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Middle East Respiratory Syndrome Coronavirus Infection During Pregnancy: A Report of 5 Cases From Saudi Arabia

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Abstract

Little is known about the effects of Middle East respiratory syndrome coronavirus (MERS-CoV) during pregnancy. In Saudi Arabia, 5 cases of MERS-CoV infection among pregnant women were reviewed, and all cases resulted in adverse outcomes. MERS-CoV infection during pregnancy may be associated with maternal and perinatal disease and death.

Keywords

Middle East Respiratory Syndrome coronavirus; pregnancy; perinatal mortality; infectious disease transmission; Saudi Arabia

Middle East respiratory syndrome coronavirus (MERS-CoV) is known to cause severe respiratory illness and large nosocomial outbreaks in humans with death recorded in 35%–40% of reported cases [1]. Approximately 80% of confirmed cases worldwide have been reported from Saudi Arabia [1–3].

Case reports documenting outcomes among pregnant women infected with MERS-CoV have been previously published, including reports of a stillbirth in Jordan [4], a maternal death in the United Arab Emirates [5], and severe maternal disease with survival of mother and infant reported from Saudi Arabia [6]. To further understand the impact of MERS-CoV infection during pregnancy, we describe 5 additional cases from Saudi Arabia.

METHODS

In Saudi Arabia, reporting is required for all patients with clinical or radiologic evidence of respiratory infections and a positive real-time reverse-transcription polymerase chain

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Notes

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reaction test result for MERS-CoV [7]. All positive cases so identified at facilities outside the Saudi Arabia Ministry of Health (MoH) require confirmation at MoH laboratories. To identify patients for inclusion in this study, we reviewed available line lists of laboratory-confirmed MERS-CoV cases reported by the MoH to the World Health Organization (WHO) from November 2012 to February 2016. Records meeting these criteria were reviewed, and information was collected regarding patient demographics, medical history, prenatal course, maternal and newborn hospital course, and outcome. When necessary, we attempted to contact patients or proxies by telephone to supply missing information, such as infant outcomes. This investigation was part of an emergency public health response and was determined to be nonresearch by the MoH and the US Centers for Disease Control and Prevention and therefore not subject to institutional review board review.

RESULTS

From November 2012 to February 2016, a total of 1308 laboratory-confirmed MERS-CoV cases were reported by Saudi Arabia to WHO, including 449 with patients listed as female. Age information was available for 400 of the 449 female patients; 179 were of reproductive age (15–45 years), and death was documented in 16 (8.9%) of the 179.

Among 1308 reported cases of MERS-CoV, 5 were documented by the MoH to have occurred in pregnant women (Table 1). Three cases were from the city of Riyadh, and the other 2 were from the cities of Makkah and Unayzah (Qasim Region). The patient's ages ranged from 27 to 34 years, all pregnancies were in the second or third trimester, and 2 patients were healthcare workers. Two of the 5 patients (40%) died during their illnesses. Among the 5 pregnancies, 2 (40%) resulted in perinatal death: 1 pregnancy resulted in intrauterine fetal demise, and 1 infant died 4 hours after emergency cesarean delivery.

Patient 1 was a 34-year-old woman (gravida 7, para 6) at 34 weeks gestation and with no history of underlying medical conditions. She reported the initial onset of shortness of breath 2–3 days before presentation to a maternity hospital on 7 May 2014. On admission she was noted to have elevated blood pressure and 3+ proteinuria consistent with preeclampsia, and pneumonia was diagnosed by means of chest radiography. Fetal heart tones were absent, and intrauterine fetal demise was suspected. A stillborn infant was delivered the same day. A nasopharyngeal specimen collected on admission tested positive for MERS-CoV by polymerase chain reaction. Although the patient was admitted to intensive care unit (ICU), she did not require ventilator support and was discharged to home on 20 May 2014. No likely exposure to MERS-CoV was identified.

Patient 2 was a 32-year-old woman (gravida 2, para 1) at 38 weeks gestation and with no history of underlying medical conditions. She reported the onset of respiratory symptoms on 3 September 2014 and presented to the hospital on 9 September with fever, cough, and shortness of breath. Her symptoms worsened after admission, and her chest radiograph showed bilateral infiltrates. She delivered a healthy neonate vaginally on 10 September, with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. The patient's condition deteriorated after delivery, prompting ICU admission the same day, with worsening pneumonia, acute renal failure, and acute respiratory distress syndrome (ARDS) requiring intubation and

mechanical ventilation; a nasopharyngeal specimen tested positive for MERS-CoV. She died of multiple organ failure on 29 September 2014. No likely exposure to MERS-CoV could be identified.

Patient 3 was a 31-year-old woman (gravida 1, para 0) at 24 weeks gestation, with a history of asthma, pulmonary fibrosis, and recurrent spontaneous pneumothoraces. A healthcare worker, she was identified as an occupational contact of a patient with known MERS-CoV and reported the onset of fever on 18 October 2014. She presented to the hospital on 23 October with cough and myalgia, and chest radiography at admission showed a right lower lobe opacity. A nasopharyngeal specimen collected on 29 October tested positive for MERS-CoV. Her respiratory status deteriorated during hospitalization, and she was admitted to the ICU on 28 October for ARDS requiring intubation and mechanical ventilation. On 31 October, the patient delivered a 240-gram infant by cesarean delivery. The infant died 4 hours after birth and was not tested for MERS-CoV. The patient died on 24 November 2014 of severe refractory hypoxia and cardiac arrest.

