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Hantavirus and Middle East Public Health Challenges: A Subject Review

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Abstract

Hantaviruses are emerging zoonotic viruses belonging to the family Hantaviridae, which are typically found in rodent reservoirs and transmitted to humans through contact with contaminated saliva, aerosolized particles or excreta. There are two major clinical syndromes associated with human infections: hemorrhagic fever with renal syndrome (HFRS) — mostly reported from Europe and Asia, and hantavirus cardiopulmonary syndrome (HCPS) — mostly reported from the Americas. The Middle East has a relatively low incidence of hantavirus disease, but recent epidemiological studies have shown that the virus is circulating in several countries, including Türkiye and Iran. The emergence of hantavirus infections in this area has become a growing concern as the population increases, climate variations occur, the rodents' ecology is changing, the agriculture spreads and the surveillance of this situation is improving. There is limited surveillance, underdiagnosis, and a large clinical overlap with other febrile illnesses all of which are important challenges in quantifying the regional burden of disease. This review aims at summarizing the state of knowledge about the epidemiology of the hantavirus in the Middle East, focusing on geographical distribution, environmental factors, rodent hosts, epidemiology, clinical features, diagnostic methods and public health preparedness. Current data suggest that while human infections are rare, ecological conditions which could sustain hantavirus are present in several Middle Eastern countries, and therefore increased surveillance and research into interdisciplinary and One Health initiatives are needed. Creating closer ties between the medical, veterinary and environmental communities is crucial for early outbreak detection and prevention in the future.

Keywords: *Hantavirus, Middle East, Epidemiology, Public health.*

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Introduction

Hantaviridae is a family of enveloped, negative-sense, single-stranded RNA viruses which lead to severe disease in humans that are maintained by persistent infection of specific reservoirs of rodents, shrews, moles, or bats without causing significant disease in the natural host species (Maes et al., 2019).

Human infection is accidental by inhaling aerosolized virus particles from contaminated rodent urine, faeces or saliva, or by direct contact via rodent bites or contaminated environmental surfaces (Vaheri et al., 2013).

Hantavirus infections are a serious public health problem globally, due to their high morbidity and potentially fatal consequences. Several hantavirus species have been identified to infect humans, resulting in two major disease syndromes, which are associated with different geographic distribution and genotype. Hantaviruses from the Old World (Hantaan, Dobrava-Belgrade, Seoul and Puumala) are mainly associated with the hemorrhagic fever with renal syndrome (HFRS) while those from the New World (Sin Nombre virus) are linked to hantavirus cardiopulmonary syndrome (HCPS), a syndrome with severe pulmonary oedema and subsequent cardiogenic shock (Avšič-Županc et al., 2019). There are an estimated 100,000 to 200,000 cases of HFRS every year worldwide, with China reporting the most cases, followed by the Republic of Korea, Russian Federation, and some European countries (World Health Organization, 2025).

In the past, Middle Eastern countries have not been known as important endemic areas for hantavirus. But, there is some recent evidence that this may be because the virus is not widely prevalent and not circulating, but because there is not enough evidence that it is circulating. There are serological evidence of antibodies to hantaviruses in humans and rodents in several countries, such as Türkiye and Iran, suggesting zoonotic transmission has likely occurred for many years, but is significantly underrecognized (Keshtkar-Jahromi et al., 2011; Razzaghi-Abyaneh et al., 2022).

Since the news coverage spread internationally about sporadic cases of hantavirus infection and outbreaks in several parts of the world, there has been a significant rise in the public awareness of such infections. There is no evidence of community transmission at this time in most countries in the Middle East, however, with early clinical recognition difficult, increased awareness amongst healthcare settings and public health authorities is warranted. Early clinical signs and symptoms such as fever, headache, myalgia, nausea, and gastrointestinal signs are non-specific and can mimic other viral illnesses commonly seen in the region which include dengue fever, leptospirosis, Crimean–Congo hemorrhagic fever, COVID-19, and even influenza (Clement et al., 2020).

This review aims to provide a thorough overview of the epidemiology of hantavirus in the Middle East, including its distribution, reservoir ecology, transmission potential and mechanisms, clinical presentation, diagnosis and public health preparedness. In addition, this review points out what gaps in knowledge exist, and suggests future research needs to advance surveillance and minimize the potential for hantavirus emergence in the region.

Virology and Classification

The hantaviruses are Bunyavirales enveloped viruses (family Hantaviridae). They have a tripartite negative sense single-stranded RNA genome with small (S), medium (M) and large (L) genomic segments. They encode the nucleocapsid (N) protein, two envelope glycoproteins (Gn, Gc) and the RNA-dependent RNA polymerase (RdRp), respectively. These structural components, in combination, allow for viral attachment, replication, assembly and persistence in reservoir hosts (Maes et al., 2019; Avšič-Županc et al., 2019).

