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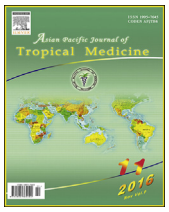

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Epidemiological status of malaria in Iran, 2011–2014

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ABSTRACT

Objectives: To aim to determine the status and epidemiological aspects of malaria in Iran in favour of gaining a better understanding of the national control of malaria.

Methods: This epidemiological study examined the status of malaria from 2011 to 2014 in Iran. Data were collected from the Ministry of Health's protocol for controlling and eliminating malaria, which is currently in use. This malaria information reporting system is automated in all Iranian provinces and cities, and all information is submitted online to the center for communicable disease control in the Ministry of Health. Information about malaria is available for researchers to evaluate.

Results: The incidence rates decreased from 2011 to 2014. There were 4.76, 2.12, 1.80, and 1.59 per 100 000 people, respectively from 2011 to 2014. During the four-year period (2011–2014), the highest numbers of cases occurred in those aged 16–25 years, by age, and in men, by sex. Most of the cases were workers and located in rural areas. An average 52.58% of cases were Iranian. The highest incidence rates from 2011 to 2014 were located in Sistan and Baluchestan province. There were 89.94, 43.9, 38.3, and 30.66 per 100 000 people. The highest numbers of malaria cases were recorded in the cities Sarbaz, Nickshahr, and Chabahar in Sistan and Baluchestan province and Bandar Abbas, Bandar Jask, and Bandar Lengeh in Hormozgan province. During the four-year period, 57.05% of cases were caused by imported factors. The majority of cases were related to the trophozoite lifecycle of parasites. Regarding surveillance, there was inactive care in the majority of cases. Vivax malaria was the most prevalent.

Conclusions: Despite the recently declining trend in reported cases, the expansion of local transmission, especially in areas with cross-border travel, is very worrying. Improved malaria control interventions can be effective for elimination of malaria in Iran; these can include programs to control border travel and focused interventions for high incidence areas and high-risk groups such as rural residents, men, workers, and people <35 years old.

1. Introduction

Malaria is a global tropical and semi-tropical parasitic disease that is considered a major public health problem [1]. Malaria is a vector-borne disease caused by protozoan parasites that belong to the genus *Plasmodium*. The parasites are transmitted from person to person by infected female anopheles mosquitoes [2]. According to the 2013 World Malaria Report by the World Health Organization (WHO), there were 207 million cases of malaria worldwide (uncertainty interval, 135–287 million) and 627 000 deaths caused by malaria in 2012 [3]. Of the estimated 3.4 billion people that are at risk of malaria, 1.2 billion are at high risk. In high-risk areas, more than one malaria case occurs per 1000 population [4].

This disease remains an important cause of mortality and morbidity in many parts of the world, and it could have adverse health and socioeconomic impacts on the population [5]. The total international and domestic funding committed to malaria control was estimated to be US $2.5 billion in 2012, which is substantially less than the amount that will be needed to reach

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the global targets [6]. Iran has a population of more than 75 million people and is located in West Asia. It covers an area of approximately 1.648 million km^2, of which mountainous regions and arid deserts comprise 50% and 25%, respectively [7].

The first reports of malaria in Iran date back to 1921, when cases were found along the northern borders with Azerbaijan and the Caspian Sea [8]. In 1924, more than one-third of Iran's 13 million people had contracted malaria, and it was considered a deterrent to the economic development of the country [9,10]. Now, after more than 50 years of control interventions against malaria in Iran starting in 1956, malaria is still considered an acute health concern, particularly in the south and southeast of Iran [1]. In the Eastern Mediterranean Region, the Islamic Republic of Iran and Saudi Arabia are in the elimination phase. The number of indigenous cases decreased from 1710 in 2011 to 787 in 2012 (consisting of 756 indigenous, 12 introduced, and 19 suspected relapsing cases) [11]. Therefore, malaria is still prevalent in many areas [1,12].

