

Evaluation of Maternal and Fetal Outcomes in Pregnant Women with COVID-19 based on Different Trimesters

Minoo Movahedi¹, Khadijeh M. Siahafshari¹, Maryam Hajhashemi¹, Farzin Khorvash², Milad Saeidi³, Zahra Allameh¹

¹Department of Obstetrics and Gynecology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran, ²Infectious Diseases Department, Isfahan University of Medical Sciences, Isfahan, Iran, ³School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract

Background: COVID-19 is the leading cause of the recent pandemic in the globe. This disease might have different effects on the maternal and fetal outcomes in pregnancy. The aim of this study was to assess these outcomes in pregnant women with COVID-19 infections in different trimesters.

Materials and Methods: This is a prospective cohort study that was performed in February 2020 to August 2021 in Isfahan on 430 pregnant women with definite diagnosis of COVID-19 infection admitted to our medical centers. The included cases were followed based on the gestational age in which they were diagnosed with COVID-19 infection. Patients were divided into three groups (first, second, and third trimesters) based on COVID-19 infection.

Results: The frequency of requiring mechanical ventilation was higher in mothers with COVID-19 in the second trimester ($P = 0.049$) and the frequency of PIH was significantly higher in mothers with COVID-19 in the third trimester compared to other women ($P = 0.009$). Fetal growth restriction (FGR) was also observed in 22 patients (5.3%) that was mostly observed with COVID-19 in the third trimester ($P = 0.012$). Oligohydramnios and fetal distress leading to C/S were observed in 19 patients (4.6%) and 12 patients (2.9%), respectively. The majority of maternal mortality was among cases with COVID-19 infection in the third trimester (44.4%).

Conclusion: We observed higher maternal and fetal complications in women especially those in the third trimester. Our results were in line with the findings of previous studies. Women with COVID-19 infection in the third trimester had highest frequencies of preterm labor and FGR.

Keywords: COVID-19, neonate, outcomes, pregnancy

Address for correspondence: Dr. Khadijeh M. Siahafshari, School of Medicine, Hezar Jarib St., Isfahan, Iran.

E-mail: kh.moradi8489@gmail.com

Submitted: 25-May-2022; **Revised:** 06-Jul-2022; **Accepted:** 16-Jul-2022; **Published:** 30-Jun-2023

INTRODUCTION

COVID-19 is a disease currently known as the coronavirus causing respiratory distress syndrome (SARS-Cov-2).^[1] The virus was first discovered in Wuhan, China, and soon led to an epidemic around the world.^[2,3] The incubation period of the disease is reported to be between 2 and 14 days.^[4]

Pregnancy increases the risk of side effects on mother and baby in many respiratory viral infections.^[5] Physiological and immunological changes that occur as a natural component of pregnancy can increase the risk of complications from

respiratory infections.^[6] Changes in the oxygen consumption and decreased lung capacity, as well as the development of immunological adaptations that allow the mother to tolerate the fetus with different antigens.^[7,8]

Data from several studies have shown that influenza increases the morbidity and mortality of pregnant women compared to nonpregnant women.^[9] This association has previously been seen in two older viruses of the corona family that cause Middle East Respiratory Syndrome (MERS).^[10,11]

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Movahedi M, Siahafshari KM, Hajhashemi M, Khorvash F, Saeidi M, Allameh Z. Evaluation of maternal and fetal outcomes in pregnant women with COVID-19 based on different trimesters. *Adv Biomed Res* 2023;12:165.

Access this article online

Quick Response Code:



Website:
www.advbiores.net

DOI:
10.4103/abr.abr_173_22

At present we have very little information about the complications of COVID-19 pregnancy.^[12] Limited information has been provided during studies conducted in Wuhan, China, regarding the pregnancy complications caused by a new virus in the COVID-19 epidemic.^[13]

In a recent study, the polymerase chain reaction (PCR) result of the virus in samples were taken from maternal neonatal blood, and neonatal throat samples were all negative.^[14] These results indicated that the probability of vertical transmission of this newly discovered virus during the third trimester of pregnancy was very low.^[15] Regarding the importance and prevalence of COVID-19 and the possible maternal and fetal complications due to the infections, here in the present study we aimed to assess these complications.

