An overview and mapping of Malaria and its vectors in Iran

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Original Article

Abstract

Introduction: In spite of public health level improvement in Iran, Malaria is still an important health problem in the southeast corner of the country. Mapping distribution of endemic diseases with their relations to geographical factors has become important for public health experts. This study was carried out to provide the distribution maps of the geographical pathology of Malaria in Iran with emphasis on its vectors.

Methods: A systematic literature review was performed and the data and/or metadata were used for evaluation of findings. All available articles and books were used for mapping vectors and parasites, data of Malaria cases were obtained from Iran Center for Diseases Control, Ministry of Health in 2010. Incidence or prevalence of the diseases and also scientific names of vectors with collection details were arranged and mapped as a shapefile in ArcGIS software.

Results: About 28 different *Anopheles* species are found in Iran. Seven maps provided for the main vectors in the country. Distribution maps generated for *Plasmodium falciparum*, *P. vivax* and co- infection cases. Distribution maps of transmission and endemic areas are provided. Out of 11668 indigenous and transmitted malaria from imported cases in three years leading to 2010, about 9400 cases occurred in south parts of the country where the weather is influenced by Afrotropical zoogeographic region, while 2200 cases occurred in the southeast corner of the country where the weather is influenced by Indo-malayan and only 25 cases were reported in the typical Palearctic area of Iran.

Conclusion: Most malaria cases occurred in the southeast corner in Sistan Baluchistan, Hormozgan and south parts of Kerman. There are similarities between malaria transmission conditions in Iran and many tropical and subtropical countries. Such information on vectors, incidence of all cases and environmental factors can be used to set a Malaria Early Warning System and help to prevent and control of malaria.

Key words: Malaria – Anopheles – Mapping - Iran

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Introduction:

According to the reports by WHO, Malaria is the most important parasitic disease in the world (1). At the time of the present study, around 3.3 billion individuals (half of the world's population) live in malarious areas, and almost 660'000 people die due to this disease per annum (2). Although malaria is the most important parasitic human disease, human is not its definitive host. In the life cycle of malaria, sexual proliferation occurs in some Anopheline species as definitive hosts. Parasite transmission to human is mainly through being bitten by infected Anopheles mosquitoes, although there are other less important transmission routes including blood transfusion, transplantation, trans-placental transmission and infected needles. Generally, the epidemiology of malaria is defined based on the biology and ecology of Anopheles mosquitoes.

Documents indicate that a considerable part of Iran has climatologic potentiality for malaria transmission. According to Gilmore (1924) malaria was one of the most important diseases in Iran and even used to affect population growth rate in this country. Gilmore reported the ecological niches of the disease and larval habitats of the vectors in rural and urban areas: 1) flooding irrigation used in agriculture created man-made larval habitats in rural areas, and 2) traditional multi-purpose water reservoirs and pools used in old houses in urban areas. He also stated that there were geographical zones in Iran as described in climatology of Iran (3).

Although malaria was eradicated or eliminated in northern and central parts of Iran, there still exist indigenous cases in some subtropical areas in south-east areas of the country. Malaria can be simply seen anywhere due to imported cases (4). Basically, malaria transmission requires particular climatologic conditions and it is not observed in inappropriate geographic conditions. Malaria early warning systems are based on disease mapping, epidemiologic variables and distribution of Anopheles mosquitoes (5).

From about 490 identified Anopheles species, 70 species are capable of transmitting malaria disease. Out of that number, 40 species are recognized as the major vectors. In addition to malaria transmission, Anopheles has the capability of transmitting filariasis and arbovirus infections. Anopheles genus belongs to Family Culicidae and Class Diptera, Order Insecta and Kingdom Animalia. From taxonomical point of view, the genus Anopheles is one of the most problematic insects with medical importance. Anopheles mosquitoes are less found in heights more than 2500 meters, although they are found above 2800 meters considering the global warming. The genus Anopheles has complete metamorphosis and its life cycle includes egg, larva, pupa and adult.

Anopheles mosquitoes live in aquatic environments at premature stages. The aquatic environments required for Anopheles laying egg (larval habitats) are usually fresh, stagnated and clean water, although some species are capable of egg-laying in brackish and nearly-brackish water, and even polluted water. The size of larval habitats ranges from some water accumulated from either water droplets or air-conditioned and water accumulated in a tin can to a relatively large pond. The three stapes occur in ponds: 1) four larval stages which take about 10 days (8 to 12 days) depending on the environmental temperature, 2) a pupa stage for 2 to 4 days in optimum temperature (27ºC to 28 ºC) and 3) emerging imago (adult) and leaving the pond which takes place between 10 to 16 days after laying eggs. This period can be shortened to 7 days or extended 20 days if the ambient temperature changes to 31ºC and 20ºC, respectively.

