

**Original Article****Spatial Modelling of Malaria in South of Iran in Line with the Implementation of the Malaria Elimination Program: A Bayesian Poisson-Gamma Random Field Model****Amin Ghanbarnejad<sup>1</sup>; Habibollah Turki<sup>2</sup>; Mehdi Yaseri<sup>1</sup>; Ahmad Raeisi<sup>3,4</sup>; \*Abbas Rahimi-Foroushani<sup>1</sup>**<sup>1</sup>Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran<sup>2</sup>Infectious and Tropical Diseases Research Center, Hormozgan Health Institute, Hormozgan University of Medical Sciences, Bandar Abbas, Iran<sup>3</sup>Departments of Medical Parasitology and Mycology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran<sup>4</sup>Center for Communicable Diseases Control, Ministry of Health and Medical Education, Tehran, Iran**\*Corresponding author:** Dr Abbas Rahimi-Foroushani, E-mail: rahimifo@tums.ac.ir

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**Abstract****Background:** Malaria is the third most important infectious disease in the world. WHO propose programs for controlling and elimination of the disease. Malaria elimination program has begun in first phase in Iran from 2010. Climate factors play an important role in transmission and occurrence of malaria infection. The main goal is to investigate the spatial distribution of incidence of malaria during April 2011 to March 2018 in Hormozgan Province and its association with climate covariates.**Methods:** The data included 882 confirmed cases gathered from CDC in Hormozgan University of Medical Sciences. A Poisson-Gamma Random field model with Bayesian approach was used for modeling the data and produces the smoothed standardized incidence rate (SIR).**Results:** The SIR for malaria ranged from 0 (Abu Musa and Haji Abad districts) to 280.57 (Bandar-e-Jask). Based on model, temperature (RR= 2.29; 95% credible interval: (1.92–2.78)) and humidity (RR= 1.04; 95% credible interval: (1.03–1.06)) had positive effect on malaria incidence, but rainfall (RR= 0.92; 95% credible interval: (0.90–0.95)) had negative impact. Also, smoothed map represent hot spots in the east of the province and in Qeshm Island.**Conclusion:** Based on the analysis of the study results, it was found that the ecological conditions of the region (temperature, humidity and rainfall) and population displacement play an important role in the incidence of malaria. Therefore, the malaria surveillance system should continue to be active in the region, focusing on high-risk areas of malaria.**Keywords:** Bayesian; Spatial; Poisson-gamma; Hormozgan; Malaria elimination**Introduction**

Malaria is the third most important infectious disease after tuberculosis and AIDS and one of the tenth diseases under investigation by the WHO as part of a program, called Tropical Disease Research. Malaria threatens more than 40% of the world's population. It is estimated that about 2.5 billion people worldwide are at risk of malaria (1). According to the report by WHO in 2019, about 80 countries are

facing with malaria transmission which had led to 228 million infected cases and 405,000 death (1). The disease is present in most tropical, subtropical and even temperate regions of the world. Due to the nature of the disease and the complexity of malaria epidemiology, it is not possible to solve the disease problem with a single strategy. Malaria is not only an infectious disease of the tropical areas, but also a

health problem related to climatic, social, economic and developmental conditions in the world.

Iran is located in an endemic area of malaria according to the malaria's global distribution map (2). Although ongoing efforts to combat malaria in the last five decades have led to a significant reduction in malaria in Iran, there are still positive cases of malaria, especially in the south and south-east of the country. The incidence of malaria in Iran has decreased from 15378 cases in 2002 to 960 cases in 2017 (3). The three provinces including Kerman, Sistan and Baluchestan, and Hormozgan are the most malaria-prone areas of Iran (4, 5). This disease has been prevalent as hyper-endemic in many parts of Hormozgan Province for many years. 12% of malaria cases reported in the south-eastern region and 10% of cases reported in Iran belong to Hormozgan Province (6). WHO had an elimination program for some countries and first phase of implementation in Iran was during 2010 to 2015 and second phase was begun in 2016 and run successfully in the region (7-10). Appropriate weather and humidity conditions throughout the year for carrier activity, adjacent to Sistan and Baluchistan Province as the main malarious area of Iran, as well as relocation and presence of immigrants infected with malaria, especially Pakistani and Afghani, are the most important factors affecting the malaria situation in this province (6). Many studies around the world have linked the incidence of malaria to weather conditions (11-19). Therefore, the use of climate variables will help to improve the prediction of malaria cases. Malaria modeling in the context of spatial models and mapping is one of the most useful approaches to study malaria in relation to climate factors. For the mapping of diseases, including malaria, the data applied are mainly the number of occurrences in each area of the country, namely province or county. One set of statistical models that is widely used in disease mapping is Bayesian hierarchical spatial models. The most commonly used