Hantaviruses are highly host specific as compared to many other zoonotic viruses. The majority of hantaviruses are associated with a single or a restricted number of mammalian reservoir hosts, typically rodents, but with a few exceptions (hantaviruses in shrews, moles, and bats). The reservoir animals do not generally have clinical disease, but the virus is able to be shed into the environment and persists in the animal for a long time through urine, faeces and saliva (Jonsson et al., 2010).

Hantaviruses are classified into 2 groups based on their geographic distribution and clinical syndromes; Old World and New World viruses. The viruses in the Old World belong to the genus Hantavirus and consist of four viruses: Hantaan virus, Seoul virus, Puumala virus and Dobrava-Belgrade virus. These viruses mainly cause the haemorrhagic fever with renal syndrome (HFRS), which features fever, leakage

of blood vessels, low platelet counts and different levels of acute kidney injury. New World hantaviruses, including Sin Nombre virus and Andes virus, are mainly known to circulate in North and South America, and cause hantavirus cardiopulmonary syndrome (HCPS), a serious respiratory illness with a high mortality rate (Vaheri et al, 2013).

The Middle East is at higher risk of encountering Old World hantaviruses as a result of the distribution of the rodent hosts of these viruses. Circulation of Puumala virus and Dobrava-Belgrade virus have been published in Türkiye, while Hantaan like and Seoul like viruses have been detected in Iran by serological and molecular methods. While known infections in humans in other countries in the Middle East are rare, the ecological environmental is favorable, suggesting that there may be more viral diversity not yet fully characterized due to limited surveillance and diagnostic testing (Razzaghi-Abyaneh et al., 2022).

Pathogenesis

Hantavirus infection appears to be primarily responsible for infection of vascular endothelial cells followed by dysregulation of vascular permeability. This suggests that increased leakiness of the capillaries is more likely to be caused by immune-mediated than by widespread endothelial cell death, since endothelial cells can support viral replication and maintain their structural integrity (Vaheri et al., 2013).

The virus enters the respiratory system by inhaling the infectious aerosols, and it is initially observed in the respiratory epithelial cells, and subsequently spreads in the blood to various organs. In HFRS, the main target is the vascular endothelium, especially in the kidneys, while in HCPS, it is in the lungs. Viral replication triggers innate immune responses, including the activation of the complement pathways, natural killer cells and dendritic cells and the activation of macrophages. There are strong adaptive immune responses, with pro-inflammatory cytokine production and cytotoxic CD8+ T lymphocytes, following these events. Tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interferon-γ (IFN-γ) and other inflammatory mediators are responsible for endothelial dysfunction, disruption of intercellular junctions and increased vascular permeability. As a result plasma leakage, hypotension, thrombocytopenia and tissue oedema occur, which are the major features of the disease causing clinical disease severity (Mittler et al., 2019).

The outcome of disease is also affected by the host's genetic factors. Some differences in susceptibility, severity, and recovery between infected individuals has been linked to variations in human leukocyte antigen (HLA) alleles and immune regulatory pathways. In addition, viral genotype is important in clinical presentation, as Sin Nombre virus is associated with severe cardiopulmonary disease; Hantaan virus is more likely to cause severe renal disease than Puumala virus; and most of the severity of the renal disease is associated with A viral genotype (Avšič-Županc, et al., 2019).

The Hantavirus epidemic in the Middle East

The Middle East has relatively few reported cases of human hantavirus infection compared with Europe and the Americas, and compared with East Asia. But the few cases published should not be taken as proof that the disease is not present. Instead, it is mostly a reflection of failing surveillance systems, poor access to molecular diagnostic tools, low clinical awareness and the non-specific clinical manifestation of hantavirus infection, which is often confused with other endemic febrile diseases like leptospirosis, Crimean–Congo hemorrhagic fever (CCHF), dengue fever and severe bacterial sepsis. As such, there is a lack of awareness about the zoonotic disease hantavirus in many parts of the region (Chinikar, et al., 2013 ; Hameed and Ahmed, 2021).

Based on existing evidence, it appears that hantaviruses are the leading viruses circulating in the Middle East. Rodent species competent to maintain these viruses, especially those of the genera Apodemus,

Microtus, Myodes and Rattus, can be found in ecological conditions of several countries. While there are very few surveillance programmes in place, the studies conducted in both serological and molecular levels suggest that the circulation of hantavirus is not limited to the countries where human cases have been reported (Ertek, et al., 2010 ; Hameed et al., 2021).

Türkiye

Türkiye has the most convincing data of endemic hantavirus transmission in the Middle East and is thought to be a key epidemiological link between Europe and Western Asia. The majority of cases has been reported from the Black Sea area where the climate is suitable for dense forestation and rodent populations. Infections in humans are mostly related to Puumala virus and Dobrava-Belgrade virus which cause hemorrhagic fever with renal syndrome (HFRS). A few outbreaks have been reported since the late 2000s, mostly in people who have come into contact with rural areas, forestry operations, farm work, military service, and rodent-infested structures. The incidence of this also has been noted to vary seasonally, being higher in seasons when there is high rodent activity. The level of national surveillance has significantly improved in the last decade, with earlier detection of individual outbreaks and improving the laboratory diagnostic capability. Although there is a lot of concern about hantavirus lately in the international arena, there are no indications of a nationwide upsurge in 2026 and it is closely monitored by the existing surveillance systems (Ertek, et al., 2010 and Turkish Ministry of Health, 2026).

