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The Mosquitoes (Diptera: Culicidae) and their Medical and Veterinary Importance in an Arid Zone of Central Iran

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ABSTRACT

Mosquitoes play an important role in transmitting a wide range of viral and parasitic diseases to humans and animals. Due to the importance of mosquitoes in human and animal health, the present study was performed to evaluate diseases transmitted by mosquitoes and the status of these diseases in Kashan County. We searched the main databases such as Web of Science, PubMed, Scopus, Google Scholar, Scientific Information Database (SID), Iran Medex, and Magiran about the mosquito-borne diseases of Iran and Kashan County up to May 2021. Also, the checklist of mosquitoes of Kashan County was prepared. There is no published information about mosquito-borne diseases in livestock and animals in Kashan. Human malaria is the only mosquito-borne disease reported in Kashan County. From 2005 to 2016 all human malaria cases in this county were only reported from Afghan immigrants and from 2017 to 2020 no human malaria case has been not reported in Kashan County. Lumpy skin disease is a vector-borne pox disease of domestic cattle that has been reported from 31 provinces in Iran. This disease has not been observed in Kashan so far, but due to the presence of the disease in livestock of neighboring provinces, there is a risk of disease for Kashan. Information about the role of mosquitoes in the transmission of pathogens in Kashan County is limited. Due to the importance of mosquito-borne diseases, mosquito surveillance is necessary for the best-integrated vector management.

Introduction

More than 17% of infectious diseases are vector-borne diseases that cause 700,000 deaths annually [1]. About 60% of emerging and re-emerging infectious diseases are zoonoses. In the last three decades, more than 30 new human pathogens have been identified, 75% of which are of animal origin [2]. In the Eastern Mediterranean Region of WHO, zoonoses are a public health threat [3]. Mosquitoes are considered the most important arthropods in medicine and health due to the transmission of pathogens causing some important infectious diseases such as malaria, filariasis, and arboviral diseases [4-6] and are present worldwide except

Antarctica [7]. Mosquitoes belong to the order Diptera, suborder Nematocera, and family Culicidae [8]. Culicidae has two subfamilies Anophelinae and Culicinae and 70 species in Iran. Mansonia uniformis was the newest genus and species that was added to the mosquito fauna in Iran [9]. Mosquito larvae are found in a variety of environments, including natural and man-made habitats, with temporary or permanent water sources, stagnant or running water, contaminated or clean water, with or without vegetation. Mosquito larvae are also found in small places where water collects, such as pots, used tires, and animal footprints [4,5]. According to the latest study conducted of mosquito fauna in Kashan, there are 3 genera and 13 species in this county including *Anopheles. claviger, An. maculipennis s.l., An. superpictus s.l., An. turkhudi, Culex deserticola, Cx. hortensis, Cx. mimeticus, Cx. perexiguus, Cx. pipiens, Cx. theileri, Culiseta annulata, Cs. longiareolata, Cs. subochrea* [10], also Cx. torrentium larva has been found at an ovitrap in Kashan County [11], and species of Anopheles multicolor, Culex modestus, Aedes caspius, and Ae. pulcritarsis have been reported from previous studies in this county [12,13]. Susceptibility to mosquito-borne diseases has increased due to globalization and led to the spread of emerging and re-emerging pathogens in new and old habitats. Economic and social factors, global trade, transport and tourism have caused the spread of vectors and diseases transmitted by them [7,14]. In livestock, mosquito bites may cause stress and pain, resulting in reduced livestock fitness. In addition, mosquitoes can also transmit pathogen between livestock reservoirs (episodic) and, humans (zoonotic diseases) [7]. Mosquitoes can transmit pathogens in Iran, including causes of arboviral diseases (avian pox, bovine ephemeral fever, dengue fever, Rift Valley fever, West Nile fever), bacterial diseases (Anthrax, Tularemia), helminthic diseases or helminthiases (mosquito-borne filariasis), protozoans (Avian malaria, Human malaria) [6]. Due to global climate change, more animal and human populations will be exposed to these pathogens [7]. Due to the importance of mosquitoes in human and animal health, the present study was performed to evaluate diseases transmitted by mosquitoes and the status of these diseases in Kashan County

Mosquito- Borne Diseases in Kashan County

To find diseases transmitted by mosquitoes, we searched the terms "mosquito-borne pathogens", "mosquito-borne diseases", "mosquito-borne infections", "mosquito-borne viruses". Data were extracted from all articles. An intensive search of scientific literature was reviewed using the search term in the following databases: "PubMed", "Web of Knowledge", "Scopus", "Google Scholar", "SID", etc. Mosquito-borne disease names including 'malaria, avian malaria, West Nile (WN) fever, Dengue (DEN) fever, Sindbis (SIN) fever, lymphatic filariasis, tularemia, tularaemia, anthrax', lumpy skin, and mosquito-borne pathogens such as *Plasmodium, Dirofilaria, Flavivirus, Alphavirus, Phlebovirus, Orthobunyavirus* were reviewed. Also, cases of mosquito-borne diseases identified in Kashan, were inquired from Kashan University of Medical Sciences and Kashan Veterinary Organization.

