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Brucellosis : Emerging and Re-Emerging Zoonosis

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Abstract - More than 500,000 human cases of brucellosis are reported each year, with Brucella melitensis being the primary cause. It is still one of the most prevalent zoonotic illnesses in the world. The CDC has categorized the bacterial pathogen as a category (B) disease, meaning that it possesses the potential to evolve into a bioweapon. It is thought that the most prevalent infections obtained in laboratories are Brucella species. The emergence or reappearance of new foci causes brucellosis to constantly shift in geographic distribution. Animals and humans are affected by the disease everywhere, with the exception of nations where bovine brucellosis has been completely eradicated. Due to brucellosis, there are significant economic losses incurred globally in both animal production and human health.

All of the region's countries have recorded cases of leishmaniasis, hepatitis A virus (HAV), and hepatitis E virus (HEV). Dengue fever, H5N1, Chikungunya, and Crimean Congo hemorrhagic fever (CCHF) have all been spreading geographically and in quantity as well as in frequency. Public health is still concerned about Middle East respiratory syndrome (MERS), which was first discovered in this area in 2012. In certain of the countries, poliomyelitis, leishmaniasis, cholera, and diphtheria control are difficult to maintain. Furthermore, just a few of the region's nations are home to Rift Valley fever (RVF) and Alkhurma hemorrhagic fever (AHF).

Furthermore, not much is known about the actual state of tularemia, Q fever, and the plague. In conclusion, EIDs and RIDs are widespread in the majority of the region's nations and may continue to spread there. Enhancing regional capacities and capabilities is essential for both preventing disease outbreaks and providing sufficient resources and expertise to contain them. Keywords: MERS-CoV, CCHF, Zoonosis, Emerging Infectious Diseases, Neglected Tropical Diseases, Eastern Mediterranean Region Copyright © 2022 Kerman University of Medical Sciences is the publisher of the author or authors. The Creative Commons Attribution License, which allows for unlimited use, distribution, and reproduction in any format as long as the original work is properly attributed, governs the dissemination of this open-access article.

***Key Words*:** AIDS, West Nile fever, and Legionnaires' diseaseZoonosis, MERS-CoV, CCHF, neglected tropical diseases, emerging infectious diseases, and the Eastern Mediterranean region.

1. INTRODUCTION

Emerging infectious diseases (EIDs) are those that have just recently been observed in a population, or whose geographic range or incidence is expanding quickly or poses a short-term threat to do so. Infectious diseases that were once under control but have resurfaced as a serious hazard to public health are known as re-emerging diseases (RIDs).1, 2

In recent years, there has been a global surge in the emergence of high-threat dangerous illnesses.2. Nearly 75% of newly discovered human diseases have zoonotic roots.2. Acute and ongoing humanitarian crises have

impacted several nations in the World Health Organization's (WHO) Eastern Mediterranean Region (EMR), either directly or indirectly. As a result, there are remarkably large numbers of internally displaced people and refugees living in cramped, overcrowded camps with scant or nonexistent access to basic medical and social services.3. High-threat pathogenic illnesses are emerging or reemerging due to a variety of causes, such as host behavior (migration, travel abroad, contact with animals, poverty, climate change, and industrial and economic development) and host adaptation or resistance.4Interconnections between social, economic, biological, technical, and ecological aspects lead to both EIDs and RIDs.

Many diseases spread due to factors such as climate and living conditions, and ecological changes are a major factor in the resurgence of infectious diseases.9. A further risk to EID and RID outbreaks is the recurring large-scale pilgrimage to Saudi Arabia and Iraq in the EMR.10 Other significant factors that raise the chance of many diseases spreading include increased political unrest and violence in the area, which result in significant population movements (eg, diphtheria, cholera, and leishmaniasis).

