

소아에서 중동호흡기증후군의 역학적 특징 및 임상 양상

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Middle East Respiratory Syndrome Coronavirus Infection in Children

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Since 2012, outbreaks of the Middle East respiratory coronavirus (MERS-CoV) have been reported, including the Republic of Korea. To date, most of the people infected with the virus are adults. Herein we describe the clinical characteristics of cases of MERS-CoV infection among children. As of October 29, 2015, MERS-CoV has caused 34 pediatric infections, which accounts for 2.1% of all cases. The median age was 13 years (range 9 months to 17 years) and where gender has been reported (n=33), 57.6% cases were male. About half of the patients were asymptomatic and the majority of the symptomatic patients had respiratory symptoms. In general, the clinical outcome in children was favorable. Among the four patients who died of progressive pneumonia, three had documented comorbidities. MERS-CoV infection in children has a lower incidence and mortality compared to adults.

Key Words: Middle East respiratory syndrome coronavirus, MERS-CoV, Korea, Outbreak, Children

Introduction

After the identification of the Middle East respiratory syndrome coronavirus (MERS-CoV) in June 2012¹⁾, outbreaks have been reported worldwide. During September 2012 and October 29, 2015, the World Health Organization (WHO) has been notified of 1,611

laboratory-confirmed cases of infection, including at least 575 related deaths (case fatality ratio 35.7%)²⁾. Twenty-six countries have been affected and most of the cases were adults³⁾. Infections in adults show high morbidity and mortality. However, only a few cases of MERS-CoV in children have been reported in the literature^{4,5)}. Herein we describe the epidemiology and clinical characteristics of cases of MERS-CoV infection among children.

Epidemiology of MERS-CoV in children

Since the discovery of MERS-CoV, the cases with infection have been identified in twenty-six countries. Most of the cases have been reported in Saudi Arabia,

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United Arab Emirates, Jordan and Qatar. Outside the Middle East, the largest outbreak occurred in the Republic of Korea. Cases have also been reported from Oman, Egypt, France, Germany, Tunisia, Italy, Algeria, Iran, the Netherlands, Greece, Kuwait, Lebanon, Malaysia, Philippines, Yemen, Austria, Turkey, United Kingdom and the United States⁶⁾.

Up to October 29, 2015, there have been 34 reports of MERS-CoV infection in children under 18 years of age^{4,5,7)}. Cases of MERS-CoV infection in children have been reported mostly from Saudi Arabia by 28 cases. There were three cases in the United Arab Emirates, two cases in Jordan and one case in the Republic of Korea. These children all showed laboratory confirmation of MERS-CoV infection according to the interim case definition of the WHO.

The exact source and mode of transmission of MERS-CoV to humans is not known. There are reports suggesting that MERS-CoV originated in bats or camels, however this is still not fully revealed. However, human-to-human transmission has been confirmed in epidemiologic and molecular studies of cases associated with hospital and household outbreaks⁸⁾. Mode of transmission has been found mostly through large droplets and contact, however airborne or fomite transmission has also been reported as a possibility. Most cases in outbreak reports are associated with close contact and history of exposure to MERS-CoV infected patients. Healthcare exposure is the most important risk factor for transmission^{6,9)}. The R_0 for MERS-CoV is estimated to be less than 0.7, which means sustained transmission is unlikely unless the virus gains mutation¹⁰⁾. These characteristics of the transmission of the virus may be the reasons for the relatively scarce reports of MERS-CoV infection in children compared with the adult population.

Clinical features of MERS-CoV infection in children

The clinical manifestations of MERS-CoV infection range from asymptomatic infection to severe pneumonia

with acute respiratory distress syndrome, septic shock, and multiorgan failure resulting in substantial morbidity and mortality in adults. Subjects with a comorbid underlying disease have a higher mortality rate¹¹⁾. The incubation period ranges from 2-14 days⁹⁾. MERS-CoV infection has been reported in various age groups, ranging in a child as young as 9 months up to an elderly subject of 99 years of age^{2,5)}. However the majority are adults with a median age of 50 years. There is a male predominance in reports among adult cases^{11,13)}. Typical MERS begins with fever, chills, cough, shortness of breath, sore throat, myalgia and arthralgia. Gastrointestinal symptoms including diarrhea have also been reported. Severe illness can lead to respiratory failure that requires mechanical ventilation and other supportive care in an intensive care unit. Risk factors for development of severe disease include patients of older age, immunocompromised patients and those with chronic diseases such as cancer, cardiac disease, chronic lung disease and diabetes^{8,13-15)}.

For the 34 cases in children, the median age was 13 years (range 9 months to 17 years old). Among the 33 cases where the sex was reported, 19 were male (male: female ratio, 1.36). Documented exposure history was available for 26 children, all which had contact history within a hospital or household contact. Among the children with MERS-CoV infection, 50.0% were asymptomatic. Reports on the cases with symptoms are limited, however most cases were reported to have fever or respiratory symptoms. Patients with severe symptoms accounted for 20.6% of all confirmed cases. Among the 34 cases, 4 cases died with a mortality rate of 11.8%. Three of the children with mortality had a comorbid disease, such as cystic fibrosis, infantile nephrotic syndrome and brain tumor (craniopharyngioma). One case did not have document of comorbid disease.

Discussion

We thoroughly reviewed previously published literatures and data provided by the World Health Organization and the Ministry of Health Saudi Arabia^{2,4,5,8)}. As of

October 29, 2015, MERS-CoV has caused 34 pediatric infections, which accounts for 2.1% of all cases. The median age was 13 years (range 9 months to 17 years) and where gender has been reported (n=33), 57.6% cases were male. About half of the patients were asymptomatic and the majority of the symptomatic patients had respiratory symptoms. Most of the asymptomatic cases were accounted in contact investigation of confirmed cases. In general, the clinical outcome in children was favorable. Among the four patients who died of progressive pneumonia, three had documented comorbidities: cystic fibrosis, infantile nephrotic syndrome and craniopharyngioma. MERS-CoV infection in children has a lower incidence and mortality compared to adults. Little is known about the reason for this. However, we should keep in mind, even in children, subjects with an underlying disease can have a more severe disease.

Infected children without comorbidities present mild manifestations and have good clinical outcome.

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요약

중동호흡기증후군 코로나바이러스(Middle East respiratory coronavirus, MERS-CoV)로 인한 질환은 2012년부터 보고되었다. 현재까지 대부분의 질환은 성인에서 발생하였으며 소아에 대한 보고는 매우 부족한 실정이다. 그리하여 본 연구에서는 소아에서 MERS-CoV 감염증의 역학적 특성과 임상 양상을 분석하였다. 전세계적으로 MERS-CoV에 감염된 소아는 34명이었으며(2015년 10월 29일 기준), 이는 전체 환자의 2.1%를 차지하였다. 소아 환자들의 중앙 연령은 13세(범위, 9개월부터 17세까지)이었으며, 성별이 보고된 자료(n=33) 중 57.6%가 남자였다. 전체 환자 중에서 약 반은 무증상 감염이었으며, 대부분의 증상이 있는 환자는 호흡기 증상을 동반하였다. MERS-CoV에 감염된 환자들의 예후는 대부분 양호하였으나, 사망한 환자는 4명이었으며 이 중 3명은 기저 질환이 있었다. 전세계적으로 소아에서 발생한 MERS-CoV 감염에 대한 보고 자료를 분석한 결과 MERS-CoV 감염은 소아에서 발생이 낮고 성인에 비해 예후가 좋은 것으로 나타났다.