MATERIALS AND METHODS

This is a prospective cohort study that was performed in February 2020 to August 2021 in Al-Zahra and Amin hospitals affiliated to Isfahan University of Medical Sciences. The current study was conducted on all pregnant women with definite diagnosis of COVID-19 infection admitted to our medical centers. All of the pregnant mothers that were hospitalized with COVID-19 infection in our facilities were followed until termination. The study protocol was approved by the Research Committee of Isfahan University of Medical Sciences and the Ethics committee has confirmed it (Ethics code: IR.MUI.MED.REC.1399.717).

The inclusion criteria were pregnant women admitted to our medical centers, and definite COVID-19 infection by PCR test and/or CT scan findings. The exclusion criteria were previously diagnosed medical diseases including cardiovascular, renal or hepatic failures, vasculitis, antiphospholipid syndrome, history of pregnancy-induced hypertension (PIH), and history of neonatal problems in previous pregnancies including fetal growth restriction (FGR).

All pregnant women were included in February 2020 until August 2021 with the mentioned criteria that were admitted to the medical centers during the study period using census method. The included cases were followed based on the gestational age in which they were diagnosed with COVID-19 infection. As a result, we divided our data in to three groups (first, second, and third trimesters). Information of the study population were collected using a checklist by the means of interview and physical examinations. They were all followed until termination and the visits were repeated every month. After the termination of the pregnancy, we collected data of the neonates using a checklist.

The collected data related to the mothers were mother's age, gestational age, weight, body mass index (BMI), blood pressure, requiring mechanical ventilation, O₂ saturation, ICU admission fetal weight, percentile of fetal weight and amniotic fluid index (AFI). The data regarding the neonates were birth weight, Apgar score in 1 and 5 min after birth, and gestational

age, requiring NICU admission, mechanical ventilation, and neonatal mortality.

The obtained data were analyzed with SPSS software version 24. *P* value <0.05 was considered as significance threshold.

RESULTS

In the present study, data of 509 pregnant women with COVID-19 infection were reviewed. 73 patients were excluded due to lack of follow up, and 6 cases were excluded due to history of FGR (2 cases) and previous diagnosis of hypertension (4 cases). Data of 430 cases were analyzed. 23 women (5.4%) were diagnosed with COVID-19 in the first trimester, 88 women (20.5%) in the second trimester, and 319 women (74.1%) in the third trimester. Initial analysis of demographic data showed that the mean age of the mothers was 31.62 ± 5.61 years. Totally, 138 women (32.1%) had normal vaginal delivery (NVD) and 292 women (67.9%) had cesarean section (C/S). 63 women (15.2%) were admitted to the ICU of the medical centers and 19 women (4.6%) required mechanical ventilation. Pregnancy-induced hypertension (PIH) occurred in 49 women (11.9%).

Data were compared between women with COVID-19 in different trimesters. These data showed that the frequency of requiring mechanical ventilation was higher in mothers with COVID-19 in the second trimester ($P = 0.049$) and the frequency of PIH was significantly higher in mothers with COVID-19 the third trimester compared to other women ($P = 0.009$). By comparing the other data between mothers with COVID-19 infections in different trimesters, we observed no significant differences regarding age ($P = 0.188$), delivery type ($P = 0.864$) and ICU admission ($P = 0.291$). These data are indicated in Table 1 and Figure 1.

Totally, 89 women (21.5%) had preterm labor with majority in women with COVID-19 in the third trimester [Table 2 and Figure 2].

FGR was also observed in 22 patients (5.3%) that was mostly observed with COVID-19 in the third trimester ($P = 0.012$). Oligohydramnios and fetal distress leading to C/S were observed in 19 patients (4.6%) and 12 patients (2.9%), respectively. There were no significant differences between mothers with COVID-19 in different gestational ages regarding the preterm labor, oligohydramnios, and fetal distress ($P > 0.05$) [Table 3].

Based on our findings, the majority of maternal mortality was among cases with COVID-19 infection in the third trimester (44.4%). On the other hand, we observed higher mortality rates in cases with COVID-19 infection in the first trimester (8.7%) compared to other cases ($P = 0.019$). These data are shown in Table 4 and Figure 3.

