

Retrospective Epidemiological Study of Malaria from 1999 to 2016 in Khash, Iran: A Region on the Verge of Malaria Elimination

Hadi Mirahmadi, Ph.D. ¹, Aboozar Kord ², Allahbakhsh Kord, B.Sc. ³, Narjes Sargolzaie, M.D. ⁴, Seyed Mehdi Tabatabaei, M.D. ⁵,
Mohamad Kazem Momeni, M.D. ⁶, Hafez Mirzanejad-Asl, M.Sc. ⁷, Reza Shafiei, Ph.D. ⁸, Alireza Badirzadeh, Ph.D. ⁹

1- Assistant Professor, Infectious Diseases and Tropical Medicine Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran

2- Medical Student, Infectious Diseases and Tropical Medicine Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran

3- Health Promotion Research Center, Zahedan University of Medical Sciences, Zahedan, Iran

4- Assistant Professor, Ph.D., Infectious Diseases and Tropical Medicine Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran

5- Associate Professor, Ph.D., Health Promotion Research Center, Zahedan University of Medical Sciences, Zahedan, Iran

6- Assistant Professor, Department of Internal Medicine, Faculty of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

7- M.Sc. of Medical Parasitology, Department of Medical Parasitology, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

8- Assistant Professor, Vector-borne Diseases Research Center, North Khorasan University of Medical Sciences, Bojnurd, Iran

9- Assistant Professor, Department of Parasitology and Mycology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
(Corresponding author; E-mail: badirzadeh.ar@iums.ac.ir)

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Abstract

Background: Malaria infection is still one of the most important public health concerns globally. The aim of this study was to evaluate retrospective epidemiological study of malaria in Khash City, Sistan and Baluchestan Province of Iran from 1999 to 2016.

Methods: This was a retrospective study, which collected official data of 26-year trend of malaria in Khash, Sistan and Baluchestan Province of Iran.

Results: The data showed that over 26 years, 5015 cases of malaria were identified in Khash; the highest number of cases was reported in 1995 with 846 patients and the lowest number was in 2016 with one patient. A total of 419 patients were Iranian (52.2%) and 383 patients (47.8%) were non-Iranian including: Afghans (323 patients, 40.3%) and Pakistanis (60 patients, 7.5%). During 17 years, 279200 blood slides for malaria were prepared in Khash of which 5014 slides were found to be positive. The highest and lowest ABER were in 2003-2004 (63.69) and 2016-2017 (0.30), respectively. *Plasmodium vivax* was identified as the main and dominant causative agent of disease in all infected patients.

Conclusions: The results revealed a significant decline in malaria incidence rate in Khash. However, based on Iran's vast borders with malaria endemic countries (Afghanistan and Pakistan) and illegal immigrants coming from these nations to country, the risk of malaria outbreaks must be considered seriously and the control and/or screening programs should be conducted constantly until the complete elimination of the infection.

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Introduction

As one of the major hygienic problems in the world, malaria is a vector-borne parasitic infection caused by unicellular protozoan parasites of different genera of *Plasmodium*, which is widely distributed around the globe (1,2). Approximately 300 million cases of malaria are reported around the globe, with about one million people, mostly children and pregnant women, losing their lives annually due to the infection (3,4).

This infection is one of the most common but neglected parasitic infections in Iran (3). The total high-risk population amounts to approximately three millions who mostly live in different infection-endemic regions of Iran, including Sistan and Baluchestan, Hormozgan, and Kerman provinces (1). Due to the malaria-control policies of the Iranian Health Ministry since 1988, the annual reported number of malaria cases has decreased, which is indicative of a sharp decline in the incidence rate of the infection. Nevertheless, malaria infection is still considered a vital health issue, particularly in the southern parts of Iran, such as Sistan and Baluchestan (5).

According to several reports, the local environment and more importantly the climate changes of the world could affect the pattern of infectious diseases, such as malaria. The predictive models of global warming indicate a striking development in the distribution of malaria cases in tropical and sub-tropical countries (6,7).

