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Coronaviruses in pregnant women in Saudi Arabia: A systematic comparative review of MERS–CoV and SARS–CoV–2

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Objective: To compare the effects of coronaviruses, such as Middle East respiratory syndrome coronavirus (MERS-CoV) or coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), on pregnant women in Saudi Arabia, and to understand the disease dynamics of these coronaviruses so as to know how to provide care and management of infected pregnant women and infants.

Methods: We conducted a systematic review of all published papers on MERS-CoV and SARS-CoV-2 infections in pregnant women in Saudi Arabia to identify knowledge gaps. Inclusion and exclusion criteria were based on the PRISMA system. The search included all papers which were published between September 1, 2012 and November 29, 2020 on pregnant women with MERS-CoV and/or COVID-19 in Saudi Arabia. Of 26 papers screened, five were included in the analysis.

Results: A total of 11 pregnant women with MERS-CoV and four with COVID-19 were reported in Saudi Arabia in the medical literature during the review period. The mean ages of the women were 33 and 31 years old for MERS-CoV and COVID-19, respectively. Maternal and fetal mortality in cases of MERS-CoV were 35% and 30%, respectively, while no maternal or fetal mortalities were reported in COVID-19 cases.

Conclusions: Very limited data has emerged from Saudi Arabia on pregnant women MERS-CoV and COVID-19. With such high mortality observed with MERS-CoV compared to COVID-19, there is a need for greater reporting of cases to truly grasp the extent of these infections in pregnant women in a country where both coronaviruses are circulating.

KEYWORDS: MERS-CoV; SARS-CoV-2; COVID-19; Pregnant women

1. Introduction

On December 31, 2019, a cluster of pneumonia cases were

reported in relation to a new coronavirus named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19)[1–3]. The World Health Organization (WHO) declared a pandemic on March 11, 2020[4].

As of November 29, 2020, COVID-19 had been reported globally in 191 countries, with 62 311 483 laboratory-confirmed cases causing 1 453 467 deaths[5]. Efforts to eliminate SARS-CoV-2 are unlikely to succeed in the long term, as they are constantly challenged by the births of new susceptible hosts and by the waning of immunity in previously infected individuals. The durability of immunity to SARS-CoV-2 is not yet fully established[6], but new births will promote virus survival. Thus, like other infectious pathogens, SARS-CoV-2 is likely to circulate in humans for many years to come[7].

The Kingdom of Saudi Arabia (KSA) is one of the top 30 countries in terms of total reported COVID-19 cases, with 356 911 laboratory-confirmed cases and 5 870 deaths[5] as of November 29, 2020. It is also the only country in the world in which a second coronavirus[8], Middle East respiratory syndrome coronavirus (MERS-CoV), has continued to cause seasonal epidemics since it was first discovered in 2012[9]. As of June 1, 2020, a total of 2 167 laboratory-confirmed cases of MERS-CoV had been reported in KSA with 842 deaths[10,11].

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Pregnant women are more prone to such infections and thus are at increased risk of maternal and fetal complications[12]. Moreover, during epidemics and pandemics, medical resources may be shifted away from reproductive health to more urgent medical needs. This can create obstacles for pregnant women to access health care, which, in turn, can lead to obstetrical complications, including stillbirths, preterm deliveries, maternal mortality, and fetal respiratory complications. To identify how these challenges might be addressed, we reviewed all published studies on pregnant women infected with these virus in KSA.

2. Materials and methods

2.1. Study design

A review was conducted for all literatures on pregnant women with MERS-CoV and/or SARS-CoV-2 infections in Saudi Arabia published between September 1, 2012 and November 29, 2020.

2.2. Search strategies

The search strategy was based on the following key terms: “pregnant women” AND “MERS CoV” or “Middle East respiratory syndrome coronavirus” or “coronavirus disease 2019” or “COVID-19” or “SARS-CoV-2” or “severe adult respiratory syndrome coronavirus-2” AND “Saudi Arabia” or “ Kingdom of Saudi Arabia.” All search terms were in the English language. The search was conducted on the Science Direct, PubMed, Web of Science, and Google Scholar databases. The search was completed independently by each of the authors, and a total of 26 articles were found.

2.3. Eligibility criteria

Articles on pregnant women with MERS-CoV or COVID-19 infections published between September 1, 2012 and November 29, 2020 were included. Studies of the disease dynamics of pregnant women without MERS-CoV or SARS-CoV-2 infection were excluded. Articles written in languages other than English were also excluded. We first examined titles and abstracts. Articles for which abstracts were not available were not included. We screened the articles by checking the abstracts and removed any duplicate articles. After screening, 13 papers were excluded for the following reasons: no abstract available ($n=2$), articles on disease dynamic without MERS or COVID ($n=10$), and non english language ($n=1$). Seven articles remained. We performed a full-text analysis of these remaining articles and removed two that did not meet the inclusion criteria. Lastly, 5 papers were included in analysis.