We also assessed the data of nine deceased cases and outcome of their children. These data are shown in Table 5.

Table 1: Evaluation and comparison of data between mothers in different gestational ages

	Trimester			P
	1 (n=23)	2 (n=88)	3 (n=318)	
Mother age (year)	30.86±7.32 ^a	32.16±5.80	31.06±5.69	0.188 ^b
Delivery type				
NVD	6 (4.34)	27 (19.56)	105 (76.1)	0.864 ^c
C/S	17 (5.84)	61 (20.96)	213 (73.2)	
Mother ICU admission	3 (4.76)	18 (28.57)	42 (66.67)	0.291 ^c
Mother mechanical ventilation (MV)	2 (10.52)	7 (36.84)	10 (52.64)	0.049 ^c
PIH	0 (0.0)	4 (8.16)	45 (91.84)	0.009 ^c
Total hospitalized cases	23 (5.36)	88 (20.51)	318 (74.13)	-

^aData is represented by mean±standard deviation or number (column%); ^bKruskal Wallis Test; ^cChi-square test and fisher test

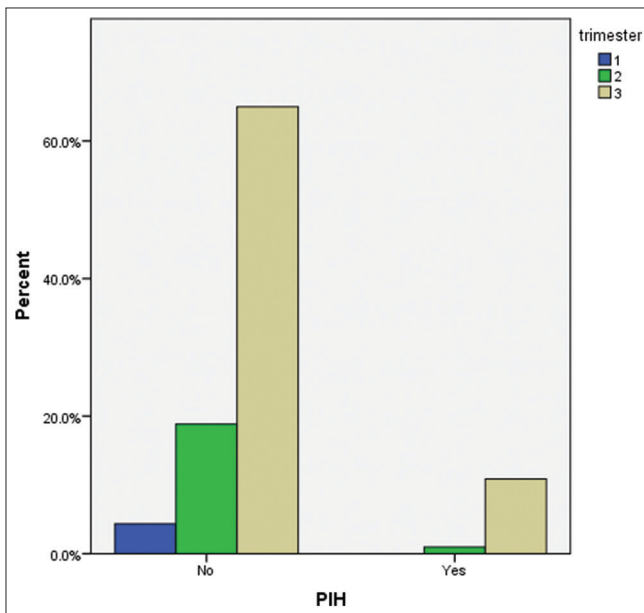


Figure 1: Evaluation of PIH based on trimester in mothers

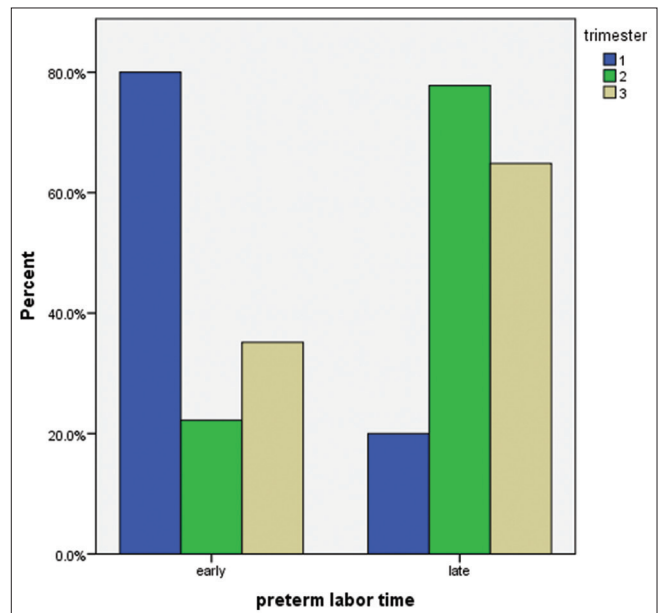


Figure 2: Evaluation of preterm labor in the study population

Further evaluations showed that IUFD was observed more among women with COVID-19 in the second trimester (9.9%) ($P = 0.001$). No significant differences were observed between women regarding NICU admission ($P = 0.182$), newborn MV/CPAP ($P = 0.334$) and newborn death. These data are shown in Table 6.

