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REVIEW ARTICLE

Vector-borne diseases in Cyprus: A detailed review of the literature

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ABSTRACT

Vector-borne diseases have been a growing health concern in recent decades due to the global warming, globalization, and increased international travel. With the typical Mediterranean climate and geographical features, Cyprus provides favorable conditions for the growth and survival of arthropod species. For the purpose of this review article, the terms "Cyprus", "vectors" and "vector-borne diseases" were searched in the National Library of Medicine ('PubMed') and the Google Scholar databases. Published articles in the literature have documented mosquito (including *Anopheles*, *Aedes*, *Culex*, and *Culiseta*), sandfly (*Phlebotomus*, *Sergentomyia*), flea (including *Ctenocephalides*, *Xenopsylla*, *Leptopsylla*), and tick (including *Rhipicephalus*, *Ixodes*, *Hyalomma*, *Haemaphysalis*) species in the island. The presence of these arthropods poses a risk to public health as they can transmit a variety of diseases to both humans and animals. Research studies in Cyprus have identified infectious agents such as West Nile virus, *Leishmania* spp., sandfly viruses, *Rickettsia* spp., *Coxiella burnetii*, and *Bartonella* spp. in the local arthropods. More importantly, West Nile virus infection and imported malaria cases (mosquito-borne diseases); leishmaniasis and sandfly fever (sandfly-borne diseases); rickettsiosis, tularemia, Q fever, anaplasmosis, tick-borne relapsing fever, and Lyme disease (tick-borne diseases); and flea-borne rickettsiosis were reported in Cyprus. Taken together with the presence of arthropod vectors, published evidence in the literature suggests that Cyprus is an important region for VBDs. In addition to its climatic and geographical conditions, international travels particularly from endemic countries pose a risk for the circulation of VBDs on the island. Therefore, vector control programs should be continuously implemented, and public awareness must be raised in the region. This review, which to the best of our knowledge is the first comprehensive report on VBDs from Cyprus, will provide insight into future islandwide studies and also will be an important contribution to the elimination of VBDs in the region.

Keywords: Arthropod; vector; vector-borne diseases; Cyprus.

INTRODUCTION

Vector-borne diseases (VBDs) refer to the infections transmitted by arthropods that cause health problems in humans and animals. Approximately 17% of infectious diseases result from vector-borne transmission. Each year the number of deaths caused by VBDs exceeds 700,000, while poor communities in the tropical and subtropical regions are the most affected populations by these infections (Cuervo *et al*., 2023).

The occurrence of VBDs does not only depend on the presence of vectors and infectious organisms in a geographical area but also on favorable environmental and climatic factors of the region. Indeed, change in climate has affected VBD transmission globally as well as in the European region. Due to climate change, disease vectors now cover more extended areas in Europe. In addition to climatic factors, globalization and international travel also facilitate the spread of both microorganisms and vectors among countries (Semenza & Suk, 2018).

Certain species of mosquitoes, sandflies, fleas, lice, ticks, bugs, flies, and snails are vectors that have an important role in disease transmission. For example, *Aedes* mosquitoes are the primary vectors of Dengue, yellow fever, Zika, and Chikungunya virus, while *Culex* spp. are more commonly involved in West Nile virus transmission. *Anopheles* mosquitoes which mainly transmit malaria are also vectors for lymphatic filariasis. Sandflies (*Phlebotomus* spp.) transmit both parasitic (leishmaniasis) and viral (sandfly fever) diseases. Other infections that are transmitted by vectors include flea-borne (plague and murine typhus), lice-borne (epidemic typhus and louse-borne relapsing fever), and tick-borne diseases (Crimean-Congo hemorrhagic fever, Lyme disease, tick-borne relapsing fever, spotted fever, Q fever, tick-borne encephalitis, and tularaemia). Triatomine bugs and tsetse flies are known vectors for American and African trypanosomiasis, respectively, while onchocerciasis is transmitted by blackflies, and schistosomiasis is acquired through aquatic snails (WHO, 2014; WHO, 2023a).

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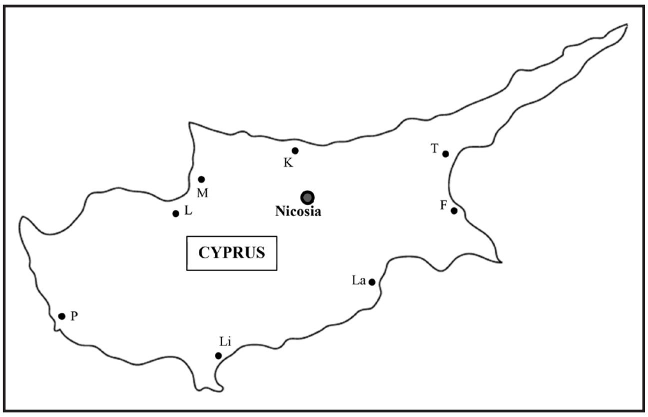

Figure 1. Map of Cyprus. Apart from the capital Nicosia; the map shows Kyrenia (K), Famagusta (F), Morphou (M), Lefka (L), and Trikomo (T) in northern Cyprus; and indicates Paphos (P), Limassol (Li), and Larnaca (L) in southern Cyprus (The map was adapted from: https://www.worldatlas.com/maps/cyprus).

Cyprus island (Figure 1), home to various arthropod species, is located in the east of the Mediterranean region between 34° and 35° northern latitudes and 32° and 34° eastern longitudes. Due to its Mediterranean climate, summers are mostly hot and dry and winters are mild on the island (Ruh & Taylan Özkan, 2019). The climatic and geographical features present in Cyprus have provided favorable growth and survival conditions for disease vectors. Published articles in the literature have identified mosquito (including *Anopheles*, *Aedes*, *Culex*, *Culiseta*) (Violaris *et al*., 2009; Drakou *et al*., 2020), sandfly (*Phlebotomus*, *Sergentomyia*) (Demir *et al*., 2010; Mazeris *et al*., 2010; Töz *et al*., 2013), flea (including *Ctenocephalides*, *Xenopsylla*, *Leptopsylla*) (Psaroulaki *et al*., 2006a; Christou *et al*., 2010) and tick species (including *Rhipicephalus*, *Ixodes*, *Hyalomma*, *Haemaphysalis*) (Ioannou *et al*., 2011; Chochlakis *et al*., 2012) in the island.

Apart from indigenous arthropod species, international travels from endemic countries make Cyprus also an important focus for VBDs. For many years, the island has been a popular tourist spot that attracts travelers from different regions. Moreover, Cyprus receives a large number of international students, most of whom come from African countries for university education. According to the Turkish Republic of Northern Cyprus (TRNC) Ministry of Education (2023), out of 107,936 students registered to the universities in the 2021-2022 academic year, 50,375 came from foreign countries (other than Türkiye). Despite the thorough medical check-ups before their travel, imported malaria cases were detected among newly arrived students over the years (Güler *et al*., 2020). Therefore, local arthropod vectors, as well as travelers and students from endemic areas may pose a risk for the introduction of new VBDs to the island.

The aim of this review is to provide detailed information about vectors and VBDs in Cyprus. To the best of our knowledge, this is the first comprehensive review of VBDs on the island.

MATERIALS AND METHODS

For the purpose of this review article, VBDs in Cyprus were searched using the National Library of Medicine ('PubMed') and the Google Scholar databases from 1970 to 2023. In order to search for the articles in detail, the following terms were used: "Cyprus", and "mosquito" (including *Anopheles, Aedes, Culex, Culiseta*), "sandfly" (*Phlebotomus, Sergentomyia*), "tick" (including *Rhipicephalus, Ixodes, Hyalomma, Haemaphysalis*), or "flea" (including *Ctenocephalides, Xenopsylla, Leptopsylla*). To identify infectious agents, similar databases were used with the terms "Cyprus" and "mosquito-borne", "*Plasmodium*", "malaria", "West Nile virus", "sandfly-borne", "*Leishmania*", "leishmaniasis", "*Phlebovirus*", "sandfly fever", "tick-borne", "*Rickettsia*", "rickettsiosis", "*Francisella*", "tularemia", "*Coxiella*", "Q fever", "*Ehrlichia*", "*Anaplasma*", "anaplasmosis", "*Borrelia*", "tick-borne relapsing fever", "Lyme disease", "louse-borne", "*Bartonella*", "flea-borne", or "acari-borne". Publications on experimental research studies such as drug discovery were excluded from the list of the articles referred.

RESULTS

Mosquito-borne diseases

Increasing temperatures in the European Region are now providing more favorable conditions for the presence of mosquito species. For this reason, the areas affected by mosquitoes have expanded over the years (ECDC, 2023a). Due to its warm climate, Cyprus island hosted different species of mosquitoes since early times. Despite the lack of detailed information on the mosquito fauna, control campaigns were applied for the mosquitoes on the island in the 1940s. Studies carried out between the early 1930s and 2000s identified the presence of various mosquito species in Cyprus. According to the report of Violaris *et al*. (2009), 23 species of mosquitoes belonging to six genera and 10 subgenera were identified within this period. Among them eight *Anopheles* spp. (*An. algeriensis*, *An. claviger* s.l., *An. hyrcanus*, *An. maculipennis* s.s., *An. sacharovi*, *An. marterii*, *An. superpictus*, *An. multicolor*), four *Aedes* spp. (*Ae. aegypti*, *Ae. caspius*, *Ae. detritus*, *Ae. mariae*), seven *Culex* spp. (*Cx. mimeticus*, *Cx, perexiguus*, *Cx. pipiens pipiens*, *Cx. theileri*, *Cx. hortensis*, *Cx. impudicus*, *Cx. martinii*), three *Culiseta* spp. (*Cs. longiareolata*, *Cs. annulata*, *Cs. subochrea*), and one *Uranotaenia unguiculata* (Violaris *et al*., 2009) were identified. A more recent study has reported *Cx. pipiens*, *Ae. detritus*, *Ae. caspius*, *Cs. longiareolata*, and *Cs. annulate* in Limassol in southern Cyprus. Among those, *Cx. pipiens*, *Ae. detritus* and *Ae. caspius* were the predominant species, and the highest population densities were reported between February and April (Drakou *et al*., 2020).

The presence of the arthropods mentioned above has resulted in the occurrence of several mosquito-borne diseases on the island, which are reviewed in the following section. The arthropods and VBDs discussed in this review article are also summarized in Table 1 and 2, respectively.

