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A Twenty- Four Years Study on the Malaria Trend in Southwestern Iran (1995-2018)

Hamid Kassiri[1]*, Iman Khodkar[2], Vali Safari[3], Masoud Lotfi[4]

[1] Department of Medical Entomology and Vector Control, School of Health, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
[2]Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
[3] Communicable Diseases Department, Gotvand County Health Center, Dezful University of Medical Sciences, Dezful, Iran.
[4] Abdanan Health Center, Ilam University of Medical Sciences, Ilam, Iran.

ABSTRACT

Iran has attained more than 96 percent reduce in indigenous malaria cases, and is classified in the elimination phase. Almost all malaria transmission happens in the southeastern regions of the country. Most of autochthonous malaria cases in Iran are due to Plasmodium vivax. In Iran, there is a significant decrease in disease burden; however, the overall trend of malaria prevalence is not investigated or well-documented in different localities. Hence, this study is aimed to investigate the epidemiologic features of malaria cases in Gotvand County from 1995 until 2018. This descriptive cross-sectional survey investigates malaria-related factors during a 24-year period of time based on existing data and information extracted at Gotvand's Health Services Center during 1995-2018. Malaria infected cases were confirmed by direct microscopy and treated with normal antimalarial agents. For each positive case a questionnaire containing demographic and epidemiologic data was filled out. Data analysis has been done by SPSS software. The obtained data from the reviewed forms included 46 positive cases in Gotvand County. The total number of malaria cases has been decreased in 1995 and 2012 compared to 1998. The highest (23, 5 and 5) cases of malaria were occurred in 1995, 1996 and 2006, respectively. The majority of cases (67.4%) were male. Most cases of malaria were due to P. vivax (97.8%) followed by P. falciparum (2.2%). About 69.6% of cases were Iranian and 30.4 % non-Iranian (Afghan). Most cases of the disease (32.7%) were in age group of 20-29 years old. The highest number of infections was seen in the occupational group of workers with 19 (41.3%) cases. With respect to suitable environmental conditions for transmission of malaria in this area, necessary plans should be conducted in Khuzestan Province to prevent the reoccurrence of malaria in this county.

Keywords: Malaria, Epidemiology, Trend, Prevalence, Iran.

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Corresponding author: Hamid Kassiri
E-mail ✉ Hamid.Kassiri @ yahoo.com
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INTRODUCTION

Malaria is an important problem affecting 300–500 million people in the world and causes nearly 2.7 million deaths yearly. At present, no vaccine protects against malaria, and resistance to anti-malaria drugs is spreading and increasing geographically. Meanwhile, anti-malarial drugs are costly and mostly uneconomical to low-income countries [1].

Malaria is the major parasitic infection in many tropical and subtropical areas [2]. The incidence of malaria has been continually decreasing in Iran from 16747 to 632 through 2001 to 2015, with the most of patients imported. Malaria cases in the country have reached less than 100 cases in 2017 and currently, 90% of malaria cases are imported from Afghanistan and Pakistan. The most cases affected with malaria are reported from southeast of Iran in Sistan and Baluchestan, Kerman, and Hormozgan Provinces. Iran is now concentrated on malaria elimination, and the methods performed are

indoor residual spraying, larviciding, using insecticide - impregnated bed nets, rapid diagnosis and no fees access to anti malaria - medicines through the health service systems, enhanced surveillance, integrated vector management, and sleeping in the long-lasting insecticide-treated nets. Iran has made salient progress in reducing its malaria burden since the early 1990s and has a national objective to interrupt *P. falciparum* transmission by the end of 2015 and to eliminate malaria by 2025. Seven anopheline species are vectors of malaria in Iran namely *Anopheles stephensi* Liston, *A. superpictus* Grassi (s. l.), *A. culicifacies* Giles (s. l.), *A. dthali* Patton, *A. fluviatilis* James (s. l.), *A. maculipennis* Meigen (s. l.) and *A. sacharovi* Favre. *A. superpictus* (s. l.), *A. maculipennis* (s. l.) and *A. sacharovi* are pertinent across the central, northern and northwestern Iran and *A. stephensi*, *A. culicifacies* (s. l.) and *A. fluviatilis* (s. l.) are pertinent in south of Iran [1-9]. *A. sacharovi*, *A. dthali,* and *A. stephensi* are reported as definite vectors of malaria in Khuzestan Province [10].

