{\theta^\theta}{\Gamma\theta} \, \tau_i^{\theta - 1} \; e^{-\theta \tau_i}$.

Then

$$f(y_i \mid x_i) = \int_0^\infty \frac{e^{-\mu_i \tau_i} (\mu_i \tau_i)^{y_i}}{y_i!} \frac{\theta^\theta}{\Gamma\theta} \tau_i^{\theta-1} e^{-\theta \tau_i} \; d\tau_i$$

$$= \frac{\Gamma(y_i + \theta)}{y_i \Gamma\theta} \left(\frac{\mu_i}{\mu_i + \theta} \right)^{y_i} \left(\frac{\theta}{\mu_i + \theta} \right)^{\theta}$$

Substituting $\alpha = \frac{1}{\theta} > 0$, the Negative Binomial distribution is rewritten as

$$f(y_i \mid x_i) = \frac{\Gamma(y_i + \alpha^{-1})}{y_i \Gamma\alpha^{-1}} \left(\frac{\mu_i}{\mu_i + \alpha^{-1}} \right)^{y_i} \left(\frac{\alpha^{-1}}{\mu_i + \alpha^{-1}} \right)^{\alpha^{-1}}$$

The conditional mean is $E(Y_i \mid X_i) = \mu_i = \exp(X_i' \beta)$ and conditional variance is $V(Y_i \mid X_i) = \mu_i (1 + \alpha \mu_i) > E(Y_i \mid X_i)$. This reduced to the Poisson distribution if $\alpha = 0$.

The parameters of the negative binomial regression model i.e., regression coefficients $\beta's$ and dispersion parameter α have been obtained from the maximum likelihood estimation method. The logarithmic likelihood function given by Cameron (2013) is

$$L = \sum_{i=1}^{n} \begin{bmatrix} \ln\{\Gamma(y_i + \alpha^{-1})\} - \ln(\Gamma\alpha^{-1}) - \ln(\Gamma y_i + 1) - \alpha^{-1} \ln(1 + \alpha\mu_i) \\ - y_i \ln(1 + \alpha\mu_i) + y_i \ln(\alpha) + y_i \ln(\mu_i) \end{bmatrix}$$

$$= \sum_{i=1}^{n} \begin{bmatrix} \left(\sum_{j=0}^{y_i - 1} \ln(j + \alpha^{-1}) \right) - \ln(\Gamma y_i + 1) - (y_i + \alpha^{-1}) \ln(1 + \alpha\mu_i) \\ + y_i \ln(\alpha) + y_i \ln(\mu_i) \end{bmatrix}$$

Differentiating with respect to β and equating to zero

$$\frac{\partial L}{\partial \beta} = \sum_{i=1}^{n} \left(\frac{y_i - \mu_i}{1 + \alpha\mu_i} \right) X_i' = 0$$

Differentiating with respect to α and equating to zero

$$\frac{\partial L}{\partial \alpha} = \sum_{i=1}^{n} \left\{ \begin{array}{l} \frac{1}{\alpha^2}\left[\ln(1+\alpha\mu_i) - \sum_{j=1}^{y_i-1} \frac{1}{j+\alpha^{-1}} \right] \\ + \frac{y_i - \mu_i}{\alpha(1+\alpha\mu_i)} \end{array} \right\} = 0$$

Solving these two equations for $\hat{\beta}$ and $\hat{\alpha}$ simultaneously using Fisher scoring iteration method.

III. RESULTS AND DISCUSSIONS

In this study, annual data on malaria cases in India has been analysed using R program, employed Spearman's correlation to know the relationship between the response variable i.e., malaria cases and other independent variable shown in Table 1 and also applied the Negative Binomial regression to know the significant impact of independent variables i.e., time, annual average rainfall, Humidity, Minimum and Maximum temperature, percentage of migrants and forest cover growth rate shown in Table 2.

Spearman's correlation analysis showed that annual average rainfall only positively correlated with annual malaria cases but insignificant. All other variables humidity, minimum temperature, maximum temperature, percentage of migrants and forest cover growth rate are negatively correlated with annual malaria cases. Percentage of migrants,minimum and maximum temperature and Forest cover growth rate are respectively 1%, 5% and 10% level of significance (See Table 1).

To apply Negative Binomial Regression we check the goodness of fit test, for the intercept only model the null deviance is 470.33 on 25 degree of freedom and the p-value is 0.0000 that indicates the only intercept model is rejected. For the predictors include model, the residual deviance is 26.022 for 18 degrees of freedom and the p-value is 0.0992 that indicated the predictors include model is accepted. Hence all predictors are important for the model. Dispersion parameter is $\theta = 203$ which indicate the data is over dispersed.

