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A comprehensive overview on sandfly fever

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ABSTRACT

Sandfly fever is a febrile emerging arboviral illness which is a huge threat posed to public health. Sandfly fever viruses (Sicilian, Naples, and Toscana) are endemic to the Mediterranean region. Evidence suggests an increase in the activity of sandfly-borne phleboviruses and their extension to other places. The infection is relatively benign but may cause severe clinical manifestations and complications. Sandfly fever viruses belongs to the genus *Phlebovirus* (family Bunyaviridae), and the four main serotypes include sandfly fever Sicilian virus, sandfly fever Naples virus, sandfly fever Cyprus virus, and Toscana virus. Sandfly fever has flu-like symptoms such as fever, headache, photophobia, malaise, myalgia, and retro-orbital pain. The incubation period of the disease is 4-8 days, and the patient usually recovers within a week. The first infection provides the host with immunity. Sandfly fever viruses are transmitted through the bites of infected female sandflies, thus, the epidemiology of sandfly fever is closely related to the presence and activity of sandfly species that act as the vectors for transmission. Cases and outbreaks of the disease have been reported worldwide for more than 100 years. All in all, this disease is important for non-endemic countries because it is a travel-related and/or imported illness.

KEYWORDS: Sandfly fever; *Phlebovirus*; Global distribution; Epidemiology; Iran

1. Introduction

Sandfly fever, also called three-day fever, phlebotomus fever, or papatasi fever, is a viral disease transmitted by the bite of a species of phlebotomine sandfly, of the family Psychodidae (Newman 1834). Sandflies are small insects that live in rural or suburban areas, and places closed to domestic animals and humans. Rodents' burrows and cavities of other animals as well as the nest of birds

and chickens are desirable places for them to live. Their activity peaks during the summer. Their bites are painful and usually occur at night, and only females are blood feeding[1,2-6].

Insects of the family Psychodidae are distinguished by a dense covering of hairs on the body and wings. Only the Phlebotominae subfamily has piercing-sucking mouthparts. They are small with a body length seldom exceeding 3 mm. Meanwhile, the phlebotomine sandflies have a brittle and elongated body. Their color ranges from nearly white to nearly black. Three features of phlebotominae sandflies are exclusive to distinguish them from other members of the family: (1) They are hairy; (2) When they want to bite, they hop around the host before settling down to feed, and their attack is silent; (3) When resting, they keep their wings at an angle above the abdomen (V shape). The live area of this subfamily are always near to the larval habitats, and the maximum sphere rarely exceeds one kilometer from their breeding sites. Phlebotomine sandflies are nocturnal but some may forage during daylight. They are prone to rest in some cool and humid places. Most species of them are exophagic and exophilic and cannot be effectively killed by residual spraying[7-10].

According to the classification currently widely used, the subfamily Phlebotominae includes the genera *Phlebotomus* (13 subgenera) (Loew 1845), *Sergentomyia* (10 subgenera) (França and Parrot 1920), and *Chinius* (4 species) (Leng 1987) in the Old World, and the genera *Lutzomyia* (26 subgenera and groups) (França 1924), *Warileya* (6 species) (Hertig 1948), and *Brumptomya* (24 species)

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(França and Parrot 1921) in the New World[1,11-14].

Of the more than 800 known sandfly species, approximately 464 are found in the New World and 375 in the Old World. Species of the *Phlebotomus* genus feed mainly on mammals, although there are exceptions. This genus includes many species that feed on humans, some of which are endophilic. Most species of *Sergentomyia* probably feed more on cold-blooded vertebrates, but others occasionally bite mammals. None of the species of *Brumptomyia* bites humans.

Sandfly fever is transovarially and horizontally transmitted by Phlebotomine sandflies. Infection is found in males and females suggesting transovarial and venereal transmission during mating[10]. Generally, *Phlebotomus papatasi* (*P. papatasi*) (Scopoli 1786) was incriminated vector of phleboviruses. Nevertheless, in the past years, the viruses have also been detected in *Phlebotomus perfiliewi* (*P. perfiliewi*) (Parrot 1930), *Phlebotomus perniciosus* (*P. perniciosus*) (Newstead 1911), *Phlebotomus longicuspis* (Nitzulescu 1930), *Phlebotomus sergenti* (Parrot 1917), and *Sergentomyia minuta* (*S. minuta*) (Rondani 1843), indicating sandflies have low specificity for these viruses[4].