Adult Anopheles mosquitoes mate usually around dusk once forever. Life span of female anopheles is usually about 10 to 14 days, and in some species it is up to 4 weeks. Temperature and humidity influence the life span of the mosquitoes. If either temperature or humidity goes beyond the tolerability thresholds of the insect, its population decreases. For example, the population of Anopheles stephensi increases in spring after a reduction in winter; and also population decreased at the beginning of unbearable summer heat and then increases at the end of summer. In this way, two picks are observed in the population chart of the mosquito. Female Anopheles requires a blood meal for development of eggs. Taking blood meal, digest it and finally oviposition takes within 2 to 4 days in 23º C which is referred to as gonotrophic cycle. Anopheles mosquitoes do not usually fly 2 to 3 kilometers far from larval habitat. However, this is various in different species. Although various environmental and climatologic factors influence the population of anopheles; and in turn on malaria, the factors which should always be considered include temperature, humidity and rainfall in the malarious areas.

Methods:

At the beginning, all available books, articles or online databases about distribution of anopheles and malariology in Iran including IRANMEDEX and Pubmed were studied. Then using ArcGIS software, each species of anopheles was separately mapped to the location of the related research. According to the principles of Logics, no report of anopheles species in a region means absence of the vector. Therefore, the areas which are depicted in white do not mean clean areas. Two colors (Black and hachure) are used in the cartography of the maps. Black which denotes anopheles report with the exact name of the district and hachure denotes provincial reports of the vector without details. In fact, entomological studies are not separately carried out in each district to identify the fauna. The results obtained from the neighboring districts are generalized to less important areas. The exception can be malarious areas where vectors are identified more precisely. It can be concluded that no reports of particular Anopheles specie can be considered as absence of that specie in malarious areas including Hormozgan Province, South of Kerman Province and Sistan & Baluchistan Province, while it can be considered suspicious for other provinces.

On contrary, there are two reasons that no reports of malaria mean a clean area. Firstly, malaria monitoring is an active procedure in Iranian Health System and its treatment is free. Secondly, the nature of the disease forces the patient to seek treatment. Therefore, patients are inevitably identified.

Results:

There are 28 definitive reported species, 33-34 biological forms and geographical races of Anopheles in Iran. Seven of them are the main vectors of malaria in Iran (6):

Anopheles stephensi (A. stephensi)
Anopheles culicifacies (A. culicifacies)
Anopheles fluviatilis (A. fluviatilis)
Anopheles superpictus (A. superpictus)
Anopheles dthali (A. dthali)

Anopheles sacharovi (A. sacharovi)
Anopheles maculipennis s.l. (A. maculipennis)

Although malaria vectors in Iran possess their individual features, the first four species among the above items are most important regarding Iran epidemiologic conditions. Most of them are zoophilic; prefer to rest in animal shelters after blood feeding. However, anthropophilic index of the insect exactly depends on season, environmental conditions, and occurrence of livestock (7).

Other anopheles mosquitoes of Iran include:

Anopheles algeriensis, Anopheles apoci Anopheles atroparvus, Anopheles claviger, Anopheles hyrcanus, Anopheles labranchiae, Anopheles sergenti,Anopheles marteri, Anopheles melanoon, Anopheles marteri, Anopheles messeae, Anopheles mongulensis, Anopheles multicolor, Anopheles persiensis, Anopheles turkhodi, Anopheles plumbeus, Anopheles nigerrimus, Anopheles pseudopictus, Anopheles pulchrimus, Anopheles subpictus, Anopheles peditaeniatus

It is noteworthy to mention that some species of Anopheles in Iran are in fact isomorph or cryptic species (sibling species) may differ biologically.

Anopheles superpictus

A. superpictus as the most widespread anopheles in Iran is distributed in central plateau, northern mountainous areas and southern hilly areas of the country. This specie is even found in Sistan & Baluchistan Province (small population). In appropriate conditions, it has the potentiality of transmitting malaria. Presence of this specie has been reported from Bandar Abbas, Bashagard, Jiroft, Tabriz to Kaleibar, Hemedan, Ilam, Ivan Gharb, Tehran, Varamin, Ferdos, Sabzevar, Mashhad, Nahavand and Borazjan. There are 3 varieties (x, y, z) in Iran. The x form exists in all parts of the country except Sistan and Baluchistan;

and the y and the z forms are just found in Sistan & Baluchistan Province. Figure 1 shows the distribution of A. superpictus in Iran according to the reported documents.

This specie is found up to 2000 meters from the sea level and its flight distance ranges from 2 to 7 kilometers. It rests in human and cattle facilities (zoophilic and anthropophilic). Larval habitats of A. superpictus include pits, holes at the bottom of rivers, agricultural water channels, shallow waters with plants and grassland.

The specie has been reported from 437 districts in Iran, an area covering 944086.6 square kilometers accounting for about 50.5% of the country. It is predicted that this estimation may increase by more complementary field researches in unsurveyed districts. In comparison with other species, widespread distribution of A. superpictus does not imply to more population density. For example, the population density of this species in Kaleibar (Eastern Azerbaijan Province) was 1/6 of A. sacharovi in summers of 2004 and 2005 (8).