The implementation of a regional strategic plan for controlling malaria is one of the most important reasons for the pre-elimination stage of malaria in Iran. WHO recommendations, including preventing the resettlement of pollution in malaria-free zones and eliminating the disease in areas where malaria transmission, are highly limited. Therefore, elimination of the disease and prevention of the return of malaria (re-introduction) in Iran, which is an endemic area, are of high importance. The elimination of the disease and prevention of the return of malaria (re-introduction) in a country where the disease is endemic is optimal. Therefore, three operational-technical approaches and four backup strategies to eliminate malaria have been proposed. The major strategies include: (1) Improving access to prompt and effective treatment of malaria; (2) Improving access to preventive services by strengthening integrated vector management (IVM); (3) Strengthening the disease surveillance system with an emphasis on appropriate and timely responses. And the backup strategies include: (1) Strengthening and developing a monitoring and evaluation system of interventions for malaria elimination; (2) Conducting applied research; (3) Using the capacity of all stakeholders for malaria elimination; (4) Building human capital capacity and mobilizing resources for malaria elimination [13].

Although previous efforts have reduced the disease burden in various areas, the malaria elimination program has faced several challenges because Iran borders malaria-prone countries. If malaria is not eliminated, economic development will be threatened, and tourism and cultural-scientific and commercial exchange will be restricted in addition to the consequences of the disease burden. Hence, it is essential for policy makers to focus all of their efforts on malaria elimination. Understanding the aspects of the disease throughout the country is important for the national control of malaria [13]. This study aimed to evaluate the status of malaria and determine the various epidemiological aspects of the disease in Iran.

2. Materials and methods

This epidemiological study examined the status of malaria in Iran from 2011 to 2014. In this study, the data were collected from the Ministry of Health's protocol for controlling and eliminating malaria, which is currently in use. To find patients, we initially collected blood samples from people with suspected malaria. The samples were collected from health houses, urban and rural community health centres, public and private hospitals, and patio tables. In the patio table method, blood samples are collected by health professionals from people who have a fever or prior history of malaria to discover parasite carriers. Sampling was performed by health centre workers and disease control experts.

The samples were sent to laboratories under the supervision of the city health centres. The results of the sample analysis (active or passive) were submitted online to the center for communicable disease control in the Ministry of Health and Medical Education on a daily basis, within 12 h from sampling. The results of the analysis for active cases as well as the full details of the patients were reported monthly to the center for communicable disease control in the Ministry of Health by the unit fighting against diseases at the city health centre. The variables in this study included sex, age, place of residence, nationality, occupation, province, city, month, epidemiologic classification of cases, the parasite life stages, type of care, type of parasite, disease symptoms, travel history to contaminated areas, history of malaria for the past 12 months, history of malaria for the past 12 months, history of blood transfusion, intensity of malaria, treatment outcome, type of service, and result of the disease.

In this research, the data of intervention programs of CDC Iran's ministry of health and medical education has been used. All the ethics have been applied.

Malaria surveillance was conducted using two main methods: passive or active case finding (Table 1).

Table 1

Current malaria surveillance in Iran, including passive and active case finding.

	Passive surveillance	Routine	Active surveillance (Active foci)
Target group (for detection of blood smear)	People with fever, recent malaria cases (for follow up)	Suspected malaria cases, infected people in the interval between two case finding activities, foreign people (Afghani & Pakistani)	Persons who feel ill, were infected in the last month, with history of malaria, from other countries (Afghani & Pakistani)
Target regions	Nationwide	Households in the villages, mobile villagers in local malaria regions	Active foci (in urban areas and villages that have >50 households, around the reported cases; in villages with <50 households, the entire village)
Service centres	Malaria labs, health houses, hospitals	Health workers, mobile malaria team	Health workers, mobile malaria team
Remark		Active surveillance is usually conducted with an interval of two weeks, unless during transmission season, when it is conducted weekly. In areas with no malaria transmission, on a monthly basis	First active case detection is within 24 h of case detection and continued for four consequent weeks

Source of information: Raeisi *et al.* Determination of malaria epidemiological status in Iran's malarious areas as baseline information for implementation of malaria elimination program in Iran.