Sandfly fever is prevalent in various geographical areas. Although it is a self-limiting benign disease, it may cause severe clinical manifestations in some people. Therefore, the differential diagnosis of sandfly fever in patients with myalgia, fever, headache with thrombocytopenia and leukopenia should be conducted[15]. Sandflies can transmit several arboviruses of the families Reoviridae, Rhabdoviridae, and Bunyaviridae. In the family Bunyaviridae, sandfly-borne arboviruses belong to the genus *Phlebovirus*[16]. *Phlebovirus* genus includes sandfly fever Sicilian virus (SFSV), sandfly fever Naples virus (SFNV), Toscana virus (TOSV), sandfly fever Turkey virus (SFTV), and Punta Toro virus. Sandfly-borne viruses of the families Reoviridae and Rhabdoviridae belong to the genera *Orbivirus* (such as Changuinola virus) and *Vesiculovirus* (such as Chandipura virus), respectively[17-19]. Changuinola virus which is associated with several outbreaks in humans is highly pathogenic. Outbreaks of acute encephalitis, characterized by rapid onset of fever and central nervous system involvement with high mortality, have been reported in Asia. Chandipura virus is currently endemic only in India[18,20,21].

In the Mediterranean region, many phlebovirus arboviruses are circulating between vectors and reservoirs in nature, as evidenced by virus isolation and molecular detection in sandflies. TOSV, sandfly fever Naples and Sicilian viruses are endemic to the Mediterranean region and can spread to the more temperate regions of Europe where vectors are present. Some of these arboviruses have low pathogenicity, but some of them, such as Toscana, Naples, and Sicilian viruses, can be very debilitating even in mild cases. TOSV shows a strong neurotropism and can cause acute meningitis or meningoencephalitis[13].

The genus *Phlebovirus* contains 37 known viruses, including sandfly fever viruses, which are mostly transmitted to vertebrates by Phlebotominae subfamily sandflies. However, other species

of mosquitoes may also be involved in the transmitting of these viruses[22,23]. Phleboviruses that cause sandfly fever are geographically distributed in Europe, Africa, Central Asia, and America[24,25].

Little is known about the animal reservoirs of sandfly fever. Isolation tests and serological assays of some animal species have mainly identified gerbils as candidates for the disease reservoir, although their role as an effective reservoir has not yet been determined[25,26]. The animal appears to play a role in enhancing the horizontal transmission of the virus, which can nevertheless ensure its vertical transmission. These arboviruses are present in the vector's body and are transmitted to the next generation through the transovarial transmission. That means the infected vectors also act as the reservoir. Vectors get the infection from animal reservoirs. In these cases, horizontal transmission is seen. Wild mammals are considered to be, but it has not been proven, the reservoirs, while novel serological studies indicate that domestic dogs may be an important part of the transmission cycle[27-30].

Sandfly fever is one of the most common viral diseases in the world and of great importance in terms of public health. It is a benign disease but is of concern because it may cause severe clinical manifestations in some people. It is also of particular importance to tourists and soldiers traveling from non-endemic to endemic areas, doubling the need to pay attention to it. Therefore, this study aims to investigate different aspects of sandfly fever.

2. Data collection

Using keywords such as three-day fever, sandfly fever, papatasi fever, phlebotomus fever, vectors, reservoirs, clinical symptoms, treatment, global distribution, and epidemiology as well as prevention and control, this review study was conducted through searching the internet and websites related to the reputable medical-health journals, scientific databases such as Web of Science, Ovid, PubMed, Scirus, Science direct, Scopus Google scholar, and Medline to access articles published from 1971 to 2019. Finally, 109 valid articles were selected, studied, and analyzed based on the study objectives.

All data were analyzed according to the relevant laws and guidelines of the ethical standards of the Declaration of Helsinki. All English and Persian articles that passed the essential evaluation stages, and also received the needed quality scores, were entered in the review. At first, the titles, then the abstract, and the main text of the papers were consulted to regain the studies fit for this review. The results of all articles were carefully reviewed and any duplicated study was excluded. Studies without obvious results for patients, those without ethical considerations, abstracts presented in congresses without full text, and case-control studies were excluded from the review step. After including the selected articles in the research and approving the quality of the articles, required data were extracted from all the accepted studies.