Furthermore, it was observed that the Apgar score in 1 and 5 min after birth were highest in patients with COVID-19 infection in the first trimester and women with COVID-19 infection in the third trimester had the lowest Apgar scores ($P = 0.008$ and $P = 0.040$, respectively) [Table 7 and Figure 4].

DISCUSSION

Based on our findings, by evaluating 430 women, the mortality rate was 2.1% in mothers with highest rate in mothers with COVID-19 in the third trimester, and 2.1% mortality and abortion in neonates. It was observed that 67.9% had C/S type of delivery and 15.2% were admitted to the ICU. The frequencies of mechanical ventilation and PIH were highest

in mothers with COVID-19 in the second and third trimesters, respectively.

In addition, women with COVID-19 infection in the third trimester had highest frequencies of preterm labor and FGR.

These data indicate the importance of COVID-19 infection in pregnant women especially those in the third trimester. This highlights the role of prevention and proper treatments in pregnant women. It should be noted that despite high frequencies of infected cases, we did not have higher rates of mortality compared to other studies. As mentioned earlier, various research have been conducted on the effects of COVID-19 in pregnant women.

The prevalence of different pregnancy-related complications have been assessed among normal populations. Based on recent data, the prevalence of preeclampsia was accounted 4--5%, the prevalence of abortion was 11--12%, the prevalence of FGR was 3--7%, the prevalence of oligohydramnios was 1--2%, the prevalence of IUFD was 13.9 per 1,000 birth and the prevalence of preterm labor was 10%. It could be observed

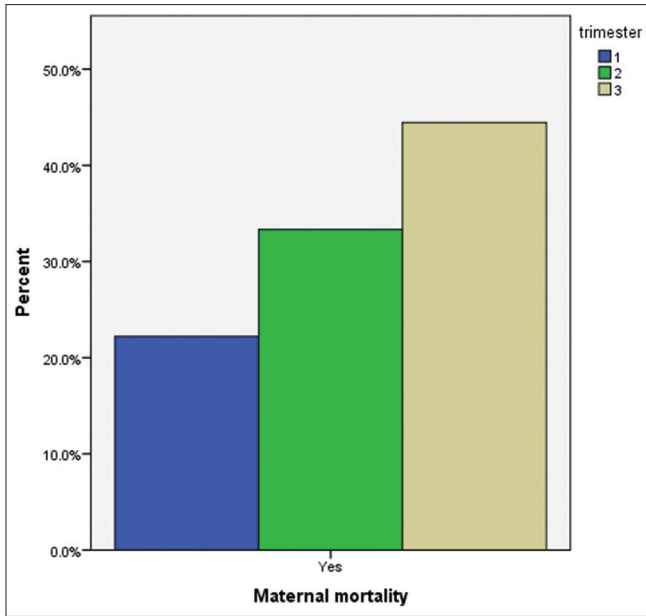


Figure 3: Comparison of maternal and fetal mortalities

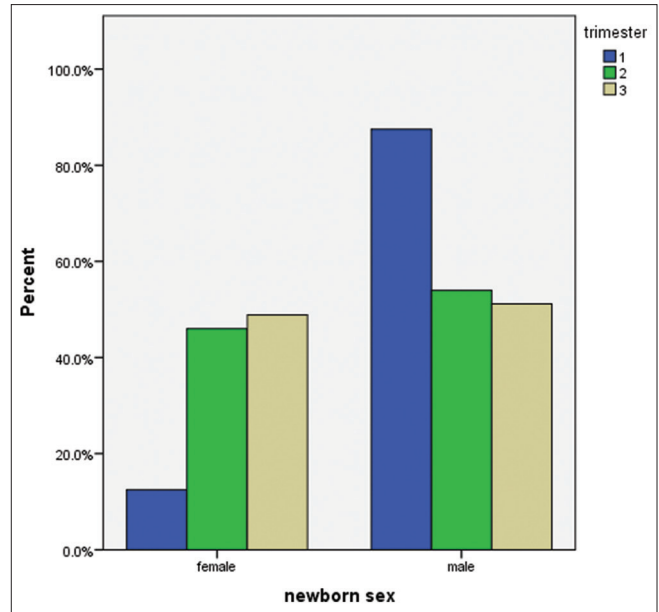


Figure 4: Evaluation of neonatal information

Table 2: Evaluation of preterm labor in the study population

Pre-term labor	Trimester			P
	1 (n=23)	2 (n=88)	3 (n=318)	
Early	4 (12.50)	2 (6.25)	26 (81.25)	0.549 ^b
Late	1 (1.78) ^a	7 (12.50)	48 (85.72)	
Total pre-term labor	5 (5.68)	9 (10.21)	74 (84.11)	
Total hospitalized cases	23 (5.36)	88 (20.51)	318 (74.13)	-