Patient 4 was a 27-year-old woman (gravida 1, para 0) at 22 weeks gestation with no underlying conditions noted at admission. She reported symptom onset, including fever, shortness of breath, and cough, on 1 February 2015 and presented to the hospital on 7 February with worsening symptoms. She was noted to have bronchopneumonia with a left lobar infiltrate. Her respiratory status deteriorated, prompting admission to the ICU on 8 February; testing of a respiratory specimen collected that day confirmed MERS-CoV. She did not require intubation or mechanical ventilation and did not deliver during this hospitalization. She recovered, was discharged on 22 February 2015, and subsequently gave birth to a healthy infant at term. No likely exposure to MERS-CoV was identified.

Patient 5 was a 30-year-old woman (gravida 1, para 0) at 23 weeks gestation and with no underlying conditions; she was working as a healthcare professional at a hospital during a large MERS-CoV outbreak. She reported the onset of cough, fever, chills, and chest pain on 24 July 2015 and presented to the hospital on 28 July with worsening respiratory symptoms. Testing of a respiratory specimen collected on the day of admission confirmed MERS-CoV. Pneumonia was diagnosed, and the patient’s condition deteriorated during hospitalization; ARDS developed, requiring ICU admission from 1 August to 28 August, with intubation and mechanical ventilation. The patient did not deliver during this hospitalization. She recovered, was discharged on 6 September 2015, and subsequently delivered a healthy infant at term.

DISCUSSION

We identified 5 pregnant MERS-CoV patients reported to WHO from Saudi Arabia between November 2012 and February 2016. All 5 pregnant MERS patients required ICU care. The birth outcomes were also notable: 1 infant was stillborn at 34 weeks, and 1 was surgically delivered at 24 weeks and died after 4 hours of life.

Our findings of severe disease and death are similar to previous reports of pregnant women with MERS-CoV [4–6]. Other respiratory pathogens, including severe acute respiratory

syndrome coronavirus [8] and influenza [9], have also been associated with severe maternal and perinatal outcomes. Physiologic changes occur during pregnancy to reduce inflammatory immune responses that otherwise might lead to fetal rejection [10]. Disease pathogenesis is also affected, secondary to the reduced activity of natural killer cells, inflammatory macrophages, and helper T cells [10]. In addition, mechanical and biochemical factors affect gas exchange and pulmonary function during pregnancy; functional residual capacity and residual volume are both decreased in pregnancy [11].

Understanding the association of pregnancy with adverse maternal and perinatal outcomes among MERS-CoV infected patients should be accompanied by efforts to prevent high-risk exposures. Since 2013, the Saudi Arabia MoH has requested that pregnant women postpone travel to Saudi Arabia for Hajj and Umrah [12]. Additional measures to decrease risk of exposure may be warranted for pregnant women in areas where MERS-CoV has been reported, such as avoiding camel contact, minimizing contact with sick persons, particularly in hospitals, and avoiding occupational healthcare exposures where feasible.

Our investigation has limitations. We retrospectively evaluated data collected as part of the public health response to MERS-CoV in Saudi Arabia. Since the identification of MERS-CoV in 2012, case definitions, testing practices, and testing locations have changed as the response evolved, and practices might not have been uniformly conducted or exhaustively reported to MoH, potentially limiting the scope of our investigation. Although we systematically assessed records of all confirmed cases during the study period to identify women reportedly pregnant, pregnancy testing was not routinely offered to women of reproductive age with MERS, leaving the possibility of missed cases. Moreover, we were not able to evaluate the MERS-CoV infection status of infants born to these mothers.

Although the overall impact of MERS-CoV on maternal and birth outcomes requires further evaluation, we conclude that MERS-CoV may pose serious health risks to both mothers and infants during pregnancy. Additional data are needed to further define this apparent association. Pregnancy testing for women of reproductive age infected with MERS-CoV should be considered to inform clinical management and contribute to a better understanding of epidemiologic risk. Efforts to limit exposure of pregnant women to MERS-CoV should be strengthened, and extended where possible.

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Table 1

Patient Characteristics and Pregnancy and Birth Outcomes in Confirmed Cases of Middle East Respiratory Syndrome Coronavirus in Saudi Arabia

Patient Characteristics and Outcomes	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Patient age, y	34	32	31	27	30
Gravida (G), para (P)	G7, P6	G2, P1	G1, P0	G1, P0	G1, P0
Gestational age at illness onset, wk	34	38	24	22	23
ICU admission	Yes	Yes	Yes	Yes	Yes
Maternal comorbid conditions	Preeclampsia	None	Asthma, pulmonary fibrosis, recurrent spontaneous pneumothoraces	None	None
Maternal outcome	Survived	Died	Died	Survived	Survived
Fetal outcome	Died	Survived	Died	Survived	Survived
Delivery details	Intrauterine fetal demise at 34 wk gestation	Vaginal delivery at 38 wk gestation	Surgical delivery at 24 wk gestation	Delivery at term	Delivery at term

Abbreviation: ICU, intensive care unit.