Table 2 show the negative binomial regression coefficients, every one-unit increased in the time, and the expected log number of annual malaria cases decreased by 0.21. Since 1996, number of malaria cases got declined gradually. Rainfall is a very major variable which helps in reproduction of Anopheles misquotes. Standing water is the breeding centre for the Anopheles misquotes. But sometimes heavy raining is also reason for distraction of the breeding centres. So many studies have been carried about to say the significant effect of rainfall on the malaria cases gives the different results. Total rainfall is influential in only few of the zones of Chennai city, India (Chatterjee, 2009). Rainfall is significant factor for the transmission of malaria and moderate rain only helps in incubation of Anopheles misquotes (Srimath-Tirumula-Peddint, 2015). But different result is found, that is rainfall is not a significant factor for the transmission of malaria disease (Nath, 2013). In our study, average annual rainfall is showing insignificant factor for the transmission.

Relative humidity is a major factor for Anopheles misquotes longevity. Greater than 60% humidity can increase the life span of misquotes than can help in development of malaria parasites (P. Falciparum and P. Vivax) within misquotes body and contact the human host. Below 60% humidity, the longevity of misquotes decreased and were unable to develop the parasites within the body (Akimbobola et al., 2013). In our study, we have considered annual average humidity which is not showing significant impact on the malaria transmission because of average of all month's humidity is considered. That's why it is not showing affect on transmission of malaria in our study.

Minimum temperature increased by 1^0C, the expected log number of annual malaria cases increased by 0.33 and increase in the maximum temperature by 1^0C, the expected log number of annual malaria cases decreased by 0.21. Minimum temperature is affecting positively with 1% level of significance and maximum temperature is affecting negatively with 10% level of significance. Minimum temperature is also a major factor for the betterment in life span of the Anopheles misquotes. In particularly, P. Vivax parasites survive in minimum temperature (15^0C) than the P. Falciparum parasite (18^0C). Duration of the survival of the parasites has been dependent on the variation in the temperature. Temperature ranged between 20^0C to 30^0C is enough for the Anopheles misquotes to live (Wilmot et al., 1995).

One percentage increase in the migration, the expected log number of annual malaria cases increased by the 0.67. When non-climatic factor considered, Migration has played a crucial role in transmission of malaria disease. Migration process may transfer the malaria infected individual to the area in which malaria is not present either non infected individual moving to the infected area. These two ways can help in spreading the malaria disease. When people move from their non malaria-endemic areas to malaria-endemic areas especially for the cropping and harvesting in the field in that season malaria in its peaks, they are more vulnerable to malaria disease because of lack of immunity. People move for a number of reasons, including environmental deterioration, economic necessity, conflicts, and natural disasters. These factors are most likely to affect the poor, many of whom live in or near malaria- endemic areas (Martens et al., 2000). One unit of increase in the forest cover growth rate, the expected log number of annual malaria cases has decreased by 0.10. Impact of forest cover growth rate on the annual malaria cases is statistically significant with 1% level of significance. In our study period deforestation happened in the year 1996 i.e., forest cover growth rate (-0.43) per square km in the negative sign that indicates deforestation and simultaneously malaria cases reached its pick in the decade. Deforestation leads to high incidence of malaria because of pools of water in the forest open for the sunlight, that gives the sufficient temperature and humidity to Anopheles misquotes for breeding and development of malaria parasites (Austin et al., 2017).

IV. CONCLUSION

Malaria disease seems to be under control, although it remains most danger in India because of development in the drug resistant malaria parasites. The climatic and non-climatic variables are the major keys for the transmission of malaria disease. Study concludes that annual average rainfall is positively correlated with malaria cases while remaining variables show negative correlation. Since the malaria disease is more in rainy season because it is a favourable condition for the reproduction of malaria mosquitoes. Increase in the duration of rainfall is directly proportional to increase in the mosquito's density.

Time, maximum temperature and forest cover growth rate are significant and have negative impact on the number of annual malaria cases and minimum temperature, and percentage of migrants have significant and positive impact on the number of annual malaria cases. Impact of percentage of migrants more is than the other variables on the transmission of malaria. This result is obtained because of considering annual data so that climatic effect is not shown much.

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Table 1: Correlation between annual malaria cases and climatic and non-climatic variables.

Independent Variables	Annual malaria cases	p- value
Annual average rainfall	0.315	0.117
Humidity (%)	-0.163	0.426
Minimum Temperature	-0.432**	0.028
Maximum Temperature	-0.428**	0.029
Percentage of Migrants	-0.879***	0.000
Forest cover growth rate	-0.366*	0.066

***indicates 10% level of significance, **indicates 5% level of significance and ***indicates 1% level of significance**

Table 2: Regression coefficients of independent variables and p value.

Independent variables	**Coefficients**	**Standard error**	**p- value**
Intercept	-2.2909	3.0118	0.4469
Year	-0.2085	0.0200	0.0000***
Annual Average rainfall	-0.0038	0.0026	0.1461
Humidity	-0.0160	0.0167	0.3380
Minimum Temperature	0.3296	0.1181	0.0052***
Maximum Temperature	-0.2146	0.1250	0.0861*
Percentage of Migrants	0.6703	0.0797	0.0000***
Forest cover growth rate	-0.1039	0.0289	0.0033***

***indicates 10% level of significance, **indicates 5% level of significance and ***indicates 1% level of significance**