Legend: ^adata is represented by number (column%); ^bChi-square test and fisher test

Table 3: Evaluation and comparison of fetal complications in mothers with COVID-19 in different gestational age

	Trimester			P
	1 (n=23)	2 (n=88)	3 (n=318)	
FGR	2 (9.09)	0 (0.0)	20 (90.91)	0.012 ^b
Oligohydramnios	1 (5.26)	1 (5.26)	17 (89.48)	0.500 ^b
Polyhydramnios	0 (0.0)	1 (100)	0 (0.0)	-
Fetal distress	0 (0.0)	3 (25)	9 (75)	0.830 ^b
Total hospitalized cases ^a	23 (5.36)	88 (20.51)	318 (74.13)	-

Legend: ^adata is represented by number (column %); ^bChi-square test and fisher test

Table 4: Frequency of maternal mortality in the study population

Maternal mortality	Trimester			P
	1 (n=23)	2 (n=88)	3 (n=318)	
Number	2	3	4	0.019 ^b
% of total mortality	(22.22) ^a	(33.33)	(44.45)	
% of total hospitalized cases	(8.7%)	(3.4%)	(1.2%)	

Legend: ^adata is represented by number (column%); ^bChi-square test and fisher test

that the prevalence of these complications is higher among mothers with COVID-19 infection but the prevalence of FGR is similar to the general population.^[16] Therefore, we state that currently, there are no hard evidence that COVID-19 infection during pregnancy could increase risks of FGR and this could be due to small sample size.

In 2020, a study was conducted by Zhang and colleagues in China on 16 pregnant women with COVID-19. It was shown that all cases underwent C/S delivery and 18.8% were admitted in the ICU.^[17] Another study was performed by Pirjani and colleagues in Iran. They showed that 6.06% of women with COVID-19 were admitted to ICU, and 52.76% had C/S delivery.^[18] These results were in line with the findings of our study. It was observed that 67.9% of women had C/S type of delivery and 15.2% were admitted to the ICU. This shows higher rates of C/S delivery and ICU admission.

In a study by Zaigham and Andersson, data of 108 pregnancies were evaluated. Based on their findings, 91% of the women were delivered by C/S. It was reported that 20% of women presented in earlier gestational weeks and were discharged, undelivered, without any major complications. The mortality rate for mothers and neonates were reported 0% and 1%, respectively.^[19] It was indicated significantly higher C/S delivery in women compared to NVD and almost similar mortality rates were reported. Nevertheless, it was observed various maternal and fetal complications in women with COVID-19 infection in the first trimester. It is believed that lack of proper follow-up could be a limitation of the study by Zaigham and Andersson.

Another important point in our study was that we evaluated maternal mortality due to COVID-19 infection and found that the mortality rate in the first trimester was significantly higher than the other trimesters. These data could be due to the issue

Table 5: Information of maternal mortality and their children

Cases	Maternal age (years)	Gestational age (week + day)	Fetal outcome	Fetal weight (gram)	APGAR score
1	26	29w + 6d	IUFD before maternal death	-	-
2	31	26w + 3d	IUFD before maternal death	-	-
3	27	36w + 5d	New borns	2600	9/10 10/10
4	35	24w	IUFD before maternal death	-	-
5	25	7w + 3d	-	-	-
6	35	33w + 1d	New born	2400	9/10 10/10
7	21	26w	IUFD before maternal death	-	-
8	32	39w	New born	3300	9/10 10/10
9	26	10w	-	-	-

