EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 6
226-231
Year: 2020

COVID-19 POTENTIAL MATERNAL AND INFANT OUTCOMES: LESSON FROM THREE EPIDEMICS

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Article Received on 09/04/2020 **Article Revised on 29/04/2020** **Article Accepted on 20/05/2020**

ABSTRACT
In early December 2019 a cluster of cases with pneumonia of unknown etiology was identified in Wuhan. Further investigation revealed a newly identified coronavirus, initially termed 2019-nCoV responsible for causing this infection. The infection moved rapidly through China, and spread to more than 200 countries world-wide. It is certain that 2019-nCoV will infect women who are pregnant. With physiological adaptive changes during pregnancy, pregnant women could be more susceptible to COVID-19 infection than the general population. Unfortunately, there is limited literature with coronavirus infections during pregnancy. In order to assess the potential affect of new coronavirus on maternal, fetal and neonatal morbidity and other poor obstetrical outcomes, this article reviews the published data addressing the epidemiological and clinical effects of SARS, MERS, and covid-19 infections on pregnant women and their infants.

KEYWORDS: Coronavirus, Middle East respiratory syndrome, severe acute respiratory syndrome, SARS-CoV, MERS-CoV, SARS-CoV-2, COVID-19, pregnancy, maternal mortality, maternal death, pregnancy complications, maternal morbidity, pneumonia, epidemic, China.

INTRODUCTION
Coronaviruses are spherical, enveloped positive-strand RNA viruses. They are known to have a wide range of host, including birds, farm animals, pets, camels, and bats, in which they are primarily responsible for causing respiratory and gastrointestinal diseases.[1,2]

Table 1: Over view of coronavirus.

Family	Coronaviridae
Sub-family	Orthocoronaviridae
Genera	Four: Alpha, Beta, Delta, Gamma
Species	Seven : HCoV-229E, HCoV-NL63 (Alpha genus) HCoV-OC43, HCoV-HKU1, MERS-CoV, SARS-CoV, COVID-19 (Beta genus)

In humans, they are responsible for causing very mild illnesses including the common colds. However, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV)—are known to be causing severe lower respiratory tract infections and responsible for epidemics in 2003 and 2012 respectively.

In late December 2019, an outbreak of pneumonia in Wuhan, China was seen which was characterized by fever, dry cough, fatigue and occasional gastrointestinal symptoms.[3] On January 30, 2020, the International Health Regulations Emergency Committee of the World Health Organization (WHO) declared the outbreak as a "Public Health Emergency of International Concern" (PHEIC). On 11 February 2020, WHO announced a name for the new corona virus disease: COVID-19. Till now it affects more than 200 countries worldwide.

It is certain that 2019-nCoV will infect women who are pregnant. With immune-compromised status and physiological adaptive changes during pregnancy, pregnant women could be more susceptible to COVID-19 infection than the general population. In order to address the potential obstetrical outcomes of infection to both mother and infant, the present communication describes the current state of knowledge regarding the effects of other coronavirus infections in pregnancy.

