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Geographical mapping and Bayesian spatial modeling of malaria incidence in Sistan and Baluchistan province, Iran

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ABSTRACT

Objective: To present the geographical map of malaria and identify some of the important environmental factors of this disease in Sistan and Baluchistan province, Iran. **Methods:** We used the registered malaria data to compute the standard incidence rates (SIRs) of malaria in different areas of Sistan and Baluchistan province for a nine-year period (from 2001 to 2009). Statistical analyses consisted of two different parts: geographical mapping of malaria incidence rates, and modeling the environmental factors. The empirical Bayesian estimates of malaria SIRs were utilized for geographical mapping of malaria and a Poisson random effects model was used for assessing the effect of environmental factors on malaria SIRs. **Results:** In general, 64 926 new cases of malaria were registered in Sistan and Baluchistan Province from 2001 to 2009. Among them, 42 695 patients (65.8%) were male and 22 231 patients (34.2%) were female. Modeling the environmental factors showed that malaria incidence rates had positive relationship with humidity, elevation, average minimum temperature and average maximum temperature, while rainfall had negative effect on malaria SIRs in this province. **Conclusions:** The results of the present study reveals that malaria is still a serious health problem in Sistan and Baluchistan province, Iran. Geographical map and related environmental factors of malaria can help the health policy makers to intervene in high risk areas more efficiently and allocate the resources in a proper manner.

1. Introduction

Malaria is the most prevalent human parasitic disease and the most common mosquito-borne disease in the world. Although reliable estimates are not available, rough calculations suggest that globally, 250 million new cases occur each year and 1.5 to 2.7 million people dying[1-4]. About 45% of the populations of the Eastern Mediterranean Region live with the risk of contracting both *Plasmodium vivax* (*P. vivax*) and *Plasmodium falciparum* (*P. falciparum*) malaria, and an additional 5% are at risk of contracting *P. vivax* alone. Some 95% of the total numbers of malaria cases in the Region are found in four countries in the Region (including Afghanistan)[5].

In Iran, 12% of the population lives in areas with sporadic malaria transmission, mostly of *P. vivax*, and only 6% in areas of continuous transmission with a high proportion of *P. falciparum*. The latter areas include the south-eastern provinces of Sistan and Baluchistan, Hormozgan and part of Kerman province, with a population of about three million. Some 77% of the total numbers of reported cases are found in this region, and the source of many cases elsewhere in the country can be traced to this area[5].

Malaria is an important tropical disease in many parts of Middle East countries, particularly Iran. In the 1950s, national malaria control programs resulted in the considerable reduction in malaria incidence. This program led to the eradication of the disease from some areas such as Caspian Sea region in the north of Iran. In addition, a high reduction in malaria incidence was observed in coastal plains in the north of the Persian Gulf by 1977. In the period between 1977 and 1994, malaria was restricted to the southeastern provinces of Iran (Sistan and Baluchistan, Hormozgan and Kerman). In the 1990s, the independence of the Republic of Azerbaijan and Armenia in northwest of Iran and large displacement of people in the provinces neighboring these countries, in addition to high immigration

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from Pakistan and Afghanistan to the east and southeast provinces of Iran increased the malaria incidence rate in these areas[6]. According to the published reports, the annual malaria cases were at least 15 000 during 2001 and 2006. Among these cases, about 60% were reported from a vast province in the east and southeast of Iran, named Sistan and Baluchistan[7,8].

The malaria parasite is transmitted from human to human via the bite of infected female *Anopheles* mosquitoes. Transmission depends on the distribution and abundance of the mosquitoes which are sensitive to environmental factors mainly temperature, rainfall, elevation and humidity. By determining the relations between the disease and the environment, the burden of malaria can be estimated at places where data on transmission are not available and high risk areas can be identified. Reliable maps of malaria transmission can guide intervention strategies and thus optimize the use of limited human and financial resources to areas of most need. In addition, early warning systems can be developed to predict epidemics from environmental changes. Geographic Information Systems (GIS) has emerged over the last 15 years as a powerful tool for linking and displaying malaria information from many different sources such as environmental and disease data, in a spatial context[9-17].