Table 6: Comparison of maternal and fetal mortalities

	Trimester			P
	1 (n=23)	2 (n=88)	3 (n=318)	
Abortion	4 (57.14)	3 (42.86)	-	0.001 ^b
IUFD	-	8 (57.14)	6 (42.86)	0.001 ^b
NICU admission	4 (4.04)	13 (13.13)	82 (82.83)	0.182 ^b
newborn MV/CPAP	3 (8.82)	2 (5.88)	29 (85.3)	0.334 ^b
newborn death	-	1 (50)	1 (50)	-
Total hospitalized cases ^a	23 (5.36)	88 (20.51)	318 (74.13)	-

Legend: ^adata is represented by number (column%); ^bChi-square test and fisher test

Table 7: Evaluation of neonatal information

	Trimester			P
	1 (n=23)	2 (n=88)	3 (n=318)	
Newborn sex				
Female	3 (1.5) ^a	41 (20.5)	156 (78)	0.131 ^b
Male	20 (8.73)	47 (20.52)	162 (70.75)	
Newborn weight	2789.23±667.84	2918.77±647.07	2838.04±617.20	0.550 ^c
Apgar 1 min	9.6±0.5	9.2±1.1	8.7±1.5	0.008 ^c
Apgar 5 min	10	9.8±0.5	9.6±0.7	0.040 ^c
Total hospitalized cases	23 (5.36)	88 (20.51)	318 (74.13)	-

Legend: ^aData is represented by number (column%) or mean±standard deviation; ^bChi-square test and fisher test; ^cKruskal Wallis Test

that women with COVID-19 infections in the first trimester often do not refer to medical centers until their disease progress to higher stages but in the second and third trimesters, women with signs of COVID-19 infection refer immediately to medical centers. Therefore, we observed lower mortality rates in the third trimester. The important points of our study were larger study population compared to most of the previous studies and comparing the pregnancy outcomes in women with COVID-19 infections during different gestational ages. By comparing these results, it was observed higher rates of different complications in pregnant women in their third gestational age.

In addition, different studies have been conducted on the pregnancy outcomes in COVID-19 infection. The most common complications were increased frequencies of C/S section, ICU admission, preterm labor, and fetal distress.^[20-22]

Smith and colleagues also evaluated nine articles regarding the pregnancy outcomes in women with COVID-19 infection.

By evaluating data of 92 patients, it was reported that 63.8% of women had preterm births, 61.1% had fetal distress, and 80% had a C/S.^[23] These data are not consistent with our findings. It was observed preterm labor in 20% and NICU admission in 23% of cases. These differences could be due to the variations in the study populations. In the present study, data of 430 pregnant women were assessed that could increase the validity of our data.

The rates of maternal mortality due to COVID-19 infection could vary in different populations. Metz and colleagues reported that this rate could be up to 5%.^[24] In another study by Nakamura-Pereira and others, it was stated that the mortality rates of pregnant women with COVID-19 could reach almost 4% in South American countries.^[25] Therefore, it is believed that our mortality rate in this study is not higher than previous studies. We believe that special care should be provided for similar cases to minimize the mortality rates.

The limitations of our study were conducting this study in two centers. Therefore, different managements in these two centers could be a shortcoming of this study. It is believed that the multicentric studies with similar treatment guidelines should be conducted in this regard. However, our data could have high clinical importance. We emphasize that the preventive and therapeutic strategies against COVID-19 should be conducted with higher priorities in pregnant women in the third trimester.

CONCLUSION

Our data were indicative of higher maternal and fetal complications in women especially those in the third trimester. Women with COVID-19 infection in the third trimester had highest frequencies of preterm labor and FGR. The Apgar score in 1 and 5 min after birth were lowest in patients with COVID-19 infection in the third trimester. It is emphasized that the preventive and therapeutic strategies against COVID-19 should be conducted with higher priorities in pregnant women in the third trimester.