Malaria is one of the most important and costly infectious diseases worldwide. Despite long-term control programs by the World Health Organization (WHO), drug resistance to this disease and the number of insecticide-resistant species of mosquitoes are increasing in different parts of the world, specifically in African tropical countries [11]. Several species of mosquitoes that carry arboviruses and affect people showed high rates of abundance in anthropogenic ves-sels and various types of capture [12]. Malaria is an acute or sub-acute febrile infectious disease, caused by inoculation of protozoan parasites of *Plasmodium* and transmitted by infected female *Anopheles* bites. Other malaria transmission manners include organ transplantation, blood transition, and transfer through the placenta. The malaria parasites grow and propagate in the liver and red blood cells [13, 14].

Malaria is caused by four protozoan species of the genus *Plasmodium* including *P. falciparum*, *P.vivax*, *P. malariae*, and *P. ovale*. In this regard, *P. vivax* and *P. falciparum* account for the majority of malaria cases, the latter causing the most severe form of malaria. Africa has the highest rate of *P. falciparum* infection; however, *P. vivax* has a broader geographical distribution than *P. falciparum* [15]. In the light of the emerging epidemiological data, *P. knowlesi* should be added to the four above-mentioned pathogenic agents, as the fifth etiological species of malaria [16].

Malaria has become a significant public health issue in Iran due to relatively good climatic and geographical conditions in the south and southeast, its adjacency to Afghanistan, Pakistan and Iraq, and uncontrolled migration from these countries. Before implementation of malaria control in Iran, it affected 4-5 million individuals per year, out of which 30% did not survive [17, 18]. It has incurred huge social and financial burden so far.

Khuzestan Province, due to its proximity to Iraq, a Free Trade Zone, its special geographical characteristics and situation, climatic and social conditions, agricultural and being economic center and an immigration zone in Iran is at risk of malaria. Gotvand, a county in Khuzestan Province (southwestern Iran), is under the malaria-elimination program. There are few annual reported cases of malaria in this county. Due to the lack of adequate information about the disease trend in recent years in Gotvand, we intended to investigate the trend of malaria in this county in the past 24 years (1995-2018) to evaluate the health surveillance system and malaria-control programs. According to the results of this study and the existing conditions and equipment, correct decisions can be made to implement the malaria-elimination program by regional authorities.

MATERIALS AND METHODS

Gotvand County (32°15′05″N 48°48′58″E) is a county in Khuzestan Province in Iran. At the 2016 census, its population was 65468 (51.6% males and 48.4% females). The area of this county is 966 km^2. Literacy rate is 83.1%. About 68.2% of the population lives in the citied and the rest are in the villages. The climate of this county is hot and dry for most of the year.

A cross-sectional descriptive study was carried out in Gotvand County between 1995 and 2018 years. Malaria surveillance was done using two main methods: passive or active case finding. The data were collected with questionnaire including some demographic-epidemiologic details such as gender, age, nationality (Iranian

or non- Iranian), causative agent (*P. vivax*, *P. falciparum*), and other details. The blood samples from all suspicious malaria subjects were taken by sterile lancet. Thick and thin blood smears were prepared for the microscopic examination for all study participants. Thick and thin peripheral blood smears were prepared according to a standard method. The smears air-dried, and then only the thin film was fixed using methanol. All slides were stained with 10% Giemsa and examined at 100x magnification with oil immersion in order to detect parasite by a trained microscopist. All data were analyzed using SPSS software, version 18.

ETHICAL CONSIDERATIONS

This study has been ethically approved by the research ethics committee of the Ahvaz Jundishapur University of Medical Sciences, Iran. Ethical subjects (comprising twice publication and/or submission, plagiarism, informed consent, supplying data and/or falsification, abundance, confidentiality of the records, misbehavior, and so on) have been entirely noticed by the authors.

