REVIEW ARTICLE

A Systematic Review of the Arthropod-Borne Rickettsial Diseases with a Special Emphasis on Iran

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Received: 20 July 2021
Revised: 14 August 2021
Accepted: 28 September 2021

Abstract

Background: Rickettsial infections occur worldwide. *Rickettsia spp.* are mandatory intracellular Gram-negative bacteria that can cause mild to severe disease. Recently, with increasing international travel to high-risk areas, the risk of rickettsia transmission has increased. These infections are also important because of their possible use as bioterrorism agents. In this study, we investigated arthropod-borne rickettsial diseases.

Methods: This systematic review study was performed based on PRISMA guidelines. All Persian and English language articles published until the end of 2019 were extracted during the search in the scientific databases of Web of Science, PubMed, Scopus, Cochrane Library, Science Direct, Google Scholar, Medlib, Irandoc, Magiran, and SID.

Results: A total of 62 studies related to the field of arthropod-borne rickettsial diseases between 1940 and 2020 were included in the systematic review. Rickettsiae are related to arthropods which will act as vectors and reservoirs within the bacteria life cycle. To date, ticks (Acari: Ixodidae), lice (Phtiraptera), and fleas (Siphonaptera) have been identified as the main suitable vectors of rickettsiae. Recently, mosquitoes have been suggested as potential vectors for *R. felis*.

Conclusion: One of the most important rickettsial diseases in Iran has been typhus. Historically, typhus has been one of the main health problems with a financial effect in Iran; be that as it may, there are constrained data on the prevalence of typhus within the past centuries. In Iran, there were both epidemic and endemic typhus. Health care officials and physicians should always consider the potential risk of typhus outbreaks under certain conditions. Natural disasters, famines, and overcrowded camps increase the risk of transmission of these infectious diseases.

Please cite this article as: Soltani A, Borouji F, Abdollahi S, Pourtabatabaei AS. A Systematic Review of the Arthropod-Borne Rickettsial Diseases with a Special Emphasis on Iran. J Health Sci Surveillance Sys. 2021;9(4):208-217.

Keywords: Arthropods, Communicable diseases, Iran, Rickettsia infections

Introduction

Rickettsial infections occur worldwide[1] and are associated with patients who have been bitten by ectoparasites such as ticks, fleas, lice, and mites.[2,3] *Rickettsia spp.* are mandatory intracellular Gram-negative bacteria that can cause mild to severe disease[4] and are also one of the most important pathogenic zoonotic factors in humans worldwide. Rickettsial diseases are widely spread around the world.[5] *Rickettsia prowazekii* was responsile for 3-5 million deaths within the Soviet Union amid and after World War I, and *Orientia tsutsugamushi* is now responsible for almost 1 Million non-severe scrub typhus per yearwhile more than 1 billion individuals are in danger.[4]

Both epidemic and endemic typhus are re-emerging diseases. It is assessed that 30 million cases of epidemic typhus happened in 1918 and 1922 in the Soviet Union and Eastern Europe, killing three million people. This illness is related to a high prevalence of contaminated body lice and has as of late re-emerged in destitute conditions and poor wellbeing, including in jails and homeless individuals. Murine typhus, which has not been detailed in Japan since the 1950s, has as of late been returned to that country.[6, 7]

Mortality rates of Rickettsia vary from species to species. Rickettsial infections are an important factor for non-malarial febrile illnesses in Africa.[8] Today, these infections are common in populations living in unsanitary conditions due to the spread of urbanization to suburban environments around the world (such as the emergence of endemic typhus to the southern area of California, USA).[9] National surveillance in the United States between 2008 and 2012 shows that 8.9 cases per million people are reported for Spotted fever infections each year, and the annual prevalence has increased over the past two decades.[10-21]

Methods

The present study is a systematic review in the field of arthropod-borne rickettsial diseases in the world with emphasis on Iran which was performed based on PRISMA-guideline for systematic review studies.[22] All stages of research including search, selection of articles, quality assessment of the articles, and data extraction were performed by three researchers independently.

Search for Articles

In the initial search, all Persian and English language articles published until the end of 2019 were extracted during the search in the scientific databases of Web of Science, PubMed, Scopus, Cochrane Library, Science Direct, Google Scholar, Medlib, Irandoc, Magiran, and SID. All articles with medical subject headings (Mesh) and keywords including arthropods, rickettsia, communicable diseases, ticks, insect, lice, flea, mosquitoes, and Iran were searched in the valid above-mentioned databases in the title, abstract, and text individually and combined using operators AND and OR.