models in this domain are Markov random field models proposed for the first time by Besag et al. in 1991 (20) and the ecological regression model developed by Clayton and Bernardinelli in 1992 (21).

In the aforementioned models, spatial quality and resolution of the risk surface function is similar to the resolution at which the data is measured. To overcome this limitation, Wolpert and Ickstadt (1998) (22), presented an extension of the random field to the hierarchical model introduced by Clayton and Kaldor (1987) (23), in which the spatial resolution of risk surface function could be independent of where the data measured. This model was applied in epidemiology by Best et al. (2005) (24) and covariates were used to improve the risk surface function in the model. In this study, the relationship between malaria incidence and climate factors will be assessed based on extended Poisson-Gamma random field model and produce the malaria risk map in Hormozgan Province at county level. The main goal of this study was to design and develop a model to investigate and predict the conditions of malaria transmission in the endemic region of Hormozgan in accordance with successful implementation of the malaria elimination program.

## Materials and Methods

### Study area

Iran has diverse climate and is in the endemic area of the global malaria spread map (2). Most of the positive cases are in the south and south-east of the country, where malaria elimination program is in progress. The three provinces of Kerman, Sistan and Baluchestan and Hormozgan are malaria-prone areas of Iran. Hormozgan Province is one of the malaria-prone areas of the country and has been hyper-endemic for many years (25). Hormozgan Province is located in south of Iran, has about 1,000km of coastline. Its population was 1,578,183 based

on 2016 census data. Its area is 70,697km<sup>2</sup> and its provincial capital is Bandar Abbas.

**Data collection**

Data on malaria incidence during April 2011 to March 2018 in Hormozgan Province was used for analysis. These data are collected from communicable disease center in Health Deputy of Hormozgan University of medical sciences. The data were grouped based on location of occurrence and categorized at county level. The data on climate variables gathered from Hormozgan meteorological organization (HMO). The variables temperature, humidity and rainfall were available as monthly record. For analysis, we calculated mean of the variables in each year, then averaging on 6 surveyed years and considered it as mentioned covariate for each district in the model.

**Statistical Model**

For response variable, we analyzed observed numbers of malaria cases (i: county (1, ..., 14)). The model used in this paper was a Poisson-gamma random field model with rainfall, temperature and humidity as covariates, the following Bayesian hierarchical structure was considered for modeling framework:

Level 1: Points:

$$N(dy) \sim \text{Pois}(\Lambda(y)w(dy)), y \in \mathcal{Y}$$

Intensity:

$$\Lambda(y) = (\theta_0 + \sum_{j \in JA} a_j \theta_j + \sum_{s \in S} k(y, s) \gamma_s \theta_s) \times \exp(\sum_{j \in JM} a_j \theta_j)$$

Level 2: Latent sources:

$$\Gamma(ds) \sim \text{Gamma}(\alpha(ds), \beta(ds))$$

Level 3: Parameter:  $\theta \sim \pi(\theta)d\theta$

In the above context, the number of observed malaria cases in each region is modelled by a Poisson process  $N(dy)$  on  $Y$  with mean  $\Lambda(y)w(dy)$ , where  $w(dy)$  is the population reference measure.  $\Lambda(y)$  as mean of the Poisson process depends on a set of covariates which their effect can be considered as excess risk (JA) or relative risk (JM). The spatial effect is introduced with a latent covariate  $X_s$  which is modelled as a Gaussian kernel mixture of a random measure  $\Gamma(ds)$  on space  $S$ . We choose

