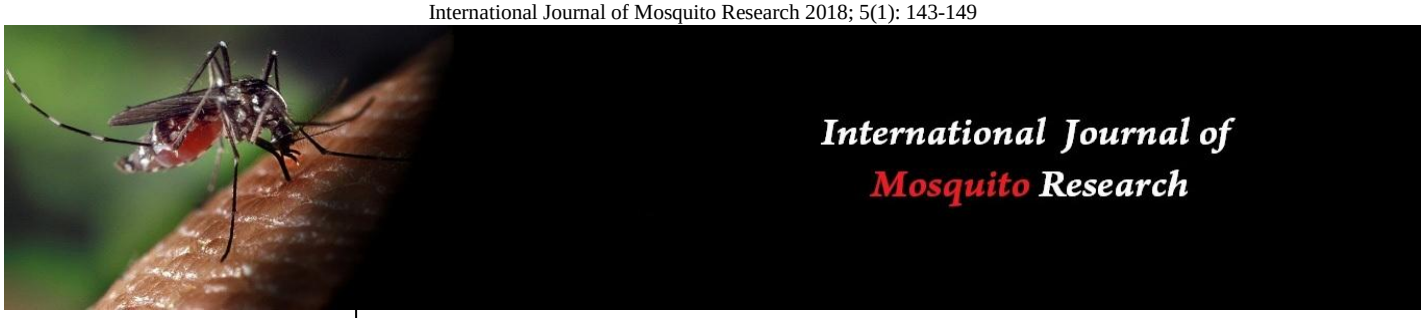

ISSN: **2348-5906**
CODEN: **IJMRK2**
IJMR 2018; 5(1): 143-149

Received: 20-11-2017
Accepted: 21-12-2017

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Imported malaria and epidemiologic components of this infection in Qeshm Island, Iran

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Abstract
Malaria threat a human health and economic status of endemic areas. It has established in many regions in spite of investment on control interventions. This study included the epidemiological characteristics of malaria disease relying on the imported malaria in Qeshm Island, south of Iran. In total, 161 (93.06%) of malaria cases were male and 12 (6.93%) were female. Vivax and falciparum malaria involved 160 (92.48%) and 13 (7.51%) respectively. All falciparum malaria (Fm) were foreign immigrants. Furthermore, no case of fm was seen in <10 age group. Similarly, 82.08% of vivax cases inhabited in rural and developing areas. API ranged from 0.17 to 0.03 per 1000. The pattern of malaria incidence dramatically changed since 2008 so that imported malaria increased due to huge travel of migrants to the south of Iran.

Keywords: Malaria, Qeshm, Imported cases, *Plasmodium vivax*, Iran

1. Introduction
Anopheles spp. a sporozoites stage of plasmodium parasite into human host by their proboscis and invade liver cells subsequently enter the bloodstream as merozoites. In fact, the malaria infection beings when merozoites multiply and rapture the red cells after certain incubation period depending on plasmodium species [1]. Although, 445,000 deaths reported from malarious regions worldwide, 21 countries distinguished with the potential to eliminate malaria by the year 2020 [2]. Plasmodium vivax malaria is a pivotal parasite in under the elimination phase and responsible for half of the malaria cases in these territories [3]. Iran has a practical experience into malaria control program that commences since 1951 [4] consequently introduced into malaria elimination since 2010-2011 to interrupt local transmission by 2025 [5]. Ministry of Health of Iran have invested to control and the indigenous malaria transmission from defined geographies but it remained annoying infection for their inhabitants. Many factors and conditions such as susceptibility of vectors to insecticides, parasite drug resistance, socio-economical pattern and illegal migrants should be considered in the anti-malaria campaign [6]. *Anopheles stephensi, A. fluviatilis, A. culicifacies, A. pulcherimus, A. dthali, A. superpictus, A. sacharovi,* and *A. maculipennis* are chiefly competent vectors of malaria in Iran [7]. A wide range breeding sites and ambient humidity and temperature due to agricultural activities create a long survival of *Anopheles* in order to transmission of the malaria parasite to a human in mountainous and plain areas of Hormozgan province, south of Iran [8]. Many works have been carried out for assessment of epidemiologic aspects of malaria in various districts of Hormozgan Province e. g. Bashagard [9], Bandar Abbas [10], Minab [11], Rudan [12], Bandar Lengeh [13] and Haji Abad [14]. Imported cases even menace the European countries where has been certificated free of malaria a long time ago. Illegal and tourists mostly from endemic districts figured this situation [15]. Irrespective side effects, chemoprophylaxis drugs prevent illness in traveler that visit endemic countries [16]. Notably, vulnerability (the estimation of infected people from another country introduced to new areas) and receptivity (the ability of a defined regions to spread transmission of malaria) are two milestone point into manage intervention of malaria in endemic spots [3]. In recent years, migrant workers make a disturbance into elimination programme that most of them are from east neighborhood countries of Iran [17, 18]. The intention of this document is to provide the analyze the epidemiologic feature of Malaria in Qeshm island. No investigation has been implemented in