Malaria

Malaria is a life-threatening, acute febrile parasitic disease caused by *Plasmodium* parasites. *P. falciparum* and *P. vivax* have the highest importance among the five species of *Plasmodium* parasites. While *P. falciparum* has the highest fatality rate in the African Region, *P. vivax* is the predominant species in most countries. Other *Plasmodium* spp. are *P. ovale*, *P. malariae,* and *P. knowlesi* (WHO, 2023b).

Plasmodium parasites are transmitted by the bite of female *Anopheles* mosquitos, mostly in tropical countries. There are 400 different species of *Anopheles* mosquitos, where 40 species are considered as vectors of malaria. Therefore, the identification of local mosquitos and local vector control programs are of great importance (WHO, 2023b).

WHO launched the 'Global Malaria Eradication Programme' (GMEP) aiming universal eradication of malaria. As a result of the efforts of countries, the disease was eradicated in several regions (WHO, 2016a). In Cyprus, the eradication program for *Anopheles* mosquitoes was initiated in 1946 (Aziz, 1947). By 1967, Cyprus was declared to have eradicated malaria (Emms *et al*., 2020).

Despite the fact that most European countries have been free of malaria for many years, *Anopheles* spp. still exist in some regions. The presence of the vector poses a significant threat to the possible re-emergence of malaria in some countries, as climate change may create conditions that are more favorable for the spread of the disease (El-Sayed & Kamel, 2020).

Table 1. Summary of arthropods of medical importance reported from Cyprus (studies conducted in northern Cyprus are written in bold)

Arthropod group	Species	Agents found	Reference
Mosquito	*Anopheles algeriensis, An. claviger, An. hyrcanus, An. multicolor, An. sacharovi, An. superpictus*		Violaris *et al*., 2009; Pallari *et al*., 2022.
	Anopheles maculipennis s.s., *An. marteri*		Violaris *et al*., 2009.
	Aedes caspius, Ae. detritus		Violaris *et al*., 2009; Drakou *et al*., 2020; Pallari *et al*., 2022.
	Aedes aegypti, Ae. mariae		Violaris *et al*., 2009.
	Aedes cretinus		Pallari *et al*., 2022.
	Culex pipiens	One pool (from Deftera, Nicosia, southern Cyprus) that contained *Culex pipiens* was detected positive for West Nile Virus RNA (Pallari *et al*., 2022).	Violaris *et al*., 2009; **Ergunay *et al*., 2014(a)**; Drakou *et al*., 2020; Pallari *et al*., 2022.
	Culex martinii, Cx. theileri		Violaris *et al*., 2009; Pallari *et al*., 2022.
	Culex hortensis, Cx. impudicus, Cx. mimeticus, Cx. perexiguus		Violaris *et al*., 2009.
	Culiseta annulata, Cs. longiareolata		Violaris *et al*., 2009; Drakou *et al*., 2020; Pallari *et al*., 2022.
	Culiseta subochrea		Violaris *et al*., 2009; Pallari *et al*., 2022.
	Uranotaenia unguiculata		Violaris *et al*., 2009.
	Phlebotomus tobbi	*Leishmania infantum* was identified in eight pools of *P. tobbi* in Kyrenia district (three pools from Lapithos, five pools from Panagra), northern Cyprus. Toscana virus was identified in one pool of *P. tobbi*. One of the *L. infantum* positive pools from Panagra was also positive for Toscana virus (Ergunay *et al*., 2014b).	Mazeris *et al*., 2010; **Demir *et al*., 2010**; **Töz *et al*., 2013**; **Ergunay *et al*., 2014(b)**; **Yetişmiş *et al*., 2022**.
	Phlebotomus papatasi	*Leishmania major* was detected in *Phlebotomus papatasi* in northern Cyprus (Yetismis *et al*., 2022).	Mazeris *et al*., 2010; **Demir *et al*., 2010**; **Töz *et al*., 2013**; **Ergunay *et al*., 2014**; Dokianakis *et al*., 2018; **Yetişmiş *et al*., 2022**.
	Phlebotomus major s.l.		**Yetişmiş *et al*., 2022**.
	Phlebotomus alexandri		Mazeris *et al*., 2010; **Demir *et al*., 2010**; **Töz *et al*., 2013**; **Yetişmiş *et al*., 2022**.
	Phlebotomus galilaeus, P. sergenti		Mazeris *et al*., 2010; **Demir *et al*., 2010**; **Töz *et al*., 2013**.

Sandfly	*Phlebotomus perfiliewi* s.l.	Toscana virus was identified in two pools of *P. perfiliewi* s.l. in northern Cyprus. Also, sequences that belonged to novel phleboviruses (named as Girne 1 and Girne 2 viruses), were identified in two *P. perfiliewi* s.l. pools (Ergunay *et al*., 2014b).	**Ergunay *et al*., 2014(b)**.
	Phlebotomus kyreniae		**Demir *et al*., 2010**; **Töz *et al*., 2013**.
	Phlebotomus economidesi		Mazeris *et al*., 2010; **Demir *et al*., 2010**.
	Phlebotomus mascittii		Mazeris *et al*., 2010.
	Phlebotomus neglectus		**Demir *et al*., 2010**.
	Phlebotomus jacusieli		**Demir *et al*., 2010**; **Ergunay *et al*., 2014(b)**.
	Phlebotomus killicki		Dokianakis *et al*., 2018.
	Laroussius spp.		**Ergunay *et al*., 2014(b)**.
	Sergentomyia azizi		**Demir *et al*., 2010**; **Töz *et al*., 2013;** **Ergunay *et al*., 2014(b)**.
	Sergentomyia minuta		**Demir *et al*., 2010**; **Töz *et al*., 2013**; **Ergunay *et al*., 2014(b)**; Dokianakis *et al*., 2018; **Yetişmiş *et al*., 2022**.
	Sergentomyia fallax		**Demir *et al*., 2010**; **Töz *et al*., 2013**; **Yetişmiş *et al*., 2022**.
	Sergentomyia dentata		Dokianakis *et al*., 2018; **Yetişmiş *et al*., 2022**.
Tick	*Rhipicephalus sanguineus*	*Coxiella burnetii* was detected in *R. sanguineus* and *Hyalloma* spp. ticks (Psaroulaki *et al*., 2006). *C. burnetii* was detected in *Rhipicephalus turanicus, R. sanguineus, R. bursa* (Ioannou *et al*., 2011). *C. burnetii* was detected in 60% of *R. sanguineus* (Psaroulaki *et al*., 2014a).	Le Riche *et al*., 1974; Psaroulaki *et al*., 2006; Psaroulaki *et al*., 2008; Ioannou *et al*., 2011; Psaroulaki *et al*., 2014(a); Tsatsaris *et al*., 2016; Chitimia-Dobler *et al*., 2019; Diakou *et al*., 2022.
	Rhipicephalus turanicus	*C. burnetii* was detected in *Rhipicephalus turanicus, R. sanguineus,* and *R. bursa* (Ioannou *et al*., 2011). *C. burnetii* was detected in 28% of *R. turanicus*, (Psaroulaki *et al*., 2014a).	Le Riche *et al*., 1974; Psaroulaki *et al*., 2008; Ioannou *et al*., 2011; Psaroulaki *et al*., 2014(a); Tsatsaris *et al*., 2016; Chitimia-Dobler *et al*., 2019.
	Rhipicephalus bursa	*C. burnetii* was detected in *Rhipicephalus turanicus, R. sanguineus,* and *R. bursa* (Ioannou *et al*., 2011). *C. burnetii* was detected in 39% of *R. bursa*, (Psaroulaki *et al*., 2014a).	Le Riche *et al*., 1974; Ioannou *et al*., 2011; Psaroulaki *et al*., 2014(a); Tsatsaris *et al*., 2016.
	Rhipicephalus pusillus		Psaroulaki *et al*., 2014(a); Tsatsaris *et al*., 2016.
	Ixodes crenulatus		Le Riche *et al*., 1974.
	Ixodes gibbosus		Le Riche *et al*., 1974; Ioannou *et al*., 2011; Psaroulaki *et al*., 2014(a); Tsatsaris *et al*., 2016; Diakou *et al*., 2022.