Despite of high incidence rate of malaria in Sistan and Baluchistan province (SBP), analysis of its incidence across the entire province has been assessed and published rarely[18-20]. Previously published articles in this field are generally related to other aspect of this disease in SBP, such as incidence and prevalence rates, description of the demographic characteristics of the patients, and plasmodium distribution[20-23].

In recent years, there is a strong interest in assessing the association between climate variability and malaria incidence and concerns about recent climate change has increased this interest. According to our searches, we find few published article about using advanced statistical methods for geographical mapping and modeling of the effect of environmental factors on malaria incidence rate in this province[18,20]. Therefore, we decided to use more complex statistical approaches to describe the status of malaria incidence in SBP and identify the impact of different environmental factors on malaria standard incidence rate (SIR) more accurately. To do this, we first report the malaria SIR in SBP over a nine-year period. Then, we use an empirical Bayesian method for estimating the malaria SIRs and representing the geographical map of this disease in SBP. Finally, we apply a Bayesian random effects model for assessing the statistical relationship between different environmental variables and malaria incidence.

2. Materials and methods

2.1. Study area

This epidemiologic research was carried out in SBP in southeastern Iran. That is the second largest province of Iran. Covering a surface area about 187 500 Square kilometers, it's twice England. This province consisted of two main parts. The north part, named Sistan, in the neighborhood of Afghanistan, and the south part, named Baluchistan, in the neighborhood of Pakistan and Oman Sea. Sistan and Baluchistan has 10 cities, 37 districts and 97 sub-districts (Figure 1). Zahedan is the capital of the province. It is a distance of 695 km from its north to the west. SBP has a common border about 1 100 km with southeastern neighboring countries (Afghanistan and Pakistan). In general, it's hot and dry in Loot Desert vicinity but in southern part, it's hot and burning because of severe winds.2.2. Data source

Figure 1. Geographical map of Sistan and Baluchistan province, Iran.

According to the national health policy of Iran, diagnosis of malaria should be based on visualization of parasites by light microscopy of Giemsastained blood smear in febrile cases.

There are active and passive surveillance systems in the country. All febrile cases, family and neighbors of a definite malaria case and a random sample of the population are regularly screened for malaria by expert microscopists using microscopic methods. The weekly malaria cases should be reported to the district health organization by rural health workers and microscopists. The acceptable quality of routinely collected information on malaria is described elsewhere[24]. Generally, it seems that nearly all cases of malaria are enrolled in the monthly surveillance forms in urban and rural health centers.

In this study, a copy of original monthly surveillance forms from urban and rural health centers were collected. The paper sheet consist of names of the patients and their parents, age, sex, type of surveillance (active or passive), type of accommodation (permanent or temporary), nationality (Iranian or immigrant), location (name of village or city), and the date of taking and reading blood films. In this study, the registered data in Sistan and Baluchistan Province during a nine-year period (from 2001 to 2009) was considered for malaria mapping and statistical modeling.

Paper sheet data convert to the spread sheet in MS-Access. The repeated episodes within subjects and immigrant cases were identified. Immigrant cases removed from the entire data bank and repeated episodes of a subject were considered just as an observed subject for each year. Repeated cases were found based on their names, parents' names, date of birth and also their locations. As denominator for the incidence calculations, midyear population from 2001 to 2009 was extracted using the published results of the last national census by the Statistics Center of Iran[25]. In addition, the required climate information for Bayesian modeling was obtained from the published reports of I.R. of Iran's Meteorological Organization[26]. The climate data comprises monthly averages of rainfall, temperature and humidity at each monitoring station in SBP.

2.3. Statistical analysis

For describing the gathered malaria data, the SIR values were computed for the total population and for the males and females, separately in different areas of SBP[27]. The analytical section of this paper consists of two different parts; geographical mapping of empirical Bayesian malaria SIR estimates and random-effects modeling for determining the effective environmental factors on malaria incidence.

2.3.1. Geographical mapping

For geographical mapping of malaria data in SBP, some researchers use the raw SIR or SMR values to estimate the underlying risk. However, when raw rates are used to estimate this underlying risk, differences in population size result in variance instability and unreal outliers. In this context, smoothing is a well-known methodology for overcoming the problem of variance instability. Essentially, rates are smoothed and thus stabilized by borrowing strength from other spatial units[28-30]. The empirical Bayesian smoothing method is a common approach for stabilizing the variance. This smoother borrows strength from a prior distribution to correct for the variance instability associated with rates that have a small base. It is empirical because the prior distribution is based on global characteristics of the existing observations[31,32]. In this paper, we used the empirical Bayesian estimates for geographical mapping of malaria SIRs in SBP.