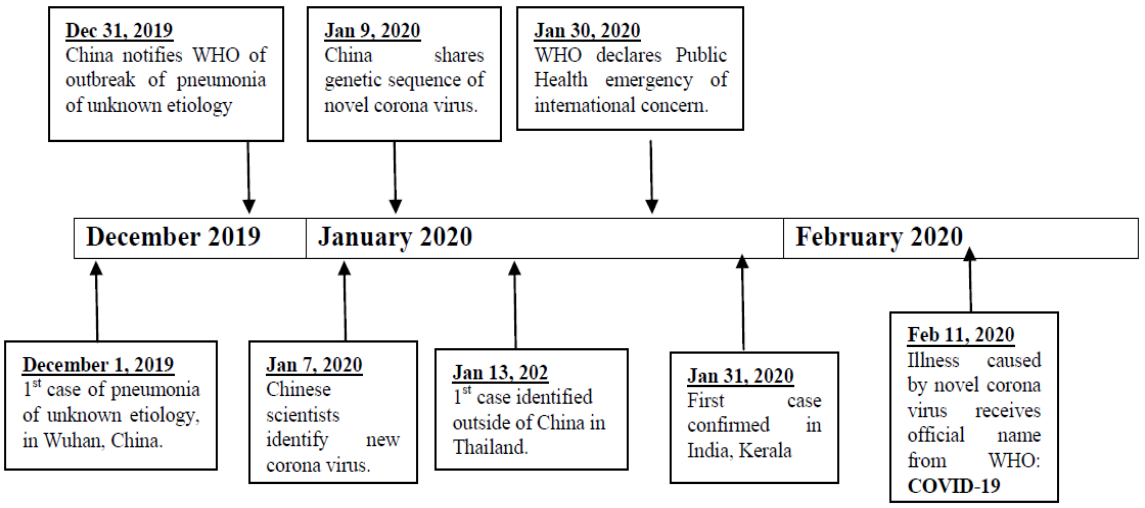


Figure 1: Series of event related to covid-19 outbreak.

Table 2: Characteristics of SARS, MERS, COVID-19.

Characteristics	SARS	MERS	COVID-19
First patients reported	Guangdong, China, November 2002	Zarga, Jordan, April 2012, and Jeddah, Saudi Arabia, June 2012	Wuhan, China, December 2019
Virus	SARS-CoV	MERS-CoV	SARS-CoV-2
Type of coronavirus	Betacoronavirus	Betacoronavirus	Betacoronavirus
Animal hosts	Bats (natural reservoir), masked palm civet and raccoon dogs may be intermediate hosts	Bats (natural reservoir), dromedary camel (intermediate host)	Bats, animals sold at the seafood market in Wuhan might represent an intermediate host[35]

SARS and its effects on pregnant women

A case series in Hong kong was done on 12 pregnant women with SARS during 2003 SARS outbreak. 7 women in 1st trimester and 5 in 24 weeks reported with SARS infection. Three deaths occurred among the 12 patients, with a case fatality rate of 25%. Four women had spontaneous miscarriage that presented during the 1st trimester. Major medical complications due to SARS during pregnancy included adult respiratory distress syndrome, disseminated intravascular coagulopathy (DIC), renal failure, secondary bacterial pneumonia, and sepsis. 4 pregnant females delivered preterm at 26,28 and 32 weeks of gestation. These babies had appropriate birth-weights. Two of the preterm born at 26 and 28 weeks gestation had respiratory distress syndrome and with one later developing broncho-pulmonary dysplasia. Gastrointestinal complications including jejunal perforation and necrotizing enterocolitis with ileal perforation was present in preterm born at 26 and 28 weeks' gestation. Whether these complications were related to SARS or its treatment or were secondary to preterm delivery was unknown. Two mothers recovered without delivery, had intrauterine growth restriction. No clinical, radiologic, or laboratory evidence for transmission from mother to fetus was observed.[4]

A case-control study was done at the Princess Margaret Hospital in Hong Kong to determine the effects of SARS on pregnancy. 10 pregnant and 40 non-pregnant women with SARS were enrolled under this case-control study. Three deaths of pregnant women with SARS were reported from whereas no deaths were occurred in the non-pregnant group. Renal failure (P = 0.006) and disseminated intravascular coagulopathy (P = 0.006) were major complication developed more frequently among pregnant SARS patients then the non-pregnant SARS group. Admission to the intensive care unit (ICU) among pregnant women was 60% (6 women) and 4out of them required endotracheal intubation. The ICU admission rate among the non-pregnant group was only 17.5% compared with a 12.5% intubation rate.[5]