this area so far. Therefore, these data can enhance and prompt the information system surveillance and update the applied strategies into the national programme of malaria elimination.

2. Material and Methods

2.1 Study area

The required information collected from control disease and prevention center (CDC) of Qeshm Island. This area coordinates 26°41′43″N 55°37′06″E with an area of 1,491 km^2 opposite the Bandar Abbas County, the capital of Hormozgan province in the Persian Gulf, south of Iran (Figure 1). It's the largest Iranian island in term of area space (length: 135, width: 40 km). The average temperature is approximately 27 °C (81 °F). The warmest months are June to August, and the coldest from October to January moreover, the average rainfall is 183.2 mm. The island comprises 69 towns and villages with a population of 136,548 at the 2016 Census. The distance from Qeshm city (seaport) as the largest city to Bandar Abbas is 20 km (12.42 mi). Mesh Island to Bandar Abbas is 27-65 km. typically, most of urban or village's line along coastal areas of the island where relative humidity is higher than other places. In General, Qeshm is known as the important free economic zone (FEZ) subjected to commercial trade administrations. Commodities stored, reconfigure and re-export to other geographic areas operated in large scale in this zone. Many parts such as Suza, Tabl, Basaidu, Drgahan and suburban regions involve fishing, mining as well as traditional markets in this island. Many migrants visit this place for working and trade annually. In addition, tourism is one of a source of income for this territory due to its natural resources such as Hara forest and the Noopark crocodile park. Also, Qeshm geotourism industry is attractive for traveler due to geographical sense such as Strait of Chahkuh, Stars Valley and Namakdan cave etc. [19]. Furthermore, Portuguese castle is historical places in term of cultural heritage tourism.

Fig 1: Map of study site, Qeshm Island, Iran

2.2 Collected data and analysis

All malaria cases were diagnosed by professional health providers and skilled laboratory technicians within active and passive detection in health and clinical units. Stained blood film under microscope and rapid diagnostic test (RDTs) were two procedures using for identification of cases. In total, 173 malaria cases were registered in our database between 1 January 2008 and 31 December 2017. This project was approved by the research ethics committee of Hormozgan University of Medical Sciences (HUMS). All cases consented to use their information in our project affirmatively. Informed consent was endorsed by each person or guardian. They treated based on national malaria guideline. Furthermore, they received a follow-up plan from health workers or physicians regularly. Demographic features of patients were recorded and classified exactly. Effective variables included into two group general features of patient and specified characteristics of infection. These indicators are listed as follows: gender, age, residency, and occupation, and citizenship, type of plasmodium parasite (vivax/falciparum), stage of parasite life cycle, history of infection, month and year of transmission. Finally, our data were analyzed by Chi-square test. P-value of ≤0.05 was employed for point of Significant difference.