As a brief illustration of the empirical Bayesian method, suppose an independent Poisson distribution for the cases in district i (in our application, i=1,...,7) with the unknown parameter λ_i. In addition, assume that the parameter λ_i has an unknown prior distribution with the mean of π and variance of σ^2. Then the distribution of the total cases in district i, that is m_i, can be written as Poi($n_i \lambda_i$), where the n_i is the total at risk population of the ith district.

In the past decades, the empirical Bayesian or shrinkage estimation for smoothing regional data was developed based on Maximum Likelihood Estimation (MLE)[33] and modified by Method of Moment Estimator (MME) [34]. The modified method resulted in the following estimates for the prior mean and variance

where $P_i = \frac{m_i}{n_i}$ is the crude estimate of the parameter λ_i and $\bar{n}$ denote the district mean at risk population. With shrinkage weights of $w_i = \frac{\hat{\sigma}^2}{\hat{\sigma}^2 + \frac{\hat{\pi}}{n_i}}$, the empirical Bayesian estimates are as follows The R software, version 2.11, was used for computing the empirical Bayesian estimates and the ArcMap software, version 9.2, was utilized for geographical mapping of malaria in SBP.

2.3.2. Random-effects modeling for assessing the environmental factors

To examine the impact of different environmental factors on malaria incidence rates, we fitted a Poisson random effects regression model. To do this, we assigned a log-normal prior distribution to λ_i values where the mean and variance are defined as a linear function of common intercept term α and two independent random effects.

Therefore, the applied random effects model can be written as

$log\,\lambda_i = \alpha + \sum_{j=1}^{5} \beta_j X_{ij} + u_i + v_i$ where $X_{ij} = (x_{1j}, \ldots, x_{mj})$ is the environmental vector of model covariates, β is a 5×1 vector of regression coefficients, u_i is the correlated heterogeneity random term reflecting local spatial structure by incorporating the influence of neighboring geographic areas (structured variation) and v_i is the uncorrelated heterogeneity that does not depend on geographic location (unstructured variation).

In the described random effects model, we considered five environmental explanatory variables (rainfall, humidity, elevation, average minimum temperature and average maximum temperature) as the potential effective factors on malaria SIRs. The model fitting process was performed using the statistical package R. To obtain more detailed information about the prior distributions of the model parameters and the Bayesian analysis, the interested reader can refer to the previously published papers[10, 35-38].

3. Results

Table 1 shows the total population, new malaria cases, some demographic information about the cases and estimated malaria SIRs, separately for years 2001 to 2009. Among 64 926 new malaria cases, 42 695 patients (65.8%) were male and 22 231 patients (34.2%) were female. In addition, this study showed that 4 205 (6.5%) of these patients were children less than 5 years old and, 46 253 cases (71.2%) were adults older than 15 years. Among the detected new cases, 9 127 cases (14.1%) were from the urban and 55 799 cases (85.9%) were from the rural areas. Figure 2 shows the trend of malaria incidence in SBP during nine-year period under study.

As mentioned before, we used an empirical Bayesian

Table 1

Demographic characteristics of malaria new cases and the estimated malaria SIRs in Sistan and Baluchistan Province from 2001 to 2009.