	Ixodes ventalloi	Three *I. ventalloi* ticks were positive for *Rickettsia* spp. and *C. burnetii* (Ioannou *et al.*, 2009). *C. burnetii* was detected in 50% of *I. ventalloi* (Psaroulaki *et al.*, 2014a).	Ioannou *et al.*, 2009; Psaroulaki *et al.*, 2014(a); Tsatsaris *et al.*, 2016.
	Hyalomma anatolicum excavatum / Hyalomma excavatum (currently known as *Hyalomma excavatum)*	*C. burnetii* was detected in *H. a. excavatum, H. sulcata*, and *H. punctata* (Ioannou *et al.*, 2011). *C. burnetii* was detected in 13% of *Hyalomma anatolicum excavatum*, 12% of *H. sulcata* and 100% of *H. puncata* (Psaroulaki *et al.*, 2014a).	Le Riche *et al.*, 1974; Psaroulaki *et al.*, 2008; Ioannou *et al.*, 2011; Psaroulaki *et al.*, 2014(a); Tsatsaris *et al.*, 2016; **Hekimoglu & Ozer, 2017**.
	Hyalomma anatolicum anatolicum (currently known as *Hyalomma anatolicum*)		Le Riche *et al.*, 1974.
	Hyalomma spp.	*C. burnetii* was detected in *R. sanguineus* and *Hyalloma* spp. ticks (Psaroulaki *et al.*, 2006).	Psaroulaki *et al.*, 2006.
	Hyalomma marginatum		Le Riche *et al.*, 1974; Ioannou *et al.*, 2011; Psaroulaki *et al.*, 2014(a); Tsatsaris *et al.*, 2016.
	Hyalomma marginatum rufipes / Hyalomma rufipes (currently known as *Hyalomma rufipes)*		Le Riche *et al.*, 1974; Tsatsaris *et al.*, 2016.
	Hyalomma marginatum turanicum (currently known as *Hyalomma turanicum*)		Le Riche *et al.*, 1974.
	Haemaphysalis punctata	*C. burnetii* was detected in *H. sulcata*, and *H. punctata. Rickettsia* spp. was detected in *H. punctata* and *H. sulcata.* (Ioannou *et al.*, 2011). *C. burnetii* was detected in 12% of *H. sulcata* and 100% of *H. puncata* (Psaroulaki *et al.*, 2014a).	Ioannou *et al.*, 2011; Psaroulaki *et al.*, 2014(a); Tsatsaris *et al.*, 2016.
	Haemaphysalis sulcata	*C. burnetii* was detected in *H. sulcata*, and *H. punctata. Rickettsia* spp. was detected in *H. punctata* and *H. sulcata.* (Ioannou *et al.*, 2011). *C. burnetii* was detected in 12% of *H. sulcata* and 100% of *H. puncata* (Psaroulaki *et al.*, 2014a).	Le Riche *et al.*, 1974; Ioannou *et al.*, 2011; Psaroulaki *et al.*, 2014(a); Tsatsaris *et al.*, 2016.
	Argas persicus		Le Riche *et al.*, 1974.
	Boophilus annulatus		Le Riche *et al.*, 1974.
Flea	*Ctenocephalides felis*	*Rickettsia felis* was detected in *C. felis* (Psaroulaki *et al.*, 2006). *C. canis* (38%), *C. felis* (16.6%), and *X. cheopis* (10.8%) were found to be positive for *C. burnetii* by PCR (Psaroulaki *et al.*, 2014b).	Psaroulaki *et al.*, 2006; Christou *et al.*, 2010; Psaroulaki *et al.*, 2014(b); Diakou *et al.*, 2022.
	Ctenocephalides canis	*C. canis* (38%), *C. felis* (16.6%), and *X. cheopis* (10.8%) were found to be positive for *C. burnetii* by PCR (Psaroulaki *et al.*, 2014b).	Christou *et al.*, 2010; Psaroulaki *et al.*, 2014(b); Diakou *et al.*, 2022.
	Xenopsylla cheopis	*Rickettsia typhi* was detected in *X. cheopis* and *Leptopsylla segnis. Rickettsia felis* was detected in *X. cheopis* (Christou *et al.*, 2010). *C. canis* (38%), *C. felis* (16.6%), and *X. cheopis* (10.8%) were found to be positive for *C. burnetii* by PCR (Psaroulaki *et al.*, 2014b).	Christou *et al.*, 2010; Psaroulaki *et al.*, 2014(b).
	Leptopsylla segnis	*Rickettsia typhi* was detected in *X. cheopis* and *L. segnis.* (Christou *et al.*, 2010).	Christou *et al.*, 2010.
	Nosophylla fasciatus		Christou *et al.*, 2010.
	Echidnophaga gallinacea		Diakou *et al.*, 2022.
Louse	*Pthirus pubis*		**Dağdelen *et al.*, 2013**.
Mite	*Neotrombicula autumnalis*		Giannoulopoulos *et al.*, 2012.

Table 2. Summary of vector-borne diseases reported in humans in Cyprus (studies from northern Cyprus are written in bold)

Transmission-route	Disease	Case definition	Year	Reference
Mosquito-borne	Malaria	Thirteen imported malaria cases (*Plasmodium falciparum,* n=10; *P. vivax*, n=2; *P. ovale,* n=1) were reported in northern Cyprus.	2016-2019	**Güler *et al*., 2020.**
		Three tourists who visited Esentepe (Agios Amvrosios) in the Kyrenia District (northern Cyprus) were diagnosed with *P. vivax* malaria after returning to the United Kingdom.	2017	**Emms *et al*., 2020.**
		A 22-year-old woman who was six-month pregnant and travelled to northern Cyprus from the Democratic Republic of Congo was diagnosed with *P. falciparum* malaria.	2022	**Güler *et al*., 2023.**
	West Nile Virus	A case of WNV was detected in Larnaca District.	2016	Pallari *et al*., 2022; Paphitou *et al*., 2017.
		A case of WNV was detected in Nicosia District.	2018	Pallari *et al*., 2022.
		An outbreak of WNV including 22 autochthonous cases [Nicosia (n=9), Famagusta (n=8), and Larnaca (n=5)] occurred.	2019	Pallari *et al*., 2022.
		Three cases of WNV were detected in northern Cyprus.	2019	**Balaman *et al*., 2020.**
		Among 760 blood donors in northern Cyprus, two (0.3%) and 31 (4.1%) were WNV IgM- and IgG-positive, respectively.	2017-2018	**Balaman *et al*., 2020.**
		WNV IgG positivity was detected in 5% of 327 samples, and IgM positivity was found in 13% of 127 symptomatic patients in Nicosia, Limassol, Larnaca, and Famagusta.	2013-2014	Billoud *et al*., 2019.
Sandfly-borne	Leishmaniasis	Three CL and two VL cases were caused by *Leishmania donovani* MON-37 was reported from southern Cyprus.	2006	Antoniou *et al*., 2008.
		CL caused by *L. donovani/infantum* complex was detected in a person after staying in Polis southern Cyprus.	NA	Poeppl *et al*., 2011.
		CL due to *L. donovani* complex was diagnosed in a person after staying in Lapithos (Kyrenia District), northern Cyprus.	NA	**de Silva *et al*., 2015.**
		Three pediatric cases of VL caused by *L. infantum* were detected (one in Kyrenia District, and two in Karpasia Peninsula) in northern Cyprus.	2011-2012	**Sayili *et al*., 2016.**
		A family cluster of four CL cases caused by *L. donovani* was reported from Paphos, southern Cyprus.	NA	Koliou *et al*., 2014.
		Out of 249 individuals three (1.2%) seropositive cases were found. Besides seven (2.8%) past CL cases (including the seropositive persons) were detected in Kyrenia District, northern Cyprus.	2014	**Ruh *et al*., 2017.**
		A CL case caused by *L. infantum* was detected in Kyrenia District, northern Cyprus.	NA	**Ruh *et al*., 2020.**
		L. infantum seropositivity was 4.7% in a study conducted in Nicosia, Kyrenia, Famagusta, Morphou, Lefka, Trikomo and Karpasia, in northern Cyprus.	NA	**Özdoğaç *et al*., 2022.**

	Sandfly fever	Among 11 Swedish soldiers in Cyprus, three were seropositive for SFNV, seven for SFSV, and one for TOSV.	1985	Eitrem, 1990.
		Neutralizing antibodies against sandfly fever viruses SFNV, SFSV, and TOSV were detected among healthy individuals.	1985-1986	Eitrem, 1991.
		During a febrile illness outbreak among Greek Army soldiers in Cyprus, 13 soldiers were found to be IgM- and IgG-positive for SFSV, SFNV, and TOSV. Also, Cypriot strain of SFSV was defined as the agent of this outbreak.	2002	Konstantinou, 2007.
		A retrospective study reported anti-SFV IgG seropositivity in Cyprus to be 28%.	2013-2014	Billioud *et al.*, 2019.
		A sandfly fever case developed by SFSV was detected in a tourist who visited northern Cyprus.	NA	Stahn *et al.*, 2018.
Tick-borne	Rickettsiosis	Six (2.0%) of 300 hunters were found to be SFG IgG-positive in northern Cyprus.	2017-2018	Ruh *et al.*, 2022.
	Tularemia	A pediatric case of systemic tularemia caused by *F. tularensis* was detected in Nicosia district of northern Cyprus.	2018	Uncu *et al.*, 2017.
		Seropositivity for *F. tularensis* was reported to be 0.93% in northern Cyprus.	2022	Yeni *et al.*, 2022.
		A 25-year-old woman was diagnosed with oropharyngeal tularemia by using tube agglutination test in northern Cyprus.	NA	Ünal Evren *et al.*, 2019.
	Q fever	Eighty-seven cases of Q fever developed by *C. burnetii* were detected among British Army soldiers located in Cyprus.	1974-1975	Spicer *et al.*,1977.
		Seropositivity for *C. burnetii* was detected to be 59.5% and 52.9%, respectively, among humans in two villages of southern Cyprus.	2006	Loukaides *et al.*, 2006.
		The seroprevalence of IgG antibodies against *C. burnetii* phase II antigen was detected to be 52.7% in southern Cyprus.	2006	Psaroulaki *et al.*, 2006.
	Anaplasmosis	A case of anaplasmosis was detected in a 9-year-old girl from the Nicosia district of southern Cyprus. Of 22 individuals including her parents and neighbors, 55% were seropositive for *A. phagocytophilum*.	2006	Psaroulaki *et al.*, 2008.
		In a 27-year-old woman from Famagusta, southern Cyprus, IgG antibodies against *A. phagocytophilum* were detected in serum, and *Anaplasma ovis* was detected in the blood sample by PCR.	2007	Chochlakis *et al.*, 2010.
	Tick-borne relapsing fever	A 24-year-old male from England was diagnosed with tick-borne relapsing fever after spending 3 weeks in Cyprus	1985	Simon, 1985.
	Lyme disease	Sixteen (17.6%) of 91 individuals were IgG-positive, and two of these individuals were also IgM-positive for *Borrelia burgdorferi* in northern Cyprus.	2000	Altındiş *et al.*, 2002.
Flea-borne	Rickettsiosis	Twenty-one children were found to be seropositive for *R. typhi*.	2000-2006	Koliou *et al.*, 2007(a).
		A pregnant woman from Larnaca was detected to be seropositive for *R. typhi*.	NA	Koliou *et al.*, 2007(b).
		A total of 193 human murine typhus cases were reported.	2000-2008	Psaroulaki *et al.*, 2012.

* WNV: West Nile virus; CL: Cutaneous leishmaniasis; VL: Visceral leishmaniasis; SFNV: Sandfly fever Naples virus; SFSV: Sandfly fever Sicilian virus; TOSV: Toscana virus; IgM: Immunoglobulin M; IgG: Immunoglobulin G; PCR: Polymerase chain reaction; NA: Not applicable

Despite being certified as a malaria-free region in 1967, sporadic cases of malaria have been reported on the island, mostly among individuals coming from malaria-endemic countries. A study published in 2020 reported 13 imported malaria cases diagnosed in a university hospital in northern Cyprus within the years 2016-2019. Ten cases were caused by *P. falciparum*, while two patients were infected with *P. vivax*, and one case was caused by *P. ovale*. Eleven of the 13 cases were from Nigeria, and two were from Turkey. One of the Turkish patients (infected with *P. falciparum*) was working in Africa and visited northern Cyprus for a holiday. The other patient from Turkey (diagnosed with *P. vivax*) had a history of malaria in the past, therefore the result was interpreted as a relapse (Güler *et al*., 2020).