Zhang et al. described SARS-CoV infections in 5 primagravidas from Guangzhou, China during SARS epidemic. Two of the mothers were in the 2nd trimester, and 3 in their 3rd trimester. All 5 pregnant women were admitted with fever and abnormal chest radiographs. Four pregnant women had cough, chills or rigor and latter developed hypoalbuminemia. Other manifestation was elevated liver enzyme (Alanine Aminotransferase levels), decreased lymphocytes and platelets count. One pregnant woman's health deteriorates and latter admitted to the intensive care unit, but all recovered and there were no maternal deaths. All the infants born were healthy with no clinical evaluation none evidence of SARS.[6]

A 38-year-old woman with 7 week gestation from USA, had travel history to Hong Kong during the SARS epidemic. Following her return , her husband was found to be positive for SARS, and after that she developed fever, myalgia, chills, headache, coryza, and a productive cough with shortness of breath and wheezing. She was confirmed with SARS infection. Following her hospitalization, her serum samples was taken on 28 and 64 days post-onset of illness and found to be positive for antibodies to SARS-CoV. A cesarean section was performed at 36 weeks gestation due to preterm rupture of membranes and fetal distress. Newborn was healthy baby boy. At the time of delivery, the mother's serum samples were positive for antibodies to SARS-CoV, but samples taken of umbilical cord blood and placenta were negative. Breast milk sampled 12 and 30 days after delivery were also negative for SARS-CoV antibodies.[7]

Yudin et al reported a 33-year-old pregnant woman at 31 weeks gestation was admitted to the hospital with a fever, dry cough, and abnormal chest radiograph. She contacted SARS from her infected family member. She was positive for coronavirus (SARS-CoV). She had a normal labor and delivery and her newborn girl had no evidence of infection.[8]

Fortunately, there were no cases of vertical transmission identified among pregnant women infected with SARS-CoV during the 2002–2003 Asian epidemics.

MERS and pregnancy

A 33-year-old nurse in her 3rd trimester became infected with MERS. During hospital admission, she was present with respiratory failure and put on mechanical ventilation. Dexamethasone as prophylaxis for the fetus was also administered to her. A preterm delivery following an emergency cesarean section at 32 weeks gestation was done. The preterm baby was healthy and latter discharged along with his mother.[9]

A pregnant female with 5 month gestational age present with a complaint of fever, fatigue, headache, cough, vaginal bleeding and abdominal pain. She was confirmed to have antibody to MERS-CoV. She had a history of unprotected contact with family members who later tested positive for the virus. On the 7th day of symptoms, she had a fetal death. This was the first documented occurrence of stillbirth during maternal infection with MERS-CoV.[10]

In 2015 in South Korea a 39-year-old patient was exposed to infection during her t 3rd. She was present with abrupt vaginal bleeding and ruptures of membranes. The patient recovered fully and delivered a healthy infant at 37 weeks and 5 days gestation. Subsequent testing of the infant's blood for IgG, IgM, or IgA antibodies to MERS-CoV was found to be negative.[11]

Current Literature of COVID-19 Infection of pregnant women and neonate outcomes

A retrospective study, on 7 pregnant women with COVID-19 admitted to Tongji Hospital from January 1 to February 8, 2020 in Wuhan, China was done. The mean age of the patients was 32 years (range 29–34 years) and the mean gestational age was 39 weeks plus 1 day (range 37 weeks to 41 weeks plus 2 days). Pregnant women were present with fever, cough, shortness of breath and diarrhoea. All the patients had caesarean section. The outcomes of the pregnant women and neonates were good. Three neonates were tested for SARS-CoV-2. Nucleic acid test for the throat swab of one neonate was positive at 36 h after birth; whereas other two were negative. The neonate had no fever and cough, with mild shortness of breath symptoms. Chest x-ray revealed mild pulmonary infection.[12]