95%CI	SIR	Mean±SD Age	Malaria new cases	SBP Total population	Sex	Year
[0.039 – 0.044]	0.041	24.20±18.07	4 103	1 011 570	Male	
[0.017 – 0.019]	0.018	23.70±17.64	1 759	1 005 606	Female	2001
[0.028 – 0.031]	0.029	23.90±17.98	5 862	2 017 176	Total	
[0.034 – 0.038]	0.036	22.70±16.93	3 733	1 045 081	Male	
[0.016 – 0.018]	0.017	21.90±18.76	1 758	1 038 921	Female	2002
[0.025 – 0.028]	0.027	22.20±17.35	5 491	2 084 002	Total	
[0.088 – 0.099]	0.093	22.90±17.16	9 935	1 078 172	Male	
[0.040 – 0.045]	0.042	21.90±17.49	4 464	1 071 827	Female	2003
[0.064 – 0.072]	0.067	22.50±17.28	14 399	2 150 009	Total	
[0.036 – 0.040]	0.038	23.40±16.29	4 178	1112977	Male	
[0.018 – 0.020]	0.019	22.70±17.79	2 058	1 106 416	Female	2004
[0.027 – 0.030]	0.028	23.20±16.83	6 236	2 219 393	Total	
[0.053 – 0.059]	0.055	23.50±16.21	6 308	1 148 423	Male	
[0.032 – 0.037]	0.034	24.00±18.31	3 866	1 141 653	Female	2005
[0.042 – 0.047]	0.045	23.60±16.96	10 174	2 290 076	Total	
[0.037 – 0.041]	0.039	25.30±15.23	4 625	1 221 277	Male	
[0.018 – 0.022]	0.020	24.50±17.19	2 824	1 184 465	Female	2006
[0.027 – 0.030]	0.028	25.00±15.84	7 449	2 405 742	Total	
[0.038 – 0.043]	0.041	25.90±17.36	5 148	1 262 569	Male	
[0.018 – 0.022]	0.020	23.50±17.05	2 764	1 224 512	Female	2007
[0.029 – 0.034]	0.032	25.20±17.13	7 912	2 487 081	Total	
[0.015 – 0.019]	0.017	25.20±16.85	2 219	1 304 021	Male	
[0.008 – 0.012]	0.010	24.50±17.12	1 248	1 264 720	Female	2008
[0.011 – 0.015]	0.013	24.90±16.94	3 467	2 568 741	Total	
[0.016 – 0.021]	0.018	25.70±16.44	2 446	1 345 662	Male	
[0.009 – 0.013]	0.011	24.10±16.86	1 490	1 305 106	Female	2009
[0.013 – 0.017]	0.015	25.10±16.58	3 936	2 650 768	Total	

Table 2

Posterior estimates of the random effects model for assessing the environmental factors on malaria SIRs in Sistan and Baluchistan Province.

95%CI	Estimate	Parameter
[–0.793 , 7.145]	3.105	Alpha
[–4.878 , –0.171]	–2.435	Rainfall
[0.243 , 2.295]	1.257	Elevation
[0.682 , 2.461]	1.765	Humidity
[1.634 , 3.124]	2.289	Average maximum monthly temperature
[0.369 , 2.907]	1.623	Average minimum monthly temperature
[0.013 , 0.162]	0.084	Variance U
[0.152 , 0.562]	0.382	Variance V

method based on the Poisson model to present the geographical map of malaria SIR estimates for total population of SBP (Figure 3). This Figure shows that Zabol, Zahak and Khash had the lowest and Nikshahr, Sarbaz and Iraanshahr had the highest malaria SIRs among the SBP districts. In general, this figure demonstrates that the Baluchistan has considerably higher malaria incidence rate than Sistan. Moreover, Figures 4 and 5 displays the estimated malaria SIR map, separately for female and male population of the province based on the empirical Bayesian approach. Comparing these figures tells us that the pattern of malaria is nearly similar for males and females in this province.

We also used the described random effects model to identify some of the most important environmental factors of malaria incidence in SBP. Table 2 shows the results of the Bayesian estimates for the model parameters. Regarding these findings, one can conclude that all of the model covariates including rainfall, humidity, elevation, average minimum temperature and average maximum temperature had statistically significant effect on malaria incidence (none of the 95% credible intervals includes zero). As another conclusion, we can observe that humidity, elevation, average minimum temperature and average maximum temperature had positive relationship and rainfall had negative relationship with malaria incidence rates in SBP. This means that increasing in humidity, elevation and temperature raises the malaria incidence and increasing in annual rainfall decreases the risk of malaria. Finally, statistically significant random terms reveal that the environmental covariates do not explain all the variability in the malaria SIRs, because a significant part of SIR variation could be captured by the regional structured and unstructured random effects (none of the 95% credible intervals for variances of U and V includes zero).