Anopheles maculipennis

In the Palearctic ecozone, there are 12 species of *Anopheles maculipennis* complex. Molecular methods have confirmed 6 species in Iran, although some researcher state there is the seventh species in Iran using morphologic methods. In this complex, *Anopheles maculipennis s.s.* is known as the main malaria vector in Iran. The members of this complex have a widespread distribution in Iran and have been reported from many provinces including West Azerbaijan, East Azerbaijan, Ardebil, Gilan, Mazandaran, Golestan, Khorasan, Isfahan, Fars, Kohgiloye and boyerahmad, Kermanshah, Kurdestan, Zanjan, Izeh in Khuzestan province, and north of Tehran. Figure 2 shows the distribution of this Anopheles in Iran.

Flight distance of this species is about 1 to 1.5 kilometers. It is an endophilic and endophagic mosquito, and its blood feeding timing is usually before midnight.

Anopheles persiensis is one of the members of the same complex, and species similar to *A. maculipennis*. Based on *A. persiensis* distribution and ecology, it is suspected to be probably involved in malaria transmission.

Anopheles sacharovi

This specie is a member of *A. maculipennis* complex which can be detected by morphologic methods. *A. sacharovi* along with *A. maculipennis* are the major malaria vectors in northern parts of Iran.

This specie is distributed in Fars province and some other regions in the country. In many parts of its distribution regions, it is known as endophilic vector, although it has been found in both human and animal shelters.

Flight distance of this anopheles is remarkable and has been reported from 8 to 14 kilometers. This vector prefers nearly brackish water and fresh water for laying eggs. It chooses midnight for blood feeding. Figure 3 shows reports related to *A. sacharovi*.

Anopheles stephensi

Anopheles stephensi is the most prevalent vector in southeast of Iran (7) and is the most important malaria vector in Iran and southeast of the country, especially in Hormozgan province. Unfortunately, resistance of the vector to some important insecticides has been reported. High density of the vector is observed in some distribution areas. In some of southeast regions of Iran, 44.5% of the captured Anopheles was *A. stephensi* (9). Anthropophilic index of A. stephensi was reported 19.8%. The ratio of the rest period to hemophagy of this vector in mosquitoes captured indoors is 4.4 and to those captured outdoors is 2.9% (Endophilic Ratio is 1.51). This means that the vector is endophilic (7).

Larval habitats of this specie can be near the streams, marshes and sumps. It can also use stagnated water and relatively contaminated and brackish, even water left in tin cans and so for egg-laying.

This anopheles is known as main malaria vector in urban epidemics in south of Iran.

A. stephensi is observed from Sarbaz district – most eastern point of Iran - to Khuzestan province. This specie is present in all southern regions of Sistan and Baluchistan, Hormozgan, Bushehr, Kerman, Fars, Khuzestan, Kohgiloye and Boyerahmad, Ilam, and south of Kermansh province. Figure 4 depicts distribution of *A. stephensi* in Iran.

Anopheles culicifacies

Anopheles culicifacies is a complex of at least five species which differ from each other from the view point of distribution, seasonal activity, sensitivity and transmission of malaria parasite, host preference, resistance to insecticides and vectorial capacity. The members of this complex are distributed in Sistan and Baluchistan, south of Khorasan, South of Kerman, Fars, and somewhat Hormozgan province. Flight distance of *A. culicifacies* is about 1 kilometer. Although it is mainly known as zoophilic anopheles, its anthropophilic index is reported as 16.4%. *A. culicifacies* rests in both human and animal shelters. This species is mainly captured from indoor resting places in hot and dry region in southeast of the country where there found less in outdoor resting places.

In spite of low density, this vector is an effective malaria vector. It is a major malaria vector in Baluchistan (south of the province) although it is seen in Sistan region (north of the province).

Anopheles dthali

Anopheles dthali is mostly distributed in southern regions of Zagros Mountain ranges in Sistan & Baluchistan, Kerman, Fars, Khuzestan, and Kermanshah provinces, although there are reports from centers in Yazd, Mahallat, Hamadan, Tabas and Isfahan (Fig. 6). The anthropophilic index of *A. dthali* has been reported variably up to 35%. Although it has been captured from indoor resting places in south part of Iran in some studies, it is mainly exophilic. *A. dthali* mostly exhibits exophagic behavior in cattle breeding areas where cattle are available for hemophagy. This anopheles lays eggs in wells, stagnated water and edges of pond.

Anopheles fluviatilis

Anopheles fluviatilis is distributed throughout southern regions including Sistan and Baluchistan, Kerman, Khuzestan, and Fars provinces. It is known as semi-stable malaria vector in the country. Although it was an endophilic vector before application of long-lasting residual insecticides, it nowadays presents exophilic behavior in the distribution regions.

A. fluviatilis is considered a species complex. Based on polytene chromosomes it includes S, T and U species, and based on genomic characteristics it has 7 genotypes. The species are different from each other from the viewpoints of biology, ecology and malaria transmission. Recent studies indicate the relationship between *A. fluviatilis* of Iran with a species complex distributed in East of Asia.