Entry and Exit Criteria

All published articles on the field of arthropod-borne rickettsial diseases with desirable quality were included in the study. Articles that were of poor quality, irrelevant to the subject, or articles with unknown location of the study, review studies, meta-analysis, case report, or series of cases were excluded.

Quality Assessment of the Articles

The quality of the articles was assessed using the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist.[23] This checklist has 22 parts, which are scored based on the importance of each section; the lowest score of this checklist is 15 and the highest score is 33. In this study, score 20 was considered acceptale.[24]

Data Extraction

First, the title and abstract of all articles were reviewed independently by three researchers considering the inclusion and exclusion criteria. Then, the researchers reviewed the full text of the articles and if all three researchers had rejected the articles, the reason would have been mentioned and in case of disagreement between them, a forth researcher judged the article. Data were extracted using a prepared checklist that included the place of study, time of the study, and type of disease.

Selection of Studies

824 articles were extracted by searching databases. Initially, the articles were entered into Endnote software and after initial review, 287 articles were removed from the study due to duplication. Then, by reviewing the titles and abstracts of articles, 475 articles were deleted due to irrelevance, and finally, 62 articles entered the systematic review process.

Results

A total of 62 studies related to the field of arthropod-borne rickettsial diseases between 1940 and 2020 were included in the systematic review.

Rickettsiae and Their Diseases

These are bacteria of the order Rickettsiales, known as short, gram-negative, and rod-shaped bacteria, which require eukaryotic cells to grow and multiply.[25]

Rickettsiales consist of three families, Rickettsiaceae, Bartonellaceae, and Anaplasmataceae.[26] The Rickettsiaceae family comprises three tribes, Rickettsiae, Ehrlichiae, and Wolbachiae, and the rickettsiae tribe is divided into the three genera Coxiella, Rickettsia, and Rochalimaea. Rickettsia (R) is divided into three groups based on its morphological, antigenic, and metabolic characteristics:

The Typhus Group (TG), whose members are *R. typhi*, *R. prowazekii*, and *R. Canada*.[14, 15, 17, 19, 27, 28]

The Spotted Fever Group (SFG), which includes 20 diverse species of rickettsiae (including *R. felis*).[11, 19, 27, 28]

The Scrub Typhus Group, which includes *O. tsutsugamushi*.[1, 17, 27, 28]

Rickettsiae are intracellular parasites[25, 29] that

require host cells to multiply. SFG rickettsiae are found in the host cell nucleus and TG rickettsiae are found exclusively in the cytoplasm. The size of the rickettsial genome is small and of all sequenced rickettsial genomes, plasmids occur exclusively in *R. felis*.[30] Rickettsiae are dependent on arthropods that can transmit microorganisms to vertebrates through salivary (biting) and fecal secretions. Rickettsiae are transmitted to people through infected arthropods, but tissue contamination and blood transfusions have also been reported.[31, 32] Hard ticks (Ixodidae) are vectors of SFG rickettsia and *R. canada*; Mites can transmit *R. akari* and *O. tsutsugamushi*; Lice are the main vectors of *R. prowazekii* and fleas are responsible for the transmission of *R. typhi* and *R. felis*.[33] Epidemic typhus transmitted by lice throughout history has been the main cause of some death and large-scale migration during wars and famines.[34] Many rickettsiae are pathogenic to humans, although, except for *R. prowazekii*, humans have a secondary role in the natural transmission cycle of other *rickettsiae spp.* At present, several species of rickettsia have been detected from infected cases, including *R. prowazekii*, the causative agent of the epidemic typhus, *R. typhi*, the causative agent of the flea-borne (murine) typhus, *R. rickettsii*, the causative agent of the Rocky Mountain spotted fever (RMSF), and *R. conorii*, the causative agent of the Mediterranean spotted fever (MSF). The main symptoms of the rickettsial infection are fever, headache, and skin rashes.[11, 14] The clinical symptoms of these infections are mild to severe. One of the challenging problems with the rickettsial disease is the accurate and timely diagnosis of these infections. Furthermore, surveying the hazard of the rickettsial infections by looking at the presence and dispersion of rickettsia in vectors and vertebrate hosts is complicated due to the issue of detecting and distinguishing rickettsiae using culturing, staining, and immunological methods.[4, 14, 35] Clinical knowledge of the rickettsial diseases, widespread utilization of cell culture processes, and the improvement of particular and sensitive molecular techniques have permitted the revelation of new rickettsial diseases and the identification of common rickettsial infections in places where no rickettsial disease has been distinguished. Most recently discovered deadly rickettsiae were first detected in arthropods and afterward in human cases. In 1937, *Rickettsia parkeri* was detected in Gulf Coast from a hard tick (*Amblyomma maculatum*), and 60 years later, the first case of this infection was reported in humans. Molecular studies have fundamentally altered Rickettsia systematic studies and have shown a wide variety of Rickettsia variants depending on the host range, the effects on the host preference, and the geographical distribution. Many Rickettsia species have been identified in various invertebrates and non-blood-sucking arthropods, including herbivorous arthropods, proteases, worms, and leeches.[6]