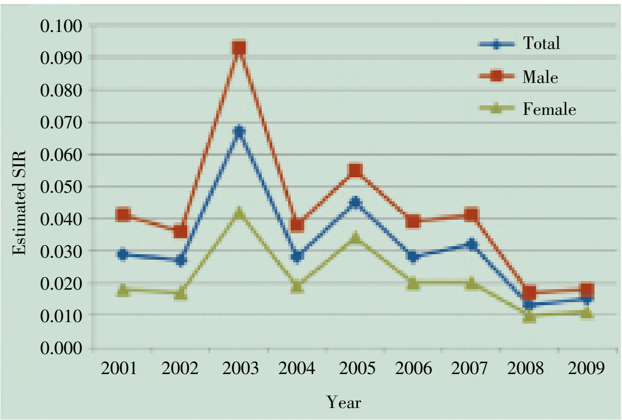

Figure 2. Estimated malaria SIRs from 2001 to 2009 in Sistan and Baluchistan Province, Iran.

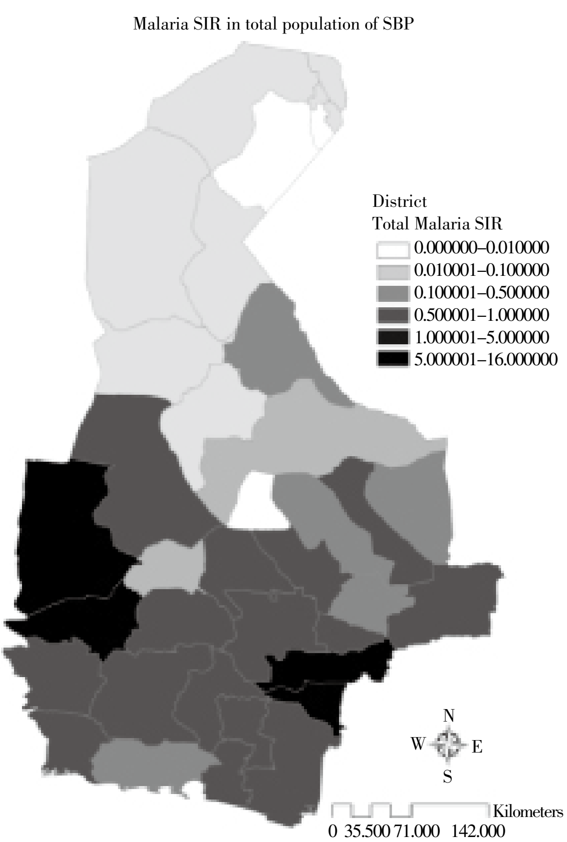

Figure 3. Estimated malaria SIRs based on empirical Bayesian method from 2001 to 2009 in total population of Sistan and Baluchistan Province.

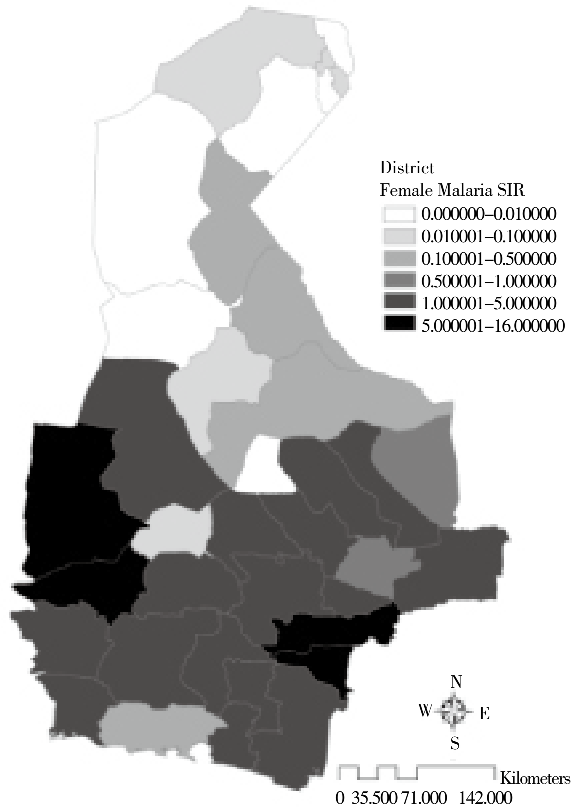

Figure 4. Estimated malaria SIRs based on empirical Bayesian method from 2001 to 2009 in female population of Sistan and Baluchistan Province, Iran.