$S$  as bounding box of area of Hormozgan Province. In this paper, a Gamma random field  $\Gamma(ds)$  with shape measure  $\alpha(ds)$  and inverse scale function  $\beta(ds) > 0$  was used.  $\Gamma(ds)$  included latent sources  $s, s \in S$ , located at  $\mu_s = (\mu_1, \mu_2)$  with size  $\gamma_s$ . Bivariate Gaussian kernel  $k(y, s)$  with correlated longitude and latitude is as follow:

$$k(y, s) = \exp\left\{-\frac{1}{2(1-\rho^2)}\left[\frac{(y_1-\mu_1)^2}{\sigma_1^2} - \frac{2\rho(y_1-\mu_1)(y_2-\mu_2)}{\sigma_1\sigma_2} + \frac{(y_2-\mu_2)^2}{\sigma_2^2}\right]\right\}$$

We consider four latent sources at fixed location of each kernel  $\mu_s = (\mu_1, \mu_2)$  for modelling.

The SIR (Standardized Incidence Ratio) was calculated as below:

$$SIR = \frac{y_i \text{ (# of malaria cases)}}{e_i \text{ (# of expected cases)}}$$

$e_i$  is the expected number of malaria cases in region  $i$  which calculated as,  $e_i = rN_i$ ,  $r$  is the total rate of malaria in the study region.

**Results**

**Descriptive statistics**

The study included 882 registered cases in period from April 2011 to March 2018. Based on epidemiological classifications, 716 cases (81.2%) were imported. Demographic characteristics of the cases are presented in Table 1. About half of the registered cases were located in rural areas. Majority of cases were non-Iranian (81.5%). Mean age of the patients was 24.3±13.68 and ranged from infants to 96 years old person. Men are more infected than women (84.96 versus 13.44 per 100,000 populations). The data was aggregated and grouped in administrative district, county for model fitting. The incidence rate of malaria per 100,000 persons was calculated as number of case in each region divided by population multiplied by 100,000 and showed in Fig. 1. The Incidence rate ranged from 0 (Abu Musa and Haji Abad Districts) to 280.57 (Bandar-e-Jask). Calculated SIRs are presented in Fig. 2.

The distribution of cases according to year and moth is shown in Fig. 3. As seen in this

figure, the trend of registered malaria cases overall declined from 2011 to 2018. Also, there is a peak in summer every year. The descriptive statistics of meteorological covariates are presented in Table 2. As mentioned in the table, the variation of temperature is small because Hormozgan Province is located in a warm area, but the humidity has wide range variability from approximately 30% to 71%, this is because of the diversity of land cover of area. In the study period, annual rainfall ranged from 5mm to 16.62mm.

model was fitted to the data through MCMC and Gibbs sampling method with 200000 iterations after burning of first 50000 iterations. The regression coefficients and risk ratio of covariates influence on malaria incidence with the 95% Bayesian credible intervals are reported in Table 1. As mentioned in Table 2, the effects of temperature and humidity on malaria incidence are positive although rainfall has negative impact on malaria incidence. The smoothed SIR for malaria incidence are estimated from the model and shown in Fig. 3.