The flight distance of *A. fluviatilis* is about 1 kilometer. A larval habitat of the Anopheles is streams, channels and rice fields. Its hemophagy is at midnight and is even dangerous in sparse populations.

Despite widespread efforts of the Ministry of Health and Medical Education (MOHME), malaria is still transmitted in southeastern Iran. In some parts of the country, it is considered as an endemic disease. As per definition, a malaria endemic area is a region in which malaria is transmitted in three consecutive years. In Iran, 11282 cases of malaria were reported in three years leading to 2010. According to the above definition, the endemic districts in Iran included Iranshahr, Saravan, Chabahar, Jask, Roudan, Minab, Jiroft and Kahnouj in 2011. The area covers 140000 square kilometers. It is 8.5% of the total area of the country, and about 1200000 people (1.5% of the total population of the country) live there.

The Iranian malaria reports are comprehensive in which imported cases are also included. This is the reason why some areas with no appropriate climatologic nature for malaria transmission seem to be dangerous. It may mislead the users. Figure 8 shows the reported cases of *P. falciparum* in Iran in 2008. Figure 9 indicates the reported cases of *P. vivax* in Iran in 2008.

Table 1 shows a summary of malaria condition in Iran in three consecutive years leading to 2010.

Imported cases of malaria can be seen almost in any area because either Iranian of non-Iranian immigrants may indwell in any of urban or rural areas. Based on this fact, imported cases of malaria are excluded from the study to better understand the geographic pathology of malaria.

Malaria transmission maps in Iran indicate that 99.65% of malaria transmitted within the past three years occurred in southeastern Iran. In fact, the only provinces involved in transmission of malaria are Sistan and Baluchistan, Hormozgan and Kerman. The main cause of the disease in Iran is *P. vivax*, and *P. falciparum* is the cause of 11% of the rest. It is possible to find some cases of *P. malarie* as reported previously, while *P. ovale* cannot be seen.

The results obtained from map analysis by Geographic Information System (GIS) showed that there is a significant relationship between malaria and temperature (P=0.00). It was observed that the average annual temperature above 25.3°C is the prevalence level of malaria in Iran (P=0.011). It was surprising to see there was significant relationship between some regions in Iran and low level of rainfall (P=0.025). But it is not observed in larger areas, and no relationship is seen between malaria and rainfall.

Malaria in Iran has been seen sporadically in different parts of Iran. This is misleading for understanding the width and climatologic variety of the country for understanding the ecology of the disease. Hence, it seems studying the three malaria endemic provinces better provides information for the ecology of malaria in Iran.

In endemic regions, i.e. the provinces in southeastern Iran, there are significant relationships between malaria transmission and Normalized Difference Vegetation Index (NDVI) (P=0.012), temperature (P=0.010) and height (P=0.041)

The extent of significance for prevalence of 15 cases of transmission for NDVI was 111.82 (P=0.013) and for temperature was >25.3° C (P=0.026). The minimum and maximum temperature for malarious areas in Iran was 20 ° C and 30 ° C, respectively. The extent for the height of the malarious areas was <920 meters (P=0.00). Classifying the rainfall rates in the three malarious provinces, it is found that areas with more than 15 cases had less than 115mm rainfall per annum (P=0.031). Studies did not indicate significant relationship between humidity rate and malaria transmission. A reason for this, like rainfall phenomenon, is malaria transmission in districts where rainfall rate and humidity are low. Such districts are located in Sistan and Baluchistan province, and more specifically Nikshahr. Apart from the above exception, there is significant relationship between malaria transmission and humidity rate in other parts in southeastern Iran (P=0.011).

Malaria transmissions in non-malarious regions of the country are limited to 1 or sometimes to 2 cases in a district in three years. The only exceptions are Farashband in Fars province and Behbahan in Khuzestan provinces which are the record holders of epidemic regions. Throughout Gilan and Mazandaran provinces which are climatologically appropriate for malaria transmission, the rate for transmission is similar to other parts of the country. This shows the effectiveness of the health system controlling programs. In this way, the transmission of the disease is not reportable. This is another bias towards malaria maps in Iran, on contrary to the map of imported malaria cases which can be misguiding.

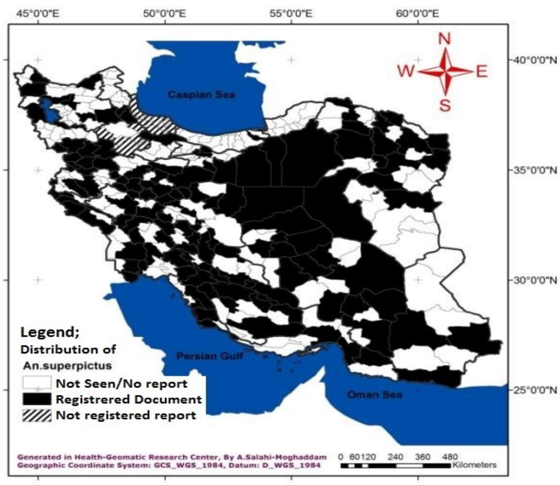

Figure 1. Reports distribution of anopheles superpicturs in Iran (10,11), (16), (6), (8), (7), (18)