Variations in the patterns of tropical and sub-tropical weather conditions, especially those of temperature and rainfall, are reported to have a decisive effect on increasing malaria infection risk. Some other elements, including changes in the land use pattern and probably the construction of water control systems have also been determined to exert marked effects on the transmission of malaria (7). In addition, the migration of infected refugees from a malaria-endemic country to another country can affect the distribution of the infection so easily in several ways (8). In this regard, infected refugees could transfer the parasites or their new strains to the host country and lead to the outbreak of the infection (8,9). In this respect, the arrival of refugees to Iran from malaria-endemic countries, such as Afghanistan and Pakistan, as well as having long common borders with these countries are among the main reasons for the increase in the incidence rate of malaria cases; therefore, most malaria cases have been imported to Iran. However, the malaria incidence rate in Iran has decreased and is in the pre-elimination phase (10).

Malaria infection is caused by eukaryotic microorganisms from genus *Plasmodium* (*P*), with three major human-specific species, including *P. vivax*, *P. falciparum* and *P. malariae*. Most malaria cases in Iran have been reported to exist in the southeast and south regions, with *P. vivax* as the dominant species (11). These regions in Iran

are considered as the main malaria-endemic zones, constituting about 95% of the total cases (11,12).

Creating a clear image of different aspects of this tropical disease throughout the country is a crucial factor in the national and subnational control of the disease and its elimination. Therefore, the current retrospective study was conducted to assess the status of malaria infection and the evolution of various epidemiological aspects of this infection in Khash, Sistan and Baluchestan Province of Iran, from 1999 to 2016, by analyzing malaria incidence rate within a 25-year period.

Materials and Method

The malaria's data collection in this retrospective study was done within the period from 1999 to 2005 in Khash, a strategic city in the south of Zahedan in Sistan and Baluchestan Province, southeastern Iran ($28^{\circ} 14' N$, $61^{\circ}12' E$), which is very close to Pakistan (Figure 1). Khash has a hot and dry climate with an approximate annual rainfall of 154mm. The temperature in this city ranges from $18^{\circ}C$ in winter to $44^{\circ}C$ in summer. The average humidity ranges from 11.9% in September (summer) to 73.4% in January (winter). According to the Statistical Center of Iran (SCI), the total population of the city is about 130,000 (13).



Figure 1. Map of Iran showing Khash located in Sistan and Baluchestan Province and its borders with malaria endemic countries (Afghanistan and Pakistan) (Created by Arc GIS version 10.2).

The current study was approved by the Ethics Committee of Zahedan University of Medical Sciences, Zahedan, Iran. In this descriptive cross-sectional study, the 20-year trend of malaria was studied in Khash. The officially organized and registered data relevant to malaria were documented from 2001 to 2016 (Figure 2), but the old data were incomplete (1990-2001). Therefore, all officially registered data from 2001-2016, including the records of 802 malaria patients who had referred to Khash Malaria Health Center were analyzed statistically. Each patient received a questionnaire, which included data on sex, age, job, nationality, place of living, duration of the disease, time of slide preparation, kind of slide, sampling time, time of treatment and parasite species. In addition, slide positive rate (SPR), annual blood examination rate (ABER) of malaria and annual parasite incidence (API) were investigated as the factors of the study.

ABER was used to show the number of slides examined per a population of 100 ($ABER = 100$ (the number of slides examined/total population)). Likewise, API was utilized to compare the rate of malaria within

specific geographically distinct human populations ($API=1,000$ (the number of positive slides/total population)). Moreover, SPR represented the number of positive slides per the total number of slides examined (2,14).

The collected data were statistically analyzed by SPSS 20 software. In addition, t-test and chi-square test were conducted to examine the relationship between quantitative and qualitative variables, respectively. In the current study, p-values less than 0.05 ($P < 0.05$) were considered statistically significant for all tests.

Results

The results of the old (1990-2001) and officially registered data (2001 to 2016) showed that over the 26-year period, a total number of 5015 cases of malaria were identified in Khash (Figure 1). Accordingly, the highest number of cases was reported in 1995 with 846 patients and the lowest was in 2016 with one patient. In fact, the number of malaria cases decreased over the course of the 26-year period (Table 1 and Figure 2).