3. Symptoms

The incubation period of the sandfly fever in humans is 4-8 days after being infected. The viremia duration is usually less than 7 days. Viral load is low in the cerebrospinal fluid. Sandfly fever has flu-like symptoms that start suddenly. Most viral infections of the disease are subclinical and cause high rates of seroprevalence in endemic areas. Cases with clinical symptoms are relatively few. Symptomatic infections are often self-limiting with headache, severe fever, sometimes up to 40 degrees, pain in the back of the eye when moving the eyeball, conjunctival hyperemia, contusion, lethargy, nausea, pain in the arms and legs and back, myalgia, abdominal pain, and leukopenia. Pharyngitis, the presence of blister-like lesions in the oral mucosa, and inflammation of the cervical lymph nodes are other symptoms of the disease. These symptoms may be severe but not lead to death, but they may cause long-term depression after recovery[19,30-33].

The virus that causes the disease has a variety of strains, some of which, such as TOVS (*Phlebovirus*), are dangerous and can cause encephalitis meningitis, and peripheral neuropathy. Most Toscana infections are asymptomatic, and if do, symptoms encompass headache, fever, vomiting, nausea, and nuchal rigidity. In addition to TOSV, SFTV can cause serious illness, including rare central nervous system infections[19,34-36]. In recent years, TOSV has been isolated from Mediterranean countries such as Italy, Cyprus, Portugal, Spain, Algeria, and France. Infected patients become immune only against the same strain of the virus and may be infected with other strains of the virus[37-43].

4. Diagnosis and treatment

Diagnosis of sandfly fever is based on clinical and laboratory findings in the early stages. In general, serological, cell culture, or molecular methods are used to confirm the diagnosis of sandfly fever[17]. Detection of specific antibodies against sandfly fever virus in serum samples is performed using indirect immunofluorescence and enzyme immunoassay[44]. Enzyme-stimulated immunity has been developed to detect sandfly fever virus-specific human G and M immunoglobulins using fixed antigens of infected cells or pure viruses[25]. Serological methods are commonly used to diagnose the disease. The levels of anti-virus antibodies are also determined in patients. The level of antibodies in the patients' body increases to 4 times or more after 14-21 days after the onset of fever. Anti-virus antibodies remain in the body for the rest of the patients' life and they are immune for good, but this immunity is specific to the same serotype of the virus, and there is a possibility of infection with other serotypes[26,45-47].

Vaccines against the sandfly fever virus are still under development. Viruses of the Bunyaviridae family are generally sensitive to ribavirin which is an antiviral and interferon-inducing medication. Interferon has been effective in inhibiting these viral infections in animal models[48]. Laboratory studies have shown the anti-

SFSV activity of ribavirin, interferon- α , 6-azauridine, glycyrrhizin, suramin sodium, dextran sulfate, and pentosan polysulfate. Ribavirin inhibition and interferon- α occur late in the SFSV replication cycle, whereas glycyrrhizin and sodium suramine are active in the early stages of SFSV replication, and sulfated polysaccharides can inhibit virus uptake into cells[49]. Lab results also show that human interferon-induced MxA protein can inhibit Phleboviruses and other members of the Bunyaviridae family by interacting with the early stage of virus replication[50]. These data suggest that the synergistic antiviral effect of the interferon- α ribavirin combination should be evaluated for viruses of the Bunyaviridae family. Although the benign course of infections caused by sandfly fever viruses and the lack of randomized studies on humans currently does not support any medication, a combination of interferon-ribavirin should be administered in critical conditions, such as critically-ill patients with the deteriorating condition[15].

5. Epidemiology

The Bunyaviridae family, which contains more than 350 RNA viruses, includes 5 genera including *Orthobunyavirus*, *Nairovirus*, *Hantavirus*, *Phlebovirus*, and *Tospovirus*. The sandfly fever viruses group belongs to the Bunyaviridae family and the genus *Phlebovirus*. So far, more than 60 serotypes of this genus have been reported, which fall into two main groups of the sandfly fever group and the Uukuniemi group. The sandfly fever group viruses are transmitted by phlebotominae sandflies and mosquitoes, and the Uukuniemi group viruses are transmitted by ticks. Phleboviruses are RNA-coated viruses with a tripartite genome. Their genomes are made up of S, M, and L fragments, have three nucleocapsids and grow in the cell cytoplasm[51,52].