Epidemiology of Rickettsial Diseases

The Emergence of Rickettsial Diseases

Considering different rickettsioses, morbidity and mortality rates vary; however, mortality rates for diseases such as scrub typhus, Rocky Mountain spotted fever (RMSF), and epidemic typhus can be as high as 50 percent. For various rickettsial diseases, attack rates also differ and can be as high as 30 percent for African tick-bite fever and 60 percent for scrub typhus[36]

Recently identified data on Rickettsiae species have changed our attitudes about the clinical and epidemiological manifestations of known rickettsial diseases. In addition to the classic triple symptoms, fever, rash, and headache, which are intended the main clinical features for identifying the rickettsial disease, each disease is characterized by certain characteristics, such as the severity and extent of the scar.[37] The process of globalization and global warming are two complementary factors that may affect the transmission of infections, especially arthropod-borne rickettsial diseases.[38] High temperature increases the risk of invasion by *Rhipicephalus sanguineus* (the brown dog tick), leadingto an increase in their attacks on humans.[37, 39]

During recent years, possibility of arthropods prevalence and the risk of ricketsial transmission has increased due to increasing international travel to far-flung places, recent measures to protect wildlife, and rehabilitation and land management measures, especially forestry.[37, 39-41] When travelers return from some high-risk areas like sub-Saharan Africa, rickettsial pathogens, mainly spotted fever tickborne, might be more prevalent in comparison with typhoid or dengue fever.

The most important neglected rickettsial diseases in the world are *Rickettsia rickettsii*, *Rickettsia prowazekii*, *Rickettsia typhi,* and *Rickettsia conorii*. These infections are also important because of their possible use as bioterrorism agents.[37]

Arthropod as Vectors and Reservoirs

Rickettsiae are related to arthropods which act as vectors and reservoirs within the bacteria life cycle. To date, ticks (Acari: Ixodidae), lice (Phtiraptera), and fleas (Siphonaptera) have been identified as the main suitable vectors of rickettsiae.[6, 42] Recently, mosquitoes (including *Anopheles gambiae*) have been suggested as potential vectors for *R. felis*.[43] Arthropods can obtain the infection through feeding or vertical transmission, which happens when a variety of arthropods feed together in a host.[44] When Rickettsiae are effectively transferred transstadially