In August 2017, the United Kingdom (UK) reported three malaria cases originating from northern Cyprus. Two siblings (10 years old and 12 years old) and another independent traveler stayed in a village called Esentepe (Agios Amvrosios) in Kyrenia district, northern Cyprus. Emms *et al*. (2020) reported that the two siblings developed symptoms shortly before returning to the UK. The patients mentioned that they did not visit any malaria-endemic countries, and moreover, one of the siblings reported multiple insect bites. After performing microscopy and molecular tests, they were diagnosed with *P. vivax* malaria. The cases recovered after the treatment (Emms *et al*., 2020).

A recent case report from northern Cyprus documented a pregnant woman diagnosed with malaria. A 22-year-old woman who was six-month pregnant traveled to northern Cyprus from the Democratic Republic of Congo 14 days before the hospital admission. In addition to microscopic examination, rapid diagnostic test was conducted, and the patient was diagnosed with *P. falciparum* malaria. The patient was successfully treated with artemether-lumefantrine with complete recovery (Güler *et al*., 2023).

Since ECDC reported that *An. algeriensis*, *An. claviger, An. sacharovi* and *An. superpictus* are still present on the island (ECDC, 2017), and also taken together with the above-mentioned cases, it is crucial to maintain a state of vigilance and preparedness to prevent and control the possible re-emergence of malaria in Cyprus. This can be achieved through the implementation of effective prevention and control measures, and also by maintaining surveillance of the mosquito vectors (El-Sayed & Kamel, 2020).

West Nile virus infection

Belonging to the Japanese encephalitis virus complex, West Nile virus (WNV) is a *Flavivirus* in the Flaviviridae family. Although the primary vectors of WNV are the *Culex* mosquitoes, particularly *Cx. pipiens*, studies have found the virus in additional genera such as *Aedes* and *Culiseta* (Pallari *et al*., 2022). WNV causes an enzootic infection between birds and the mosquito vectors, where the birds are the principal reservoir for the virus allowing its replication. WNV infection, as a result of mosquito bites, also occurs in humans and horses. However, these are referred to as dead-end hosts, because the virus levels are not high enough to be transmitted to the vectors (Pallari *et al*., 2021). WNV is the cause of West Nile fever, and also, West Nile neuroinvasive disease (Pallari *et al*., 2022). The former is mostly seen as a mild and flu-like illness including fever, malaise, myalgia, and skin rash. The latter, which is rare but a severe form, can manifest itself with encephalitis, meningoencephalitis, or meningitis. This clinical form affects particularly people at older ages and has a mortality rate of 10% (Billioud *et al*., 2019).

In Cyprus, the first case of human WNV infection was reported from Larnaca district in 2016 (Pallari *et al*., 2022). A 75-year-old and non-immunosuppressed man who traveled to Greece developed symptoms of meningoencephalitis and flaccid paralysis. Due to the clinical picture of the patient, first, Guillain-Barré syndrome was included in the differential diagnosis. However, WNV RNA was detected in the cerebrospinal fluid (CSF) sample and later in serum and urine samples. Also, WNV-specific IgM and IgM/IgG were detected in CSF and serum samples, respectively. Taken together with the clinical characteristics, the patient was diagnosed with WNV neuroinvasive disease (Paphitou *et al*., 2017). Following this, the second human WNV case was reported from the Nicosia district in 2018 (Pallari *et al*., 2022). Notably, an outbreak of WNV occurred in 2019. Twenty-two autochthonous cases of WNV infection in southern Cyprus were detected in the districts of Nicosia (n=9), Famagusta (n=8), and Larnaca (n=5). WNV neuroinvasive disease was reported in a minimum of 15 patients, whereas the others developed West Nile fever (Pallari *et al*., 2022). Interestingly in July 2019, the first three cases of human WNV infection were reported from northern Cyprus (Balaman *et al*., 2020).

Although WNV is primarily transmitted via mosquito vectors, the infection can also be contracted as a result of blood transfusion as well as tissue or organ transplantation (Balaman *et al*., 2020). In line with this, a study was conducted in northern Cyprus that searched for antibody responses in blood donors. Serological tests revealed that, out of 760 individuals two (0.3%) were IgM-positive, and 31 (4.1%) were IgG-positive, while no participants was positive for both IgM and IgG. The plaque reduction neutralization test (PRNT) was found to be negative for both (100.0%) of the IgM-positive samples, and it was also negative in 5 (16.1%) of 31 IgG-positive specimens. IgG avidity was high in 21 (67.7%) of the 31 samples (indicating previous infection), while one (3.2%) sample showed low avidity (indicator for recent infection), 6 (19.4%) were within borderline values, and three (9.7%) specimens were interpreted as negative (below detection levels of relative avidity index). Of note, PRNT-confirmed IgG-positive samples had high (n=21/26) or borderline (n=5/26) values for avidity. None of the seropositive samples were found positive for WNV RNA. The study highlighted the need for serological screening and confirmation as well as the application of an avidity test before blood transfusion (Balaman *et al*., 2020).

A serological study on human WNV (and sandfly virus; SFV) infection was also conducted in southern Cyprus. During the 2013-2014 period, 327 sera from the leftover samples and 127 serum specimens collected from symptomatic patients (compatible with WNV or SFV infections) were tested for IgG and IgM antibodies, respectively. The IgG positivity rate was found to be 5%, while IgM antibodies were detected in 13% of the symptomatic patients. Importantly, two of these patients had neuroinvasive manifestations. In the study, seropositive cases were detected from different localities including Nicosia, Limassol, Larnaca, and Famagusta (Billioud *et al*., 2019).

In addition to the human infections, the presence of WNV was also searched in vectors and animal hosts on the island. A study originating from Turkey also included northern Cyprus and collected mosquito samples from Nicosia, Kyrenia, Famagusta, and Morphou districts. *Cx. pipiens* sensu lato was the only mosquito species found in northern Cyprus, while no WNV RNA was detected in the mosquitoes collected from the region (Ergunay *et al*., 2014a). In a study from southern Cyprus, mosquito samples were collected in 2019, the same year that the human WNV outbreak occurred. Among the mosquito species defined, *Cx. pipiens* pools (n=126) were subjected to further molecular analysis. One (0.8%) pool that was collected from Deftera village in southern Nicosia, was detected to be positive for WNV RNA. The authors noted that this finding confirms the circulation of the virus in the region. Despite the absence of reported human infections in Deftera, it was stated that three human WNV cases in 2019 were detected in localities 6-20 km from this village. Therefore, all these suggest that transmission to humans probably resulted from the *Culex* vectors present on the island (Pallari *et al*., 2022).

Another study searched for the WNV seropositivity among avian samples (migratory and resident birds) collected from 2015 to 2020 in southern Cyprus. Of 44 avian species, *Sylvia atricapilla*, which is a migratory bird, was predominant. Eleven (1.3%) of 836 avian samples were found positive for WNV IgY (equivalent of mammalian IgG) antibodies suggesting a past WNV infection in these birds. Seven of the 11 seropositive samples belonged to *S. atricapilla*. The authors indicated that the migratory birds might be infected in regions where WNV infection was documented, such as Africa and Europe, and carry the virus while migrating to Cyprus. Importantly, seven of the seropositive birds were captured in the Famagusta district, where 36% of the human cases were detected in the 2019 outbreak. In addition, three of 11 seropositive birds were captured in Larnaca district, where several human infections were documented during the outbreak (Pallari *et al*., 2021).

Taken together, the published evidence indicates that, apart from the human cases, WNV infection is also present in *Culex* vectors and birds on the island. Moreover, WNV was reported in horses in Cyprus, and also WNV antibodies were detected in a horse that was born in Cyprus and later imported to the United Kingdom (Fooks *et al*., 2014; Pallari *et al*., 2022). Given the presence of human cases and avian infection in the Famagusta district, the region could be considered an important focus for WNV transmission. However, this does not rule out the possibility of infections in other districts due to the presence of *Culex* vectors (Nicosia) and infected birds (Larnaca) (Pallari *et al*., 2021, 2022). Therefore, islandwide control programs should be implemented to prevent further WNV outbreaks.

Other mosquito-borne diseases

Zika virus is another agent that is transmitted by *Aedes* mosquitoes, primarily *Ae. aegypti*. Additionally, *Ae. albopictus* was shown to be a possible vector for Zika virus (WHO, 2016b). Since *Aedes* mosquitoes had already been detected in Cyprus, concerns were raised about the possible presence of Zika virus infections on the island. However, according to the recent ECDC report on the Zika virus, no data/case has been documented from Cyprus between 2017 and 2021 (ECDC, 2023b). Apart from this, a retrospective study in northern Cyprus that included 91 samples collected from a blood bank found no IgG positivity against Zika virus (Abushoufa *et al*., 2021). Although no case related to the Zika virus has been detected so far on the island, due to the presence of potential vectors, health authorities should consider the possible emergence of mosquito-borne diseases in the region.

Sand fly-borne diseases

Phlebotomine sandflies are an important public health concern since they can be vectors for viral (sandfly fever), bacterial (bartonellosis), and parasitic (leishmaniases) infections (Ergunay *et al*., 2014b). Sandflies are classified in the order Diptera, family Psychodidae, and subfamily Phlebotomina. These blood-sucking flies are mostly present in the regions with warm climate (Lafri & Bitam, 2021). Infections caused by sandfly bites reach their highest levels in the summer months in endemic areas, as high temperatures in summer provide more favorable conditions for the reproduction and growth of these vectors (Guler *et al*., 2012).

Large-scale studies conducted on the island revealed the presence of various *Phlebotomus* species. In both northern and southern Cyprus, *P. tobbi*, *P. galilaeus,* and *P. papatasi* were among the commonly detected sandfly species (Demir *et al*., 2010; Mazeris *et al*., 2010; Töz *et al*., 2013). While previous studies mostly based on morphological diagnosis, a study from 2018 used DNA barcoding technique and identified *P. papatasi*, *P. killicki*, as well as *Sergentomyia minuta* and *S. dentata* in Cyprus (Dokianakis *et al*., 2018).

Due to the presence of various *Phlebotomus* species, clinical cases resulting from sandfly bites have been documented in both parts of the island. Sandfly-borne diseases, the causative agents, and their vectors detected in Cyprus are reviewed in detail below.