Protozoal Diseases

Human Malaria

Malaria is a health threat. This disease is caused by a parasite that is transmitted to humans through the bite of infected Anopheles mosquitoes and can be prevented and treated. In 2019, almost half of the world's population was at risk for malaria. Most deaths occur in sub-Saharan Africa. However, Southeast Asia, Eastern Mediterranean, Western Pacific, and Americas also have the case of diseases and deaths. In 2019, cases and the number of deaths due to malaria were 229 million and 409,000, respectively. *Plasmodium falciparum* and *Plasmodium vivax* are the most important parasite species of human malaria [15,16], which are biologically transmitted by some anopheline mosquitoes [17]. Many effective efforts have been done for malaria control in the past that caused decreased morbidity and mortality in Iran [18,19]. At the present, malaria has been eliminated in most parts of Iran [20]. A malaria pre-elimination program started in Iran in 2009, restricted the local transmission of this disease [21]. The results of a study showed that the imported cases (from the eastern neighboring countries) have increased from 2009 onward, compared to indigenous cases [20]. WHO (2020) reported the Islamic Republic of Iran had no indigenous malaria cases in 2018 and 2019[15].

Kashan County is located in the central plateau region of Iran, where have a lower risk of malaria infection compared to southern/ southeastern parts. Seven Anopheles species (*An. maculipennis Meigen s.l., An. sacharovi Favre, An. culicifacies Giles s.l., An. dthali Patton, An. fluviatilis James s.l., An. stephensi Liston, An. superpictus Grassi s.l.*) are malaria vectors in Iran [22]. *Anopheles superpictus s.*l. species is the most abundant and distributed among Anopheles in Kashan County [10,12,13], and is one of the seven species of malaria vectors in Iran [22,23], also *An. maculipennis s.l.* [10,12], An. claviger [10,12,13], *An. multicolor* [12,13], and *An. turkhudi* [10] have been reported from Kashan County. *An. maculipennis s.l.* is the main vector in the Caspian coast in northern Iran [24]. In Kashan County, from 1986 to 1997, a total of 498 malaria patients have been reported, of which 95% were Afghan immigrants and 5% were Iranian travelers or immigrants from other parts of the country [13]. There are malaria cases from 2005 to 2020 and parasite species in Table 1, all malaria cases in these years were reported from Afghan immigrants.

Table 1: Human malaria cases and parasite species from 2005 to 2020 in Kashan County.

Year	*P. vivax*	*P. falciparum*	*P. vivax* and *P. falciparum*	*P. malariae*	Total
2005	3	0	1	0	4
2006	3	0	0	0	3
2007	1	1	0	0	2
2008	3	0	1	0	4
2009	3	0	0	0	3
2010	1	0	0	0	1
2011	2	0	0	0	2
2012	1	1	0	0	2
2013	1	0	0	0	1
2014	0	0	0	0	0
2015	1	0	0	0	1
2016	0	1	0	0	1
2017	0	0	0	0	0
2018	0	0	0	0	0
2019	0	0	0	0	0
2020	0	0	0	0	0

Avian Malaria (Bird Malaria)

Culicidae mosquitoes belonging to different genera (*Culex, Coquillettidia, Aedes, Mansonia, Culisetta, Anopheles, Psorophora)* transmit many species of avian Plasmodium [25-29]. Bird malaria has been reported in some provinces of Iran including Fars Province [30,31], and Mazandaran Province [32,33]. Kalani et al. for the first time, reported two hematozoa, including *Aegyptianella and Plasmodium* in Isfahan Province [34]. But no information is available about the vectors of this disease in birds in these provinces. *Culex pipiens* is the main vector in some countries including Austria [35], Japan [28], Portugal [36], Spain [37], and Turkey [38]. In Austria *Cx. torrentium* is also main vector [35]. *Culex theileri* in Portugal and Spain are known as a vector [36,37]. *Aedes caspius s.l., Cx. modestus and Cx. perexiguus* are vectors in Spain [37]. No avian malaria has been reported from birds in Kashan County, but there are species of *Aedes caspius s.l, Cx. pipiens, Cx. torrentium, Cx. theileri, Cx. modestus and Cx. perexiguus* in different districts of the county [10-12].