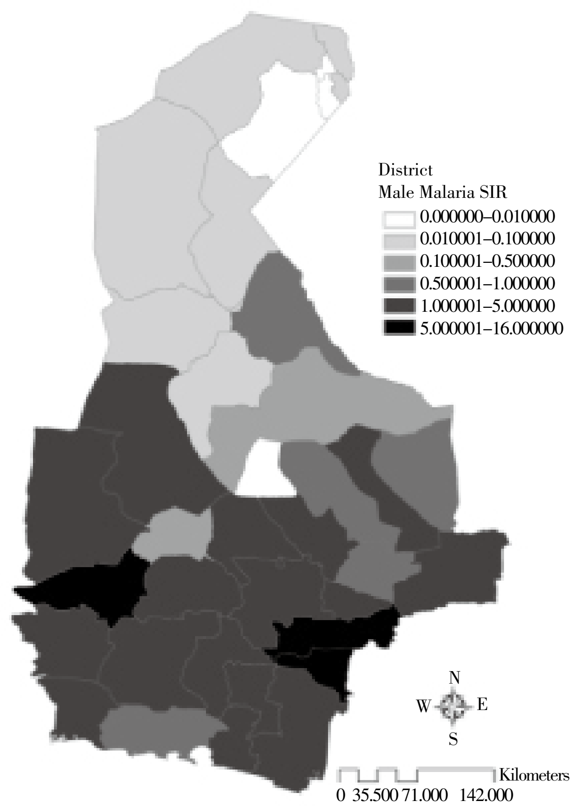

Figure 5. Estimated malaria SIRs based on empirical Bayesian method from 2001 to 2009 in male population of Sistan and Baluchistan Province, Iran.

4. Discussion

Malaria had being widely prevalent in many societies and it still remains as a major concern in the Eastern Mediterranean countries and in Iran. In 1949, Iran began a program for malaria eradication. This program has changed to malaria control in 1985 and all malaria control activities have been integrated in primary health care system since 1988. However, malaria is still the most important parasitic and vector-borne disease in Iran and one of the main health problems in southeast provinces. Ministry of Health and Medical Education of Iran started to investigate possibility of malaria elimination. The WHO/EMRO supported this initiative for situation analysis and providing recommendations for the program to start planning for strengthening the control program and preparing the required environment for malaria elimination[7,39].

Although Iran is among the Eastern Mediterranean region countries with low malaria endemicity, in some area of this country (especially in south and south east of Iran near the Persian Gulf and Oman Sea), there is still a rather high risk of malaria transmission[40]. WHO/EMRO categorized countries of Eastern Mediterranean countries in three groups based on the number of malaria cases: Group 1 consists of countries that have eliminated malaria or with very limited malaria transmission in residual foci (Bahrain, Egypt, Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Morocco, Oman, Palestine, Qatar, Syrian Arab Republic, Tunisia and United Arab Emirates), group 2 includes countries with low malaria burden limited to certain areas and with effective malaria programs (Iran, Iraq and Saudi Arabia), and group 3 includes countries with weak health systems and/or complex emergencies in them the number of recorded and estimated cases of malaria is moderate or high (Afghanistan, Pakistan, Djibouti, Somalia, Sudan and Yemen)[41].

In the previous decades, one of the main applications of GIS in disease research and control is mapping the incidence or prevalence. This kind of application is the basic GIS utility and consists of mapping incidence or prevalence of under study disease over some geographic area. The goal of this study is to detect and visualize any possible exception of correlation between disease incidence or prevalence and populations at risk[42-44]. Over the past decade, advanced GIS approaches and softwares have enabled us to get more information about malaria and use this information to combat this disease[44]. While there is a growing body of literature on the use of GIS for malaria research and control throughout the world, there have been few issues on malaria indexes in Iran. Because of lack of required information, we could not present the geographical malaria map for total population of Iran. Therefore, we decided to gather this information for a province with high incidence and prevalence rates of malaria in our country and present the geographical map of malaria for this region. According to our searches, this is the first effort for providing the geographical map of malaria using the advanced geo-statistical methods in a vast part of Iran. In general, the depicted maps in SBP showed a rather high incidence rate of malaria in southern part of this province (Baluchistan) in the neighborhood of Pakistan in the east, Oman Sea in the south and two other provinces of Iran (Kerman and Hormozgan) in the west. The high rate of immigrants from Pakistan to the Baluchistan section of SBP may be the main reason for this issue.