Table 1. Slide positive rate (SPR), annual parasite incidence (API) and annual blood examination rate (ABER) of malaria in Khash, Sistan and Baluchestan Province of Iran, from 1999 to 2016

Year	City population	Prepared slides	Positive slid	ABER	API	SPR
1990-1991	106646	25387	813	23.80	7.62	0.03
1991-1992	105127	27753	348	26.40	3.65	0.01
1992-1993	105216	29527	374	28.06	3.55	0.01
1993-1994	110286	18135	381	16.44	3.45	0.02
1994-1995	110386	7908	465	7.16	4.21	0.05
1995-1996	117198	9064	846	7.73	7.21	0.09
1996-1997	123634	8206	383	6.63	3.09	0.04
1997-1998	122426	4486	224	3.66	1.82	0.04
1998-1999	130939	4480	157	3.42	1.19	0.03
1999-2000	135622	5641	150	4.16	1.11	0.02
2000-2001	139403	5819	71	4.17	0.51	0.01
2001-2002	144639	7169	162	4.95	1.12	0.02
2002-2003	135972	8646	87	6.35	0.63	0.01
2003-2004	142074	9477	150	63.69	1.05	0.00
2004-2005	145450	6442	94	4.43	0.64	0.01
2005-2006	148185	6670	80	4.50	0.53	0.01
2006-2007	152261	3716	103	2.44	0.67	0.02
2007-2008	159077	1920	56	1.20	0.35	0.02
2008-2009	163011	1257	21	0.77	0.12	0.01
2009-2010	162314	1251	14	0.77	0.08	0.01
2010-2011	165219	1112	14	0.67	0.08	0.01
2011-2012	168304	1084	13	0.64	0.07	0.01
2012-2013	170056	978	4	0.57	0.02	0.00
2013-2014	172543	895	3	0.51	0.01	0.00
2014-2015	173146	643	1	0.37	0.005	0.00
2015-2016	175200	534	0	0.30	0	0
Total	3684334	279200	5014	7.578032	19.75	0.001