Leishmaniasis

Cyprus has been an important region for leishmaniasis for many years. Apart from the human leishmaniasis cases, the sandfly vectors and canine leishmaniasis (CanL) were documented on the island. Of the four clinical forms, cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL) were detected in both northern and southern parts of Cyprus, while there has been no evidence of mucocutaneous leishmaniasis and post kala azar dermal leishmaniasis (PKDL) to date in the island (Ruh & Taylan Özkan, 2019; Kerkuklu & Guran, 2020).

In northern Cyprus, although sandfly species were detected in different localities, the species diversity was found at the highest levels in Lapithos (Kyrenia district) and Leonarisso (Demir *et al*., 2010). Moreover, a paper published in 2014 revealed *Leishmania infantum* in *Phlebotomus tobbi* pools collected from Lapithos, and a nearby village Panagra (Ergunay *et al*., 2014b). In a recent study from northern Cyprus, *L. major* was detected in *P. papatasi* and the rate of infection was found to be 2.63% (n=1/38;) among the blood-fed sandfly specimens (Yetişmiş *et al*., 2022).

CanL seroprevalence was reported at varying levels (Töz *et al*., 2013; Beyhan *et al*., 2016; Çanakçı *et al*., 2016) in northern Cyprus. Notably, the highest rate (13.2%) was reported from the Kyrenia region (Çanakçı *et al*., 2016). The infecting *Leishmania* spp. was not identified in these studies. In southern Cyprus, the seroprevalence of CanL was found as high as 14.9%, and *L. infantum* MON-1 was the predominant zymode detected (Mazeris *et al*., 2010). Apart from dogs, the presence of *Leishmania* parasites was also detected in cats. Attipa *et al*. (2017a) identified *L. infantum* in 2.3% of the feline samples and also found that 4.4% of the cats tested were seropositive for *L. infantum* in southern Cyprus. Moreover, Psaroulaki *et al*. (2010) found that 7.3% of the rats tested were seropositive for *L. infantum* in southern Cyprus.

According to the published articles, today human cases of leishmaniasis are known to exist on the island. A report from northern Cyprus documented three pediatric VL cases aged between 16 months and 34 months (one patient from Kyrenia district, and two patients from Karpasia Peninsula). The causative agent was identified to be *L. infantum*. The patients were treated with liposomal amphotericin B with complete recovery (Sayili *et al*., 2016). Another study from Kyrenia district found that three (1.2%) of 249 participants were seropositive for leishmaniasis. In the study, seven (2.8%) participants, including the seropositive individuals, had a previous diagnosis of CL (Ruh *et al*., 2017). More recently, a 79-year-old man from Kyrenia district was diagnosed with CL and the infecting agent was identified as *L. infantum* by real-time PCR (Ruh *et al*., 2020). Another recent study that included participants from different residential places in northern Cyprus (Nicosia, Kyrenia, Famagusta, Morphou, Lefka, Trikomo, and Karpasia) found *L. infantum* seropositivity rate to be 4.7%. The authors noted that the positivity was higher among hunters, farmers, and those involved in animal husbandry, as well as dog owners (Özdoğaç *et al*., 2022).

Studies from southern Cyprus also reported human leishmaniasis cases in different years. In 2006, three CL (aged 44, 50, and 55 years) and two VL patients (aged 9 months and 73 years) were detected, and the infecting agent was identified as *L. donovani* MON-37 (Antoniou *et al*., 2008). Additionally, a case report in 2014 documented that four patients (aged between 6 and 60 years) belonging to an extended family in Paphos District were diagnosed with CL and the agent was defined as *L. donovani*. While the skin lesion of one case healed spontaneously, the other patients were treated with liposomal amphotericin B (Koliou *et al*., 2014).

Apart from the local cases, leishmaniasis was also detected in people who traveled to Cyprus. A 59-year-old woman who stayed in Polis (Greek Cypriot territory) was diagnosed with CL eight months after her visit. The agent was detected to be *L. donovani/infantum* complex and the patient was completely cured after miltefosine treatment (Poeppl *et al*., 2011). Furthermore, a 54-year-old man developed CL six months after staying in Lapithos in northern Cyprus. The agent was identified as *L. donovani* complex, and the patient completely recovered after sodium stibogluconate treatment (De Silva *et al*., 2015).

Considering the previous data, one can conclude that there are two major transmission cycles of leishmaniasis in Cyprus. In the first cycle, *L. infantum* causes CanL, while in the second, anthroponotic transmission of *L. donovani* results in CL and VL (Koliou *et al*., 2014). Although molecular characteristics of the infecting species were identified in southern Cyprus, the transmission cycles in the north of the island still need to be elucidated. Molecular studies have already reported *L. infantum* in humans in northern Cyprus (Sayili *et al*., 2016; Ruh *et al*., 2020). However, considering the presence of *L. donovani* in the Greek Cypriot community (Antoniou *et al*., 2008; Koliou *et al*., 2014), and also the genetic relationship with the isolates in Turkey (Koliou *et al*., 2014; Gouzelou *et al*., 2012), the occurrence of *L. donovani* infections is also possible in northern Cyprus. Furthermore, the recent identification of *L. major* in *P. papatasi* (Yetişmiş *et al*., 2022) suggests that CL infections caused by this species are also likely to occur in the region (Karmaoui *et al*., 2022). Thus, to better understand the transmission cycles of the infecting *Leishmania* spp., comprehensive molecular studies covering more residential areas will be essential in northern Cyprus.

Sandfly fever

Sandfly fever, also called "Pappataci fever" or "Phlebotomus fever" is a viral, febrile disease, caused by phleboviruses in the Bunyaviridae family. Phleboviruses are medically important, enveloped, single-stranded RNA viruses with a three-segmented genome (Ergunay *et al*., 2017). The serologic classification of phleboviruses includes sandfly fever Sicilian complex, sandfly fever Naples complex, and Salehabad complex, which are present in the Old World (Ayhan & Charrel, 2017). Old World sandfly-borne phleboviruses (SBPs) are primarily observed in the Mediterranean, Middle East, Africa, India, and Asia (Ergunay *et al*., 2017). Besides these, Candiru virus, Chilibre virus, Bujaru virus, Frijoles virus, and Punta Toro virus are present in the New World. Sandfly fever Naples virus (SFNV) and sandfly fever Sicilian virus (SFSV) are the causative agents of febrile disease while Toscana virus (TOSV) which is one of the species listed in the SFNV complex, is related to neuroinvasive sandfly fever infections (Ergunay *et al*., 2017). SFSV, SFNV, TOSV, and sandfly fever Cyprus virus (SFCV) are reported as the major *Phlebovirus* serotypes detected in the Mediterranean region (Guler *et al*., 2012). SFCV which is included in the Sicilian complex was detected among Swedish soldiers in Cyprus (Alwassouf *et al*., 2016). On the other hand, sandfly fever Turkey virus (SFTV), Adana virus (ADAV), Toros virus (TORV), and Zerdali virus (ZERV) are the four novel phleboviruses identified in Anatolia, Turkey, between 2008 and 2013 (Ergunay *et al*., 2017). It is known that more than 70 phleboviruses (which are classified into ten species) have been identified worldwide and novel viruses are still being discovered, increasing the risk of human infections (Lee *et al*., 2020).

Sandfly fever is transmitted to humans via infected female *Phlebotomus* sandflies (Ergunay *et al*., 2017). Following the bite of the vector, the incubation period of the disease is 3-6 days. In endemic regions, patients can develop unspecific symptoms including fever, headache, myalgia, malaise, back pain, and retro-orbital pain. Since the fever ends in a maximum of 72 hours, the disease is also called "three-day fever" (Guler *et al*., 2012).

In the regions where sandfly fever is endemic, asymptomatic seroconversion and mild disease are observed among local populations (Ergunay *et al*., 2017; Lee *et al*., 2020). Importantly, as a result of travel to endemic regions such as Mediterranean countries, outbreaks can occur that affect non-immune individuals (Lee *et al*., 2020). In 1944, Cyprus was declared to be an endemic region for phleboviruses. In 1984, the first cases of SFSV were reported among the military personnel of a Swedish UN army on the island (Niklasson & Eitrem, 1985; Papa *et al*., 2006; Konstantinou *et al*., 2007). In 1985, another Swedish UN army that served for six months in Cyprus developed symptoms related to sandfly fever after returning from the island. By performing indirect immunofluorescence antibody test, seroconversion was detected for SFSV (seven cases), SFNV (three cases), and TOSV (one case) (Eitrem *et al*., 1990). In addition to the cases detected in the military staff, sandfly fever infections were also reported in tourists between 1986 and 1989 in southern Cyprus (Papa *et al*., 2006; Konstantinou *et al*., 2007).

In a study conducted in 1991, the neutralizing antibodies against SFNV, SFSV, and TOSV were investigated among healthy individuals in southern Cyprus. The study included a total of 479 serum samples, and the results showed that the seroprevalence of SFNV, SFSV, and TOSV were 57%, 32%, and 20%, respectively. The study found that the frequency of dual and triple infections was higher than expected (Eitrem *et al*., 1991). Another study included 47716 febrile patients administered to a military hospital in northern Cyprus between 1997 and 1999. The authors mentioned that 7.09% of patients were pre-diagnosed with sandfly fever based on their symptoms. They also reported that the most cases were observed between May and November, and the highest number of cases were observed in June. However, no information was provided regarding the infecting *Phlebovirus* strains in the study (Ergin & Yılmaz, 2002).

Papa *et al*. (2006) and Konstantinou *et al*. (2007) reported a self-limited febrile illness among soldiers of the Greek Army Forces in Cyprus between May 2002 and September 2002. In addition to flu-like symptoms, at least one insect bite was documented in the clinical examination of all individuals. Whole blood samples, convalescent serum samples, and acute phase serum samples were collected randomly among soldiers. Papa *et al*. (2006) reported that 11 of 18 acute phase serum samples, and four of five whole blood samples were detected positive for sandfly fever viruses by PCR. Also, according to Konstantinou *et al*. (2007), 13 of 18 serum samples taken in the acute phase of the disease were found to be IgM- and IgG-positive for SFSV, SFNV, and TOSV. Further sequencing and phylogenetical analysis showed that the causative agent of this outbreak was a Sicilian-like strain of phlebovirus (Cypriot strain of SFSV) which was found to be different from SFSV at the amino acid and nucleotide levels (Papa *et al*., 2006; Konstantinou *et al*., 2007).