3. Results

In this project, 173 cases were recognized as malaria infection in healthcare and prevention center of Qeshm Island between 2008 and 2017 years. Out of 173 cases, 96 (80%) was an illness from 2008 to 2011 continued with lower incidence rate toward 2017 (Figure 2). Overall, 161 (93.06%) were male and 12 (6.93%) were female. 151 (87.28%) of them were laborers in term of occupation. Student, fisherman and other jobs consist 0.57, 0.57 and 11.56 % of our patients. The correlation relationship was found between occupation and incidence of disease (P=.000). 31(17.91%) and 142 (82.08%) lived in urban and rural areas respectively. Vivax malaria involved 160 (92.48%) and 13 (7.51%) were plasmodium falciparum cases (Table 1). All falciparum malaria (FM) were foreign migrants. At the same time, no case of Fm was seen in <10 age group (Figure 3). Similarly, 75% of vivax cases inhabited in rural and developing areas. Further results showed that the two-thirds of patients were Pakistani followed by Afghanistani, Iranian and other nationalities. Relapsing vivax was detected in 3 (1.73%) of malaria cases originating from Pakistan. September was the predominant month of disease so that up to 33 (19.07%) of cases reported in this month (Table 2). Trophozoites and gametocytes stages of parasite life cycle together have been more detected (52.6%) through blood tests followed by trophozoites (34.1%) alone. 6 (3.46%) had the history of infection upon >1years ago that all of them were foreign residents. The significant difference was shown related to the type of nationality and prevalence of infection (P=.000). Clearly, 21-30 age group accounted the dominant class of infected persons (Table 1). API (Annual Parasite Incidence) ranged from 0.17 to 0.03 per 1000. ABER (Annual Blood Examination Rate) was calculated 3.76 to 3.67% from 2008 to 2017. Also, SPR (Slide Positivity Rate) value was high level along with 2011 (Table 3). 62 (35.83%) and 111 (64.16%) of cases were diagnosed by active and passive surveillance respectively through. All cases were examined via blood film and rapid test kit.

Table 1: Epidemiologic profile of malaria in Qeshm Island

Epidemiologic variables	Value	Total
Sex	Male Female	161(93.06) 12(6.93)
Residency	Urban Rural	31(17.91) 142(82.08)
Occupation	Worker Student Fisherman Others	151(87.28) 1(0.57) 1(0.57) 20(11.56)
Age group	≤5 6-10 11-20 21-30 >30	11(6.35) 8(4.62) 45(26.01) 72(41.61) 37(21.38)
Citizenship	Iranian Pakistani Afghanistani Others	20(11.56) 115(66.47) 32(18.49) 6(3.46)
Type of parasite	*P. vivax* *P. falciparum*	160(92.48) 13(7.51)
Surveillance	Active Passive	62(35.83) 111(64.16)

Table 2: Monthly distribution of malaria in infected people

Months	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
Number	1	0	2	2	16	28	21	17	33	30	15	8	173
Percent	0.57	0	1.15	1.15	9.24	16.18	12.13	9.82	19.07	17.34	8.67	4.62	100

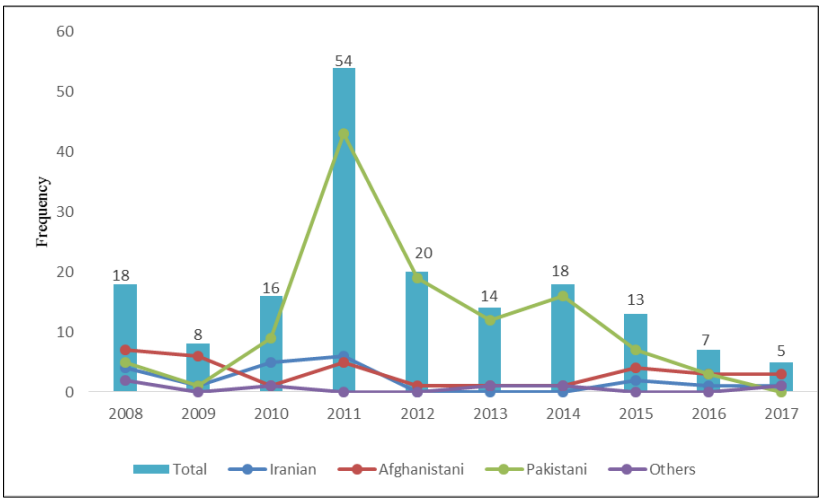

Fig 2: Distribution of malaria cases based on citizenship during 2008-2017

4. Discussion

In our view, the incidence of malaria has been decreasing over the one-decade period whereas a sharp slope progressively presented in 2011. As reported earlier the foreign citizen particularly Pakistani was the largest troop that acquired malaria (Figure 2). They worked in the construction of commercial and residential buildings. Some of them have been employed for the fishing industry. As regarding Qeshm is known as free economic zones (FEZ), many foreign workers intend to work in this destination. On the other hand, they cross the borders of neighboring countries illegally introduced and the rural and suburban areas with poor sanitary conditions as the preferred sites for the living. Notably, predominant immigrants entered to our site study since 2011. For this reason, the highest level of malaria incidence presented in 2011. In reality, there was a lot of undocumented Pakistanis without identified ID card lived in remote and rural regions. The previous research supported this result [20]. They ordinarily lacked sufficient knowledge of malaria surveillance. Unfortunately, most of them didn't have bed-net or any equipment (e. g. air conditioner) for ventilation in their house due to poverty. Up to half of laborers also became ill in their own countries subsequently they confirmed as malaria cases in Iran. In certain scenarios, refugees moved to Iran whereas they stopped antimalarial treatment. Therefore, they received incomplete treatment regarding relapsing vivax was emerged in 3 (1.73%) of them. An unfinished regimen maybe causes plasmodium resistance/tolerance [21]. Occasionally,