A study on 10 neonates born to 9 mothers with confirmed 2019-nCoV infection in China was done. Four mothers develop fever and cough before birth, two on the day of birth and three after birth. 4 neonates were full term whereas 6 were born preterm. Six neonates had shortness of breath, two were present with fever, two newborns had thrombocytopenia accompanied by abnormal liver function, and one had pneumothorax. Four newborns showed gastrointestinal symptoms such as feeding intolerance, bloating, refusing milk, and gastric bleeding. Chest radiography showed abnormalities in 7 newborns at admission, which included infections in 4 newborn, neonatal respiratory distress syndrome (NRDS) in 2 neonates and pneumothorax in one baby. Latter 5 newborns had been cured and discharged, 1 died, and 4 newborns remained in hospital in a stable condition.[13]

A case study on 4 four mothers who were symptomatically infected with COVID-19 during the 3rd trimester was done. Clinical manifestation present at admission was fever, cough, myalgia or fatigue and headache. Only one patient felt reduced fetal movement and one experienced dyspnea. Lab results showed decreased Lymphocytes and platelet counts. Coagulation function and blood biochemistry of all the mothers were normal. Throat swab of four women was found to be positive COVID-19. Abnormalities in chest CT images and bilateral involvement were detected among all pregnant women. A cesarean section was performed for three patients while one patient underwent vaginal delivery. All infants were isolated from their mother immediately after birth. All the babies were having normal apgar score as well as weight according to gestational age. Three of the four infants tested negative for COVID-19 using a throat swab specimen in RT-PCR after 72 h after birth and one baby's parents did not provide consent for the test .Three mothers of the infants recovered from their COVID-19 infections and were released 3–5 days after delivery. However, one mother suffered severe dyspnea after delivery which required respiratory support, latter she survived. All four infants

and their mothers were healthy upon a post-discharge follow-up.[14]