RESULTS

In general, 46 cases with malaria have been recorded in Gotvand in this mentioned period (1995-2018). The highest incidence rate was observed in 1995 with 23 cases, followed by a decline and reached zero between 2012-2018 (Figure 1). The annual parasitic incidence from 1995 to 2018 was 3.8 per 100000 populations. According to the results, 31 patients (67.4%) were male and 15 (32.6%) were female; the highest number of patients was in the age range of 20-29 years with 15 patients (32.7%) and the lowest was over 60 years old with one patient (2.2%); 32 patients (69.6%) were Iranian and 14 patients (30.4%) were Afghan; 45 cases (97.8%) were infected by *P. vivax* and only one case was infected by *P. falciparum*. In addition, 45.7% of the cases were diagnosed by an active method. In this type of care, the populations at the risk were screened in terms of symptoms and history of malaria in the past month through going house to house by the health surveillance staff. The peripheral blood samples of the suspicious cases were taken and examined with a rapid diagnosis test kit or by direct microscopic examination. Moreover, 54.3% of the patients were diagnosed using the passive method. In this method, the populations at risk were provided with diagnosis and treatment equipment to give them access to health surveillance services. In terms of occupation, the majority of the patients were workers (41.3%) and students (19.6%) (Tables 1 and 2). Despite high variations in different months of the year, the highest incidence rate was observed in August with 21.7% and October with 17.4%, and the lowest rate in February and March with 0% (Figure 2). The epidemiological status of malaria disease between 2001 and 2014 in the southwest of Iran, Khuzestan Province are provided in figures 3-7.

Table 1: Distribution of malaria cases based on gender, nationality, and age group in Gotvand County, southwestern Iran (1995-2018)

Years	Gender		Nationality		Age Group						
	Male No (%)	Female No (%)	Iran No (%)	Afghan No (%)	1-9 No (%)	10-19 No (%)	20-29 No (%)	30-39 No (%)	40-49 No (%)	50-59 No (%)	>60 No (%)
1995	10(43.5)	13(56.5)	23(100)	0(0.0)	9(39.1)	7(30.4)	3(13.1)	4(17.4)	0(0.0)	0(0.0)	0(0.0)
1996	4(80.0)	1(20.0)	5(100)	0(0.0)	1(20.0)	0(0.0)	2(40.0)	0(0.0)	0(0.0)	1(20.0)	1(20.0)
1997	2(66.7)	1(33.3)	3(100)	0(0.0)	0(0.0)	2(66.7)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
1998	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
1999	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2000	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2001	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2002	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2003	2(100)	0(0.0))	0(0.0)	2(100)	0(0.0)	0(0.0)	2(100)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2004	1(100)	0(0.0)	0(0.0)	1(100)	0(0.0)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2005	1(100)	0(0.0)	0(0.0)	1(100)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

2006	5(100)	0(0.0)	0(0.0)	5(100)	0(0.0)	0(0.0)	3(60.0)	1(20.0)	1(20.0)	0(0.0)	0(0.0)
2007	1(100)	0(0.0)	0(0.0)	1(100)	0(0.0)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2008	2(100)	0(0.0)	0(0.0)	2(100)	0(0.0)	0(0.0)	1(50.0)	0(0.0)	1(50.0)	0(0.0)	0(0.0)
2009	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2010	1(100)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(100)	0(0.0)
2011	2(100)	0(0.0)	0(0.0)	2(100)	0(0.0)	0(0.0)	1(50.0)	0(0.0)	1(50.0)	0(0.0)	0(0.0)
2012	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2013	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2014	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2015	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2016	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2017	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2018	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Total	31(67.4)	15(32.6)	32(69.6)	14(30.4)	10(21.7(	10(21.7)	15(32.7)	5(10.7)	3(6.5)	2(4.3)	1(2.2)

Table 2: Distribution of malaria cases based on occupation, species of parasite and type of surveillance in Gotvand County, southwestern Iran (1995-2018)