Among sandfly fever viruses, Naples serocomplex and Sicilian serocomplex are the two main serocomplexes associated with human diseases. Karimabad, Arabian, Massilia, Punigue, Tehran viruses, and TOSV belong to the Naples sandfly virus serogroup. Andria, Arumowot, Odrenisrou viruses, and possibly Arabia virus are known as unclassified phleboviruses; however, Selahabad serocomplex has been suggested for them. Another widespread genotype is the SFSV. Sandfly fever Cyprus virus (SFCV) and SFTV belong to SFSV. At least 10 other new species (Adana, Alcube, Arrabida, Fermo, Granada, Medjerda Valley, Punique, Toros, Zerdali) have been isolated from the Old World sandflies. Granada virus, reported from Spain, appears to be closely related to the SFNV group. Massilia virus from France and Punigue virus from Tunisia have also been reported. New World phleboviruses such as Chagres and Punta Toro virus in Panama and Candiru and Alenquer viruses in Brazil have isolated from *Lutzomyia* sandflies[53-55].

Phleboviruses transmitted by sandflies in the Old World, *i.e.* in the Mediterranean, Africa, Middle East, and Central Asia, as well as the Indian subcontinent, is transmitted by *Phlebotomus* and *Sergentomyia*. In the New World, these viruses are transmitted by *Lutzomyia*. Pathogenicity of 7 Sicilian, Naples, Punta Toro,

Toscana, Chagres, Alenquer, and Candiru serotypes has been proven for humans. Also, vesicular stomatitis virus from the family Rhabdoviridae and genus *Vesiculovirus* has been isolated from sandflies. Chandipura virus has also been isolated from *Sergentomyia* sandflies in Gujarat, India[51]. Phleboviruses have been isolated from the Mediterranean, southern European, Central Asian, African, and American countries[18,56-58]. The seasonal prevalence of the disease in the temperate regions of the Northern Hemisphere is observed from mid-April to late October and is prevalent among military personnel and travelers traveling from non-endemic areas to the endemic areas[59,60]. Of the 22 Eastern Mediterranean countries, sandfly fever has been reported from 15 countries including Iran[26], Pakistan[61], Afghanistan, Iraq[57], Jordan[62], Israel[63], Saudi Arabia, Egypt[64], Sudan[65], Tunisia[66], Bangladesh[67], Algeria[68], Morocco, Somalia, and Djibouti, and 10 serotypes have been reported from the Eastern Mediterranean region[45].

6. Situation in Iran

The first information available in Iran about sandfly fever dates back to the 1970s, but only in a few areas[26,69,70]. Although there was limited information about the disease, researchers have studied its distribution areas and the possibility of new strains of the disease in Iran due to the growing needs and the outbreak of the Iraq war against Iran[71,72]. Various studies have been conducted on sandfly fever. To evaluate patients suspected of sandfly fever, a seroepidemiological study was conducted on soldiers with high fever, headache, and severe cramps with eyeball pain using complement fixation and hemagglutination inhibition tests as well as 2 serum samples of acute and recovery periods. The study showed that in Ilam province, 60% of the studied soldiers had antiserum against Sicilian serotype, and 46% of the same serum contained antiserum against Naples virus. In Gilan-e-Gharb County (Kermanshah province), All serum samples from sick soldiers had antibodies against the Sicilian virus, while only one sample had the Naples virus antibody. Only in Iran, the Isfahan virus has been isolated from sandflies, rodents, and patients[73-76].

Several phleboviruses have been isolated from sandflies in Iran, including Salehabad, Karimabad, and Tehran viruses in 1959, and SFSV in 1975. Karimabad and Salehabad strains are not pathogenic serotypes for humans. The active rotation of these viruses and SFNV in humans has been demonstrated by the detection of antibodies in human serum. In a recent study, the Dashli virus, which is very similar to SFSV, was reported from Iran. This virus has been isolated from *Sergentomyia* spp. and *P. papatasi*[55].