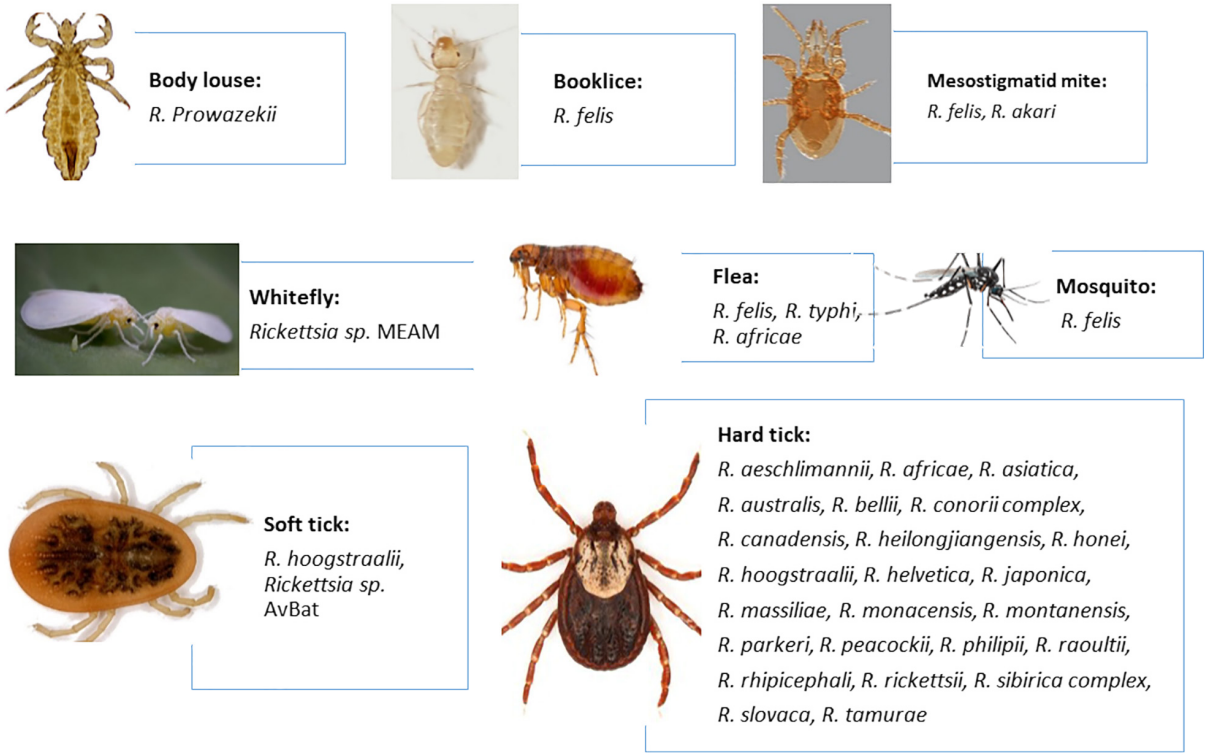

Figure 1: Potential vector/reservoir arthropods for *Rickettsia spp.*[6]

(from larvae to nymphs or from nymphs to adults) and transovarially (from females to their offspring through eggs), in a vector, this arthropod can act as a bacterial reservoir, and subsequently as a distributor of the rickettsial disease[44] (Figure 1).

Tick-borne Rickettsial Diseases

Ticks are the obligatory actoparasites of vertebrates with around 900 known species, which are now classified into three categories: Ixodidae (hard ticks), Argasidae (soft ticks), and Nuttalliellidae (with one rare African species).[45] These arthropods are known as the most important reservoirs and also vectors of the disease in most parts of the world. Using the intracellular mechanism, and having very diverse hosts along with various blood feeding stages (larvae, nymphs, adults) and a long lifespan (sometimes longer than their vertebrate hosts), facilitate the entry of pathogens into host tissues, and also increase the vectorial capacity of the ticks. Ixodidae ticks are vectors and approved reservoirs of most diseases caused by rickettsiae, including *R. rickettsii, R. africae, R. conorii conorii, R. honei, R. sibirica, R. slovaca, R. raultti, R. parkeri. R. massiliae, R. aeschlimannii,*and *R. helvetica*. Different species of the new Rickettsia have been isolated from ticks using molecular techniques, but their pathogenic potential is not yet known.[6]

Rickettsiae infect almost all organs of the invertebrate host and replicate into them. Ticks can transmit the infection to the next generation. When ticks eggs become infected with the bacterium, all stages of their life will eventually be infected with the pathogen (transstadial transmission rate is 100% in these vectors).[6] Ixodidae ticks are bloodthirsty arthropods at all stages of their development, except for some adult males in some species of Ixodes.[40, 46] Rickettsia-infected ticks can transmit the infection to the vertebrate host through the salivary glands during blood-feeding.[40] Accordingly, since all stages of the life cycle could be infectious for their vulnerable vertebrate hosts, ticks should be considered the main reservoir-host of SFG. Long-term starvation of ticks cannot eliminate their rickettsial infection, although some of its properties may change.[6] To be an effective reservoir for rickettsiae, vertebrates need to be the normal host of the vectors and sensitive to rickettsiae, whilepreserving and supporting rickettsiae in their body for a long time. If they do not meet these criteria, ticks will not be able to get rickettsiae from their host's bloodstream. Human beings are not a suitable reservoir for rickettsiae because they are rarely infected with a large number of ticks over a long period. Moreover, the life cycle of ticks can be affected by antibiotic interventions. Rickettsial infection has been reported to reduce fertility in ticks.[14]

Rhipicephalus sanguineus has a role in the transmission of *R. conorii conorii* in the Mediterranean area.