Years	Occupation						Species of *Plasmodium*		Type of Surveillance	
	Baby No (%)	Student No (%)	Housewife No (%)	Worker No (%)	Rancher No (%)	Soldier No (%)	*falciparum* No (%)	*vivax* No (%)	Passive No (%)	Active No (%)
1995	5(21.7)	8(34.8)	6(26.1)	2(8.7)	2(8.7)	0(0.0)	0(0.0)	23(100)	10(43.5)	13(56.5)
1996	1(20.0)	0(0.0)	1(20.0)	1(20.0)	1(20.0)	1(20.0)	0(0.0)	5(100)	2(40.0)	3(60.0)
1997	0(0.0)	1(33.3)	1(33.3)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	3(100)	0(0.0)	3(100)
1998	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
1999	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2000	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2001	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2002	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2003	0(0.0)	0(0.0)	0(0.0)	2(100)	0(0.0)	0(0.0)	0(0.0)	2(100)	2(100)	0(0.0)
2004	0(0.0)	0(0.0)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)	1(100)	1(100)	0(0.0)
2005	0(0.0)	0(0.0)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)	1(100)	1(100)	0(0.0)
2006	0(0.0)	0(0.0)	0(0.0)	5(100)	0(0.0)	0(0.0)	1(20.0)	4(80.0)	5(100)	0(0.0)
2007	0(0.0)	0(0.0)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)	1(100)	1(100)	0(0.0)
2008	0(0.0)	0(0.0)	0(0.0)	2(100)	0(0.0)	0(0.0)	0(0.0)	2(100)	1(50.0)	1(50.0)
2009	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2010	0(0.0)	0(0.0)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)	1(100)	1(100)	0(0.0)
2011	0(0.0)	0(0.0)	0(0.0)	2(100)	0(0.0)	0(0.0)	0(0.0)	2(100)	1(50.0)	1(50.0)
2012	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2013	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2014	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2015	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2016	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2017	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
2018	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Total	6(1.3)	9(19.6)	8(17.4)	19(41.3)	4(8.7)	1(2.2)	1 (2.2)	45(97.8)	25(54.3)	21(45.7)

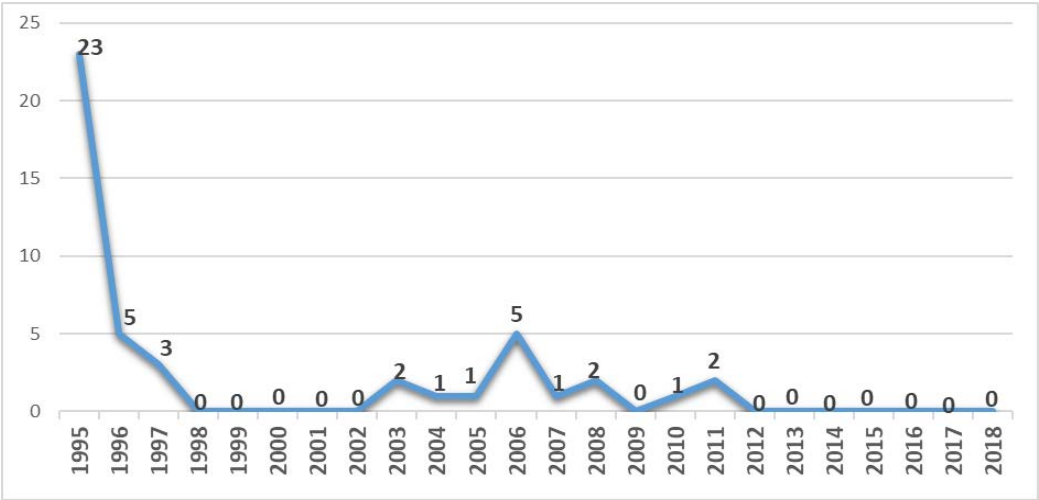

Figure 1: Distribution of malaria cases based on year in Gotvand County, southwestern Iran (1995-2018)