migrant workers treated themselves by traditional methods and they didn't seek medical attention. However, a delayed diagnosis or treatment occurred. The same result was claimed in other studies [22, 23]. Imported cases shift the resistant species of Plasmodium to the new community through competent vectors. This episode is perilous especially for children in case of *P. falciparum* [24]. Parasitemia or a thrombocytopenia were the main characteristics of imported pediatric malaria particularly in <2 years [25]. Indeed, the imported case and travelers can disperse the various parasites (i. e. *P. vivax, P. falciparum, and P. ovale*) even in non-endemic areas with low immunity [26]. *Plasmodium vivax* was the widespread parasite in all age groups in our literature in accordance with other parts of southern Iran [27] (Table 1). In contrast, *P. falciparum* (Pf) wasn't seen in <10 age group (Figure 3).

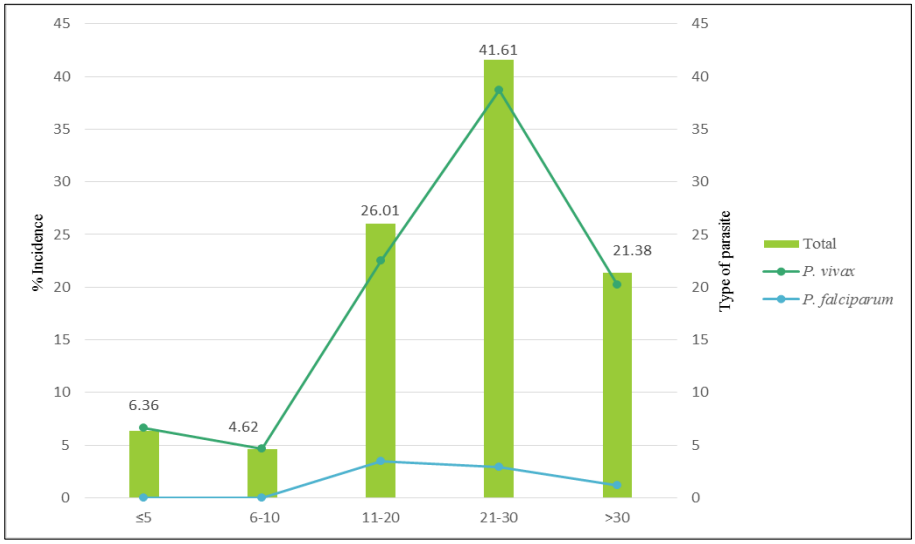

Fig 3: Burden of malaria in all age-groups according to type of parasite (Vivax/Falciparum)

In areas such as tropical Africa with high stable malaria, severe malaria was more common in children (with <5 years old) but in Iran with less endemicity, *Plasmodium falciparum* was more frequent in elder children. Maybe adult and childhood acquire a slight immunity in unstable regions [1-28]. In current respect, only 20 (11.56%) of patients had Iranian nationality as indigenous malaria cases. Most worked with other within common activity or workplaces such as fishery, market, trade etc. In this instance, introduced cases (first-generation local transmission) can occur result exposure to foreign parasite carrier [29]. Afghanistan civilians were predominant groups as malaria cases in another part of southern Iran [30]. The most incidence rate has shown from September-November (Table 2). Apparently, *Anopheles stephensi* Liston as the main vector of malaria [31] has the most density and biodiversity in autumn season in the south of Iran [32]. Significantly, environmental indicators such as humidity and temperature can establish infection in malarious areas [33, 34]. Evidence suggests that the social and economic activities grow up during this period thereby, malaria impressed with income and economic model of its region [35]. API was in high level along with 2011 compared with other years. Considerably, health provider's efforts increased parallel with prevalence of malaria in this year because ABER value has been taken increasingly. SPR can describe an operational scale into malaria elimination programme. These criteria were 0.52 synchronized with migrants that more entered in endemic zone in 2011. Although the slide positivity rate was ranked equal to second along 2010, the covered population in this year was the latest in term of examined blood smears. Therefore, the number of blood film examination should be considered in successive strategies in accordance with other scales. The declining trend of API is indicative of the fact that fight against malaria has been relatively well-developed in south of Iran (Table 3).