Moreover, in Sub-Saharan Africa, *Haemaphysalis leachi* and *Rhipicephalus simus* are responsible for its transmission.[47] But, *R. rickettsii* is associated with different ticks including *Dermacentor andersoni, Dermacentor variabilis, Dermacentor nitens,*

Amblyomma cajennense, Amblyomma aureolatum, Amblyomma americanum, Amblyomma imitator, Rhipicephalus sanguineus, and *Haemaphysalis leporispalustris*. All above-mentioned hard ticks are occasionally involved in the transmission of rickettsiae to humans and animals.[40]

Moreover, *Amblyomma variegatum* and *Amblyomma hebraeum* are vectors and reservoirs of *R. africae*.[45] This species was also detected in *Rhipicephalus spp.* and *Hyalomma* spp.[40] *R. felis* was detected in *Haemaphysalis flava, Haemaphysalis kitasatoe, Ixodes ovatus, Ixodes granulates*, *Rhipicephalus sanguineus, and Amblyoma cajennense*.[48-52] Also, *R. prowazekii* was detected in *Hyalomma spp.* in Ethiopia[53] and *Amblyomma spp.* in Mexico.[54]

The geographical distribution of Rickettsia species is determined by the spread of the host tick in a certain area. In this way, the seasonal onset of the disease coincides with the activity of the tick. It ought to be noted that the immature stages of ticks can be responsible for the transmission of the disease; whereas their prevalence patterns are different from the adult population. Infected tick bites are painless and usually, most ticks are invisible, especially when small larvae or nymphs are involved.[14]

Insect-borne Rickettsial Diseases

Louse-borne Rickettsial Diseases

Unlike SFG, the Typhus Group (TG) is associated with insects.[27] Lice are blood-sucking ectoparasitic insects that parasitize birds and mammals. About 3,200 species of lice have been identified. Three known species of lice infect humans including *Pediculus humanus humanus* (body louse) and *Pediculus humanus capitis* (head louse), both from the Pediculidae family, and sometimes *Phtirus pubis* ("crab" louse), which is a member of the Phthiridae family. Body lice are the main vector of *R. prowazekii*. To date, infections transmitted by human lice have been on the rise among poor communities such as the homeless, especially in developing and some industrialized countries. Transmission of the disease by lice occurs when infected lice feces come in contact with the bite site, or mucous membranes are in contact with the crushed body or infected lice feces. *R. prowazekii* infection can occur through aerosols caused by dried lice feces, indicating a major risk of transmitting typhus to medical practitioners who are exposed to lice-infested cases.[6] The outbreak of epidemic typhus can thus be caused by the high-speed transmission of *R. prowazekii* from person to person by infected lice. In contrast to ticks that transmit SFG, infected lice will die within 2 weeks after having a blood meal from an infected host. Given that lice eventually die due to the infection, the role of the reservoir in maintaining rickettsiae in nature is crucial. Patients with typhus as a potential reservoir can infect lice.[27]

Flea-borne Rickettsial Diseases

Fleas belong to the order Siphonaptera with about 2500 species, and they are ectoparasites of mammals and scarcely of birds. *Xenopsylla cheopis*, the oriental rat flea, is the main vector of *R. typhi*, and its transmission occurs through exposure of the bite site with flea's feces containing rickettsiae or through inhalation of the dried flea aerosol. Primitive reservoirs are mostly *Rattus rattus* and *Rattus norvegicus*, but several rodents and other animals, including domestic cats and opossums, can also act as hosts. Transstadial and transovarial transmission of *R. typhi* occur in *X. cheopis.*

Fleas are capable of multiple feedings, resulting in the transfer of rickettsiae to several hosts.[27] *R. typhi*, the agent of Murine (or endemic) Typhus, does not reduce the lifespan of flea.[27] Fleas are also the vector of other species of Rickettsia. *R. felis* has been identified in cat flea (*Ctenocephalides felis*). In various studies, the vertical and horizontal transmission of this pathogen has been well established. Previous studies indicate that these insects can act as vectors and reservoirs of the disease.[6]

