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Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection: epidemiology, pathogenesis and clinical characteristics

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Abstract. – OBJECTIVE: Middle East Respiratory Syndrome Coronavirus-(MERS-CoV) infection is an evolving worldwide health crisis. The early diagnosis and management of the disease remains a major challenge. This study designed to discuss the epidemiology, pathogenesis and clinical appearances of MERS-CoV infections.

MATERIALS AND METHODS: We conducted a broad search of the English-language literature in "PubMed" "Medline" "Web of knowledge", "EMBASE" and "Google Scholar" World Health Organization-WHO" using the key words "Middle East Respiratory Syndrome", "MERS", "MERS-CoV" "Epidemiology" "Transmission" "Pathogenesis" "Clinical Characteristics". We reviewed the literature on epidemiology, pathogenesis and clinical appearances of MERS-CoV infection and the required information was documented.

RESULTS: The global prevalence of MERS-CoV infection from June 2012 to April 2018 is 2206 people. The number of cases reported from Saudi Arabia is 1831 (83%) with mortality rate of 787 (35.67%). The main clinical manifestations are fever, chills, generalized myalgia, cough, shortness of breath, nausea, vomiting and diarrhea. The age-allied prevalence of MERS-CoV was highest amongst elderly people with chronic debilitating diseases such as pulmonary diseases, end-stage renal illness, diabetes mellitus and malignancy.

CONCLUSIONS: MERS-CoV infection is an emerging global health concern, affected people in 27 countries in the various continents. MERS-CoV infection has been identified mainly in the Middle East, Europe, Africa, Asia and North America. Early detection and management of MERS-CoV infection is of critical importance to minimize the burden of the disease.

Key Words:
Middle East Respiratory Syndrome, Coronavirus, (MERS-CoV), Epidemiology, Pathogenesis.

Abbreviations

Middle East Respiratory Syndrome (MERS), Middle East Respiratory Syndrome Coronavirus (MERS-CoV), "Institute of Scientific Information" (ISI), World Health Organization (WHO), White Blood Cells (WBCs).

Introduction

"Middle East Respiratory Syndrome coronavirus infection (MERS-CoV)" became an evolving worldwide health concern. "MERS-CoV" originally reported in 2012 a primitive cause of respiratory infection initiated by a coronavirus human pathogen[1,2]. "MERS" affected more than 2000 people in 27 countries and 4 continents[3]. In Middle East, Saudi Arabia is reflected as the epicenter of "MERS-CoV" infection[4]. Saudi Arabia has unique cultural and religious practices; millions of Muslims come across from the globe travel to Saudi Arabia to perform Hajj. The various regional appearances have provided favorable conditions for speedily transmuting viruses to appear. MERS-CoV triggered an occurrence of respiratory illness in the "Middle East with secondary spread to Europe, Africa, Asia, and North America". The diseases occurred mainly the Middle East states with a highest cases of 88% followed by "Asia 11%", "Europe 0.8%" and "USA 0.1%"[5].

"MERS-CoV" infection is transmitted from animals to humans and human to human[6]. Evidence shows that bats aided as the original host species of MERS-CoV. Interestingly, recent investigations[7] revealed that MERS-CoV in bats infect the humans. The interaction of humans with bats or their secretion is an occasional transitional

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to "MERS-CoV", and involved in transferring the virus to humans. The main cause of occurrence of "MERS-CoV" infections is exposure to animals, mainly the bats and "dromedary camels"[8-10]. In Middle-East and Africa about 90% of camels were sero-positive for "MERS-CoV"[11]. Although some other animals including goats, cows, sheep and poultry were involved in the transmission of infection[8,9]. MERS-CoV strains similar to human strains have been isolated from dromedaries camels in numerous countries "Saudi Arabia, Egypt, Oman and Qatar" [12,13]. "MERS-CoV" antibodies were found in many camels[14], then camels may serve as the intermediate host for "MERS-CoV" infections[12-15]. Humans are infected during their interactions with infected dromedary camels[16,17]. It is suspected that nasal mucous, sputum, saliva, milk or uncooked meat of infected camels are the main sources of transmission. However, the secondary infection can be through droplets or direct contact, and virus may spread through the air or fomites[18].

The early diagnosis of the disease remains a major challenge for the physicians, the epidemiology, pathogenesis and clinical characteristics play significant role to facilitate the physicians to diagnose and manage the disease. This study aimed to discuss the epidemiology, pathogenesis and clinical appearances of "MERS-CoV" infections providing current knowledge of the disease.

Materials and Methods

Materials

This observational study was conducted in the "Department of Physiology, College of Medicine, King Saud University", and "King Abdul Aziz City for Science and Technology, Riyadh, Saudi Arabia".