2. Literature review

It is a narrative review in this work. A literature study yielded an extensive list of developing and RIDs. The Delphi approach was then used to share the preliminary list with EMR 17 specialists. The specialists discussed a variety of topics, such as epidemiology, clinical infectious disease, and microbiology. A final list of infectious illnesses of global concern in EMR was selected and authorized based on the expert's judgment. An assessment of the epidemiological circumstances surrounding the RIDs and EIDs in the EMR was carried out. A thorough list of research in the topic was compiled using a methodical search strategy. Purposively examined studies were found to provide an overview of the epidemiological conditions for each targeted infectious disease in various EMR nations.

Section snippets

An ancient illness known as brucellosis may have its origins in the fifth plague that struck Egypt in 1600 BC. Recent analysis of the 750 BC ancient Egyptian bones revealed signs of osteoarticular diseases, including sacroiliitis, which are common brucellosis consequences (Pappas and Papadimitriou, 2007). In 1887, David Bruce discovered Brucella melitensis (known at the time as Micrococcal melitensis) from the spleen of a British soldier who had died from a prevalent feverish disease called Malta fever.

The etiologic agents

Gram-negative, facultative intracellular coccobacilli that are non-spore-forming and non-capsulated are called Brucella spp. Despite being classified as non-motile, Brucella species possess every gene required to form a functional flagellum, with the exception of the chemotactic system (Fretin et al., 2005). Along with Ochrobactrum, Rhizobium, Rhodobacter, Agrobacterium, Bartonella, and Rickettsia, they are members of the Proteobacteria's alpha-2 subgroup (Yanagi and Yamasato, 1993). There are nine species of Brucella.

Global distribution and economic impact

The emergence or reappearance of new foci causes brucellosis to constantly shift in geographic distribution. Due to increased international travel as well as a number of hygienic, socioeconomic, and political factors, the epidemiology of human brucellosis has evolved significantly in recent years. Human brucellosis has spread to new areas, mostly in central Asia, and the situation is fast getting worse in some Middle Eastern nations (Pappas et al., 2006b).

Zoonoses

Brucella melitensis is the most invasive and harmful species for humans, followed in descending order by B. suis, B. abortus, and B. canis. Of the nine known species of Brucella, five can infect humans (Acha et al., 2003). According to several studies (Brew et al., 1999, McDonald et al., 2006, Sohn et al., 2003), marine

brucellae (B. ceti) are zoonotic. The Centers for Disease Control and Prevention in the United States have classified B. melitensis, B. suis, and B. abortus as possible bioweapons.

Human brucellosis

Before antibiotics were discovered, one of the greatest summaries of human brucellosis was "the disease rarely kills anybody, but it often makes a patient wish he were dead" (TIME magazine, 1943). Although brucellosis typically takes 1-3 weeks to incubate, symptoms may not appear for several months. While infections with other species are typically subacute and protracted, B. melitensis is linked to acute infections (Mantur et al., 2007).

Animal brucellosis

The most common clinical symptom after a Brucella infection in livestock animals (cattle, sheep, goats, pigs, and camels) is abortion (Acha et al., 2003). The main strain that infects cattle is B. abortus; however, when cattle share pasture or facilities with infected pigs, goats, and sheep, they can also get temporarily infected by B. suis and more frequently by B. melitensis. Cow's milk can spread B. melitensis and B. suis, which pose a major risk to public health (Acha et al.,)

Diagnosis

Clinical diagnosis of human brucellosis is challenging due to the wide range of clinical symptoms that the disease displays. Every incidence of human fever with no known cause is thought to be caused by brucellosis in some endemic places. Thus, laboratory testing is required to confirm the diagnosis. Human brucellosis diagnosis must be made quickly and accurately because misinterpretation or delay in diagnosis frequently leads to treatment failure, relapses, chronic courses, localized sequelae, and a high case-fatality rate (Dahouk).

Treatment

Because Brucella is intracellular and may adapt to the environment in its replicative niche, such as a macrophage, treatment failure and recurrence rates are significant and rely on the drug combination and patient compliance (Seleem et al., 2008). Combination regimens using two antibiotics are the most effective treatment for brucellosis because monotherapies with a single antibiotic have been linked to significant rates of relapse (Pappas et al., 2005, Pappas et al., 2006a).