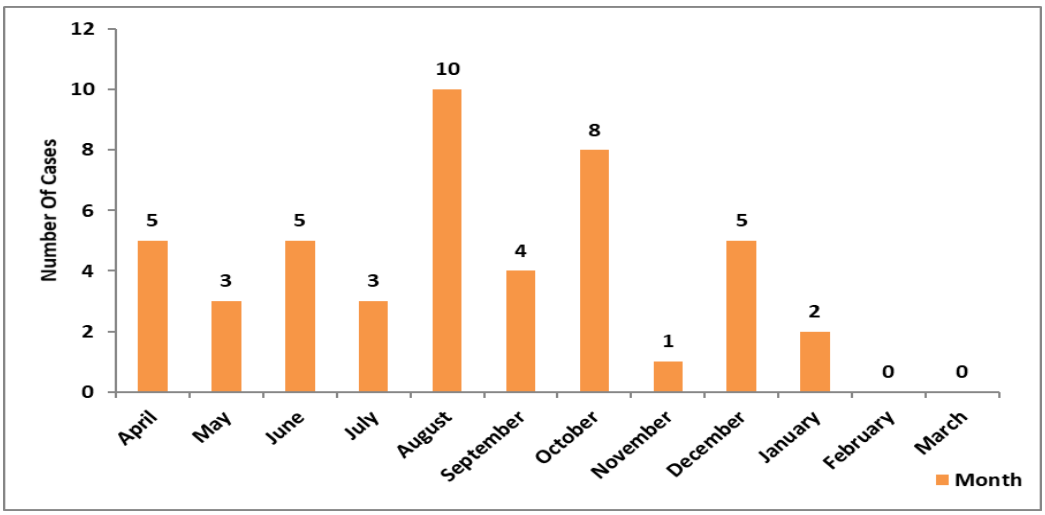

Figure 2: Distribution of malaria cases based on month in Gotvand County, southwestern Iran (1995-2018)

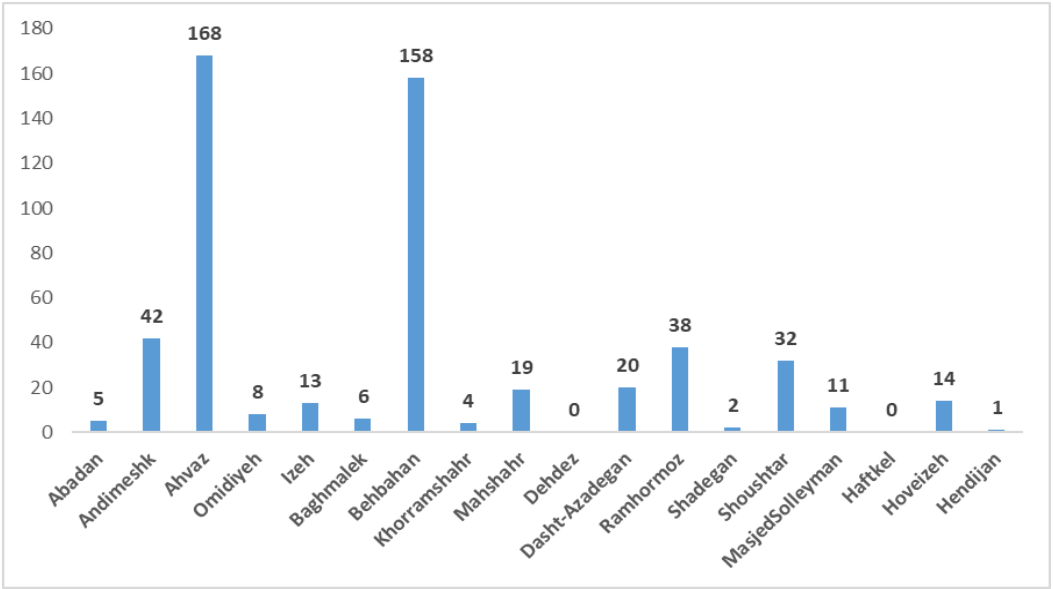

Figure 3: Distribution of malaria cases based on various counties in Khuzestan Province, southwestern Iran (2001-2014)