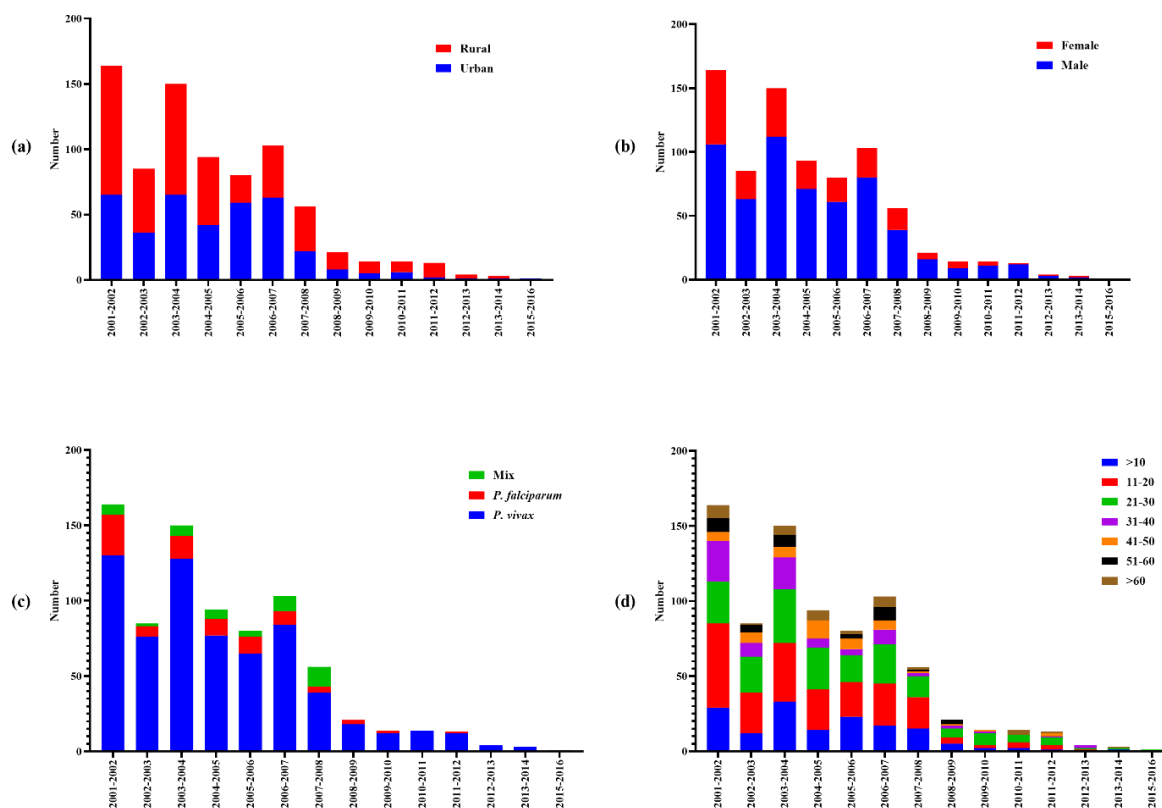


Figure 2. Epidemiological status of malaria in Khash, Sistan and Baluchestan Province of Iran, by district, sex, species and age for 802 patients from 1999 to 2016

According to the officially registered data, 802 cases of malaria have been identified from 2001 to 2016 in Khash. In addition, the highest and the lowest number of cases were reported in 2001 with 162 patients and in 2014 with one patient, respectively. However, there was no positive case reported in 2016. Most of the patients in this study were employees in Khash (212 patients, 26.4%) and the rest of them were self-employed (150

patients, 18.7%), children or students (135 patients, 16.8%), and housewives (127 patients, 15.8%).

A total of 419 patients were Iranian (52.2%) and 383 patients (47.8%) were non-Iranian, including Afghans (323 patients, 40.3%) and Pakistanis (60 patients, 7.5%) (Fig. 3). Thus, the imported cases of malaria from neighboring countries, such as Afghanistan and Pakistan had a strong effect on the outbreak of the disease in this region.

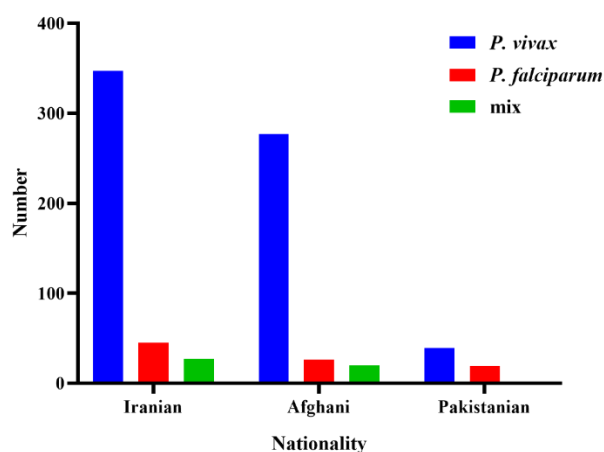


Figure 3. Epidemiological status of malaria in Khash, Sistan and Baluchestan Province of Iran, by nationality and species, for 802 patients from 1999 to 2016

During the 17-year period, 279,200 blood slides were prepared for malaria in Khash, with 5,014 slides found out to be positive. In addition, the values of SPR, ABER and API indices were calculated (Table 1). According to the results, the highest and lowest values of ABER were 63.69 (2003-2004) and 0.30 (2016-2017), respectively.

As Figure 2 and Figure 3 show, the species of the isolated parasites were identified using the parasitological method. *P. vivax* was identified as the main and dominant causative agent of the disease in all infected patients. Out of the 802 malaria patients, 663 cases (82.5%) were infected with *P. vivax*, 90 cases (11.2%) with *P. falciparum* and 49 (6.3%) cases were infected with mixed parasites (*P. vivax/P. falciparum*).

In this study, 426 (53.1%) patients lived in rural areas and the rest inhabited urban districts (Figure 2). Out of 802 infected people recruited in the current experiment, 586 (73.1%) participants were male and 216 (26.9%) were female, only one of which was pregnant (Figure 2).