**Model fitting**

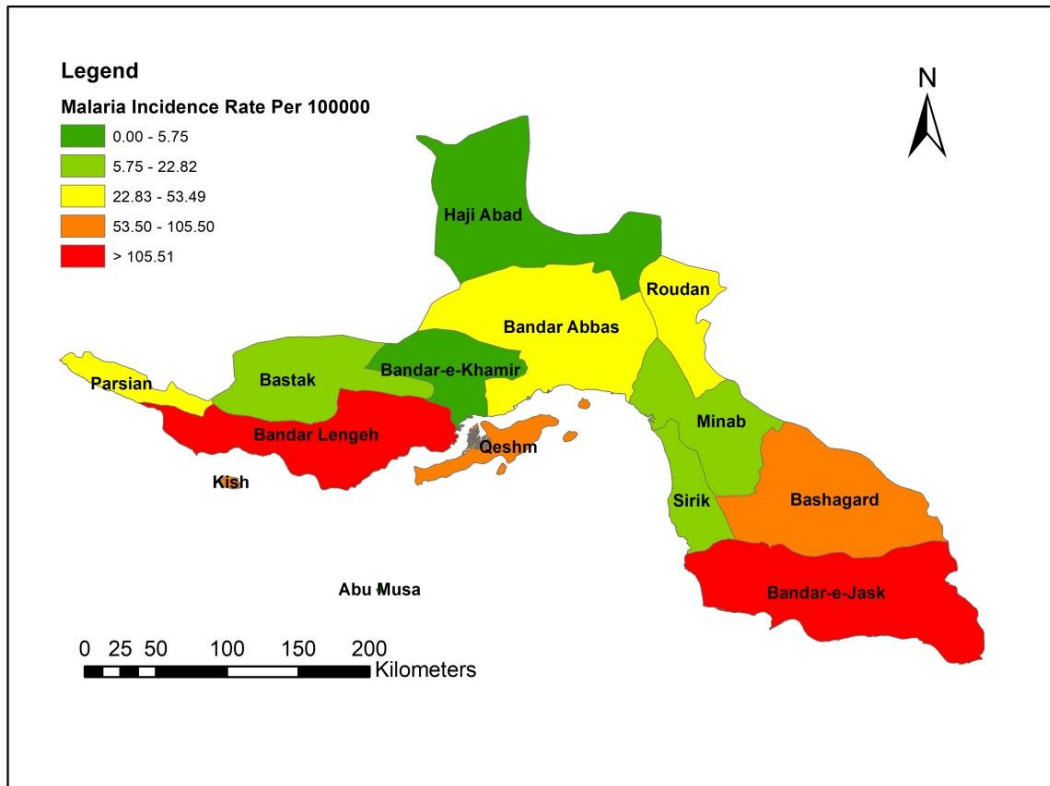
The Bayesian Poisson-Gamma random field

**Table 1.** Demographic characteristics of the patients with malaria in Hormozgan Province during 2011–2018

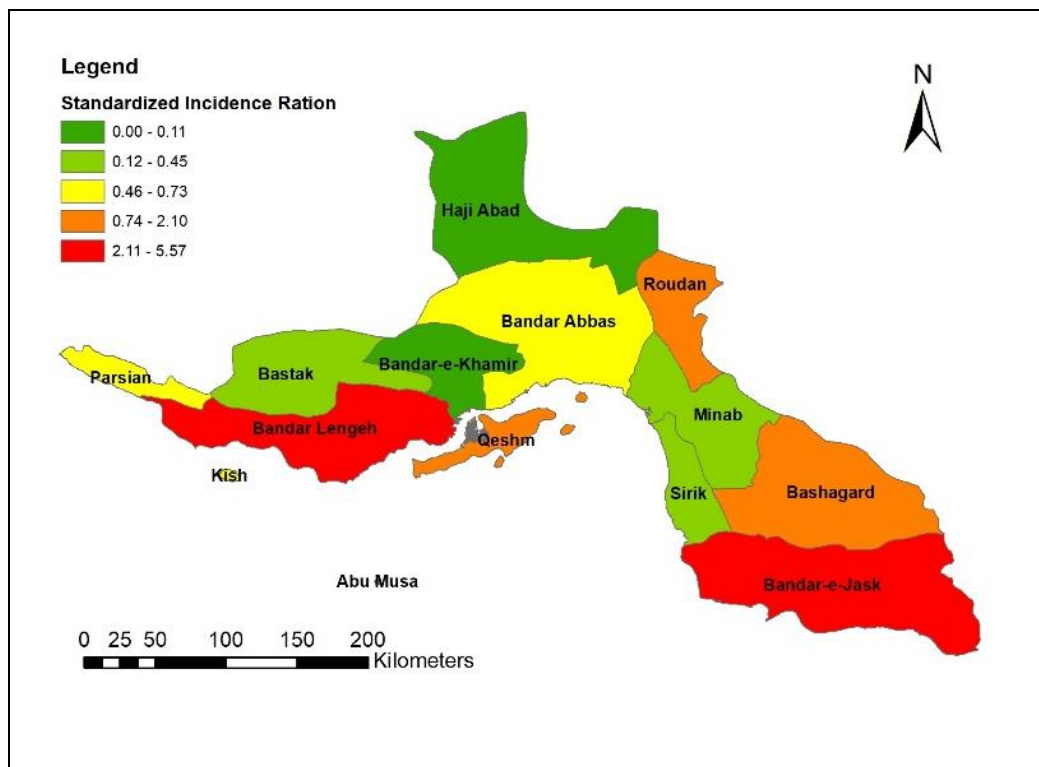
Variable	Category	No. (%)
<b>Sex</b>	Male	763 (86.5 %)
	Female	119 (13.5 %)
<b>Age</b>	Under 5 years	60 (6.8 %)
	5–15 years	116 (13.2 %)
	16–29 years	481 (54.5 %)
	30–64 years	211 (23.9 %)
	65 years and older	14 (1.6 %)
<b>Residency</b>	Urban	453 (51.4 %)
	Rural	429 (48.6 %)
<b>Nationality</b>	Iranian	163 (18.5 %)
	Afghan	270 (30.6 %)
	Pakistani	425 (48.2 %)
<b>Job</b>	Other Nations	24 (2.7 %)
	Worker	479 (54.3 %)
	Farmer	42 (4.8 %)
	Housewife	40 (4.5 %)
	School students	18 (2 %)
	Children	99 (11.2 %)
	Other	204 (23.1 %)
<b>Type of Malaria Parasites</b>	Plasmodium vivax	801 (90.8 %)
	Plasmodium falciparum	79 (9 %)
	Mixed	2 (0.2 %)