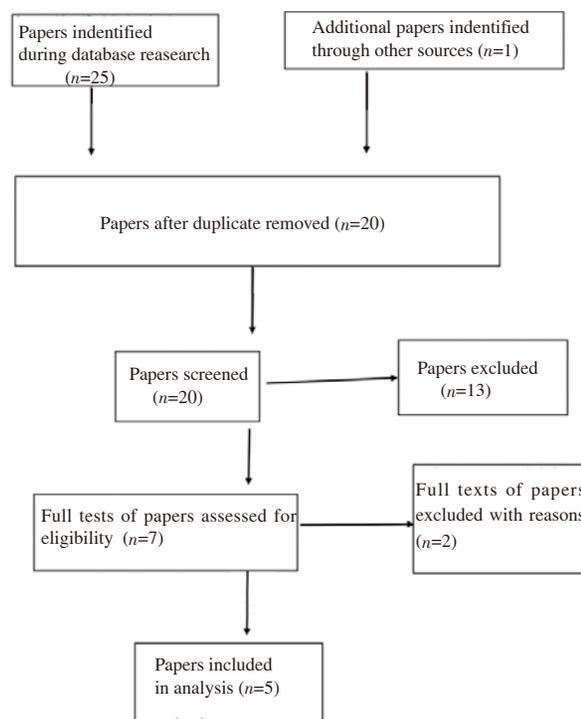


Figure 1. Flowchart of the process of identifying papers for review.

The inclusion and exclusion processes were summarized using a PRISMA flowchart (Figure 1). We collected data on pregnant women with SARS-CoV-2, vertical transmission, MERS-CoV, or COVID-19 and on the impact of these infections on newborns.

2.4. Assessment of study quality

The quality of the selected papers was evaluated by the authors. Due to the low number of studies, a meta-analysis was not performed.

3. Results

Eleven cases of MERS-CoV in pregnant women in KSA were reported in the literature. The mean age of the pregnant women was 33 years, and the mean gestational age was 28 weeks. Seven of these pregnant women (64%) were admitted to an intensive care unit (ICU), and 40% required a cesarean section. The rate of maternal fatality directly attributed to MERS-COV was 35%[13], and all deaths occurred within 2-3 weeks post-delivery. The overall fetal death rate was 30%[14]. There was one intrauterine death, one still birth, and one preterm delivery at 25 weeks with a 4-hour post-birth neonatal death. No vertical transmission was confirmed in any case[13,15–17].

Only four pregnant women with COVID-19 in KSA were reported in the literature, three of whom were asymptomatic and were

Table 1. Summary of reported studies of pregnant women with either MERS-CoV or COVID-19 in Saudi Arabia, including outcomes.

Study author	Study type	MERS-CoV / COVID-19	Number of pregnant women	Age of women (year)	Gestational age (week)	Gravidity, Parity	Comorbidities	Delivery type	Maternal outcome	Fetal outcome
Alfaraj <i>et al</i> [14]	Case series	MERS-CoV	2	29	6	G2, P1	None	Vaginal delivery at term	Survived	Healthy
				39	24	G6, P5	End stage renal disease	NR	Survived	NR
Alserehi <i>et al</i> [17]	Case report	MERS-CoV	1	33	31	G1, P0	Hypothyroidism	Cesarian section	Survived	Survived
Assiri <i>et al</i> [18]	Case series	MERS-CoV	5	34	34	G7, P6	Preeclampsia	NR	Survived	IUFD
				32	38	G2, P1	None	Vaginal delivery	Died	Survived
				31	24	G1, P0	Asthma	Cesarian section	Died	Died
				27	22	G1, P0	None	Vaginal delivery	Survived	Survived
				30	23	G1, P0	None	Vaginal delivery	Survived	Survived
Schwartz <i>et al</i> [19]	Review	MERS-CoV	3	27-34 (range)	NR	NR	NR	NR	2 died 1 survived	2 died 1 survived
Barry <i>et al</i> [20]	Case series	COVID-19	4	NR	NR	NR	NR	Two vaginal delivery, two cesarian section	All survived	All survived

MERS-CoV: Middle East respiratory syndrome coronavirus; COVID-19: coronavirus disease 2019; IUFD: Intrauterine fetal demise; G: gravidity; P: parity; NR: not reported.

detected by routine testing as part of routine obstetric care. Two women delivered vaginally, and the other two underwent cesarean sections. All the women survived, and all four babies were healthy and tested negative for COVID-19[18] (Table 1).