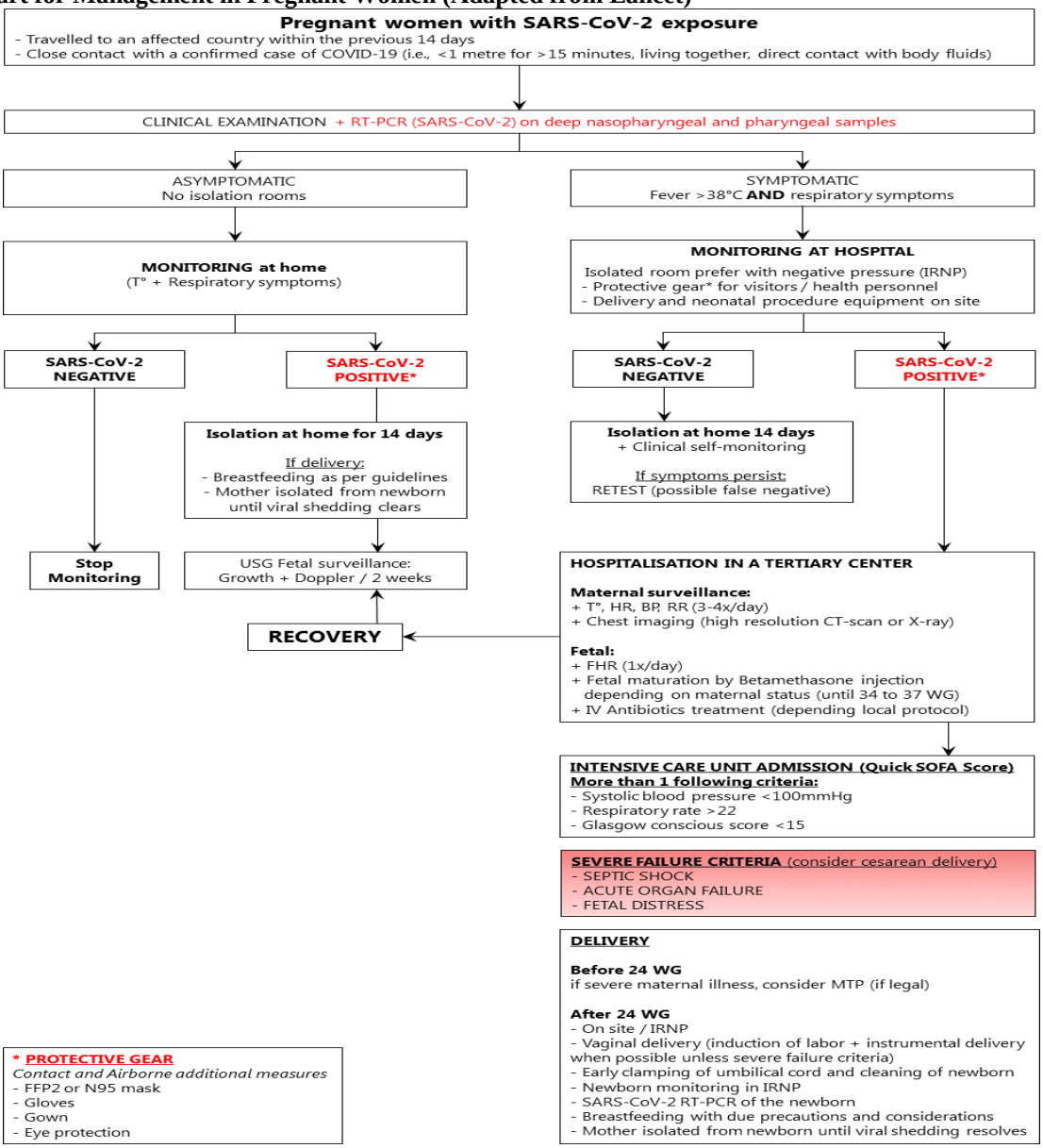
In a recent study published by Liu et al., the results showed that five out of 13 patients underwent an emergency cesarean section due to pregnancy complications. These complications were fetal distress (in three of the 13 cases), premature rupture of the fetal membrane (in one of the 13 cases), and delivery (in one of the 13 cases). The condition of six patients deteriorated during hospitalization and led them to be admitted to the Intensive Care Unit (ICU) with multiple organ dysfunction syndromes. The functional impairment syndrome included ARDS requiring intubation and mechanical ventilation, acute hepatic insufficiency, acute renal failure, and septic shock.[15]

Review showed that covid-19 during pregnancy can leads to preterm birth whereas it deteriorates the health of mother as well as newborn. It can also affect WBC and platelets count, elevate liver enzyme. Although there was no evidence of vertical transmission of covid-19 from mother to fetus.

Management of pregnant women with COVID-19

Guidance outlines on infection prevention and control precaution to be used by heath workers, when they are caring pregnant patients with suspected or confirmed SARS-CoV-2 infection. As till now there is no effective drug or a vaccine against this virus, management of this pandemic depends on effective prevention and control of disease transmission. In order to address the safety issues for the obstetrical management and delivery of pregnant women withCOVID-19 Pandemic, guidelines were prepared by ICMR.

Flowchart for Management in Pregnant Women (Adapted from Lancet)[16]



Guidance for Management of Pregnant Women in COVID-19 Pandemic ICMR, India[17]

Intra-partum Care of covid-19 positive pregnant women

- Delivery should be preferably done at tertiary care centre.
- Maternal observations including temperature, respiratory rate & oxygen saturations should be done timely.
- Confirmation of the onset of labor, as per standard care.
- Electronic fetal monitoring using cardiotocograph (CTG) should be done throughout the care.
- Hourly oxygen saturation during labor.