In a study conducted in 1977, the overall prevalence of Naples, Sicilian, and Karimabad virus antibodies in Isfahan province (central Iran) was 17%, 25%, and 66%, respectively. All sera were negative against the Salehabad virus. Karimabad and Sicilian viruses were suggested as endemic in the area, but the Naples virus was suggested as sporadic. Sandflies collected from the area (mostly *P. papatasi*) contained Karimabad and Sicilian viruses. Among the sera of the

animals tested, the infection was only proven in gerbils. Of the 38 *Rhombomys opimus* (great gerbil) (Rodentia: Gerbillidae) (Wagner 1841) tested, 34% had antibodies against the Sicilian virus and 32% against the Karimabad virus[27]. A study of military personnel on Iran's western border in 2017 indicated that 18.4% were positive for IgG antibodies to sandfly fever viruses. SFSV and SFNV were the predominant serotypes. There is a lot of doubt about the presence of TOSV and SFCV in Iran because TOSC has never been isolated from *P. papatasi* in Iran. However, in a few cases, TOSV and SFCV patients were detected using the indirect immunofluorescence test. This may be due to the cross-reactivity between virus serotypes[77]. In most areas, people may develop sandfly fever accompanied by leishmaniasis[78]. Therefore, it is important to pay attention to the set of diseases transmitted by sandflies[79].

Studies have shown that, just as the southwestern area of Iran, the border areas of western Iran can be a favorable area for the spread of sandfly fever among non-immune people. Therefore, such people should be protected against the disease[17,80]. Climate and environmental changes have helped spread the disease to areas where the disease has not been previously reported. The disease is important in terms of military considerations and became epidemic among soldiers in southwestern Iran during the Iran-Iraq war. Therefore, in this regard, there is a danger for people living in southwestern Iran in terms of sandfly fever. Also, with the more travelers to neighboring countries, convenient transportation, and prosperity of the world trade, the transmission of the disease is considered a serious threat[81].

7. Vectors and reservoirs

Sandflies belonging to the Psychodidae (Newman 1834) family are small in size of about 2 mm to 3 mm. Their body and wings are hairy and their tips are narrow, and when resting, their wings are upright above the body. The female sandfly lays eggs in crevices and holes in the moist soil of animal nests, stables, and poultry farms. The larvae feed on decaying organic materials[82,83] including fungi, leaves, vegetables, animal feces, and the decaying bodies of arthropods. After 4 larval stages, they become pupae and then mature. *Phlebotomus* sandflies overwinter in the larval stage. Female phlebotomine sandflies are blood-feeding and attack humans early in the night and sometimes at dawn. They have short mouthparts that can only penetrate naked skin. These sandflies have poor flying power so that they can only fly intermittently[84,85]. Their flight radius at night is 800 to 1500 meters from the location of the larval habitat. During the day, they rest in dark places near humans and animals, such as tree trunk holes, tree branches, animal nests, rock crevices, caves. They are one of the major health pests and vectors of leishmaniasis and carrion's disease in humans[86-89].

So far, about 44 species of sandflies have been reported in Iran, and more species are expected to be found down the line. Of these identified sandflies, 26 species belong to the genus *Phlebotomus* and 18 species belong to the genus *Sergentomyia*, which are scattered and

found throughout Iran[90-95]. Meantime, Kassiri *et al.* reported 52 species of sandflies belonging to the subgenera *Adlerius* (Nitzulescu 1931), *Euphlebotomus* (Theodor 1948), *Larrousius* (Nitzulescu 1931), *Paraphlebotomus* (Theodor 1948), *Phlebotomus*, *Synphlebotomus* (Theodor 1948), *Grassomyia* (Lewis 1987), *Parrotomyia* (Lewis and Parrot 1948), *Parvidens* (Goldman 1917), *Rondanomyia* (Theodor 1948), *Sergentomyia* and *Sintonius* (Nitzulescu 1931) in Iran[96]. In a study in Sistan-Baluchistan Province in 1997 and according to a published paper in 2020 about the check-list of Phlebotominae sandflies in Iran[96], Kassiri *et al.* reported *P. kabulensis* (Artemiev, 1978), *P. salengensis* (Artemiev, 1978), *P. similis* (Perfiliew, 1963), *S. indica* (Theodor, 1931), *S. dreyfussi turkestanica* (Theodor and Mesghali, 1964), *S. squamipleuris* (Newstead, 1912) and *S. (Rondanomyia) sp.* in Iran.

Based on serological studies on rodents in Iran, infection with Sicilian, Karimabad, and Isfahan viruses has been reported in the genus *Rhombomys opimus*. According to the same studies, *Tatera indica* (Hardwicke 1807) has been infected with the Sicilian, Naples, Isfahan viruses, and *Nesokia indica* (Rodentia, Muridae), (Gray 1830) has been infected with the Isfahan virus[26]. Isfahan virus, which is a vesicular stomatitis virus serotype, was isolated from *P. papatasi* in 1975 in Iran. The high prevalence of the Isfahan virus in human sera in some parts of Iran probably indicates its importance to public health. Isfahan virus antibodies were also observed in gerbils serum but not in domestic animals[76]. It should be noted that there are a limited number of studies on the animal reservoir of this disease in the eastern Mediterranean region. Possible reservoirs of the disease are located in most parts of Iran[76,97,98].