Vaccines

In addition to being a serious zoonosis for public health, Brucella infections in animals have a significant economic impact, particularly in underdeveloped nations where they can lead to infertility, reduced milk supply, and abortion in pregnant animals. The sole means of managing and completely eliminating this zoonosis in areas where the disease is highly prevalent is by immunizing all susceptible hosts and getting rid of diseased animals (Briones et al., 2001). The most commonly used vaccines

Perspective

The fact that brucellosis is a zoonosis that is still prevalent today and affects both humans and a wide variety of animals worldwide is a bit of a conundrum. The paradox is that although there are recognized, cost-effective methods for controlling brucellosis, many countries lack the resources or political "know how" to put these methods into practice. Building infrastructure that informs people about the disease's existence and controls animal brucellosis in undeveloped nations takes a significant amount of work.

2.1 Screening of Potentially Relevant Citation

Two researchers used predefined inclusion and exclusion criteria to evaluate abstracts and titles for relevance to the main questions. Two investigators worked independently to acquire full-text publications that either of them thought would be useful for additional review. The EndNote® reference management program (version X5, Thomson Reuters, Philadelphia, PA, USA) provided sufficient coverage for all results.

2.2 Inclusion Criteria

All eligible subjects were required to meet the following inclusion requirements, which included meeting the requirements for study designs: Included were published articles that described the epidemiological state of the targeted diseases in the area between 2001 and 2018.

The end objective, which was restricted to Arabic and English language publications, was usually to discover similar systematic reviews, review articles, case reports, and original works.

2.3 Quality Assessment

Excellent evidence served as the foundation for a narrative review. Two researchers subjectively evaluated the methodological quality of the studies that were a candidate for data extraction for this narrative review, taking into account the following factors: (a) No indication of selection bias; (b) Appropriate sample size; and (c) Minimal publication bias (for systematic reviews). Discussion was used to settle disagreements between the two investigators.

2.4 Data Abstraction and Analysis

One investigator abstracted the extracted data into a large database and a customized Excel spreadsheet, which another investigator verified. Every relevant paper that was located was thoroughly examined and concisely summarized in order to possibly be included in this report. The diseases that are covered are arranged alphabetically by common name into three groups: bacterial, viral, and parasitic EIDs and RIDs. Saudi Arabia saw the emergence of Alkhurma Hemorrhagic Fever (AHF), a zoonotic viral illness, in 1995.47 High death rates as high as 25% were recorded in the early stages of the disease discovery.48 As the illness gained more awareness and recognition, the death rates were reduced to roughly 1.3% upon the discovery of subclinical infections.49 Regarding the disease's pathways of transmission, there is currently a knowledge gap.There have been reports of 50 AHF from Egypt and Saudi Arabia.There have been reports of 51,52 seropositive cases and Amblyomma lepidum ticks contaminated with the AHF virus from Djibouti.53 H5N1 avian influenza:

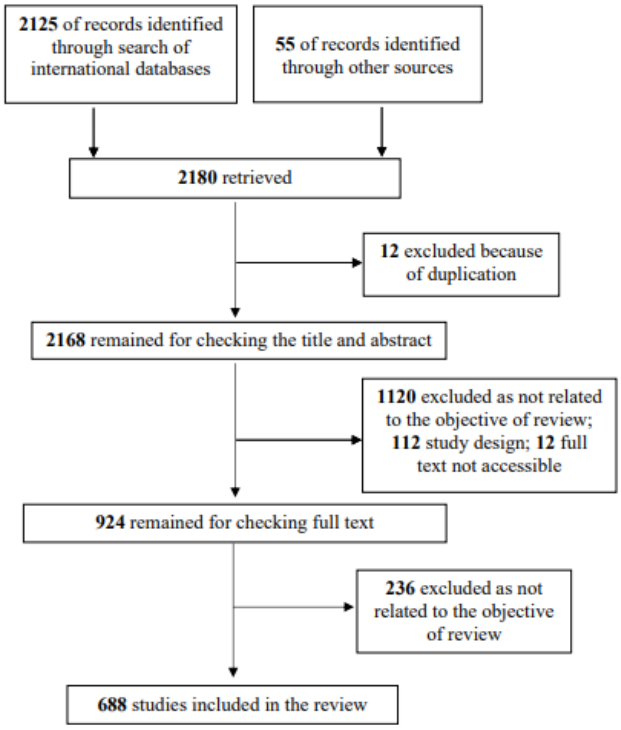

Figure 1. *A Flow Chart Depicts the Stages of Retrieving References, Checking Eligibility Criteria, and Including the Final Articles Into The Review.*

The virus is predicted to spread farther after reports of it came from 16 different nations. Large-scale nonhuman (mainly avian) epidemics of H5N1 occurred in Afghanistan, Djibouti, Egypt, Iran, Iraq, Jordan, occupied Palestinian territories, Pakistan, and Sudan in 2006. H5N1 moved quickly through the EMR throughout that year. Ever since, Egyptian poultry have developed an endemic strain of H5N1.54 It has been established that the virus is spreading over Egypt, Libya, and Saudi Arabia.55, 56 Since 2006, reports of H5N1 cases in humans have only come from Egypt and Iraq. discovered up till 2011. Since then, the overall number of infected cases has sharply climbed, from 405 instances discovered in the previous year to 8330 cases recorded in 2017.65,66 There appears to be a hidden crisis with a significant risk of transmission given the existence of competent vectors and worldwide migration of viremic patients between Eastern Mediterranean

countries and spread of the disease into neighboring chikungunya virus-free countries

2.5 Dengue: The EMR has very little information regarding the disease's current state. Dengue outbreaks have been reported in Egypt, Djibouti, Oman, Pakistan, Saudi Arabia, Somalia, Sudan, and Yemen.Furthermore, seroprevalence of dengue has been demonstrated by serological studies in Afghanistan, Iran, Kuwait, Lebanon, Qatar, and Syria.80 Aedes aegypti and Aedes albopictus, the primary mosquito vectors of dengue virus, have been found in fifteen countries in the region: Afghanistan, Djibouti, Egypt, Iran, Jordan, Lebanon, Oman, Pakistan, Palestine, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, and Yemen, among others.

However, because most of these nations lack sufficient entomological surveillance systems, nothing is known regarding the occurrence of infected vectors in other EM countries. There were 139 cases of dengue in Sudan, 245 cases in Pakistan, and 125 316 cases in Egypt in 2017. Following the start of the civil conflict in 2015, which resulted in extensive infrastructure devastation and allowed dengue to become endemic in Yemen, a total of 6777 suspected dengue cases were documented in 2015.

Human seropositive instances of West Nile fever (WNF) have been documented in Idia ,Afghanistan, Djibouti, Egypt, Iran, Iraq, Jordan, Lebanon, Libya, Morocco, Pakistan, Sudan, Tunisia, and Yemen.It was shown that Culex mosquitoes in Djibouti, Egypt, Iran, and Tunisia were infected with 134 WNF.134 This highlights the need for integrated surveillance strategies and shows how common the WNF virus is in the EMR. 2018 saw the emergence of a WNF outbreak from Tunisia that included 377 suspected patients and 49 laboratory-confirmed cases.135 Poliomyelitis:

All of the region's nations are still very vulnerable to the disease's resurgence as long as the virus is still in the EMR. Emerging and Reemerging Bacterial Infectious Diseases cholera The disease cholera is brought on by unsanitary living circumstances. The sickness is pervasive across the EMR.