During labor

- To keep oxygen saturation >94%, titrating oxygen therapy accordingly.
- If the woman has signs of sepsis, investigate and treat as per guidance on sepsis in pregnancy, but also consider active COVID-19 as a cause of sepsis and investigate according to guidance.
- Continuous electronic fetal monitoring in labor is recommended.
- There is currently no evidence to favor one mode of birth over another. Mode of birth should not be influenced by the presence of COVID-19, unless the woman's respiratory condition demands urgent delivery.
- There is no evidence that epidural or spinal analgesia or anesthesia is contraindicated in the presence of coronaviruses. Epidural analgesia should therefore be recommended in labor to women with suspected/confirmed COVID- 19 to minimize the need for general anesthesia if urgent delivery is needed.
- In case of deterioration in the woman's symptoms, make an individual assessment regarding the risks and benefits of continuing the labor, versus emergency caesarean birth if this is likely to assist efforts to resuscitate the mother.
- When caesarean birth or other operative procedure is advised, it should be done after wearing PPE.
- An individualized decision should be made regarding shortening the length of the second stage of labor with elective instrumental birth in a symptomatic woman who is becoming exhausted or hypoxic.

Postnatal Management

It is unknown whether new-born with COVID-19 are at increased risk for severe complications. Transmission after birth via contact with infectious respiratory secretions is a concern. Facilities should consider temporarily separating (e.g. separate rooms) the mother who has confirmed COVID-19, from her baby until the mother's transmission-based precautions are discontinued.

- The risks and benefits of temporary separation of the mother from her baby should be discussed with the mother by the healthcare team.
- If "rooming in" of the new-born with his/her ill mother in the same hospital room occurs in accordance with the mother's wishes or is unavoidable due to facility limitations, facilities should consider implementing measures to reduce exposure of the new-born to the virus that causes COVID-19.
- Consider using engineering controls like physical barriers (e.g., a curtain between the mother and new-born) and keeping the new-born ≥6 feet away from the ill mother.

If no other healthy adult is present in the room to care for the new-born, a mother who has confirmed COVID-19 should put on facemask and practice hand hygiene before each feeding or other close contact with her new-born. The facemask should remain in place during contact with the new-born.

Breastfeeding

- During temporary separation, mothers who intend to breastfeed should be encouraged to express their breast milk to establish and maintain milk supply.
- If possible, a dedicated breast pump should be provided. Prior to expressing breast milk, mothers should practice hand hygiene. After each pumping session, all parts that come into contact with breast milk should be thoroughly washed and the entire pump should be appropriately disinfected as per the manufacturer's instructions.
- This expressed breast milk should be fed to the new-born by a healthy caregiver.
- If a mother and new-born do room-in and the mother wishes to feed at the breast, she should put on a facemask and practice hand hygiene before each feeding.

CONCLUSION

There is limited knowledge regarding coronavirus infections that occur during pregnancy. These previous experiences with coronavirus infections in pregnancy indicate that these agents are capable of causing adverse outcomes including hospitalization, intensive care and ventilator support. Coronaviruses can also result in adverse outcomes for the fetus and infant including intrauterine growth restriction, preterm delivery, and admission to the ICU, spontaneous abortion and perinatal death. However, pregnant women should be considered to be at high risk for developing severe infection during this current outbreak of 2019-nCoV. Additional clinical research on the treatment of 2019-nCoV is necessary to understand the potential risks and benefits of novel therapies and new vaccines in pregnancy.

Source of funding: NIL.

Conflict of interest: No conflict of Interest.