During 2013-2014, 327 sera were collected in southern Cyprus to search for the seroprevalence of sandfly fever viruses (SFV) by using indirect immunofluorescence test. The study found that the prevalence of anti-SFV IgG was 28%, and the seropositivity increased with age. This suggested that previous exposure to SFV was common in the study population (Billioud *et al*., 2019).

In 2014, Ergunay *et al*. collected a total of 2690 sandflies from northern Cyprus and Eastern Thrace of Turkey. By the morphologic examination *Phlebotomus perfiliewi* sensu lato, *P. tobbi*, *P. papatasi*, *Laroussius* sp., *Sergentomyia azizi*, *Sergentomyia* sp., *S. minuta* and *Phleobotomus jacusieli* were identified in northern Cyprus. Importantly, TOSV was identified in two pools of *P. perfiliewi* s.l. and one pool of *P. tobbi* in northern Cyprus. A co-infection of TOSV and *L. infantum* was detected in one *P. tobbi* pool. Also, sequences that belonged to novel phleboviruses were identified in two *P. perfiliewi* s.l. pools. These viruses (named Girne 1 and Girne 2) had genomic similarities with TOSV and SFCV and related strains, respectively (Ergunay *et al*., 2014b).

Alwassouf *et al*. (2016) conducted a phlebovirus seroprevalence study in 2016. A total of 1250 dogs from Greece and 422 dogs from southern Cyprus were included in this study to search for neutralizing antibodies against TOSV, SFSV, and Salehabad viruses (Arbia virus and Adana virus). The authors found that SFSV had a high prevalence of 71.9% in Greece and 60.2% in Cyprus. TOSV followed SFSV with a rate of 4.4% in Greece and 8.4% in Cyprus. The prevalence of Salehabad viruses (Adana and Arbia) ranged between 0-22.6% (Alwassouf *et al*., 2016).

In 2018, Stahn *et al*. documented a sandfly fever case from northern Cyprus. A 45-year-old woman tourist developed symptoms including fever, myalgia, diarrhea, and papular rash when she returned to her country after staying in northern Cyprus for two weeks. Due to the detection of antibodies against SFSV in the laboratory tests, the patient was diagnosed with sandfly fever (Stahn *et al*., 2018).

In addition to the above-mentioned studies from Cyprus, it is known that an increased diversity of phleboviruses was documented in the other Mediterranean countries (Dvorak *et al*., 2020). Therefore, clinicians should consider the differential diagnosis of sandfly fever in febrile cases to prevent misdiagnosis, especially in travelers returning from the endemic countries (Konstantinou *et al*., 2007; Stahn *et al*., 2018).

Tick-borne diseases

Ticks are blood-sucking external parasites that can infest a wide group of animals or humans. During the blood meal, they can transfer the microorganisms harbored in their body to their host, which can pose significant health risks to the susceptible humans (Walker *et al*., 2003; Tsatsaris *et al*., 2016). The most common ticks documented include American dog tick (*Dermacentor variabilis, Dermacentor similis*), Blacklegged tick (*Ixodes scapularis*), Brown dog tick (*Rhipicephalus sanguineus*), Gulf Coast tick (*Amblyomma maculatum*), Lone star tick (*Amblyomma americanum*), Rocky Mountain wood tick (*Dermacentor andersani*), and Western black-legged tick (*Ixodes pacificus*) (CDC, 2023a). *Anaplasma* spp., *Borrelia* spp., *Ehrlichia* spp., *Coxiella burnettii*, *Rickettsia* spp., and *Bartonella* spp. are reported as the most common pathogens that can be transmitted by the bites of the above-mentioned tick species (Tsatsaris *et al*., 2016).

The climate of Cyprus enables favorable conditions for the presence and dissemination of various tick species and tick-borne pathogens, indicating the importance of active surveillance programs for ticks and tick-borne diseases on the island (ECDC, 2023c). Early studies on the island identified *Hyalomma anatolicum anatolicum*, *Hyalomma anatolicum excavatum*, *Hyalomma marginatum marginatum*, *Hyalomma marginatum rufipes*, *Hyalomma marginatum turanicum*, *Haemaphysalis sulcata*, *Ixodes crenulatus*, *Ixodes gibbosus*, and *Rhipicephalus turanicus* for the first time on the island. Additionally, the presence of *Rhipicephalus sanguineus*, *Rhipicephalus bursa*, *Argas persicus,* and *Boophilus annulatus* was also reported (Le Riche *et al*., 1974). The latest ECDC tick surveillance reports, which were published in early 2023, showed the presence of *Rh. sanguineus* and *Hy. marginatum*, while no data is available for *Ixodes persulcatus*, *Ixodes ricinus*, *Dermacentor reticulatus*, *Ornithodorus erraticus,* and *Hyalomma lusitanicum* on the island (ECDC, 2023c).

In addition to the human hosts, ticks can also infest wild animals, birds, and ruminants (Attipa *et al*., 2017b). While climate changes positively affect the life cycle and distribution of vectors, infested animal hosts also pose a risk to susceptible human populations (Chala & Hamde, 2021). It is reported that various tick-borne pathogens are endemic in these groups of animals in Cyprus. *Rh. sanguineus* was the most common tick species on the island, with a prevalence of 38.5%, and this was followed by *Rh. turanicus* and *Rh. bursa*, with a prevalence of 21.3% and 17.8%, respectively. Besides the common tick species, *Hy. excavatum* (9%) and *Hae. sulcata* (9%) were also detected in the region. The remaining 4.4% of the collected ticks were identified as *I. gibbosus*, *Ixodes ventalloi*, *Rhipicephalus pusillus*, *Hy. marginatum*, *Hy. rufipes,* and *Haemaphysalis punctata* (Tsatsaris *et al*., 2016; Chitimia-Dobler *et al*., 2019).

In a study of Diakou *et al*. (2022), tick infestation was found in 68.3% of the dogs and 22% of the cats. In the morphological identification of the ectoparasites, *Rh. sanguineus* sensu lato (found in 13 cats and 108 dogs) and *I. gibbosus* (found in two dogs) were the identified tick species (Diakou *et al*., 2022). Apart from this, Cyprus hosts more than 300 bird species, including migrating and local species, which can be infested with ticks during migration and introduce tick-borne pathogens to local human and animal populations. Between 2004 and 2006, ticks were collected from birds, and all of them were identified as *I. ventalloi* (Ioannou *et al*., 2009).

In a study conducted between 2002 and 2006, 663 ectoparasites were collected from mouflons from southern Cyprus. The ticks were identified as *Rhipicephalus* spp. (40.4%) (*Rh. turanicus*, *Rh. sanguineus*, *Rh. bursa)*, *Hyalomma* spp. (12.7%) (*Hy. anatolicum excavatum*, *Hy. marginatum)*, *Haemaphysalis* spp. (43.9%) *(Hae. punctata*, *Hae. sulcata)*, and *I. gibossus* (3.5%) (Ioannou *et al*., 2011). Tick infestation was also reported from the northern part of the island. During 2011-2015, 736 tick samples were collected from sheep, goats, cattle, cows, tortoises, and birds from 70 localities in Turkey (65 regions) and northern Cyprus (five regions). The study results showed that *Hy. marginatum* was Turkey's predominant *Hyalomma* tick, while only *Hy. excavatum* was detected in northern Cyprus (Hekimoglu & Ozer, 2017). Tick-borne infections detected on the island are discussed in the following section.

Rickettsiosis

Rickettsia spp. are gram-negative intracellular bacteria in which arthropods play an important role in transmission. The genus *Rickettsia* comprises four groups, all of which contain different species. Mainly, the spotted fever group (SFG) includes *Rickettsia rickettsii* and *Rickettsia conorii*; and the typhus group (TG) contains *Rickettsia prowazekii* and *Rickettsia typhi*. Other species of the genus, *Rickettsia bellii,* and *Rickettsia canadensis* belong to the ancestral group, while *Rickettsia akari*, *Rickettsia australis,* and *Rickettsia felis* are included in the transitional group (Guccione *et al*., 2021). *R. typhi* and *R. felis* are the agents of murine typhus and flea-borne spotted fever, respectively, and these species are detected in many regions of the world (Caravedo Martinez *et al*., 2021), which will be mentioned under the "Flea-borne diseases" heading. As the main focus of the current section, tick-borne rickettsioses, are predominantly reported in Europe (Portillo *et al*., 2015). Notably in southern and eastern parts of Europe, Mediterranean spotted fever (MSF), which is caused by *R. conorii* subsp. *conorii*, is the most prevalent rickettsial disease documented (ECDC, 2013).

The presence of rickettsiosis in humans has been reported on the island by several studies. In southern Cyprus, previous reports demonstrated seropositivity in humans against *R. typhi* and *R. conorii* (Psaroulaki *et al*., 2006a). In northern Cyprus, a recent study searched for seropositivity against SFG rickettsiae among 300 hunters. In the indirect immunofluorescence assay, using *Rickettsia slovaca* Ankara strain isolated from *Dermacentor marginatus* tick, six (2.0%) of the participants were found to be SFG IgG-positive. While all seropositive results were obtained in the regions outside the capital Nicosia, no statistical correlation was found between the residential settings and seropositivity. Other factors (gender, age, hunting years, hunting abroad, and previous exposure to arthropod bites) were also not found significant for rickettsial seropositivity (Ruh *et al*., 2022).

In southern Cyprus, Chochlakis *et al*. (2012) identified SFG rickettsiae in ticks infesting mouflons, goats, sheep, dogs, foxes, and hares. In that study, *Rickettsia aeschlimannii* (in *Hy. marginatum marginatum*), *Rickettsia massiliae* (in *Rh. turanicus* and *Rh. sanguineus*), *Rickettsia sibirica mongolotimonae* (in *Hy. anatolicum excavatum*), *Rickettsia hoogstraalii* (in *Hae. punctata*), and Candidatus *Rickettsia barbariae* (in *Rh. turanicus*) were identified (Chochlakis *et al*., 2012). Between 2002 and 2006, blood specimens as well as the infesting ticks were collected from 77 Cypriot mouflons. Of the blood samples, 30% were detected positive for 30% for *Rickettsia* spp., and among the 109 ectoparasite pools, 28.4% tested positive for *Rickettsia* spp. In the study, *Rickettsia* spp. was detected in *Rh. turanicus, Rh. bursa, Hae. punctata*, and *Hae. sulcata* (Ioannou *et al*., 2011). In another study conducted between 2004 and 2006 in Cyprus, three *I. ventalloi* ticks collected from birds were detected positive for *Rickettsia* spp. (Ioannou *et* *al*., 2009). Recently, Diakou *et al*. (2022) searched for pathogens in the ectoparasites collected from 59 cats and 161 dogs in southern Cyprus. The PCR-coupled sequencing method detected *R. massiliae*, *R. conorii*, and *R. felis* in the ticks (Diakou *et al*., 2022).