Methods

We searched literature from the English databases including "World Health Organization" "PubMed", "Medline" "Institute of Scientific Information (ISI) Web of knowledge", "EMBASE" and "Google Scholar". Two research investigators investigated, reviewed and recorded the literature using key terms "Middle East Respiratory Syndrome", "MERS", "MERS-CoV" in combination with terms "Epidemiology" "Transmission" "Pathogenesis" "Clinical Features" "Clinical Characteristics". The summaries of the research literature were reviewed to investigate the aptness for the documents. All articles with allied information were well thought out for inclusion without limitations on documents and language of the publications. We reviewed the research documents and "World Health Organization" website. 25 publications that harmonized our criteria were finally comprised and remaining papers were excluded. The suitability of the literature was considered by two investigators and differences were determined by another member.

Ethics Approval

For this study, literature based information was collected on "Middle East Respiratory Syndrome", "MERS-CoV" infection and its "Epidemiology" "Transmission" "Pathogenesis" "Clinical Characteristics" already published in databases, hence Ethical approval was not required.

Statistical Analysis

The data were computed into the computer; percentages were calculated and analyzed by using the Statistical Package for Social Sciences [SPSS for Windows, version 21.0, IBM, Armonk, NY, USA]. The level of significance was established at p-value less than 0.05.

Results

The global prevalence of "Middle East Respiratory Syndrome Coronavirus (MERS-CoV)" infections is 2206 people. These cases are reported from the different countries. From these laboratory confirmed cases, the maximum numbers of cases are reported from the Kingdom of Saudi Arabia 1831 (83%) compared to the cases reported from the other countries of the world (p-0.0001).

The age group with highest risk for acquiring as primary cases of infections is 50-59 years, and high risk for acquiring as secondary cases of infections is 30-39 years. The total number of associated mortality rate is 787 (35.67%) (Table I).

The clinical findings of "MERS-CoV" infection are different from person to person, ranging from no clinical symptoms (asymptomatic), or mild to severe respiratory illness symptoms. Most of MERS-CoV hospitalized patients had complain respiratory illness, gastrointestinal symptoms, central nervous system involvement and cardiovascular system allied symptoms. The major clinical characteristics of "Middle East Respiratory Syndrome Coronavirus (MERS-CoV)"

Table I. Facts and figures of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infections[3].

Total number of worldwide laboratory confirmed MERS-CoV cases	2206
Total number of associated mortality rate	787 (35.67%)
Total number of reported cases from Saudi Arabia	1831 (83%)
Total number of deaths reported from Saudi Arabia	713 (32.32%)
Age group with highest risk for acquiring as primary cases of infections	50-59 years
Age group with high risk for acquiring as secondary cases of infections	30-39 years
Primary cases age associate mortality	50-59 years
Secondary cases age associate mortality	70-79 years

Ref: WHO[3].

infection are fever, chills, generalized myalgia, drowsy, cough, dyspnea, shortness of breath abdominal pain, nausea, vomiting and diarrhea" (Table II).

Discussion

The global number of MERS-CoV infection cases which have been reported from June 2012 to April 2018 is 2206 people, with the maximum number of cases from Saudi Arabia 1831 (83%) with a fatality rate of 787 (35.67%) (Table I).

"MERS-CoV" is largely scattered in "Gulf Co-operation Council (GCC)" region "Saudi Arabia, United Arab Emirates, Qatar, Kuwait, Bahrain and Oman". These countries had dominant distributions of MERS-CoV infection, may be due to large number of "dromedary camels" in the Middle East region. The current literature suggests that during the breeding season of camels, the camel farmhouses become a main source of "MERS-CoV" infections. The viral incubation period is about 2 to 14 days. 93% cases of "MERS-CoV infection" were reported from Saudi Arabia. 52% cases from Riyadh, 20% Makkah, 11% Ash Sharqiyah, 4% Al-Madinah and 3% Najran. The remaining regions collectively contributed with 5% of the cases.[5] However, the other 5 GCC countries contributed 7% of the cases "United Arab Emirates" 5.0%, "Qatar" 1.0%, "Oman" 0.5%, "Kuwait" 0.2% and "Bahrain" 0.06%. The gender-based analysis demonstrated that 60% were male and 31% female[5].

Table II. Clinical characteristics of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection.