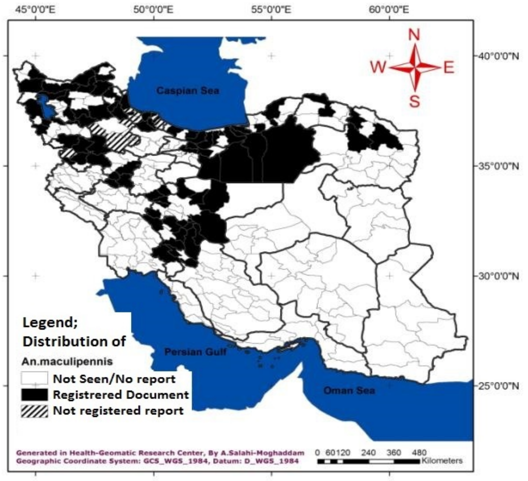

Figure 2. Reports distribution of anopheles maculipennis in Iran

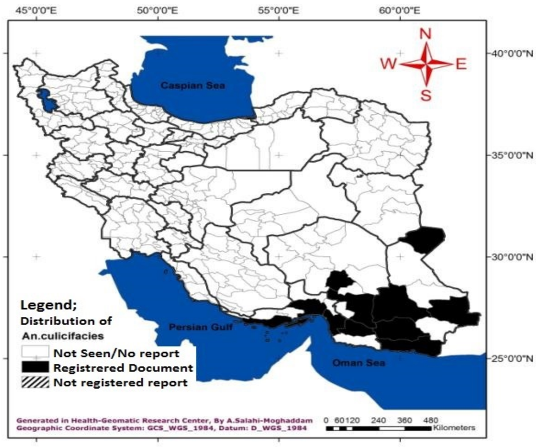

Figure 5. The map of reports distribution of An.culicifacies

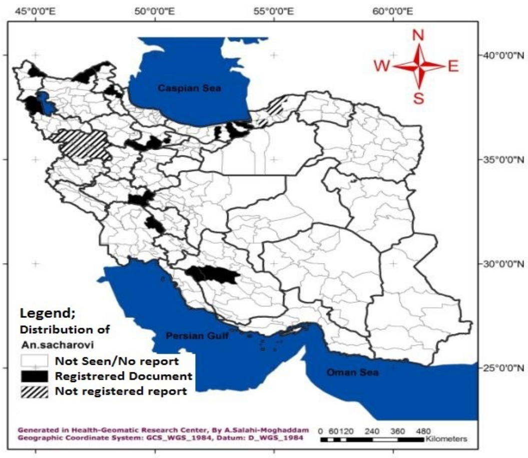

Figure 3. The map of reports distribution of An. Sacharovi in Iran

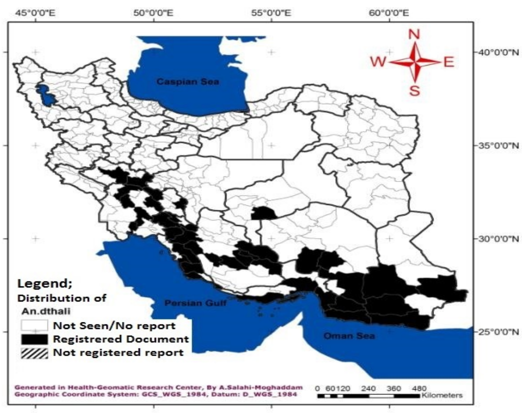

Figure 6. The map of reports distribution of An.dthali in Iran (7) (11) (16) (17,6)

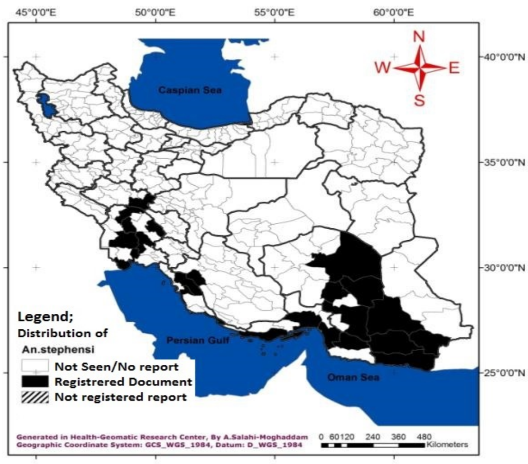

Figure 4. The map of reports distribution of An. Stephensi in Iran (16) (11) (17) (16) (18) (6)