Tularemia

Tularemia (rabbit fever or deer fly fever) is a life-threatening disease developed by the intracellular bacterium *Francisella tularensis* (Yeni *et al*., 2022). Tularemia predominantly affects rural areas (Gürcan, 2007). It can be transmitted to humans via ingestion, inhalation, direct skin contact with infected animals (including rabbits, rodents, and deers), or by the bite of infected arthropods (ticks, mosquitoes, or deer flies). Studies have shown that *Dermacentor variabilis*, *Amblyomma americanum*, *Dermacentor andersoni*, *Dermacentor occidentalis* are the most common vectors of *F. tularensis* in the United States, while *D. reticulatus* and *I. ricinus* are mostly reported in Europe (Zellner & Huntley, 2019).

F. tularensis contains four subspecies, namely *F. tularensis* subsp. *tularensis* (type A biovar), *F. tularensis* subsp. *holarctica* (type B biovar), *F. tularensis* subsp. *mediasiatica*, and *F. tularensis* subsp. *novicida* (Gürcan, 2007; Abdellahoum *et al*., 2021). Subspecies *holarctica* is frequently detected in the Northern Hemisphere. It is less virulent, and fatal cases are rare (WHO, 2007).

According to the 2018 tularemia annual epidemiological report, ECDC defined Cyprus, Greece, Iceland, Ireland, Luxembourg, Malta, and the United Kingdom (only imported cases) as free of tularemia (ECDC, 2019). However, in 2018, a case of systemic tularemia was reported from northern Cyprus. A 5-year-old female patient was admitted to the hospital with fever, pharyngitis, mesenteric and cervical lymphadenopathy, hepatosplenomegaly, bilateral periorbital edema, and hyperemia. The patient was found to be positive for *F. tularensis* by microagglutination test. This is the first case of tularemia documented in northern Cyprus (Uncu *et al*., 2017). Furthermore, nal Evren *et al*. (2019) reported a 25-year-old woman from northern Cyprus who had oropharyngeal tularemia with a high fever and cervical lymphadenopathy. The patient was found to be positive for tularemia by the tube agglutination test. Apart from these cases, a cross-sectional study published in 2022 reported the seropositivity of *F. tularensis* to be 0.93% in northern Cyprus. The study indicated the presence of tularemia, despite its low seroprevalence, in the country (Yeni *et al*., 2022).

Since tularemia has a wide range of symptoms, the disease may be misdiagnosed. As a result, there may be a lack of reports on tularemia in different countries. This highlights that awareness should be raised among healthcare providers as well as the public. Tularemia should be considered in the differential diagnosis of patients who have a history of exposure to infected animals or ticks, particularly in the endemic regions (Obaidat *et al*., 2020).

Q fever

Coxiella burnetii is another pathogen that can be transmitted via ticks. It is the causative agent of a zoonotic infection called Q fever. *C. burnetii* can infect a large scale of animals without any symptoms. Cattle, sheep, and goats, the usual reservoirs of *C. burnetii,* harbor high amounts of bacteria in tissues like the placenta, fetal membranes, and amniotic fluid. Inhalation of contaminated aerosols is another route of transmission. Also, more than 40 tick species harbor *C. burnetii* naturally in their body and enable their survival in nature.

Q fever has been recorded in Cyprus since 1951. However, number of the studies is limited (Psaroulaki *et al*., 2014a). Within the years 1974 and 1975, a total of 87 British soldiers located in Cyprus were reported to have Q fever. Despite Q fever is mostly asymptomatic in humans, 59% of the infected soldiers developed pneumonia, hepatitis, and pericarditis. Investigations showed that the source of this infection was the *C. burnetii* epidemic in livestock, and no vector-borne transmission was observed. By serological tests, a large number of asymptomatic military staff were detected positive. While it was stated that the transmission occurred through contaminated aerosols, no information was given regarding tick or flea infestation in the soldiers (Spicer *et al*., 1977).

In a study conducted in 2011 in northern Cyprus, Cantas *et al*. collected abortion material samples from 51 cows, six sheep, and two goats, and searched for *C. burnetii* by molecular methods. Among the 59 animals, 30 were infested with ticks, and 22 samples (37%) were detected positive. Results indicated that ticks, poor hygiene, and the presence of carnivores in farms were risk factors for *C. burnetii*-associated abortions in livestock (Cantas *et al*., 2011). In another study, Loukaides *et al*. (2006) conducted an epidemiological investigation of Q fever in southern Cyprus. They aimed to detect high-risk regions on the island, and search for acute clinical cases among humans and animals (goat, sheep, bovine). They defined two rural villages as high-risk regions and named them VIL1 and VIL2. They included *C. burnetii* seronegative individuals and animals from both villages in the study and followed up the study participants through an active surveillance program for one year. IgG, IgM, and IgA antibodies against the phase II antigen of *C. burnetii* were investigated monthly by indirect immunofluorescent antibody test. The seropositivity rates in humans were noted to be 59.5% in VIL1, 52.9% in VIL2, and 27.8% in children. Seropositivity in animals was 43.1% in VIL1 and this rate was 28.7% in VIL2 (Loukaides *et al*., 2006).

In another study, Psaroulaki *et al*. (2006) collected serum samples from 974 animals and 583 humans and tested IgG antibodies against the phase II antigen of *C. burnetii* by indirect immunofluorescent antibody test. They also collected 141 ticks from animals and tested *C. burnetii* positivity by PCR. The ticks were identified to be *Rh. sanguineus* (n=100) and *Hyalomma* spp. (n=41). The seropositivity was detected as 52.7%, 48.2%, 18.9%, and 24% for humans, goats, sheep, and bovines, respectively. In addition, among 141 ticks, seven *R. sanguineus* and three *Hyalomma* spp. were found to be positive for *C. burnetii*. In the study, tick infestation was defined to be one of the risk factors for Q fever seropositivity (Psaroulaki *et al*., 2006b). Within the years 2000 and 2006, Psaroulaki *et al*. (2014a) collected ticks from wildlife animals including mouflons, rats, foxes, hares, and birds in five districts of southern Cyprus. *Rh. turanicus*, *Rh. sanguineus*, *Rh. bursa*, *R. pusillus*, *Ixodes ventalloi*, *I. gibbosus*, *Hy. anatolicum excavatum*, *Hy. marginatum marginatum*, *Hae. punctata* and *Hae. sulcata* were the identified tick species in this study. A total of 1315 ticks were tested for the presence of *C. burnetii* by molecular techniques. Fifty-six (28.9%) of 195 tick pools were detected positive for *C. burnetii.* Among the tick species, *C. burnetii* was identified in 60% of *Rh. sanguineus*, 28% of *Rh. turanicus*, 39% of *Rh. bursa*, 13% of *Hy. anatolicum excavatum*, 50% of *I. ventalloi*, 12% of *Hae. sulcata* and 100% of *Hae. puncata* (Psaroulaki *et al*., 2014a). In another study, 141 ticks were collected from southern Cyprus. Ticks were identified as *Rh. sanguineus* and *Hyalomma* spp. *C. burnetii* was identified in 10% of the collected ticks (Spyridaki *et al*., 2002).

The presence of *Coxiella* in ticks was also documented by other studies. Between 2002 and 2006, 30% of blood specimens collected from the mouflons were detected positive for *C. burnetii*. In this study, 32.1% of the ectoparasite pools were positive for *C. burnetii* which was detected in *Rh. turanicus, Rh. sanguineus, Rh. bursa, Hy. a. excavatum, Hae. sulcata*, and *Hae. punctata* (Ioannou *et al*., 2011). In another study, three pools of *I. ventalloi* ticks collected from 557 birds between 2004 and 2006 were detected positive for *C. burnetii* in Cyprus (Ioannou *et al*., 2009).

The published evidence of *C. burnetii* in humans, animals, and ticks suggests that this infection can pose a risk to public health, and therefore highlights the need for the implementation of vector control programs on the island.

Anaplasmosis

Anaplasma phagocytophilum is a gram-negative intracellular bacterium that causes the zoonotic infection called anaplasmosis. White-tailed deer and white-footed mice are reported to be the most common sources of *A. phagocytophilum* in nature. Additionally, this pathogen can also infect livestock and humans. It can be transmitted to humans via *Ixodes* tick. Human infections can vary from asymptomatic or mild disease to severe disease, marked by pancytopenia, multiorgan failure, and death (Dumic *et al*., 2022). Anaplasmosis can be observed at any time of the year, but cases usually peak in June-July and October-November (CDC, 2023b).

The first case of anaplasmosis in Cyprus was detected in a 9-year-old girl from Nicosia in 2006. She had a recurrent fever of 38°C for over 3.5 months and a tick was removed from her neck before the symptoms started. The serological test was negative, while PCR was positive for *A. phagocytophilum*. For the epidemiological survey in the village, 22 blood samples from parents and neighbors, and 15 blood samples from dogs, sheep, and goats were collected. Also, 34 ticks were collected from the animals, and these were identified to be *Hy. anatolicum excavatum* (n=21), *Rh. sanguineus* (n=12) and *Rh. turanicus* (n=1). IgG antibodies against *A. phagocytophilum* were detected in 55% of the human samples, however all of these individuals were asymptomatic. All ticks were negative for *A. phagocytophilum*, while 60% of goats and 85.7% of sheep were detected positive by PCR (Psaroulaki *et al*., 2008). In another report, Chochlakis *et al*. (2010) documented a human anaplasmosis case from the Famagusta region, in southern Cyprus. In 2007, a 27-year-old woman was admitted to the hospital, with a prolonged fever after a tick bite. Three blood and serum samples were collected from the patient for serological and molecular tests. IgG antibodies against *A. phagocytophilum* were detected in one serum sample, while *Anaplasma ovis* was detected in one of the blood samples by PCR (Chochlakis *et al*., 2010).