3. Results

The incidence rates decreased from 2011 to 2014. There were 4.76, 2.12, 1.80, and 1.59 per 100000 people, respectively from 2011 to 2014 (Figure 1).

During the four-year period (2011–2014), the highest numbers of cases occurred in those aged 16–25 years, by age, and in men, by sex (Figure 2).

Malaria was most common in men, with only 18.5% of cases occurring in women over the four-year study. Most of the cases occurred in rural areas and among workers. During the four-year study, an average 52.58% of cases were Iranian. The sampling method during the four-year period for the majority of cases (49.5%) was the urban health centres' sampling unit, followed by rural health centres (35.8%) and patio table (7.6%). In addition, 0.4% of the cases had received blood in the past. Complicated and severe malaria was present in 5.6% of the cases. The treatment was successful in 83.2% of the cases. Outpatient services were used by 79.1%, and only 4.8% of patients were admitted to hospitals for treatment services. In addition, 83.8% of patients recovered, and 0.1% of cases died (Table 2).

During the four years of 2011–2014, 6542 cases of malaria were mainly found in the provinces of Sistan and Baluchestan and Hormozgan, and the highest incidence rates from 2011 to 2014 were located in Sistan and Baluchestan province. There were 89.94, 43.9, 38.3, and 30.66 per 100000 people (Table 3).

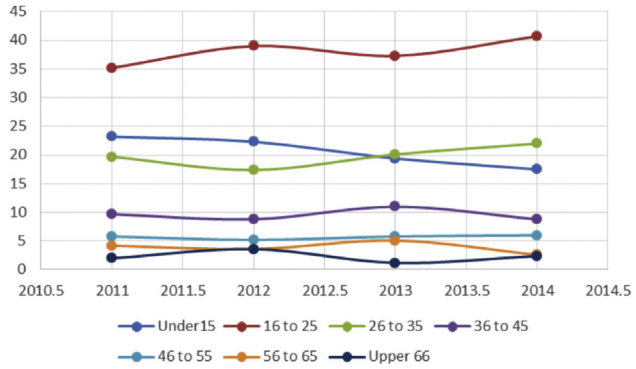

Figure 2. Distribution of the frequency of imported malaria cases, by age group.

This four-year study showed that the highest numbers of malaria cases were recorded in the cities Sarbaz, Nickshahr, and Chabahar in Sistan and Baluchestan province, and Bandar Abbas, Bandar Jask, and Bandar Lengeh in Hormozgan province (Table 3).

The number of malaria cases by month is reported in Figure 3.