3. Discussion

EMR serves as a hub for RIDs and EIDs. The amount and burden of emerging and re-emerging infectious diseases in this region are difficult to compare to other locations; however, throughout the past 20 years, there have been more outbreaks in this region due to these infectious pathogens, which has had a significant impact on social and economic growth. Owing to the prevalence of several humanitarian situations, brittle health institutions, internal conflicts, inaccurate data, fragile ecosystems, and increased population movement, the region is particularly vulnerable to outbreaks of these high-threat viruses.

For the majority of these diseases, the frequency, duration, and magnitude of disease outbreaks have increased recently. A number of disease outbreaks, including MERS in the Arabian Peninsula, cholera in Iraq, Somalia, and Yemen, Avian influenza A (H5N1) in Egypt, CCHF in Afghanistan, Iran, and Pakistan, and dengue fever in Yemen, Sudan, and Pakistan, have been identified and contained across the region (Figure 2, and Table 1). A deeper comprehension of the spread of disease, readiness for the emergence of new diseases, identification of infections and their vectors, and the use of high-impact control and preventative actions are all necessary. This is particularly challenging in light of the inadequate monitoring systems in many nations as a result of scarce diagnostic resources and personnel. extensive instruction on disease monitoring and reaction to

There is a danger of increased appearance and transmission of zoonotic diseases due to the insufficient

coordination mechanisms between the animal and human health sectors in the majority of the region's countries. The majority of the region's surveillance systems are ineffective at quickly disseminating data through standard procedures. Given that cases of several of the diseases mentioned—like chikungunya, CCHF, MERS, plague, sandfly fever, tularemia, and WNF—tend to arise as solitary occurrences and occasionally in distant places, one likely explanation is that doctors may not be properly recognizing and reporting these illnesses.

There may be differences in the data, studies, and articles that are available between nations. Further restrictions may arise from differences in each country's capacity for laboratory testing and surveillance; still, by compiling available data, the current assessment has made an effort to offer a reasonably comprehensive picture of the state of affairs in the region's countries.

Results

Viral Infectious Diseases: Emerging and Re-emerging Acute hepatitis A and E: Very little information is available regarding the prevalence of hepatitis A virus (HAV) and hepatitis E virus (HEV) from countries in the EMR, with the exception of a few published articles and outbreak reports.31 Studies conducted in Tunisia (84%), Yemen (86%), Iran (86%), Iraq (96%), Egypt (100%), and Libya (100%) have found a high prevalence of HAV and HEV. Morocco is a location where the HAV virus is intermediately prevalent.37 Due to indoor dry pit use and the drinking of sewage-contaminated water, the majority of rural areas have high antiHAV antibody prevalence. Travelers from European nations have had multiple HAV infection epidemics.

CONCLUSIONS

Large-scale population movements related to the Hajj and Arba'een pilgrimage, internally displaced people, refugees, armed groups, and transnational migrants are all ongoing issues in the EMR countries. In addition, the region's poor public health infrastructure, poverty, and climate change have made it more susceptible to a variety of EIDs and RIDs. Certain illnesses are prevalent in this area and pose a risk to visitors from other countries. Political will, financial support, collaborative international and local initiatives, widespread drug administration, immunization, and surveillance for the identification and diagnosis of less well-known agents are all crucial for the elimination of infectious illnesses in this region.

Comprehending and recording the geographical extent and patterns of these infectious disease outbreaks will be crucial in averting, swiftly recognizing, and appropriately addressing these health hazards to reduce fatalities, restrict the geographic expansion, and halt the spread of the disease through evidence-based and highly beneficial interventions. For the countries in the region, creating efficient, evidence-based public health control measures and intervention methods to reduce the risk of infection is of utmost importance (Table 2). Better planning and control strategies require research projects to understand the nature and effects of infectious illnesses in the area. In order to detect and stop the widespread appearance and reemergence of infectious diseases, more focused research efforts should be made.

Protecting the populace requires multifaceted approaches, such as collaborations between medical professionals, labs, and public health organizations, as well as well-coordinated, equipped, and prepared public health institutions. Additionally, using accurate and modern diagnostic techniques as well as surveillance helps to get better results faster.

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