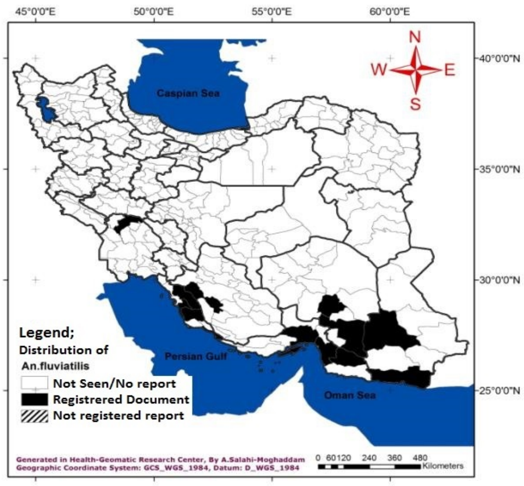

Figure 7. The map of reports distribution of An.fluvialis in Iran

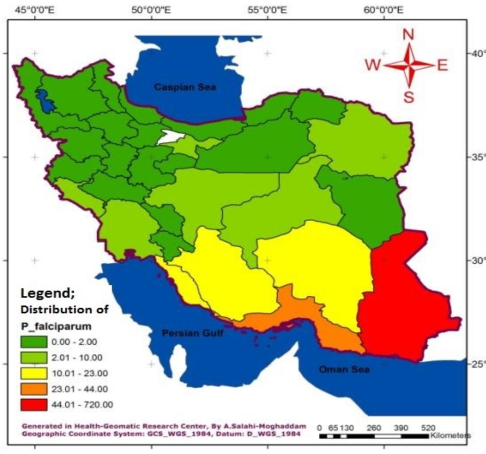

Figure 8. The map of report distribution of falciparum malaria in Iran

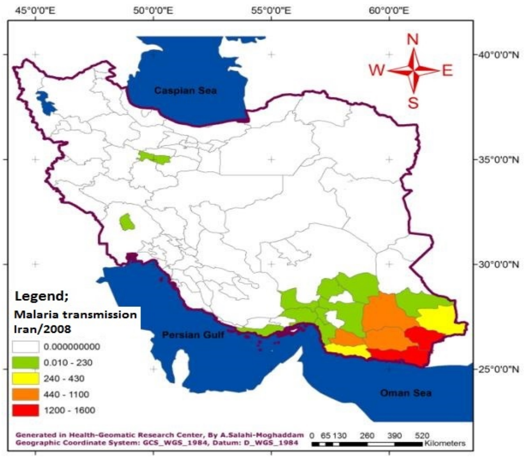

Figure 11. The map of report distribution on different malaria transmission in Iran in 2008