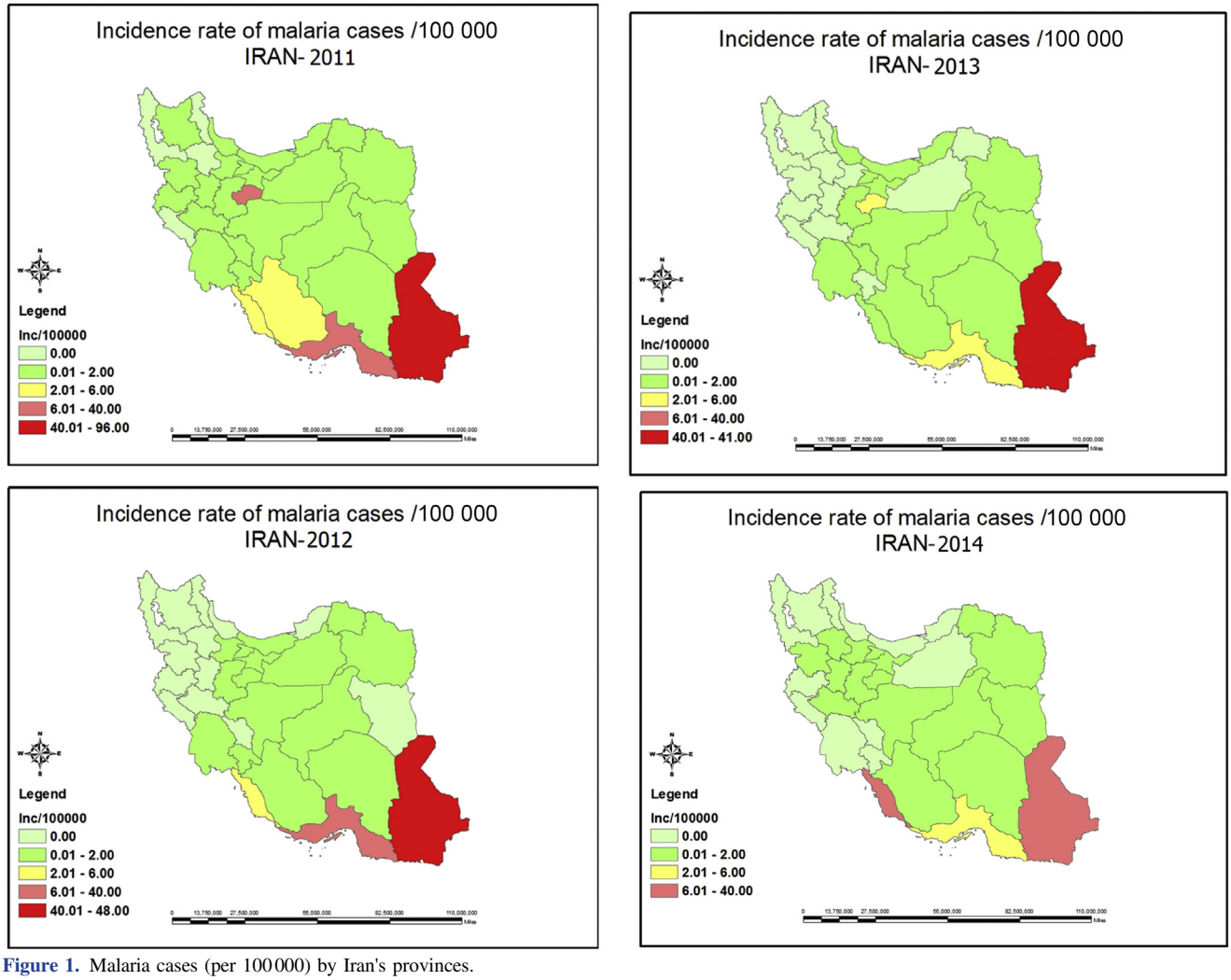

Figure 1. Malaria cases (per 100000) by Iran's provinces.

Table 2
Distribution of the frequency of reported cases based on the study variables [n(%)].

Variables	Category	2011	2012	2013	2014
Sex	Male	2810 (78.5)	1336 (82.4)	1128 (81.2)	1041 (83.7)
	Female	762 (21.3)	285 (17.6)	262 (18.8)	202 (16.3)
Residence	Urban	1254 (35.0)	553 (43.1)	385 (27.7)	434 (34.9)
	Rural	2170 (60.6)	1046 (64.5)	921 (66.3)	712 (57.3)
	Traveller	133 (3.7)	20 (1.2)	62 (4.5)	67 (5.4)
	Nomadic	15 (0.7)	2 (0.1)	4 (0.3)	11 (0.9)
Nationality	Iranian	1790 (50.0)	871 (53.7)	770 (55.4)	637 (51.2)
	Pakistani	1068 (29.8)	476 (29.4)	437 (31.4)	330 (26.5)
	Afghani	687 (19.2)	263 (16.2)	172 (12.4)	265 (21.3)
	Other	27 (0.8)	11 (0.7)	11 (0.8)	11 (0.9)
Occupation	Labourer	1565 (43.7)	695 (42.9)	462 (33.2)	508 (40.9)
	Housewife	455 (12.7)	178 (11.0)	165 (11.9)	125 (10.1)
	Student	331 (9.2)	167 (10.3)	92 (6.6)	90 (7.2)
	Farmer	189 (5.3)	52 (3.2)	86 (6.2)	48 (3.9)
	Driver	97 (2.7)	121 (7.5)	123 (8.8)	143 (11.5)