Mosquito-Borne Viruses (Arboviral Diseases)

Bovine Ephemeral Fever

Bovine ephemeral fever is an arthropod-borne disease of cattle and water buffaloes. The disease agent is from the genus *Ephemerovirus* within the Rhabdoviridae family. Biting midges (Diptera: Ceratopogonidae) and mosquitoes *Aedes, Anopheles and Culex* are known as the main vectors [39-42]. There is no information about the vectors of the virus in Iran [6]. In Iran, bovine ephemeral fever virus has been found in cattle and water buffalo in provinces Razavi Khorasan [43], Khuzistan [44], Fars, Tehran, West Azerbaijan [45], and Qazvin [46]. The virus has not been reported in Kashan County.

West Nile Fever

West Nile Virus (WNV) distributed in Africa, Europe, the Middle East, North America, and West Asia, is a member of the family *Flaviviridae*, *Flavivirus* genus, and belongs to the Japanese encephalitis complex. Human is most often infected by infected mosquito bites. Genus *Culex* is the principal vector of WNV, in particular *Cx. pipiens.* Birds are the reservoir hosts of WNV, In Europe, Africa, Middle East, and Asia [1,47]. In nature WNV is held in a mosquito-bird-mosquito transmission cycle and *Culex spp*. are the main vectors [48]. In a study, *Cx. pipiens* infection with WNV was reported in Guilan Province, north of Iran [49]. Also, it has been reported that *Aedes caspius* to be infected with the virus in the northwest of Iran [50]. West Nile virus has been identified by ELISA in horses in at least 26 of the 31 Iranian provinces and is the most important and most widespread mosquito-borne arbovirus in Iran [51-53]. *Culex perexiguus*, and *Cx. modestus* have also been reported as the principal vectors of WNV in Asia and Europe [54]. These mosquitoes have been reported from Kashan County [10,12], but no information is available about them, and birds infected with WNV in this County.

Lumpy Skin Disease (LSD)

Lumpy skin disease is a vector-borne pox disease of domestic cattle and Asian water buffalo and is characterized by the appearance of skin nodules [55]. Lumpy skin disease virus (LSDV) is a member of the genus *Capripoxvirus* and the family Poxviridae and is one of the most warning diseases in cattle from the perspective of OIE (Organization for World Health Animal Diseases), so it is mandatory that disease-free countries report it to OIE within 24 hours of confirmation of the disease [56]. The original vector is probably different in geographical areas, including the common stable fly (*Stomoxys calcitrans*), mosquitoes such as *Aedes aegypti*, and some species of African mites *Rhipicephalus and Amblyomma spp*. [55]. Lumpy skin disease (LSD) outbreaks in Kenya were caused incidence of Aedes natronius and Culex mirificus mosquitoes [57]. Culex spp. mosquitoes that feed multiple times on different hosts can increase the probability of transmission [58]. Lumpy skin disease was first seen in Zambia in 1929, then spread to all parts of the Sub-Saharan Africa as well as Madagascar. This disease was first observed in 2014 in western Iran. The outbreak of the disease in Iran followed the spread of the disease in neighboring western countries, including Turkey and Iraq. This disease has been reported from 31 provinces of the country with different prevalence percentages and epidemiological data of the disease indicate that the disease has spread epidemically among cattle and calves of different breeds. High risk provinces were including the provinces of West Azerbaijan, Kurdistan, Ilam, Khuzestan, and Kermanshah. Epidemiological data of the disease in the country show that the prevalence is less than 1% (0.55%) [59]. This disease has not been observed in Kashan so far, but due to the presence of the disease in livestock of neighboring provinces, there is a risk of disease for Kashan.

Mosquito-Borne Filariases

Dirofilariasis

Dirofilaria is a long, slender parasitic worm that infects a variety of mammals. The infection is transmitted by mosquito bites. There are many species of *Dirofilaria*, but infection in humans is usually caused by three species: *D. immitis, D. repens, and D. tenuis.* Dogs and wild dogs such as foxes and wolves are the main natural hosts of these three species. *Dirofilaria immitis* is also known as "heart worm" [60]. *Dirofilaria repens and D. immitis* infection has been found in humans and dogs in 16 provinces of Iran including Guilan [61], Garmsar [62], East Azarbijan Province [63], Gilan, Mazandaran, Golestan, East, and West Azerbaijan, Ardebil, Markazi, Isfahan, Khorassan, Khuzestan and Hormozgan [64,65], Ahvaz City [66,67], Kerman [68], and Meshkin-Shahr [69]. Vector of D. immitis in Ardebil Province is Cx. theileri [61,70]. There is no information about this disease in Kashan County.