SFNV reservoirs are unknown in the world. Various vertebrate species such as carnivores (*Mustela nivalis*), insectivores (Soricidae and Talpidae), and rodents (*Apodemus Kaup*, 1829), *Mus musculus* (Linnaeus 1758), *Rattus rattus* (Linnaeus 1758), *Clethrionomys glareolus* (Schreber 1780), *Meriones libycus* (Lichtenstein 1823), *Gerbillus aureus* (Setzer 1956) may be involved in the maintenance of SFSV. Infection of domestic and wild animals with TOSV has not been established. Transovarial transmission of TOSV in *Phlebotomus* spp. has been proved. Venereal transmission from infected male sandflies to non-infected female sandflies has also been detected in TOSV. Therefore, the reservoir of TOSV is most likely its vectors[18].

P. papatasi is the main vector of SFSV, *P. perfiliewi* (Parrot 1930) and *P. perniciosus* (Newstead 1911) are the main vectors of TOSV, and *Phlebotomus major sensu lato* is the main vector of SFTV[53]. SFSV has been isolated from *P. papatasi*, from the Mediterranean basin to Central Asia. In Algeria, SFSV was isolated from *Phlebotomus ariasi*. In Greece, the Corfou virus, which is very close to SFSV, has been isolated from *Phlebotomus neglectus* (Tonnoir 1921)[18]. In Tunisia, SFSV was isolated from *P. perniciosus*, *Phlebotomus longicuspius* (Nitzulescu 1931), and *S. minuta*. In Turkey and Greece, SFTV and Corfou virus were isolated from *P. major* complex[55]. SFNV was isolated from *P. perfiliewi* in Serbia and *P. papatasi* in Egypt[99]. TOSV, which is prevalent in Spain, France, Italy, Greece, Cyprus, Portugal, and Turkey, was isolated

from *P. perniciosus* and *P. perfiliewi*. The TOSV genome was discovered in *S. minuta*[18].

For a long time, *Sergentomyia* spp. sandflies were considered unimportant vectors because it was believed that they feed only on reptiles and not on humans and mammals. Some studies show that in some parts of the world, *Sergentomyia* spp. can be the vector of leishmaniasis. It has been reported that the *Sergentomyia* spp. has been infected with human pathogenic RNA viruses such as SFSV, TOSV, Chandipura virus, Saboya virus, and Tete virus[55].

8. Prevention and control

Sandfly fever may be epidemic among soldiers and tourists under certain conditions. Up to 75% of non-immune adults entering an infected area may become infected. The best way to control the disease is to eliminate sandflies and protect humans from being bitten by these vectors. The use of insecticide-treated nets and DEET repellent as well as providing necessary health training to people are of great importance. It is also important for travelers and soldiers to use appropriate clothing and repellents on open areas of the body when entering endemic areas. The use of various insecticides and sleeping in an insecticide-treated net as well as observing environmental hygiene can be effective in controlling sandflies[99-102].

9. Conclusions

The current study represented a comprehensive understanding of sandfly fever and its determinant factors in the globe. Since the national and international results of this study have been reported comprehensively based on scientific procedures, therefore, they can be used for policymaking and decision making. One of the limitations of this review study was the dissimilarity between studies. To solve this problem, we tried to extract our data from articles published in reputable journals and by prominent authors.

Military personnel in endemic areas of sandfly fever are at risk for the disease. Having a fever of an unknown source after returning home from an endemic area should raise suspicions about sandfly fever and other possible sandfly-borne diseases. Before going to the endemic areas in the summertime, travelers should receive the necessary training. It is recommended to accurately determine the vectors, reservoirs, and strains of the disease in different areas of the world. Also, it is suggested to provide a complete list of the potential and proven sandfly fever vectors and reservoirs for phleboviruses in the Old and New World.

Conflict of interest statement

The authors report no conflict of interest.

Ethical consideration

The university research review committee revised the research proposal according to the rule and regulation. Accordingly, the study was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences (ID: IRAJUMS.REC. 1400.114).

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Authors' contributions

All authors participated in the research design and contributed to different parts of the research.

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