The epidemiological cases were classified into the following 5 categories: imported from abroad, indigenous, domestic transmission relapsed and introduced. During the four years, 57.05% of the cases were imported from abroad.

The trophozoite lifecycle was present in most cases. Surveillance in the majority of cases was inactive care. This indicates that there were diagnostic and treatment facilities available for a high-risk population that allowed patients to

Table 3
Number of malaria cases in Iran, by city [*n* (%)].

Province	City	2011	2012	2013	2014
Sistan & Baluchestan	Sarbaz	848 (23.7)	394 (24.3)	390 (28.1)	313 (25.2)
	Chabahar	819 (22.9)	305 (18.8)	187 (13.5)	193 (15.5)
	Nikshahr	252 (7.0)	90 (5.6)	25 (1.8)	18 (1.4)
	Saravan	225 (6.3)	238 (14.7)	329 (23.7)	158 (12.7)
	Iranshahr	112 (3.1)	71 (4.4)	42 (3.0)	36 (2.9)
	Konarak	109 (3.0)	60 (3.7)	55 (4.0)	37 (3.0)
	Zahedan	52 (1.5)	6 (2.2)	45 (3.2)	18 (1.4)
	Khash	11 (0.3)	14 (0.9)	13 (0.9)	4 (0.3)
	Sibosooran				41 (3.3)
	Zabol				67 (5.4)
Hormozgan	Bandar Abbas	183 (5.1)	38 (2.3)	20 (1.4)	13 (1.0)
	Bandar Jask	150 (4.2)	37 (2.3)	12 (0.9)	15 (1.2)
	Bandar Lengeh	96 (2.7)	24 (1.5)	18 (1.3)	14 (1.1)
	Rudan	26 (0.7)		4 (0.3)	6 (0.5)
	Qeshm		20 (1.2)	14 (1.0)	18 (1.4)
	Minab	18 (0.5)	11 (0.7)	21 (1.5)	6 (0.5)
	Sirik	12 (0.3)			
	Bashagard	11 (0.3)	6 (0.4)		
Booshehr	Booshehr	33 (0.9)	45 (2.8)	9 (0.6)	52 (4.2)
	Kangan	14 (0.4)	12 (0.7)	7 (0.5)	10 (0.8)
	Dashtestan				5 (0.4)
Qom	Qom	168 (4.7)	11 (0.7)	37 (2.7)	15 (1.2)
Fars	Shiraz	102 (2.8)	35 (2.2)	18 (1.3)	34 (2.7)
	Jahrom	14 (0.4)	11 (0.7)	5 (0.4)	5 (0.4)
	Larestan	11 (0.3)	5 (0.3)		4 (0.3)
Tehran	Tehran	24 (0.7)	18 (1.1)	22 (1.6)	37 (0.3)
	Rey	14 (0.4)			
	Shemiranat			4 (0.3)	10 (0.8)
	Varamin		5 (0.3)		
Isfahan	Isfahan	21 (0.6)	12 (0.7)	10 (0.7)	16 (1.3)
Kerman	Roodbar Jonoob	15 (0.4)			
	Kerman			5 (0.4)	4 (0.3)
	Rafsanjan				7 (0.6)
Yazd	Yazd	12 (0.3)	13 (0.8)	7 (0.5)	4 (0.3)
Alborz	Karaj		10 (0.6)		
Khorasan Razavi	Mashhad			5 (1.1)	8 (0.6)
Khoozestan	Dashte Azadegan			4 (0.3)	