Table 3: Malariometric indices of Qeshm County in 2008-2017 years

Year	Population at risk	Smears examined	No. positive		API	ABER	SPR	AFI	SFR
			Pv	Pf					
2008	101,878	3,835	18	0	0.17	3.76	0.46	0	0
2009	112,615	1,947	6	2	0.07	1.72	0.41	0.01	0.1
2010	114,495	1,300	14	2	0.13	1.13	1.23	0.01	0.15
2011	119,824	10,310	50	4	0.45	8.6	0.52	0.03	0.03
2012	123,432	8,531	19	1	0.16	6.91	0.23	0.008	0.01
2013	120,258	6,564	12	2	0.11	5.45	0.21	0.01	0.03
2014	123,508	5,657	18	0	0.14	4.58	0.31	0	0
2015	130,221	5,395	12	1	0.09	4.14	0.24	0.007	0.01
2016	136,548	5,519	7	0	0.05	4.04	0.12	0	0
2017	140,573	5,170	4	1	0.03	3.67	0.09	0.007	0.01

API (Annual Parasite Incidence) = No. of positive slides for malaria parasite x 1000/Total population at risk in a year SPR (Slide Positivity Rate) = Total positive for malaria parasite x 100 /Total blood slides examined ABER (Annual Blood Examination Rate) = Smears examined/Total population per 100 SFR (Slide Falciparum Rate) = Total positive Pf x 100 / Slides examined AFI (Annual Falciparum Incidence) = Total positive Pf in a year x 1000/Total population at risk pre-1000 Pv = P. *vivax*, Pf = P. falciparum

To judge relating to control interventions all indexes should be assessed as a conjunction. It is noteworthy that the local transmission had high in the native people before 2008 in south of Iran [36] but this pattern dramatically changed since 2008 so that imported malaria increased due to huge travel of migrants to these zones. Detailed data has been shown that passive and active surveillance (AS) were implemented equally (≈60%). Both of them have advantages and disadvantages. Several signs not only fever should be considered in AS within time of visit suspected case [37]. Moreover, the antimalarial medicines can be evaluated in passive surveillance for treatment (PST) [38]. In elimination phase of malaria infection should be focused on all malaria cases substantially imported case irrespective symptoms. Clearly, illegal migrant workers inhabit in remote areas thereby, active surveillance is efficient strategy to trace them in this circumstance. Microscopy examination of note is priority method for identify and rapid diagnostic test (RDT) should be used as an axillary technic in an area with ongoing autochthonous transmission [29]. Iran has the strong national system in term of financial and qualified personnel resources. Treatment of malaria is free of charge for domestic or foreign cases in this county. Local transmission of falciparum and sever disease have been interrupted in 2014 in our site. In addition to, absence of asymptomatic malaria cases implies a successful implement policy on the limitation of malaria transmission [17].

5. Conclusion

We anticipate that Iran will be certified as malaria-free by the World Health Organization in few next years. Nevertheless, vivax malaria remain a challenge and imported malaria comprise a large proportion of problem in recent years. The roust border checkpoint should be set up along southeast of Iran where most of illegal immigrant influx of it. Continued collaboration with neighbored governments and stakeholders can help to organize the migrants, refugees and mobile people in receptive areas. Entomological monitoring, mass parasitological screening in high risk district, training, mapping, prompted report of initial cases are requirements for achieving elimination. Although some *Anopheles* spp. have presented resistance / tolerance to pyrethroids insecticide, application of these chemical compounds group through indoor residual spraying (IRS) and ITNs (insecticide-treated nets) declined the risk of malaria transmission in south of Iran. Moreover, periodical use of different class of pesticides recommended as important approach to manage insecticide resistance [39].

6. Acknowledgments

We sincerely thank staffs and Health providers of center for disease control and prevention (CDC) of 7 Qeshm county, for surveillance of malaria cases and recording the data.

7. Conflict of Interest

None declared.

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