The age of the patients ranged from 1 to 97 years. The average age of the infected patients was 25 years. The group with the oldest age (> 60) had the highest infection rate (Figure 2).

Inactive screening showed that 567 (70.7 %) patients were diagnosed with malaria while blood samples revealed that only 235 (29.3 %) patients had active infection with fever. In 90% of cases, the date of sample preparation was the same as that of slide examination due to the long distance of the villages from the sampling site or the coincidence with official holidays. Nevertheless, treatments started as soon as a diagnosis was made for all patients.

According to the incidence pattern of malaria in different months, the outbreak of the disease was more prevalent in the period from April to September than in other months of the year (Figure 4). Moreover, as Figure 4 shows, *P. vivax* was the most prevalent species of malaria from April to September.

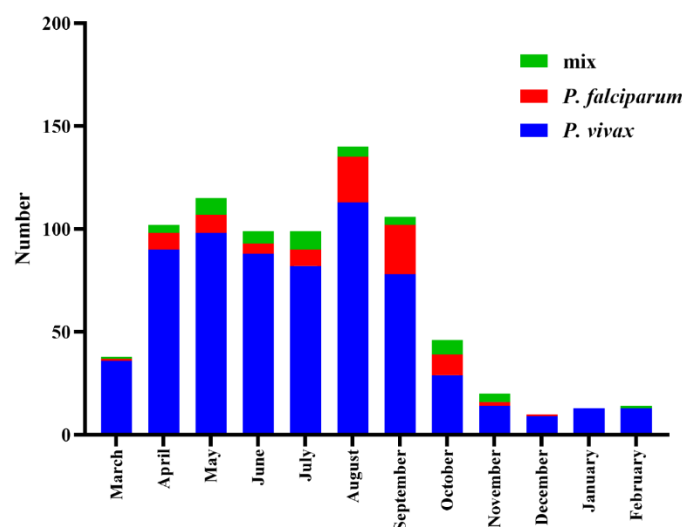


Figure 4. Epidemiological status of malaria in Khash, Sistan and Baluchestan Province of Iran, by month and species, for 802 patients from 1999 to

2016

Discussion

The present research has been the first retrospective epidemiological study to investigate malarial morbidity from 1999 to 2005 in Khash, south of Zahedan, Sistan and Baluchestan province, southeastern Iran. According to the registered statistics, the decreasing trend of malarial infections over the past 17 years has been accompanied by an increase in the return of refugees, especially Afghans to their country. This steady decline in the number of the cases of malaria due to the return of refugees to their countries has been reported in various studies, such as those carried out in Kuwait, Bahrain, Pakistan and many parts of Iran, following the decline in Afghan immigration. The results of these studies were consistent with those of the present study (8,15,16). However, in most studies conducted in Iran, the number of Afghan malaria-infected patients was higher than the number of Iranian patients, indicating

that most of the malaria cases were imported from outside Iran (16).

In the present study, 73% of patients were male, indicating that the malaria infection rate was lower in female patients than in male ones. Some other studies supported the findings of the present study. Zayeri *et al.* reported that about two-thirds of 65000 malaria cases in Sistan and Baluchestan province were male (17). Quite clearly, sex does not affect sensitivity or resistance to malaria infection straightly and naturally, but patients' occupation or type of body coverage, such as using female Islamic veil could be effective in the occurrence of the infection (17). Furthermore, men are probably more exposed to mosquito bites due to their social activities as well as their presence in outdoor work environments. Moreover, according to the present study, the higher incidence rate in male employees and especially in those aged 21-30 confirmed the discussed

hypothesis. Therefore, given that the risk of being infected with malaria was the same in both sexes, prevention and treatment strategies could be applied in the same way to both male and female people (18). Some other studies confirmed the findings of the current experiment with the highest incidence rate of malaria occurring in the age group of 21 to 30 (15).