Setariasis (Setariosis)

Setaria (Nematoda: Spirurida: Onchocercidae: Setariinae) infects ruminants. Species of *Setaria digitata, S. equina, S. labiatopapillosa, S. marshali, S. cervi* have been reported in horses, cattle, sheep, goats, donkeys, wild sheep, and water buffalo in 10 provinces [71-82]. This nematod is transmitted by mosquito species of the genera *Aedes, Anopheles, Armigeres Theobald, Culex and Mansonia* [83]. Setaria equine has been found from *Anopheles maculipennis* females in Ardebil Province [70]. There is no information about this disease in Kashan County.

Checklist of Mosquitoes (Diptera: Culicidae) of Kashan County

A checklist of mosquitoes of Kashan County is presented as follow:

Family Culicidae Meigen, 1818

Subfamily Anophelinae Grassi, 1900

Genus Anopheles Meigen, 1818

Subgenus *Anopheles* Meigen, 1818

1. *An. (Ano.) claviger (Meigen*, 1804)
2. *An. (Ano.) maculipennis s. l. Meigen*, 1818

Subgenus *Cellia* Theobald, 1902

1. *An. (Cel.) superpictus s. l. Grassi*, 1899
2. *An. (Cel.) multicolor Combouliu*, 1902
3. *An. (Cel.) turkhudi Liston*, 1901

Subfamily Culicinae Meigen, 1818

Tribe Aedini Neveu-Lemaire, 1902

Genus Aedes Meigen, 1818

Subgenus *Ochlerotatus* Lynch Arribálzaga, 1891

1. *Ae. (Och.) caspius (Pallas,* 1771*) s.l. [Oc. caspius (Pallas) s.l.]*
2. *Ae. (Och.) pulcritarsis (Rondani,* 1872*) [Oc. pulcritarsis (Rondani)]*

Tribe Culicini Meigen, 1818

Genus Culex Linneaus, 1758

Subgenus *Barraudius* Edwards, 1921

1. *Cx. (Bar.) modestus Ficalbi, 1889*

Subgenus *Culex* Linneaus, 1758

1. *Cx. (Cux.) pipiens Linnaeus*, 1758 (see Note 26)

2. *Cx. (Cux.) torrentium Martini*, 1925
3. *Cx. (Cux.) perexiguus Theobald*, 1903
4. *Cx. (Cux.) theileri Theobald*, 1903
5. *Cx. (Cux.) mimeticus Noè*, 1899

Subgenus *Maillotia* Theoald, 1907

1. *Cx. (Mai.) deserticola Kirkpatrick*, 1924
2. *Cx. (Mai.) hortensis Ficalbi*, 1889

Tribe Culisetini Belkin, 1962

Genus *Culiseta* Felt, 1904

Subgenus *Allotheobaldia* Broelemann, 1919

1. *Cs. (All.) longiareolata (Macquart*, 1838*)*

Subgenus *Culiseta* Felt, 1904

1. *Cs. (Cus.) annulata (Schrank*, 1776*)*
2. *Cs. (Cus.) subochrea (Edwards*, 1921*)*

Conclusion

Information about the role of mosquitoes in the transmission of pathogens in Kashan County is limited. Due to the construction of bird garden in Qamsar, and entry of birds from 17 different countries into this area, and importance of mosquito-borne diseases in the country, vector-borne disease surveillance, is necessary for the best integrated vector management. The life cycle of mosquitoes requires two types of environments: aquatic habitats (eggs, larvae, and pupae) and terrestrial ecosystems (adults) [17]. Control strategies of mosquitoes may be to controlling adults or larvae at the breeding sites. Methods of insecticide-treated bed nets (ITN) and indoors residual spraying (IRS) are used to control adult mosquitoes [84]. But these methods are not effective in controlling exophilic and exophagic mosquitoes [85]. Environmental management is one of the most effective and sustainable methods for controlling of vectors of diseases. The concept of environmental management for mosquito control is a range of methods including long-lasting physical transformation of larval habitats, temporary changes of larval habitats, which makes the environmental conditions unsuitable for vector breeding, and reduce human/vector/pathogen contact [86]. Application of these methods depending on the type of larval habitat can reduce mosquito populations and reduce the risk of disease transmission.

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Availability of Data and Materials

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Competing Interests

The authors report no conflicts of interest in this work.

Consent for Publication

Not applicable.

Author's Contributions

Seyed Hassan Moosa-Kazemi (SHM) and Mohammad Mehdi Sedaghat (MMS) designed and organized the work. Tahereh Sadat Asgarian (TSA) performed the literature search and wrote the manuscript. Mohsen Akbarian (MA) provided information about malaria. All authors reviewed the manuscript.

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