Between 2002 and 2006, 10% of blood samples collected from the mouflons were detected positive for *A. ovis*. Also, 10.9% of the ectoparasite pools were found to be positive for *A. ovis* which was detected in *Hae. sulcata* only (Ioannou *et al*., 2011). In another study, Attipa *et al*. found *Anaplasma platys* in one of three dogs in the Paphos district of southern Cyprus (Attipa *et al*., 2017b). Furthermore, Diakou *et al*. (2022) detected *A. platys* by PCR-coupled sequencing method in the ectoparasites of 59 cats and 161 dogs in southern Cyprus. Apart from this, the presence of *Anaplasma* spp. was also shown in birds (49%) in southern Cyprus (Ioannou *et al*., 2009). Considering that birds can be carriers of zoonotic pathogens, this issue should be considered within the One Health concept (Chochlakis *et al*., 2010).

Other tick-borne infections

Another infection is tick-borne relapsing fever which is caused by *Borellia persica*. In the past decades, this infection was detected in most of the Middle East countries. The vector of this pathogen is defined as *Ornithodoros tholozani*, a tick species that is distributed in many countries, including Turkey, Israel, Egypt, and Cyprus (Assous & Wilamowski, 2009). A previous report documented a tick-borne relapsing fever case which was acquired in Cyprus and later imported to England (Simon, 1985). A study published in 2002 demonstrated seropositivity against Lyme disease, caused by *Borrelia burgdorferi*, in northern Cyprus. The results revealed that, of 91 individuals, 16 (17.6%) were IgG-positive, and two of these individuals were also IgM-positive for *B. burgdorferi* (Altındiş *et al*., 2002).

Although *Ehrlichia canis* and *Hepatozoon canis*, which are canine tick-borne pathogens, are present in the Mediterranean region, there are only a limited number of studies from Cyprus. Of these, one study reported the presence of *E. canis*, *H. canis*, *A. platys*, *Babesia vogeli*, and *Mycoplasma haemocanis* among dogs in southern Cyprus by molecular methods (Attipa *et al*., 2017b). Despite an extensive literature search, no information was found regarding the presence of Crimean-Congo hemorrhagic fever in Cyprus (ECDC, 2023d). Likewise, the prevalence of tick-borne encephalitis (TBE) in Cyprus is unknown due to the lack of TBE surveillance systems (ECDC, 2012; Van Heuverswyn *et al*., 2023).

Lice-, flea- and acari-borne diseases

Lice-borne diseases

Lice are classified into three types due to the localization on the human host: These are body lice, head lice, and pubic lice. Body lice are arthropods of medical and veterinary importance and play a role as a vector in the transmission of pathogens like *Bartonella* spp., *Borrelia* spp., or *Rickettsia* spp. (ECDC, 2023e).

Rickettsia prowazekii, an intracellular gram-negative bacterium, is the agent of epidemic typhus and is transmitted by human body lice. Epidemic typhus has a high mortality and morbidity rate. The bacterium has the ability to reinvade other body tissues several years after the primary infection. Humans are the main reservoir of this bacterium. Recent outbreaks have been documented in different countries, and immigrants, refugee camps, and prisons are the major sources of the infection. Although epidemic typhus is not locally acquired in Europe, imported cases are reported among tourists (ECDC, 2023e). No reports of epidemic typhus or information on louse vectors have been recorded from Cyprus.

Bartonella quintana is the agent of trench fever which is transmitted by the body louse. Non-specific symptoms like fever, headache, and malaise are observed in the patients, however the infection can also result in bacteremia. Although cases were reported in different countries, *B. quintana* infection was not documented for Cyprus (ECDC, 2023e).

Another disease is louse-borne relapsing fever, which is caused by *Borrelia recurrentis*. Humans are the reservoir of the infection, and the main vector is the human body louse. In 2015, confirmed cases of louse-borne relapsing fever were reported among refugees from Africa in the European countries (ECDC, 2015). Although no case of louse-borne relapsing fever has been reported from Cyprus, a publication in 2013 documented an infestation with *Pthirus pubis* on a 4-year-old boy's eyelid in northern Cyprus. After lice and nits were removed mechanically from the eyelashes, topical treatment was applied to avoid the possibility of secondary infection, and the patient recovered completely (Dağdelen *et al*., 2013).

Flea-borne diseases

More than 2500 flea species have been defined, and those that have medical and veterinary importance are *Ctenocephalides felis* (cat flea), *Pulex irritans* (house or human flea), and *Xenopsylla cheopis* (the oriental rat flea), while *Tunga penetrans* (chigoe flea) has a limited distribution. Fleas generally infest rodents and mammals, however they can be found accidentally on the human body and transmit several infectious diseases. Flea-borne spotted fever, cat scratch disease, murine typhus, and plaque are some of the flea-borne infections of public health concern (ECDC, 2023f).

Rickettsia typhi, the agent of flea-borne (murine) typhus can be transmitted to humans via contact with infected fleas *Xenopsylla cheopsis* and the *Ctenocephalides felis*. In the studies that analyzed fleas collected from rats in southern Cyprus, *R. typhi* was detected in *X. cheopis* (oriental rat flea) and *Leptopsylla segnis* (Christou *et al*., 2010), and *R. felis* was identified in *C. felis* (cat flea) (Psaroulaki *et al*., 2006a) and *X. cheopis* (Christou *et al*., 2010). Moreover, Psaroulaki *et al*. (2010) reported that 48.6% and 41.8% of the rats tested were IgG-positive for *R. typhi* and *R. conorii*, respectively, in southern Cyprus. The authors found the rate of flea infestation to be 40.5% in that rat population.

Although there is not any published evidence of murine typhus in northern Cyprus, cases were documented in southern Cyprus. Between 2000 and 2006, 21 children under 15 years of age were reported to be seropositive for *R. typhi*. Most (71%) of the pediatric cases were living in rural regions. One of the children developed subacute meningitis as a disease complication. The patients were successfully treated with chloramphenicol and/or doxycycline (Koliou *et al*., 2007a). A case report in 2007 documented a pregnant woman from Larnaca who exhibited high IgM and IgG antibody titers for *R. typhi*. After the diagnosis of murine typhus, the patient was successfully treated with erythromycin and she gave birth to a healthy baby (Koliou *et al*., 2007b). Another study reported that 193 cases of murine typhus were detected in humans between 2000 and 2008. A high percentage (79.3%) of the cases were documented in rural regions (Psaroulaki *et al*., 2012).

In 2022, scientists from southern Cyprus collected ectoparasites from a total of 220 animals (161 dogs and 59 cats). Flea infestation was found in 39.1% of the dogs, while flea and louse infestation among the cats was reported to be 84.7% and 3.4%, respectively. In the morphological investigation of the ectoparasites, the authors found that 62 dogs and 45 cats were infested with *C. felis*, while one dog and one cat were infested with *Ctenocephalides canis*, and *Echidnophaga gallinacean*, respectively. In the study, *R. felis, Rickettsia* sp., *Bartonella koehlerae, Bartonella clarridgeiae,* and *Bartonella henselae* were detected in the fleas by PCR (Diakou *et al*., 2022).

Psaroulaki *et al*. (2014) conducted another study between 2002 and 2006. From 48 different locations in southern Cyprus, 1147 fleas were collected from rats, hares, and foxes. The flea species identified in the study were *X. cheopis* (n=729), *C. felis* (n=304), and *C. canis* (n=114). Among the 153 flea pools, 25 (16.3%) were found to be positive for *C. burnetii* by PCR. The presence of *C. burnetii* was detected in 38.1% of *C. canis*, 16.6% of *C. felis*, and 10.8% of *X. cheopis* in the study (Psaroulaki *et al*., 2014b).

On the other hand, *Bartonella henselae*, another flea-borne pathogen is the causative agent of the cat scratch disease. In 2021, a 34-year-old female patient was diagnosed with the cat scratch disease in northern Cyprus. The transmission occurred as a result of the cat injuring the human, and no flea infestation was reported in either the cat or the patient (Güler *et al*., 2021).

Acari-borne diseases

Sarcoptes scabiei is a mite which is the causative agent of scabies. As a neglected tropical disease, the case numbers are dramatically increasing worldwide (Gazi *et al*., 2022). *Sarcoptes scabiei* var. *hominis* can be acquired after a prolonged and close skin contact. Mostly children under the age of two and elderly individuals are affected. This highly contagious parasitic cutaneous disease affects approximately 200 to 300 million individuals each year (Leung *et al*., 2020). While scabies outbreaks are documented in different countries, an increase in scabies rates was also reported in Türkiye. The main reason was attributed to coronavirus disease 2019 (COVID-19) pandemic. It was documented that, due to the restrictions in the beginning of the pandemic, family members spent more time at home, increasing the contact time with each other (Ruh & Taylan Özkan, 2023). In Cyprus, the media and press have highlighted the occurrence of scabies in both northern and southern parts, however no study has been published in the literature yet.

Another mite that is important for both human and veterinary medicine is *Neotrombicula autumnalis*. In addition to dogs and cats, it can also infest other domestic and wild mammals, birds, and humans. Only the larval stage of the mite is parasitic, but in contrast, nymphs and adults are free-living. These mites are the causative agent of trombiculosis, a kind of dermatopathy. Besides the dermatologic problems, they can be potential vectors of *A. phagocytophilum* and *B. burgdorferi* sensu lato. Giannoulopoulos *et al*. reported cases of trombiculosis in Greece (in one cat and one dog), and in Limassol district, southern Cyprus (in one cat) for the first time in 2012. *N. autumnalis* larvae were detected in the microscopic examination of the skin scrappings in all three cases (Giannoulopoulos *et al*., 2012).

CONCLUSION

The island of Cyprus has been an important focus for VBDs over the years. Although control programs were implemented to eliminate diseases such as malaria on the island, the existence of disease vectors caused the emergence/re-emergence of VBDs in the region. Not only climatic and geographical conditions, but also international travel particularly from endemic countries pose a risk for circulation of VBDs. Importantly, studies conducted in the island identified various infecting agents in the arthropods which clearly indicate the ongoing circulation of diseases. Consistent with this, reports from both northern and southern parts of Cyprus have documented infections in humans acquired through arthropod vectors. Therefore, to control the transmission cycle of infective microorganisms, measures must be taken against disease vectors, and public awareness must be raised in the region. We believe that this first comprehensive literature review will provide an insight into future islandwide studies, and also will be an important contribution to the elimination of VBDs in the region.

Conflict of Interest:
The authors declare that they have no conflict of interest.

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