Regarding the estimated SIRs in the present study, one can observe a peak in year 2003 and a severe dip in year 2004 and a fairly rise in year 2005. The trend seems to be decreasing in the last years under study, especially for years 2008 and 2009. More efforts for protecting the borders by the Iranian security forces to prevent the illegal entry of people (especially from Pakistan and Afghanistan) may be one of the main reasons for the observed reduction in malaria incidence during 2006 to 2009.

In our study, the presented results demonstrate that about two third of these cases were male. Clearly, the main reason for higher incidence rate of malaria in males and adults is the need for working out of the houses and more probability of human-vector contacts. In addition, we found that the mean age of malaria new cases was between 22 and 26 years and more than 60% of them were adults more than 15 years old. The epidemiology of malaria in adults who live in malaria endemic areas is a neglected issue of research. Malaria control strategies have mostly focused on children under the age of 5 years and pregnant women, as the majority of malaria related sickness and death is seen in these two groups[45,46].

The recent advances in statistical modeling methods and related softwares provide helpful and efficient tools to assess relationships between climate, the environment and mosquito vectors of human disease[12,47]. These results tell us that increase in altitude, humidity and average temperature raises the risk of malaria in SBP. Our finding about the relationship between elevation and risk of malaria is in agreement with other studies in this context[48-51]. The elevation is SBP is generally less than 1 400 meters above the sea. Noor *et al.* reported that areas with altitude less than 500 meters above the sea level had odds of 0.59 for malaria risk compared to areas with altitude between 500 and 1 500 meters. In contrary, lower risk of malaria was reported for altitudes higher than 1 400 meters above the sea[50]. Also, the obtained positive association between humidity and malaria risk in our study is not in contrast to results of other surveys. This positive correlation has previously reported in studies conducted in Bangladesh and Mozambique[52,53]. Temperatures between 15 to 40 ℃ and humidity between 55% to 80% are suitable for the completion of the *P. falciparum* and *P. vivax* malaria parasite life cycles[53]. It seems that humidity plays important role in the life cycle of the mosquito. In the presence of high humidity values, the parasite would complete the necessary life cycle in order to increase transmission of the infection to more humans. Additionally, results of other studies about the positive correlation between temperature and malaria risk are generally in agreement with our findings. Commonly, the majority of these studies have demonstrated that temperature is an important factor in malaria transmission[53-57]. Temperature directly affects mosquito development, survival, reproduction, activity, and the extrinsic incubation rate. A study in east African highlands revealed that a 1 ℃ increase in minimum temperature with a lag time of 1-2 months and a 1 ℃ increase in maximum temperatures with a lag time of 2-5 months led to an 8-95% increase in the number of malaria outpatients[58]. In another study in Bangladesh, however, the researchers found no significant association between temperature and number of malaria cases after adjusting for other climatic confounding factors[51].

The effect of rainfall on malaria incidence is somewhat controversial. In this study, we found a negative association between the amounts of rainfall and malaria SIRs in SBP. This finding is not supported by many other studies in different areas. For instance, studies in Angola, Mozambique, Mali, Zambia, Uganda, Botswana and

Thailand reported that higher values of rainfall is associated with higher risk of malaria[13,50,53,59–62]. In contrast, other studies in some regions of India and Seri Lanka showed that rainfall is a major contributing factor for the decrease of malaria cases[53,63–67]. At the same time, some other surveys found no significant relationship between rainfall and malaria incidence[51,68]. One reason for the observed negative association between rainfall and malaria incidence maybe that high and intensive rainfall flush out breeding sites and kill the eggs[18,51,69].

In the present study, we used advanced statistical methods for geographical mapping of malaria and identifying the effective climate factors on this disease in Sistan and Baluchistan Province, Iran. We showed that the incidence rate of malaria can be accurately modeled and mapped using these approaches. In general, the present study showed that malaria is still a serious health problem, despite of national control programs and the efforts of the Ministry of Health and Medical Education of Iran for the elimination of this disease in our country. The presented maps and determined environmental factors in this study give the health policy makers an important overview of malaria situation in this province in order to intervene in high risk areas more efficiently and allocate the resources in a proper manner.

Conflict of interest statement

We declare that we have no conflict of interest.

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