**Table 2.** Descriptive statistics of meteorological covariates in Hormozgan Province during 2011–2018

Variables	Mean	Standard Deviation	Range
<b>Temperature (°C)</b>	28.04	0.86	26.09–29.76
<b>Humidity (%)</b>	52.70	14.41	29.50–70.71
<b>Rainfall (mm/year)</b>	10.14	4.17	5.07–16.62



**Fig. 1.** Incidence rate of malaria in Hormozgan Province



**Fig. 2.** Calculated standardized incidence ratio (SIR) for malaria in Hormozgan Province

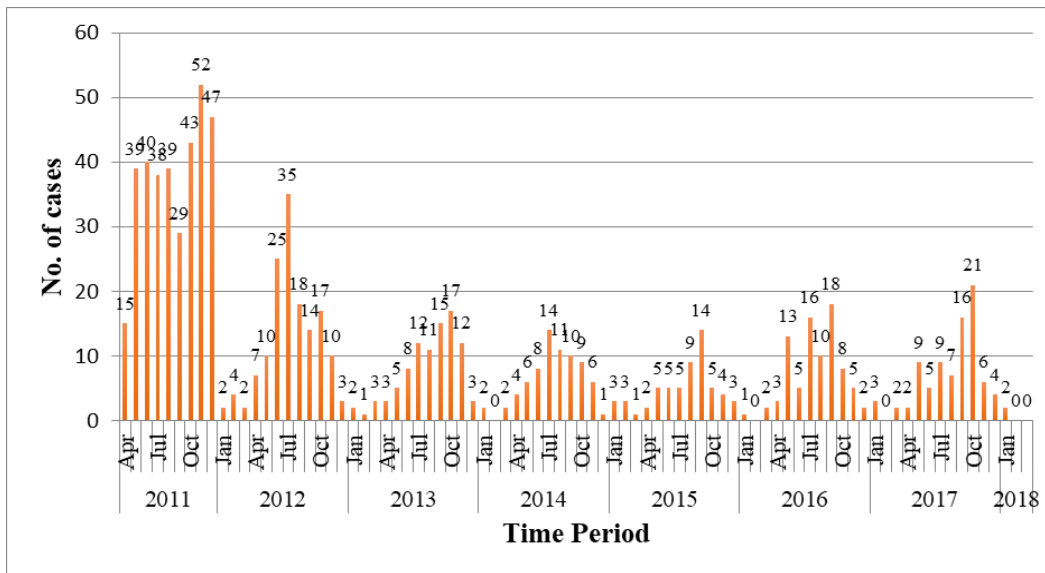
**Table 3.** Summary statistics of coefficients of Bayesian Poisson-Gamma Model