The results of this study showed that most infected patients lived in rural areas of Khash; hence, rural health centers should be more active in identifying, controlling, and educating the high-risk people. The reasons for the reduction in the number of positive cases of the disease in urban districts are the high presence of welfare indicators and more importantly the low volume of stagnant waters as larval habitats.

According to the documented data, *P. vivax* has been the dominant *Plasmodium* species of malaria infection in Iran from 1941 to 2006 (11). In the present study, most of the identified cases were related to *P. vivax*. Some other studies conducted in Iran have reported similar findings (11,19,20). Moreover, the findings of the present study were compatible with those of the study by Mendis *et al.* in Africa (21). In the same regard, Fekri *et al.* reported that *P. vivax* was the major *Plasmodium* species in Jask County, located in the southeastern corner of Iran (22). Given that *P. vivax* can recur due to hidden hypnozoites persisting in the patient's liver and then can result in severe relapses (23-26), the related cases should be identified and treated thoroughly (27).

Although active screening plays a significant role in identifying patients with malaria, most patients were

identified by passive screening in the present study. The use of highly experienced health experts in identifying, screening and treating malaria in the active surveillance method demonstrates the high motivation of malaria control program and the existence of an effective care system (28,29).

According to the current study, the API declined from 7.62 per thousand in 1990 to 0.005 per thousand in 2015, with the highest infection rates observed from 1990 to 1999. These results were consistent with those of other studies, which revealed a decrease in the API and infection rates in different cities of Iran (16,30,31). Furthermore, the findings of the present study showed that the SPR index declined from 0.03 % in 1990 to 0 in 2015, which was consistent with the country's disease trend. The trend of the indices studied in the present study was similar to that of other studies conducted in different parts of Iran.

Interestingly, the results of the present study indicated that the most positive and the least positive cases were in summer and in winter, respectively. However, these data were consistent with those of other studies conducted in Iran, in which the most positive cases were reported in spring (32). It was found out in the present study that the most prevalent period of malaria outbreak was from April to September. The findings of this study were consistent with those of the study by Ostovar *et al.*, in which malaria epidemics happened mainly from July to October (35). Another study in Kerman, southeastern Iran, reported that the highest number of malaria cases happened in October.

Some research showed that the highest number of malaria cases occurred in autumn and in summer (33).

Various conditions, such as geographical and climatic changes, irrigation systems, environmental changes, population movements especially from neighboring countries, transportation, structure of houses, illiteracy, and distance among villages as well as economic and social problems have been reported as factors leading to malaria transmission and its high prevalence in Iran (34). Although Iran is on the verge of the malaria elimination phase, the most serious problems are Iran's long borders with malaria-endemic countries (Afghanistan and Pakistan) and illegal immigrants coming from these countries to Iran (35). In addition, the results of this study showed that one of the main reasons for malaria outbreak was the imported cases of infections in Khash. The cases of malaria in this region imported from the neighboring countries, such as Afghanistan and Pakistan had a strong effect on the outbreak of malaria. Therefore, it is recommended that epidemiological indices be evaluated at national and subnational levels in the region, including Iran, Afghanistan and Pakistan to develop effective public health programs. The results of another study by Ostovar *et al.* were consistent with those of the present research since they found out that the main sources of various cases of malaria epidemics in Sistan and Baluchestan province were imported from Pakistan and Afghanistan (35).

According to the results of data analysis in the current study, a few strategies can be formulated for controlling infection rates in this region including

developing health education and prevention strategies for high-risk people and health personnel, controlling country borders in terms of immigrants' health especially in the eastern borders of the country (Afghanistan and Pakistan), detecting and treating malaria cases on time by making use of skilled experts and employing seasonal workers in accordance with the sanitary rules for the control of epidemic and contagious diseases.

Conclusion

In conclusion, the findings of the present study revealed that although malaria outbreak decreased significantly in Khash, it could still be a serious health problem in this region. Given the climatic conditions of the city and the increase in the return of refugees, the risk of malaria outbreak must be considered continually, with control programs continued constantly until the elimination of the infection. Therefore, malaria control programs and interventions can reduce the risk of infection transmission significantly. Moreover, control interventions should continue constantly until complete elimination of the infection.

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