General clinical characteristics[8,9,19]
Fever
Chills or rigors
Generalized myalgia
Malaise
Drowsy
Confusion
Pulmonary clinical characteristics
Dyspnea
Cough
Shortness of breath
Pneumonia
Extra-pulmonary clinical characteristics
Abdominal pain
Nausea and vomiting
Diarrhea
Acute renal failure
Blood analysis[20]
Increase White Blood Cells count
Decrease lymphocytes count
Decrease platelets count
Decrease Red Blood Cells count

Among GCC countries, UAE has the second largest number of "MERS-CoV" infection cases, which occurred during March 2013 to June 2016. Similarly, 9 positive "MERS-CoV" cases were confirmed from the "Sultanate of Oman" who attended a camel race or exposure to dromedary camels in the UAE. Ministry of Health, Kuwait, also reported 4 cases of "MERS-CoV infections" form the capital, Kuwait city and one case from Manama, Bahrain[5].

The transmission of "MERS-CoV" infection from human to human has been found among the family members and health care workers in the "United Kingdom, Italy, France, Saudi Arabia, United Arab Emirates, Qatar, Jordan and Tunisia" [21-23]. These cluster of cases were reported among the same family members living in same home or working in the same institute[21]. The transmission of "MERS-CoV" in family members or hospital clusters occurs through direct contact or droplets. MERS-CoV cannot easily transmit from a person to another individual except if there is close contact while managing the infected patient in a hospital. In hospitals, the

chances of transmission from human-to-human are frequent with inadequate infection prevention control practices[24,25]. Infected patient's households and infirmaries with "MERS" patients are reflected as the dominant nuclei of "MERS-CoV outbreaks"[26-30].

Nassar et al[31] reported that the pattern of "MERS-CoV infection" has been observed to have seasonal variations. The highest global seasonal occurrence of "MERS-CoV infection" was found during the summer time in the month of June and low occurrence was seen in the months of October-January during the period 2012 to Dec 2017[31].

The clinical appearances of "MERS-CoV" infection characterize a wide-ranging spectrum fluctuating from asymptomatic presentation and mild to severe acute respiratory illness to death. A distinctive presentation of "MERS-CoV" features are fever of 38°C or more, fever with chills or rigors, generalized myalgia, malaise, drowsy, confused, dyspnea[8,9], cough, shortness of breath and radiological pulmonary presentation of pneumonia (Table II). The extra-pulmonary features include abdominal disorders, nausea, vomiting, diarrhea and acute renal failure[32]. The other clinical findings are pericardium inflammation, consumptive coagulopathy, increase in White Blood Cells, mainly neutrophils, and decrease lymphocytes, platelets and red blood cells[20].

The disease appears with severity in old age, debilitated immune systems, mainly in people with chronic diseases such as diabetes mellitus, pulmonary and renal diseases. "MERS-CoV" cases are identified mainly community and hospital-acquired, old age and in patients with multiple comorbidities including influenza, upper respiratory tract infections and pneumonia[3].

The "MERS-CoV" allied morbidity and mortality is a great alarming for health officials. The "MERS CoV" infection diagnosis is established on the clinical history, complete blood analysis and chest X-ray. The early blood analysis findings including "lymphopenia", "thrombocytopenia", "leukocytosis" and "neutrophilia" are allied to progressive infection. Moreover, reduced liver and renal functions, hypoalbuminemia and elevated inflammatory markers are also found in "MERS CoV" infection. The gold standards for the diagnosis are the detection of viral RNA on RT-PCR in specimens including sputum, endotracheal aspirate, broncho-alveolar lavage, nasal or nasopharyngeal swabs, urine and feces examinations[30]. Chest radiography is found to be useful in the diagnosis of "MERS-CoV" by demonstrating lung abnormalities and in the evaluation of the progress of disease and its response to treatment[31].

The treatment of "MERS-CoV" infection is mainly supportive, no specific remedy or vaccine is presently available. As preventive measures, it is essential to avoid the close contact to camels, goats, cows and sheeps and visiting the camel farms and animal sheds. Moreover, the intake of dairy products, drinking raw camel milk and eating uncooked meat should also be evaded. If infection plays a pivotal role in the process of pulmonary fibrosis, therapeutic strategies utilizing available antiviral or antibiotic drugs may be effective in modifying the course of this dreadful condition[33,34].

Conclusions

MERS-CoV infection is an emerging global health concern affecting 2206 people. The major clinical manifestations are fever, chills, cough, shortness of breath, generalized myalgia, malaise, drowsy, diarrhea, confusion, dyspnea and pneumonia. MERS-CoV infection may cause more severe disease amongst old people with chronic debilitating diseases such as diabetes mellitus, renal, lung disease, malignancy and immunocompromised patients. The health officials should establish awareness programs, implement effective preventive policies and better standards of health and hygiene, which are essential to minimize the global burden of the disease.

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Conflict of Interest

The Authors declare that they have no conflict of interests.

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