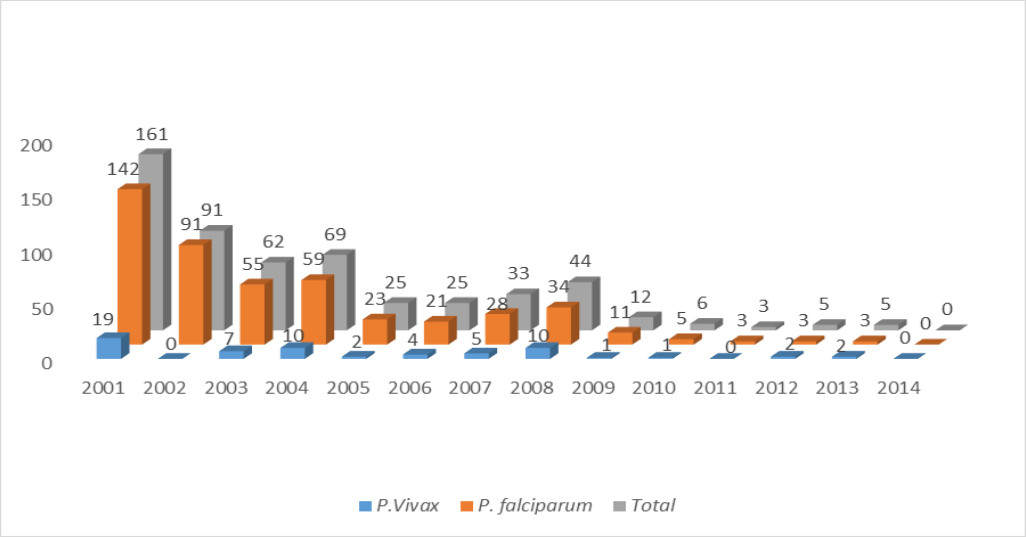

Figure 4: Distribution of malaria cases based on parasite species in Khuzestan Province, southwestern Iran (2001-2014)

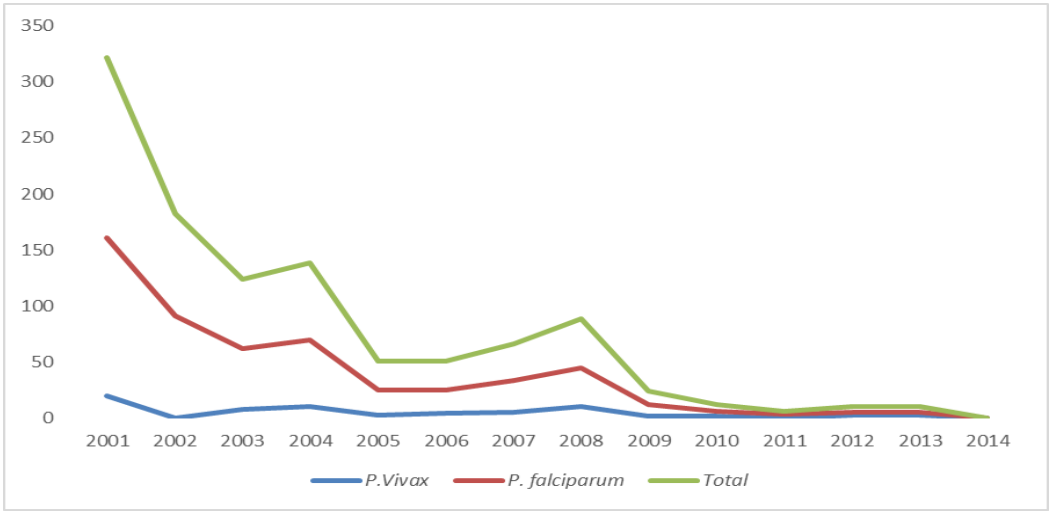

Figure 5: Trend of Malaria disease in Khuzestan Province, southwestern Iran (2001-2014)