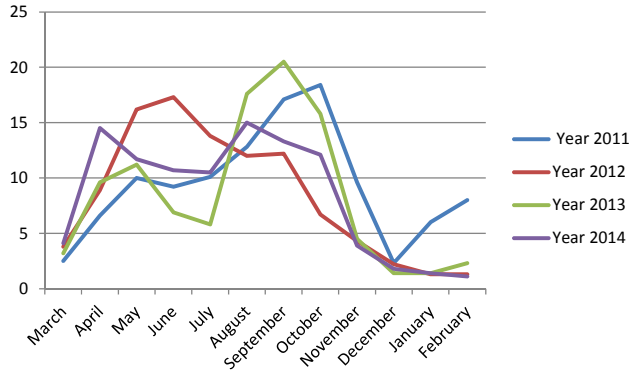

Figure 3. Distribution of the frequency of imported malaria cases in Iran, by month.

receive services such as peripheral blood smears or rapid diagnostic tests.

The medication used most frequently for treatment was artesunate, in both oral and injectable forms. The majority of patients reported a history of travelling to Pakistan. The most frequently occurring danger signs of malaria during 2011–2014 were anaemia, hypotension, and hypoglycaemia. Regarding a history of travelling to malaria-infected areas, 43.6% of patients travelled to Pakistan and 10.2% to Afghanistan (Table 4).

4. Discussion

The results of the present study showed that the incidence rates decreased from 2011 to 2014. Results of other studies also indicate a declining trend in the incidence rate of malaria in Iran [14,15]. The National Malaria Control Program reported a reduction in malaria cases, from an annual average of 16786 cases during 2001–2006 to 6122 cases in 2009 (64% decline), with 100% confirmation. The main reason might be the changing environmental conditions, i.e., drought, for anopheles breeding and survival. Integration of vector management using long-lasting insecticide-treated bed nets, active case detection and treatment through the implementation of mobile teams, and increased financial resources for the malaria control program might also have contributed.

According to Fekri *et al.*, improving the awareness, attitudes, and performance of people also helps to reduce the number of malaria cases. Although Iran is in the pre-elimination stage of malaria, the increase in locally transmitted cases and development of active centres of the disease are concerning. Furthermore, the higher burden in Fars and Isfahan provinces than in Kerman province is a serious warning for Iranian health officials. To eliminate the disease and prevent its return, we need to increase the knowledge of people regarding the control and treatment of malaria. Also, there should be health education

Table 4
Malaria information in Iran, 2011–2014.