Iran

In the Middle East, Iran has had the most published research about the hantavirus that has been conducted. The available evidence is strongly indicative that the infection with hantavirus is not a new phenomenon, but has been underdiagnosed in the past. The first reported case of HfrRS in northwestern Iran in the early 1980s, and later laboratory samples have shown human exposure in several provinces. In one of the most significant epidemiological studies, 4.5% of the workers in the city of Isfahan province had been found to be sero-positive for having been previously infected by hantavirus. Infection by rodents accounted for the highest risk factor, emphasising environmental sanitation and occupational health. Several additional studies using patients with suspected viral hemorrhagic fever confirmed the presence of antibodies against Puumala virus and Hantaan virus, suggesting a presence of Old World hantaviruses among the Iranian population. These serological results are in general agreement with endemicity of circulation for viral RNA, which is infrequently detected. Recent reviews suggest that hantavirus infection in Iran is probably underdiagnosed since physicians do not routinely consider hantavirus infections in the differential diagnosis of any acute febrile illness with thrombocytopenia or acute kidney injury. Therefore, physician education, molecular diagnostics, and improved surveillance are all considered to be key public health priorities (Esmaeili, et al., 2017).

Iraq

There is very little published information available about the epidemiology of hantavirus infection in Iraq. Large scale serological surveys and nationwide molecular surveillance studies have not been carried out so far. However, Iraq has a number of ecological features which could facilitate the circulation of hantavirus such as the prevalence of commensal rats (Rattus norvegicus and Rattus rattus), agricultural development, the presence of extensive irrigation systems, marshland ecosystems in southern Iraq and increased human–rodent interactions in urban areas caused by urbanization. Sporadic hantavirus infections may be undiagnosed, especially if they only present with a fever and low platelet count, which are common symptoms of other infections like Crimean–Congo hemorrhagic fever, leptospirosis and bacterial sepsis. Lack of reporting, therefore, does not mean that hantavirus is not present in Iraq but rather it represents an important knowledge gap. Establishing national surveillance programs and conducting rodent reservoir studies should be considered research priorities (Heyman, et al., 2011).

Saudi Arabia

At this time, there is no evidence of continued endemism of hantavirus in Saudi Arabia to humans. However, the large volume of international trade, burgeoning urban populations, growing agricultural schemes and the presence of commensal rodents, make conditions conducive to continued surveillance. Infected rodents (Rattus norvegicus) with a Seoul virus species commonly associated with this species could be introduced into major commercial ports. While human cases have not been widely reported, health care professionals need to be aware of hantavirus infection when assessing a patient for fever of unknown origin and acute kidney failure after occupational or environmental exposure to rodents. Ongoing monitoring of rodents around ports, food retail stores and in urban areas can yield useful epidemiological data (Jonsson et al., 2010).

United Arab Emirates

There are no current indications that locally acquired hantavirus infection is common in the United Arab Emirates. The dry climate in the country could limit the ecological suitability of a number of traditional hantavirus reservoir species but peri-domestic rodents are widespread in urban areas and commercial ports. Wild rodents are a source of zoonotic viruses that can emerge, and surveillance studies have identified several of these viruses, even in the absence of documented human outbreaks, thus reinforcing the need to continue monitoring wild rodents (Klempa, 2009 and UAE Ministry of Health and Prevention, 2026).

In Oman, Kuwait, Qatar, Jordan, Syria and Lebanon

There is very little information available on hantavirus epidemiology in Oman, Kuwait, Qatar, Jordan, Syria and Lebanon. Published literature is composed mostly of ecological observations or geographic review for the most part, not laboratory confirmed epidemiological studies. At present there is no convincing evidence for widespread endemic human infection in these countries. All six countries have rodent populations that can act as a potential reservoir for zoonotic pathogens, although at present little is known about these populations. Rodent ecology and potential future spillovers could change in response to environmental change, climate variability, changes in agricultural practices, humanitarian crises, population displacement and urban expansion. The absence of surveillance, however, is a major study void across the region and not evidence of the lack of disease (Mostafavi, et al., 2017).

Conclusion

Hantavirus infection is a largely overlooked, but potentially significant, zoonotic disease in the Middle East. Epidemiological evidence from various parts of the region indicates that appropriate ecological conditions and reservoir hosts exist in parts of the region, although confirmed human cases remain relatively uncommon. To accurately characterise the regional burden of disease and minimise the risk of future hantavirus emergence, efforts must be made to strengthen surveillance system and increase diagnostic capacity, encourage interdisciplinary, One Health collaboration and invest in high quality research.

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