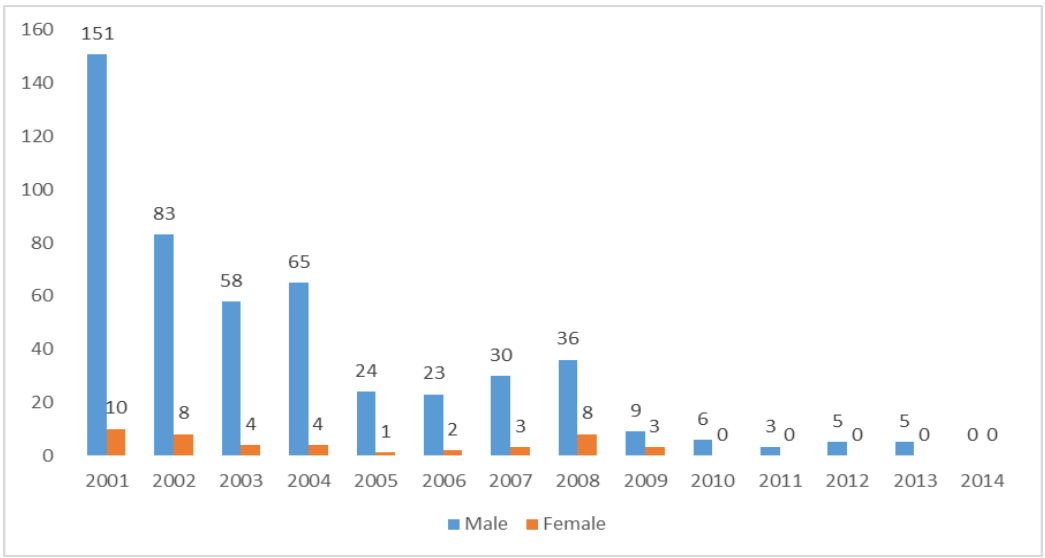

Figure 6: Distribution of malaria cases based on gender in Khuzestan Province, southwestern Iran (2001-2014)

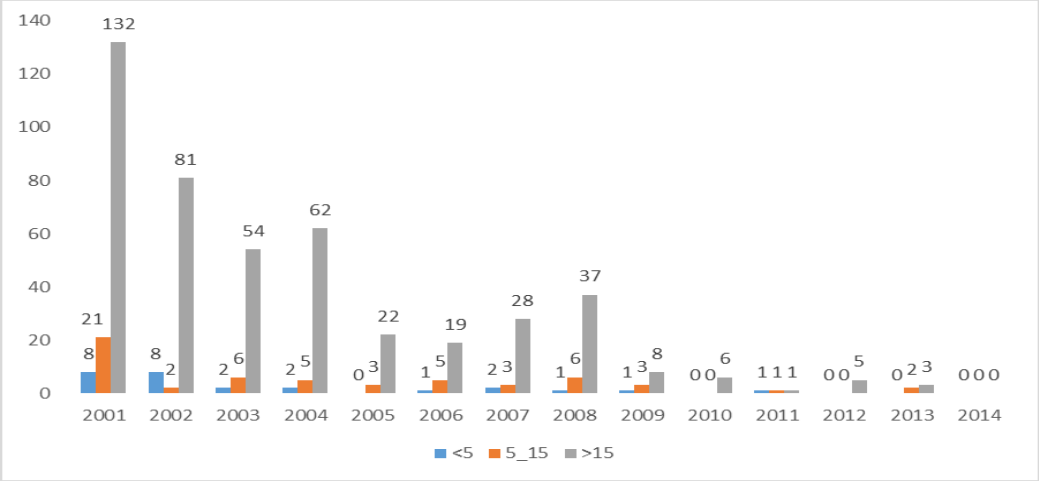

Figure 7: Distribution of malaria cases based on age group in Khuzestan Province, southwestern Iran (2001-2014)

DISCUSSION:

Nearly half of the malaria cases in Gotvand County in this period were reported in 1995. This can be due to the relatively high rainfall rate in this year, which provided a suitable condition for creation of mosquito larval habitat. Moreover, temperature reduction, which results in the abundance of vectors, can be another reason for this high incidence rate of malaria in this year. An enormous increase in the incidence rate in the neighboring countries, such as Afghanistan and Pakistan, also plays a role in this regard.

In this study, males accounted for 67.4% of all reported malaria cases. According to the reports by the Iranian Disease Management Center, males have been more prone to malaria than females in recent years [9]. This finding was also consistent with other studies with other parts of the country, such as Larestan (77%), Mazandaran (88.4%), Hamadan (80.6%) and Isfahan (93.6%) [19-22]. In a study conducted by Norouzinejad et al. in Iran (2011-2014), malaria was most common in men, with only 18.5% of cases occurring in women over the four-year study [23].

Although gender has no direct impact on the sensitivity or resistance to malaria, it may have indirect effects through occupation or clothing. The greater social activities of men and their presence outdoors expose them more to mosquito bite and more affected by malaria. Regarding that both genders are at similar risk of malaria infection, the same prevention and treatment approaches should be employed [24].