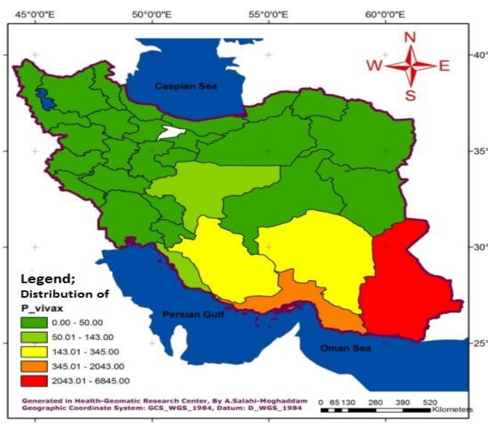

Figure 9. The map of report distrubition of vivax malaria in Iran

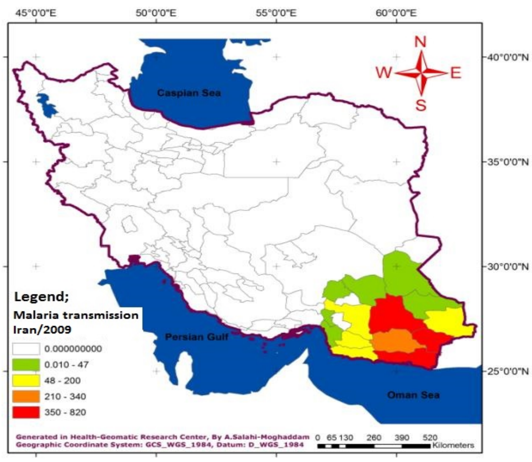

Figure 12. The map of report distribution on various malaria in Iran in 2009

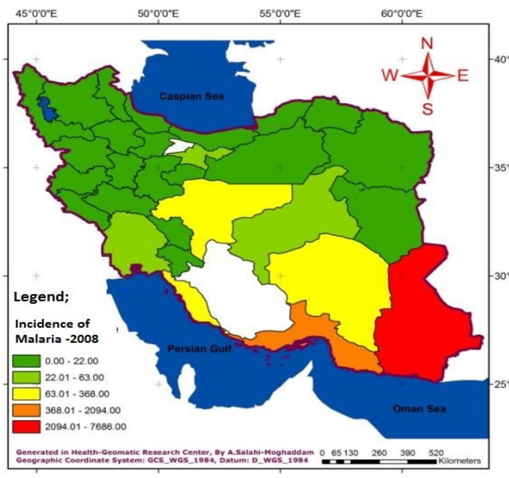

Figure 10. The map of report distribution of various malaria in Iran

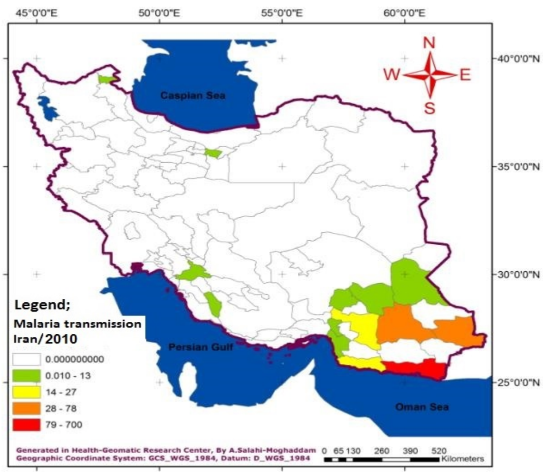

Figure 13. The map of report distribution of various malaria in Iran in 2010

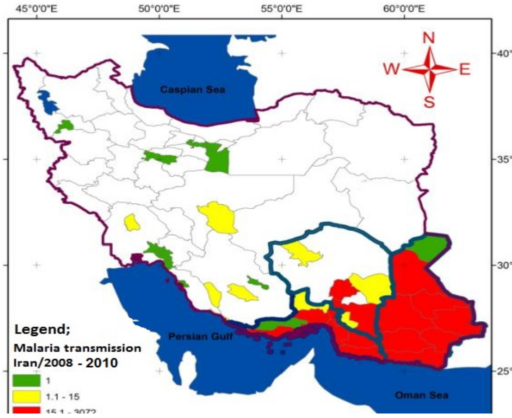

Figure 14. The cases of malaria transmission in Iran between 2008-2010

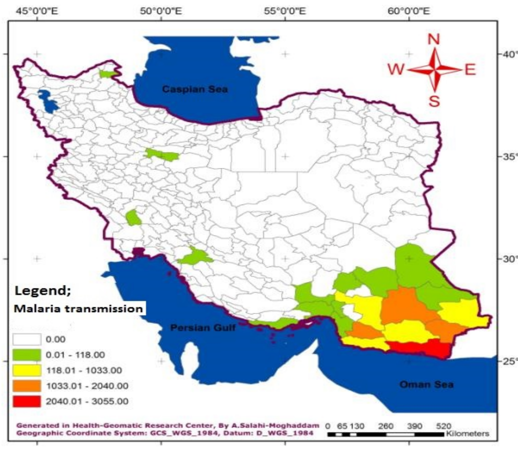

Figure 15: The cases of malariua transmission in Iran focusing upon cities and three present malaria provinces and transmission intensity

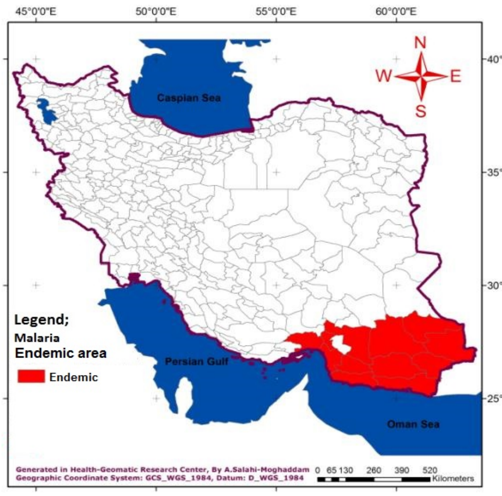

Figure 16. The malaria endomic regions in three years ended to 2011

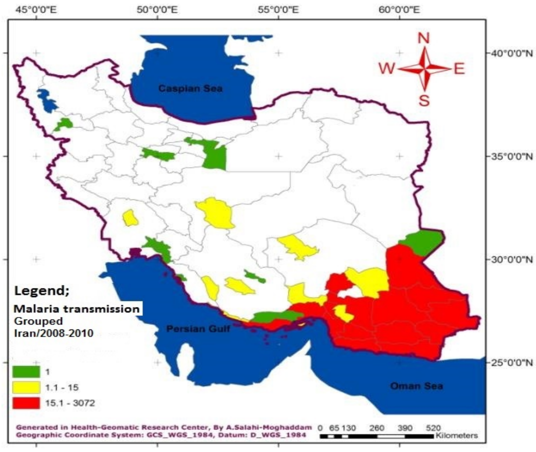

Figure 17. The vegions with higher or lower than 15 cases in the year

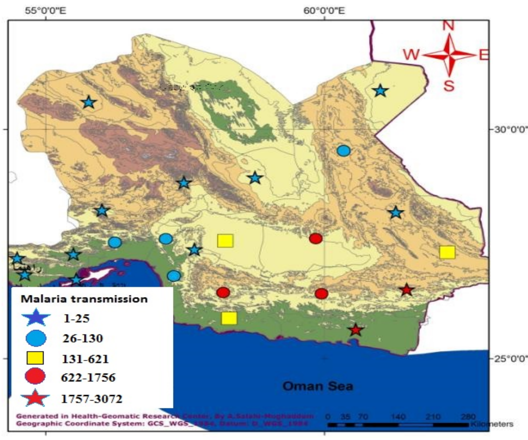

Figure 18. The map of various malaria in southeast mountains in Iran (6) (16) (17) (11) (16,7)