Variables	Category	2011	2012	2013	2014
Epidemiological classification of cases	Imported from abroad	1717 (48.0)	825 (50.9)	835 (60.1)	860 (69.2)
	Indigenous	1270 (35.5)	523 (32.3)	366 (26.3)	243 (19.5)
	Domestically transmitted	426 (11.9)	224 (13.8)	137 (9.9)	100 (8.0)
	Relapse	54 (1.5)	18 (1.1)	15 (1.1)	22 (1.8)
	Introduced	105 (2.9)	31 (1.9)	26 (1.9)	11 (0.9)
Lifecycle of the malaria parasite	Gametocytes + trophozoite	755 (21.1)	312 (19.2)	284 (20.4)	331 (26.6)
	Trophozoite	2314 (64.7)	1037 (64.0)	857 (61.7)	687 (55.3)
	Schizont	189 (5.3)	105 (6.5)	67 (4.8)	78 (6.3)
	Gametocytes	314 (8.8)	167 (10.3)	147 (10.6)	122 (9.8)
Surveillance	Passive	2113 (59.0)	937 (57.8)	849 (61.1)	717 (57.7)
	Routine	1236 (34.5)	625 (38.6)	493 (35.5)	497 (40.0)
	Active foci	223 (6.2)	59 (3.6)	46 (3.3)	28 (2.3)
Parasite species	*Plasmodium vivax*	3013 (84.2)	1410 (87.0)	1079 (77.6)	1104 (88.8)
	Mixed (vivax and falciparum)	109 (3.0)	66 (4.1)	59 (4.2)	23 (1.9)
	Plasmodium falciparum	449 (12.5)	144 (8.9)	238 (17.1)	111 (8.9)
	Malariae	1 (0.0)	1 (0.1)	1 (0.1)	1 (0.1)
Type of treatment	Oral artesunate		15 (0.9)	26 (1.9)	17 (1.4)
	Injectable artesunate		15 (0.9)	22 (1.6)	19 (1.5)
	Oral quinine		2 (0.1)	7 (0.5)	6 (0.5)
	Injectable quinine		5 (0.3)	1 (0.1)	
	Coartem		7 (0.4)		
Danger signs of malaria	Anaemia		10 (0.6)	9 (0.6)	12 (1.0)
	Hypotension		10 (0.6)	15 (1.1)	10 (0.8)
	Hypoglycaemia			18 (1.3)	7 (0.6)
	Respiratory failure		3 (0.2)	11 (0.8)	7 (0.6)
	Bleeding		1 (0.1)	5 (0.4)	1 (0.1)
	Dark urine		8 (0.5)	5 (0.4)	4 (0.3)
	Convulsions		5 (0.3)	4 (0.3)	
	Jaundice		9 (0.6)	10 (0.7)	1 (0.1)
	Disturbance of consciousness		5 (0.3)	13 (0.9)	7 (0.6)
	Gait abnormalities		9 (0.6)	12 (0.9)	5 (0.4)
History of travelling to infected areas	Pakistan	1341 (37.5)	671 (41.4)	612 (44.0)	640 (51.5)
	Afghanistan	412 (11.5)	150 (9.3)	97 (7.0)	162 (13.0)
	Other malaria-prone countries	37 (1.0)	17 (1.0)	22 (1.6)	25 (2.0)
	Inside Iran	255 (7.1)	142 (8.8)	95 (6.8)	117 (9.4)
	None	1527 (42.7)	641 (39.5)	524 (37.7)	287 (23.1)

programs to improve people's knowledge and performance in personal protection and environmental improvement to prevent the creation of new centres in border regions.

Unfortunately, neighbouring countries such as Afghanistan, Pakistan, Iraq, and some former Soviet republics have created challenges for the control of malaria in Iran [16]. It is also necessary for Iranian health officials to better control the borders and prevent irregular migration to Iran to cut off the chain of disease transmission and eliminate the disease [17,18]. Through the Malaria Case Notification System (MCNS), all of the cases of malaria have to be reported by all health care units and medical units of medical universities to the disease control and elimination of malaria office. Thus, detection and reporting of all diagnosed cases of malaria are possible in the shortest possible time, and the elimination of malaria will progress more quickly and accurately.

The highest number of cases occurred in those aged 16–25 years. The increase in malaria in people older than 16 years might be due to the increase in the number of immigrants from Pakistan and Afghanistan who are looking for jobs. However, the disease tended to decline in people <4 years old or >15 years old during 2002–2007 [12,19]. The highest incidence of the disease was present in men, which is justified by the increase in the number of immigrants from Pakistan and Afghanistan. However, the number of male patients decreased from 2002 to 2007 by approximately 12%. Sex does not naturally or directly influence the sensitivity or resistance to malaria, but it is possible that the effects are via occupation or coverage. Social activities and the presence of men outside the home increase their susceptibility to mosquito bites. The high number of workers suggests the importance of health literacy and training in this group by health care providers through avenues such as mass media [11]. The disease process in terms of location was primarily in villages during 2011–2014. This finding is consistent with the results of other studies.