Main Pathogenic Rickettsia spp. and Their Distribution in the World

R. Prowazekii: This parasite is a causative agent of epidemic typhus that is transmitted from patients or asymptomatic cases by *Pediculus humanus* (but not by other lice). There is an infectious agent in the stool of lice, that transmits the infection by scratching the bite site, causing contact with the infected feces, but in epidemics in enclosed communities, aerosol respiration from the dried feces of infected lice can transmit the disease.[33]

Typhus fever occurs in colder (i.e. mountainous) regions of central and eastern Africa, Central and South America, and Asia. In recent years, most outbreaks have taken place in Burundi, Ethiopia, and Rwanda. Typhus fever occurs in overcrowded and poor-hygiene areas such as prisons and refugee camps. Wars in underdeveloped and developing countries which lead to internally displaced people around the world make it necessary to consider such diseases. They highly need attention as these diseases can even occur in poor-hygiene areas in developed countries that are the main destinations for refugees.[55]

R. Mooseri (R. Typhi): R. mooseri causes endemic typhus infection which is transmitted by *X. cheopis*.[33] and usually infects humans in markets, grain warehouses, garbage warehouses, etc. It is usually not a serious issue but can be more aggressive

in some vulnerable people such as refugees and the homeless.

Flea-borne typhus occurs in tropical and subtropical climates around the world specifically in port cities and coastal regions with a high infestation rate of rodents. This infectious disease is well documented in the USA, Mexico, and some European countries. The higher population densities of rats and their ectoparasites are one of the most important reasons for the occurrence of this disease in coastal urban and sub-urban regions.[56]

The "Spotted Fever" Group

The "Spotted fever" group includes a large number of the rickettsial infections that are transmitted mostly by ticks from rodents, dogs, and some wild animals. Twenty-nine Rickettsia species are currently identified. Rickettsiae are found worldwide, but these parasites have limited distribution and are usually found only in places where their vectors are present. To date, 19 human spotted fever rickettsioses have been described.[56] The most important species are:

R. Rickettsia: Rocky Mountain Spotted fever implies its discovered area, but it is currently occurring mainly in the eastern parts of the US Atlantic Ocean, especially among travelers and hunters exposed to wildlife ticks.

R. Conorii: Mediterranean spotted fever (or boutonneuse fever), that occurs in the Mediterranean region, some parts of Africa, and India, is transmitted by the brown dog tick, *Rhipicephalus sanguineus* (as a vector).[57]

R. Africae: It is found in African pastures and park playgrounds, that are infested with ticks living on cows, rhinos, hippos, and some other animals, leading to African tick-bite fever.[58]

R. Australis, R. Japonica: and other similar rickettsiae that are widely distributed in Asia and Australia, infect humans through various species of animal ticks.

Orientia Tsutsugamushi: (formerly *Rickettsia tsutsugamushi*), the scrub typhus agent, is an obligate and intracellular parasite of mites, that belongs to the family Trombiculidae, is transmitted by the bite of larvae living on grasslands. This parasite was first reported in Japan by Hakuju Hashimoto in 1810. The high-risk zones include Southeast Asia, northern Australia, the Indian subcontinent, Sri Lanka, and other islands in the Indian Ocean, New Guinea, and Afghanistan (Iran's eastern neighbor), etc.[34]

Rickettsial Diseases in Iran

Historically, typhus has been one of the most important rickettsial diseases and health problems with massive economic effects in Iran; however, there are confined data on the prevalence of typhus in the past centuries. Epidemic typhus is an endemic disease in Iran, but its prevalence is restricted.[59] In the Qajar period (1925-1796), infectious diseases, including epidemic typhus, were common. In the twentieth century, the outbreak of typhus occurred in Iran. In November 1909, the outbreak of typhus appeared in the port of Gaz in the province of Golestan in northern Iran. For a long time, physicians were confused about the clinical differentiation of typhus fever from other similar infectious diseases, especially typhoid fever. According to John Gilmour, during the famine of 1918-1917 in Iran, the outbreak of typhus caused the death of a large number of the country's population. At that time, typhus was more prevalent in the fall and winter, and children were more affected than adults. During World War II, typhus was one of the most dangerous pandemics expected to occur during and after the war. Before 1939, in some countries including Morocco, Algeria, Tunisia, Egypt, Iran, Yugoslavia, and possibly Poland, typhus appeared as a small outbreak in winters, but during World War II (1945-1939), the prevalence of the disease increased sharply. In 1941, despite Iran's declaration of neutrality, it was occupied by Allied forces, and at that time typhus spread to Tehran and other major cities[60, 61]> and many people, including health workers, died of typhus. In Iran, there were both epidemic and endemic typhus.[62] Health care officials and physicians should always consider the potential risk of typhus outbreaks under certain conditions. Natural disasters, famines, and overcrowded camps increase the risk of transmission of these infectious diseases. Health experts should always keep in mind that WHO has classified typhus as a "disease under surveillance".[62]