4. Discussion

A wide spectrum of symptomatic cases of pregnant women infected with MERS-CoV has been reported, while no asymptomatic cases have been identified[19]. Regarding transmission and preventive measures, it is important that pregnant women have knowledge of the preventive measures recommended by the WHO to prevent infection of both themselves and their infants. These measures include frequent hand washing; maintaining at least 1 m distance from others; avoiding touching one's eyes, nose, and mouth with one's hands; covering one's mouth and nose when coughing or sneezing; wearing a face mask in public; and staying at home[20]. In a cross-sectional survey of 284 pregnant women, 61% had adequate knowledge of measures to prevent the spread of COVID-19, but only 30% practiced these measures[21]. No studies on pregnant women's knowledge of how to prevent MERS-CoV infection were identified. Thus far, no evidence of vertical transmission of SARS-CoV-2 has been observed in pregnant women[22]. Preterm deliveries have occurred among women infected with COVID-19 during the pandemic, but it is unclear whether they were due to COVID-19

infection itself or other complications. Cases of preterm labor have been reported to have increased during the pandemic, but this finding is not directly attributed to COVID-19[23]. No preterm labor has been reported in KSA yet. The potential risk of vertical transmission has been considered in several studies[22,24,25]. A study by Chen *et al*[26] on vertical transmission of COVID-19 infection from pregnant women to neonates indicated that pregnant women with COVID-19 did not show any different symptoms or worse disease compared to non-pregnant women with COVID-19 infection. No vertical transmission has been reported in KSA. Most studies included in a narrative review of the emerging literature on the challenges faced by pregnant women during the pandemic found no vertical transmission. However, the authors of the review suggested that special care be taken in treating pregnant women with COVID-19[27]. In their systematic review of all available studies of pregnant women with MERS-CoV, including women in KSA, Diriba *et al*[28] reported no vertical transmission. Regarding the overall clinical effects of MERS-CoV and SARS-CoV-2, a systematic review of all infected pregnant women with MERS-CoV[28] reported a 33% prevalence of preterm birth at <34 weeks of gestation, while 80% of pregnant women studied gave birth at >37 weeks gestation. Preeclampsia was reported in 6% of pregnant women infected with MERS-CoV. The rate of pregnant women with MERS-CoV admitted to ICU was 33%, while the maternal death rate from the disease was reported to be as high as 40%, which is similar to that reported in the general population[29]. The prevalence of pregnant women with MERS-CoV

who gave birth by cesarean section was 66.7%, while only 17% underwent normal delivery. Perinatal death was reported in 33.3% of newborns.

In a systematic review of all infected pregnant women with SARS-CoV-2[28], the prevalence of preterm birth at 34 to 37 weeks of gestation was 14%, while 46% of pregnant women gave birth at >37 weeks of gestation. Preeclampsia was reported in 5% of cases. Premature rupture of membranes was reported in 9% of the women studied, and the rate of fetal growth restriction was 1%. Miscarriage was reported in 2.4% of cases. Of all infected pregnant women, 28.5% were admitted to the ICU, while the rate of maternal death was 1.5%. The prevalence of cesarean section was 57%. Fetal distress was reported in 25% of cases. The rate of neonatal asphyxia was 1.6%, and the rate of perinatal death was 2.9%. Regarding recommendations for obstetrical care issued by Saudi Medical Societies early in the COVID-19 pandemic, the Saudi Anesthesia Society published several recommendations on obstetrical considerations to be addressed[30]. These included surge planning through the formation of an institutional multidisciplinary obstetric COVID-19 committee to set out clinical pathways and procedures; collaboration between hospitals that offer obstetric care to form a network for channeling scheduled cesarean deliveries to centers not in a moderate-to-crisis level surge; advice to health care workers who are pregnant beyond 28 weeks of gestation to avoid contact with suspected or confirmed COVID-19 patients and to take nonclinical assignments if necessary; early recruitment of volunteers to address possible manpower shortages; modifications to increase isolation capacity and provide high-efficiency particulate air filters to prevent airborne infection in areas such as isolation rooms; stringent visitation policies; preadmission screening for elective admissions; and contact tracing of exposed personnel. The Saudi Society of Maternal-Fetal Medicine published guidance on pregnancy and COVID-19, which included pregnancy management, medication concerns, labor considerations, and postpartum and neonatal care[31]. Neither society has published any similar recommendations for MERS-CoV.

The positive effects of adhering to these COVID-19 recommendations have not yet been published and should be assessed in further studies.

5. Conclusion

Published data on pregnant women in KSA infected with MERS-CoV and SARS-CoV-2 coronaviruses is limited, despite the fact that they are at increased risk of adverse obstetrical outcomes. Maternal and neonatal morbidity and mortality is much higher for MERS-CoV than for SARS-CoV-2. However, data on more cases is needed to truly grasp the extent of these infections in pregnant women. Additionally, gaps in obstetrics and neonatal care for those infected with these coronaviruses must be identified and further by the relevant societies.

Conflict of interest statement

The authors declare that there is no conflict of interest.

Authors' contributions

Mazin Barry and Magdoleen A. Barry contributed to the conceptualization, methodology, manuscript writing and editing equally.

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