REFERENCES

1. Hui D.S. Epidemic and emerging coronaviruses (severe acute respiratory syndrome and Middle East respiratory syndrome) Clin. Chest Med., 2017; 38: 71–86. doi: 10.1016/j.ccm.2016.11.007. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
2. Song Z., Xu Y., Bao L., Zhang L., Yu P., Qu Y., Zhu H., Zhao W., Han Y., Qin C. From SARS to MERS, thrusting coronaviruses into the spotlight. Viruses, 2019; 11: 59. doi: 10.3390/v11010059. [PMC free article] [PubMed] [CrossRef] [Google Scholar
3. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, 2020. Doi: 10.1016/S0140-6736(20)30183-5.
4. Wong S.F., Chow K.M., Leung T.N., Ng W.F., Ng T.K., Shek C.C., Ng P.C., Lam P.W., Ho L.C., To W.W., et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. Am. J. Obstet. Gynecol, 2004; 191: 292–297. doi: 10.1016/j.ajog.2003.11.019. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
5. Lam C.M., Wong S.F., Leung T.N., Chow K.M., Yu W.C., Wong T.Y., Lai S.T., Ho L.C. A case-controlled study comparing clinical course and outcomes of pregnant and non-pregnant women with severe acute respiratory syndrome. BJOG., 2004; 111: 771–774. doi: 10.1111/j.1471-0528.2004.00199.x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
6. Zhang J.P., Wang Y.H., Chen L.N., Zhang R., Xie Y.F. Clinical analysis of pregnancy in second and third trimesters complicated severe acute respiratory syndrome. Zhonghua Fu Chan Ke Za Zhi., 2003; 38: 516–520. [PubMed] [Google Scholar]
7. Stockman L.J., Lowther S.A., Coy K., Saw J., Parashar U.D. SARS during pregnancy, United States. Emerg. Infect. Dis., 2004; 10: 1689–1690. doi: 10.3201/eid1009.040244. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
8. Yudin M.H., Steele D.M., Sgro M.D., Read S.E., Kopplin P., Gough K.A. Severe acute respiratory syndrome in pregnancy. Obstet. Gynecol, 2005; 105: 124–127. doi: 10.1097/01.AOG.0000151598.49129.de. [PubMed] [CrossRef] [Google Scholar]
9. Alserehi H., Wali G., Alshukairi A., Alraddadi B. Impact of Middle East respiratory syndrome coronavirus (MERS-CoV) on pregnancy and perinatal outcome. BMC Infect. Dis., 2016; 16: 105. doi: 10.1186/s12879-016-1437-y. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
10. Payne D.C., Iblan I., Alqasrawi S., Al Nsour M., Rha B., Tohme R.A., Abedi G.R., Farag N.H., Haddadin A., Al Sanhouri T., et al. Stillbirth during infection with Middle East respiratory syndrome coronavirus. J. Infect. Dis., 2014; 209: 1870–1872. doi: 10.1093/infdis/jiu068. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
11. Jeong S.Y., Sung S.I., Sung J.H., Ahn W.Y., Kang E.S., Chang Y.S., Park S.P., Kim J.H. MERS-CoV infection in pregnant woman in Korea. J. Korean Med. Sci., 2017; 32: 1717–1720. doi: 10.3346/jkms.2017.32.10.1717. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
12. Yu N, Wei L, Kang Q, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. Lancet 2020; published online Mar 24. https://doi.org/10.1016/S1473-3099(20)30176-6
13. Zhu H P, L W, Cheng Z F, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. Transl Pediatr, 2020. published online Feb 10. DOI:10.21037/tp.2020.02.06
14. Chen Y, Peng H, Wang L, Zhao Y, Zeng L, Gao H et al. Infants Born to Mothers With a New Coronavirus (COVID-19). Frontiers in Pediatrics [Internet], 2020. [cited 28 April 2020];8. Available from: https://www.frontiersin.org/articles/10.3389/fped.2020.00104/full
15. Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy. *J Infect*, 2020. doi: 10.1016/j.jinf.2020.02.028. [PubMed: 32145216].
16. Favre G, Pomar L, Qi X, Nielsen-Saines K, Musso D, Baud D. Guidelines for pregnant women with suspected SARS-CoV-2 infection. Lancet Infectious Diseases, 2020 pii: S1473-3099(20)30157-2. [Online] March 3, 2020. Accessed on April 5, 2020.
17. Guidance for Management of Pregnant Women in COVID-19 Pandemic [Internet]. 2020 [cited 28 April 2020]. Available from: https://icmr.nic.in/sites/default/files/upload_documents/Guidance_for_Management_o