Therefore, we can conclude that malaria is a local issue in Iran. Because the migrant workforce is concentrated in cities and their borders, there were more malaria cases observed in cities than in the past [13]. In terms of nationality, the highest numbers of cases were in Iranian, Pakistani, and Afghani people. Annually, 3000–8000 cases of malaria come to Iran from neighbouring countries. From 2010 to 2011, most of the cases were non-Iranian (Pakistani, Afghani, and other nationalities). This reflects the intensification of control measures in recent years. However, in this study, an average 47.42% of patients were Pakistani or Afghani. Therefore, it is necessary to routinely conduct blood tests for Afghani and Pakistani citizens in patio care, especially at the beginning of transmission season. Because of the relative safety, these people might be asymptomatic; however, the parasite might be present in the blood. Interestingly, the present results showed that an average 26.9% of patients had a history of travelling to Pakistan or Afghanistan. Therefore, people with a history of travelling to malaria-infected areas should also be examined for the disease.

Most of the cases were detected in Sistan and Baluchestan and Hormozgan provinces. These provinces were the focus of malaria and are at risk of the return of malaria owing to the presence of predisposing factors for malaria transmission such as high population exchange with malaria-prone regions (Pakistan and Afghanistan), infectious reservoirs, favourable weather conditions (temperatures >16 °C and humidity >50%), high frequency of transmission, and large number of carriers. A malaria elimination program needs to focus not only on interrupting the local transmission but also on trying to prevent and control imported disease and the chain of its transmission to local residents. Policy makers should try to reduce the number of new autochthonous malaria cases to zero and make the high-risk areas clear regions (annual parasite index = 01) [13].

The number of cases in the provinces of Fars and Isfahan was higher than in Kerman province. However, regarding the prevalence of the disease by province, Kerman province has been ranked first or third [20]. Hence, determining the disease prevalence and consideration of the disease control program in all provinces of Iran is of high importance. Most cases were detected in the cities of Sarbaz, Chabahar, and Nikshahr in Sistan and Baluchestan province. Youssefi & Rahimi (2011) reported that there were 1464 malaria cases in the city of Sarbaz between 2009 and 2010. In the study by Sargolzaie *et al.* (2008), the highest numbers of cases were detected in Chabahar (31%), Sarbaz (24.3%), and Nikshahr (10.2) between 2008 and 2011. These rates might be related with favourable environmental conditions, including a long hot season and stagnant water, in addition to the quality of the malaria surveillance system in the cities and travel to the eastern borders [21].

Most cases were recorded during September and August. However, in 2012, most cases were reported during May and June. The highest incidence of the disease in previous studies was in summer [22]. The increase in imported cases and local transmission in addition to the decrease in domestically transmitted cases show that the number of autochthonous malaria cases is currently decreasing in Iran and that the necessity of controlling the country borders is increasingly becoming important [13]. Vivax malaria accounted for the highest rates of malaria, as in 2002 and 2007 [13], and, other than 2013, there was an increasing trend. Therefore, the falciparum infection rate is declining and being replaced by the same number of cases of vivax. This might be due to the reduced number of Afghan and Pakistani refugees and improved diagnostic and treatment services. Severe and complicated malaria was present in 5.6% of patients. This can lead to treatment failure and the need for inpatient services. Prompt disease treatment and parasite elimination from the body can prevent the disease. It also prevents uncomplicated malaria from becoming complicated and severe malaria and also disease transmission in the community.

Despite the recent declining trend in reported cases, the expansion of local transmission, especially in areas affected by border travelling, is concerning. Unfortunately, neighbouring countries such as Afghanistan and Pakistan have created challenges in controlling malaria in Iran.

To meet the ultimate goal of malaria elimination by 2025, steps should include the interruption of the local transmission of malaria; improvements in malaria control interventions, including programs to control border travel and focused interventions for high incidence areas and high-risk groups such as rural residents, men, workers, and people younger than 35 years; and interventions based on the environmental life cycle of the mosquito anopheles and the peak incidence time in the province.

Conflict of interest statement

The authors declare no conflict of interest.

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