Variable	RC*	95% CI** for RC	RR***	95% CI** for RR
Temperature (°C)	0.8287	(0.65, 1.02)	2.29	1.92–2.78
Rainfall (mm/year)	-0.079	(-0.107, -0.05)	0.92	0.90–0.95
Humidity (%)	0.43	(0.029, 0.057)	1.04	1.03–1.06
Latent Source	0.0059	(0.0003, 0.02576)		

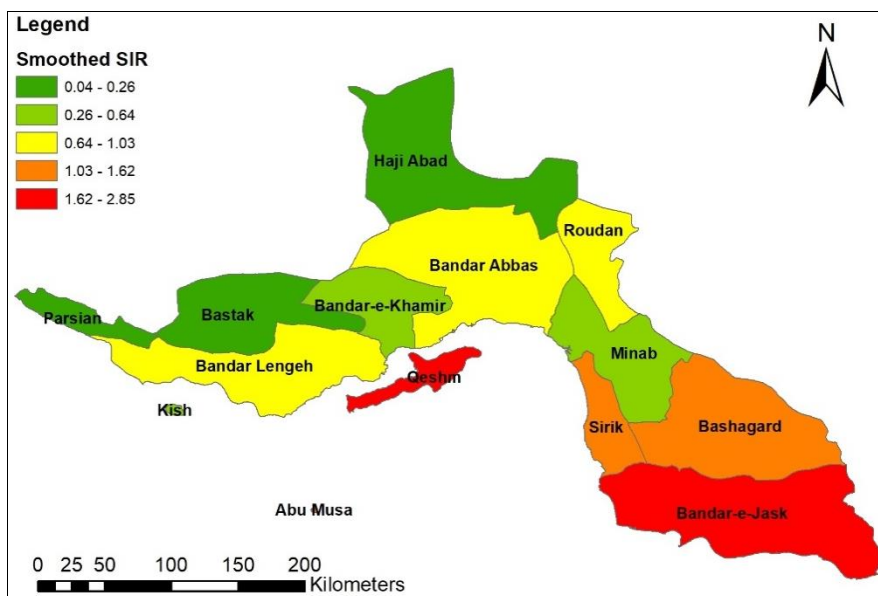
\*Regression coefficients

\*\*Credible interval

\*\*\*Risk Ratio



**Fig. 3.** Trend of malaria cases in Hormozgan Province during 2011-Apr to 2018-Mar



**Fig. 4.** Smoothed standardized incidence ratio (SIR) based on Bayesian Modelling

## Discussion

The key point of the present study was mapping malaria incidence in a region which previously known as endemic area for malaria infection and elimination program is implemented in the region. The estimated malaria risk map helps health policy makers to have better realization of the infection risk in the region and effect of climate.

As mentioned in results, there is a decline of detected malaria cases from 2011 to 2018 because of good implementation of malaria elimination program and successful malaria surveillance system.

In this paper we developed a model for analyze spatial pattern of malaria incidence in Hormozgan Province, south of Iran in presence of some climate covariates.

Visualizing standardized incidence rate (SIR) on the region map is one of the best representation of disease burden in epidemiological studies. In the Malaria disease, there are studies which produce smoothed maps via statistical modelling around the world such as works done by Taddese et al. in northwest of Ethiopia (26), Saita et al. in Tak province of Thailand (27), Bui et al. in Brazil (28), Gwitira et al. in Zimbabwe (29), Sasane et al. in India (30), Nur et al. in Indonesia (31), Hast et al. in Zambia (32).