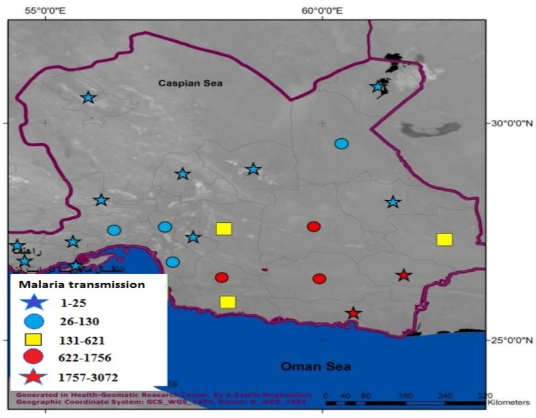

Figure 19. Distribution map of malaria cases in malarial provinces and in frequencies NDVI

Table 1. A summary of malaria status in Iran duringthree years ended to 2010

Year	Vivax	Falciparum	Cases	Recurrence (Relapse)	Transmission from entered	Transmission	Total Number
2008	10225	1203	4246	130	118	6706	11200
2009	5291	610	2314	89	95	3391	5889
2010	2527	436	1497	97	96	1262	2952
Total	**18043**	**2249**	**8057**	**316**	**309**	**11359**	**20041**

Conclusion:

From viewpoint of geographic pathology, Iran is climatologically influenced by three zoogeographical zones. Zoogeographical zones are usually classified based on the variety of vertebrates, especially birds. But considering the epidemiologic requirements in Iran, the classification has been based on a wider variety of creatures one of which is the distribution of anopheles mosquitoes. In the present study, detailed maps of the three zoogeographical zones have been presented considering the opinions of pioneering researchers in prevalence of tropical diseases including Schistosomiasis, Dracontiasis, Malaria, ecology of the region and malaria transmission cases in Iran, and political division of the country by the use of GIS.

Out of 11668 cases of malaria transmission and imported ones in the three recent years, 9400 cases are from the region influenced by Afro-tropical climate, 2200 cases from a region similar to Indo-Malayan and 25 cases in central and northern regions (Palearctic). Since the geographic divisions are not precise, the ranges of the figure given above are not error free.

A review on malaria maps leading to three consecutive years to 2011 indicates that the view of scientists in the previous century concerning the effect of southern heights on contagious diseases still remains valid. Even the distribution of the disease in Kahnouj district does not extend to further northern latitudes in Kerman province.

The georeferenced findings about malaria in Iran are relatively compatible with classical findings of malaria in other parts of the world (12, 13). Therefore, it is possible to predict malaria warning systems for Iran. Malaria distribution map in Iran is also relatively compatible with distribution of vector mosquitoes in Iran including *A. dthali, A. fluviatilis, A. stephensi and A. culicifacies* (14).

The relationship between malaria transmission and relative humidity was discovered at the time of Socrates. It was documented at Pampana the Malariology textbook in 1962. Although most of malaria cases in Iran occur in humid regions, no confirmed significant relationship between malaria transmission and relative humidity has been reported ($P=0.094$). If two important exceptions – about which will be explained later – in eastern Iran are excluded, then the relationship will be significant.

In malaria eradicated/eliminated areas, there is not any relationship between malaria and rainfall. Although rainfall and malaria in endemic regions are related to each other, it is not statistically significant (15). In some studies carried out in small areas of Sistan & Baluchistan province (Iranshahr District) reverse relationship between malaria and rainfall has been reported. According to geo-reference studies in Sistan and Baluchistan province the local vector of the disease is *A. culicifacies* (14). It is assumed that the vector rests in humid microclimates including wells and barns. In this way, the vectors escape from dry and water scarcity regions. Accordingly, tropical torrential rains in the region neither provide suitable condition for the Anopheles life cycle, nor leave the microclimates intact. It washes out all the larval habitats and breeding places. As per the results from field studies (2011) in one of the most important malaria foci of Iran – Iranshahr and Saravan – generalization of the findings was biased towards the relationship between relative humidity, rainfall and malaria transmission.

It should never be forgotten that most parts of Iran have the history of malaria transmission and climate of Iran has the potentiality for malaria transmission. But the evaluation of the disease transmission potentiality is not a simple procedure.

In the past when malaria distribution was intact, the transmission was classified as urban and rural. In urban areas, in which there was not tap water system, people used to consume unsanitary water from private and public water reservoirs. The reservoirs were suitable places for larval habitats. Moreover, in rural areas, the flooding irrigation system also provided the same condition for larval habitats. Therefore, the prevalence of the disease was widespread based on climatologic pattern. As a result, there were more pre-immune people in comparison with present situation, a phenomenon which can explain some of outbreaks.

Although international, national and local measures taken aiming to eradicate and eliminate malaria have changed natural epidemiologic pattern of malaria transmission, the predicting maps generated from this study are compatible with malaria distribution pattern a century ago. In other words, the methodology for preparing the maps and the results obtained from them are compatible with nature of malaria in Iran.

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