In terms of age, people between 9-20 years accounted for the majority of malaria cases in this period. This result is consistent with other epidemiologic studies on malaria in Iran [25, 24]. In the years with a local transmission in a focus, younger people accounted for the majority of infected cases. As a result, the incidence rate of malaria was higher in older people in the following years of the study period. In the years with high incidence among Afghan citizens, the incidence rate significantly increased in older people and reduced in other age groups. During the study period, malaria distribution varied by nationality. In general, all reported 31 cases between 1995 and 1997 were Iranian and after five years without any new case of malaria (1998-2002), all cases in the following six years (2003-2008) were Afghans living in Gotvand. It means that local transmission of the disease can be terminated through enhanced control measures among Iranian citizens and lowering the incidence of malaria as well as prevention of illegal migration.

As it was expected, *P. vivax* accounted for the majority of parasites, which is consistent with results from other studies in other parts of the world. The dominant malaria parasite in Iran is *P. vivax* [25]. In recent years, the incidence rate of *P. falciparum* infection has significantly reduced [26]. This reduction versus the increased prevalence of *P. vivax* in a region indicates an increase in local transmission of

malaria. Regarding that *P. vivax* can relapse, because of the presence of hypnozoites, these cases must be diagnosed and completely treated. According to epidemiological classification proposed by the WHO, the reported cases of malaria are categorized as, autochthonous, imported, introduced, relapse and unknown. Based on the WHO classification, the malaria endemic regions across the world are divided into stable and unstable areas. The dominant parasites in unstable and stable regions are *P. vivax* and *P. falciparum*, respectively. In this classification, Iran is among regions with unstable malaria with *P. vivax* as the dominant parasite [23].

According to the results, over the study period of 24 years, 45.7% of cases with malaria were diagnosed using the active case finding method. The patients can be diagnosed and treated timely through empowering those involved in malaria-elimination program, taking samples of suspicious people at proper time, specifically by clinical specialists and health care providers, and providing an efficient surveillance system. In unstable areas, the incidence of malaria is generally associated with high fluctuations in different months and years. In the current study, the downward and upward trends in the incidence rate of malaria in Gotvand County were correlated with economic, climatic, control program and migration conditions. The seasonal and climatic changes, as well as changes in rainfall rate and pattern may result in changes in larval breeding places which, in turn, affect seasonal and annual changes in the incidence rate of malaria. During the study period, there were high fluctuations in different months of the year with the highest rate in August and October. On the other hand, no infection was reported in February and March.

Among the factors that affect malaria transmission, the seasonal variation has a direct role [28]. Regarding the climatic conditions of the Gotvand and the presence of vector mosquitoes, there is a high potential for disease transmission cycle in this county. As a result, it is required that the malaria control programs, such as the disease report system, malaria diagnosis laboratories, case findings, timely and immediate treatment, and vector control measures, if needed, continue permanently. It is recommended to provide local health surveillance staff involved in malaria control program with adequate educational programs to enable them in timely diagnosis of clinical symptoms (*e.g.* fever in foreign citizens) to refer the patients to malaria diagnosis centers. The incidence rate of malaria reduced in the past 24 years in Gotvand, which can be attributed to changes in climatic conditions and rainfall rate, and improved health care services through control and prevention measures. Regarding that the majority of malaria cases in this region were imported by migrants, the health surveillance services should be improved through early diagnosis and treatment. Moreover, the conduction of different studies is essential to determine the fauna and biology of vector *Anopheles*, identify their habitats and eliminate them.

CONCLUSIONS

Due to the specific climatic status in Gotvand County, the optimum circumstances exist for the growth of mosquitoes as the insect's malaria vectors; thus, the risk of malaria epidemics should be considered constantly. Therefore, malaria control programs such as screening and treatment for patients as well as strengthening the intersectoral cooperation and improving educational activities should be continued until disease elimination. Meanwhile, the negative effect of malaria epidemics in our neighboring country (Pakistan) and the role of illegal immigrants should not be neglected.

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CONSENT FOR PUBLICATION

Not applicable.

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