The Bayesian framework was used to modeling the malaria incidence and create smoothed map after adjusting for climate variables: temperature, rainfall and humidity. This is the first research that uses a Bayesian modeling framework to study the relationship between climatological covariates and malaria incidence in Hormozgan Province. The last published paper for mapping malaria in Hormozgan was conducted by Hanafi-Bojd in 2012 (33), they analyzed data for only Bashagard District and produced malaria risk maps and identified hot spots. Also, there is another published work in Minab District of Hormozgan Province that assessed the association between meteorological factors with malaria incidence during 2003 to 2009 us

ing time series analysis but not considering the spatial pattern (34).

### Effect of temperature

Based on Bayesian modelling, temperature was important environmental covariate on malaria incidence. The impact of malaria was hazardous due to the approximately 2.3 risk ratio. This result is consistent with the study by Mohammadkhani et al. in Kerman, southeast of Iran (35). Because of neighboring of Hormozgan and Kerman provinces this result is feasible. Also, Umer et al. in Pakistan evaluate the relationship between climate factors and malaria incidence and their findings were in line with our study. In the study by Ikeda et al. in South Africa (36), high temperature was associated with high incidence which was similar to the present study. Kang et al. in Madagascar showed that temperature is an affecting factor on malaria (37). Laneri et al. assess the impact of climate drivers on malaria incidence in a region of Argentina and found that the temperature had positive effect (38) which is consistent with the present study. Sempiira et al. in Uganda analyzed MIS data for children under 5 years and the effect of land surface temperature was positive and significant (39). Herekar et al. in Karachi, Pakistan found the positive correlation between temperature and malaria cases (40). Liu et al. in Tengchong County of Yunnan Province in China investigated the effect of climate on malaria incidence and had found that high temperature is an important factor on malaria (41).

In some studies, there are negative impact on malaria incidence, M’Bra et al. found a negative effect of temperature on malaria incidence in Cote D’Ivoire (42). The effect of temperature on malaria incidence was negative in a research by Santos-Vega et al. in northwest of India (43).

### Effect of humidity

Another climate factor which has positive

and significant effect on malaria incidence in our study was humidity. This result is consistent with other studies around the world. Herekar et al. in Pakistan concluded the same result for humidity (40). Laneri et al. had found a complex relationship between humidity and malaria, in their study the maximum humidity above 85% had negative effect and minimum temperature had positive effect which is consistent with this study in some aspects. Simple et al. found a positive impact of humidity on malaria in Uganda (44) which is in line with our study.

### Effect of rainfall

The impact of rainfall on malaria incidence was estimated to be negative in this study which is consistent with the study conducted by Adigun et al. in Nigeria (45). Millar et al. found that the rainy season was the strongest climate predictor for malaria (46). Matthew showed that there is a strong and direct correlation between rainfall and malaria occurrence in Ile-Ife region in south-western of Nigeria (47). But in our study the rainfall had negative impact on malaria incidence. The direct effect of rainfall has been seen in the African countries which have tropical and wet climate (48) which is different from the climate of Hormozgan. The studied region has a warm and dry summer and in the winter, some of the area experienced rainy days. The spatial distribution in Hormozgan showed a hot spots pattern in the areas which have foreign workers from other provinces and other countries. There is noticeable effect of temperature on malaria incidence which is concluded that the people should be aware in hot season and policy makers must have good planning to control and eliminate the malaria in the district.

### Conclusion

Based on the analysis of the study results, it was found that the ecological conditions of the region (temperature, humidity and rainfall) and population displacement play an important role in the incidence of malaria. Therefore, the

malaria surveillance system should continue to be active in the region, focusing on high-risk areas of malaria. Country has a long history of work on malaria and publication of several papers on different aspects of malaria including insecticide resistance monitoring, sibling species, molecular study, new record, novel methods for vector control, faunistic study, use of plants for larval control, using bednets and long lasting impregnated nets, morphological studies, malaria epidemiology, ecology of malaria vectors, biodiversity, community participation, vector control, repellent evaluation, anthropophilic index of malaria vectors, training is designated as malaria training center by WHO. There are several reports on different aspects of malaria vectors recently (49-143).

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