Louse-borne Typhus (Epidemic Typhus)

Inhalation of contaminated aerosols from the body lice and contact with crushed lice transmit the infection to humans. Like other parts of the world, the vector of the disease in Iran is *Pediculus humanus* and its reservoir is humans. In the past, it was a native disease in Iran, leading to the death of large numbers of people, especially during times of famine and war. Fortunately, this disease no longer exists in Iran.[62-64]

Murine Typhus (Endemic Typhus)

Murine typhus, which is a disease of rodents, is sometimes transmitted to humans by fleas. The causative agent is *Rickettsia typhi*. The primary vector of this disease is *Xenopsylla cheopis* and secondary vectors are *Xenopsylla astia*, *Nosopsyllus fasciatus*, *Ctenocephalides felis, Echidnophaga gallinacea*, and *Pulex irritans*. This disease has been identified in Iran both by serology and by isolating the pathogen from the brain of rodents. Murine typhus is a native disease in Iran. This disease is mainly observed in the coastal areas of the north and south, including the provinces of

Mazandaran, Gilan, Golestan, and Hormozgan.[10, 64-67]

Q Fever

An obligate intracellular gram-negative bacterial pathogen called *Coxiella burnetii causes Q fever*. Domestic ruminants, including cattle, sheep, and goats, are the main reservoirs. Infected ticks can play an important role in transmitting bacteria to mammals, rodents, and other mammals, as well as wild and domestic birds. Transmission of the infection to humans is mainly through inhalation of contaminated aerosols, but the disease may also occur after consuming raw milk and contaminated dairy products. Person-to-person transmission of the disease is very rare. Q fever is an endemic disease in Iran.[66, 68, 69] Rodents have been reported to be infected with the pathogen in Iran during the 1970s; However, in recent decades there has been no report of rodent infection and transmission to humans[68] although there have been numerous reports of infection of other animals and their products with *C. burnetii* in various provinces of Iran such as Fars, Khuzestan, Yazd, Chaharmahal- Bakhtiari, Isfahan, Gilan, and Mazandaran.[66, 69, 70]

Boutonneuse Fever (The Mediterranean Spotted Fever)

Rickettsia conorii is the causative agent of Boutonneuse fever. The disease is transmitted by biting different species of ticks. Its primary vector is *Rhipicephalus sanguineus* and its secondary vectors are *Dermacentor spp.*, *Haemaphysalis spp.*, *Hyalomma spp.*, *Boophilus spp.*, and *Rhipicephalus spp.* Dogs, wild rodents, and other mammals have been reported as reservoirs for this pathogen. Most investigations on this matter in Iran have been published in the form of case reports. The results of two studies reported two cases of this disease in Tehran and Mazandaran provinces. Given that some patients with Boutonneuse fever were identified in the mentioned areas, these provinces could be identified as high-risk areas.[66, 71]

Conclusion

Historically, typhus has been one of the most important rickettsial diseases and health issues in Iran and other countries in the Middle East region. Both epidemic and endemic typhus were reported from different parts of the country at different periods. Health policymakers, health system employees, and physicians should always consider the potential risk of the rickettsial diseases outbreaks under certain conditions.

If there is no proper surveillance and monitoring system for these diseases in the country, some environmental and socio-economic factors such as natural disasters, famines, and overcrowded camps can increase the risk of transmission of these infectious diseases. If these influential factors are not well identified and managed, they can even cause the re-emergence of these dangerous vector-borne diseases in the country.

Ethical statement

This article does not contain any studies with human participants or animals performed by any of the authors.

Conflict of Interest: None declared.

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