Financial support and sponsorship

This study was financially supported by Isfahan University of Medical Sciences.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Fauci AS, Lane HC, Redfield RR. Covid-19—navigating the uncharted. *N Engl J Med.* 2020;382:1268-1269.
- Velavan TP, Meyer CG. The COVID-19 epidemic. *Trop Med Int Health* 2020;25:278-80.
- COVID GA, Group P-ACS. Post-COVID-19 global health strategies: The need for an interdisciplinary approach. *Aging Clin Exp Res* 2020;32:1613-20.
- Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. *Clin Immunol* 2020;215:108427.
- Talbot L, MacLennan K. Physiology of pregnancy. *Anaesth Intensive Care Med* 2016;17:341-5.
- Rafiee Zadeh A, Ghadimi K, Mohammadi B, Hatamian H, Naghibi SN, Danaeiniya A. Effects of estrogen and progesterone on different immune cells related to multiple sclerosis. *Casp J Neurol Sci* 2018;4:83-90.
- Fisher JJ, Bartho LA, Perkins AV, Holland OJ. Placental mitochondria and reactive oxygen species in the physiology and pathophysiology of pregnancy. *Clin Exp Pharmacol Physiol* 2020;47:176-84.
- Pascual ZN, Langaker MD. Physiology, Pregnancy. *StatPearls.* 2021.
- Somerville LK, Basile K, Dwyer DE, Kok J. The impact of influenza virus infection in pregnancy. *Future Microbiol* 2018;13:263-74.
- Verma S, Carter EB, Mysorekar IU. SARS-CoV2 and pregnancy: An invisible enemy? *Am J Reprod Immunol* 2020;84:e13308.
- Alfaraj SH, Al-Tawfiq JA, Memish ZA. Middle east respiratory syndrome coronavirus (MERS-CoV) infection during pregnancy: Report of two cases & review of the literature. *J Microbiol Immunol Infect* 2019;52:501-3.
- Chen M, Zeng J, Liu X, Sun G, Gao Y, Liao J, *et al.* Changes in physiology and immune system during pregnancy and coronavirus infection: A review. *Eur J Obstet Gynecol Reprod Biol* 2020;255:124-8.
- Rasmussen SA, Kelley CF, Horton JP, Jamieson DJ. Coronavirus disease 2019 (COVID-19) vaccines and pregnancy: What obstetricians need to know. *Obstet Gynecol* 2021;137:408-14.
- Laresgoiti-Servitje E, Cardona-Pérez JA, Hernández-Cruz RG, Helguera-Repetto AC, Valdespino-Vázquez MY, Moreno-Verduzco ER, *et al.* COVID-19 infection in pregnancy: PCR cycle thresholds, placental pathology, and perinatal outcomes. *Viruses* 2021;13:1884.
- Lu D, Sang L, Du S, Li T, Chang Y, Yang XA. Asymptomatic COVID-19 infection in late pregnancy indicated no vertical transmission. *J Med Virol* 2020;92:1660-4.
- Tsakiridis I, Dagklis T, Zerva C, Mamopoulos A, Athanasiadis A, Papazisis G. Depression in pregnant women hospitalized due to intrauterine growth restriction: Prevalence and associated factors. *Midwifery* 2019;70:71-5.
- Zhang L, Jiang Y, Wei M, Cheng B, Zhou X, Li J, *et al.* Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province. *Zhonghua Fu Chan Ke Za Zhi* 2020;55:166-71.
- Pirjani R, Hosseini R, Soori T, Rabiei M, Hosseini L, Abiri A, *et al.* Maternal and neonatal outcomes in COVID-19 infected pregnancies: A prospective cohort study. *J Travel Med* 2020;27:taaa158.
- Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. *Acta Obstet Gynecol Scand* 2020;99:823-9.
- Oltean I, Tran J, Lawrence S, Ruschkowski BA, Zeng N, Bardwell C, *et al.* Impact of SARS-CoV-2 on the clinical outcomes and placental pathology of pregnant women and their infants: A systematic review. *Heliyon* 2021;7:e06393.
- Moradi B, Kazemi MA, Gity M, Hantoushadeh S. Do we expect important complications of COVID-19 infection during pregnancy? *J Matern Fetal Neonatal Med* 2022;35:3000-1.
- Wong YP, Khong TY, Tan GC. The effects of COVID-19 on placenta and pregnancy: What do we know so far? *Diagnostics* 2021;11:94.
- Smith V, Seo D, Warty R, Payne O, Salih M, Chin KL, *et al.* Maternal and neonatal outcomes associated with COVID-19 infection: A systematic review. *PLoS One* 2020;15:e0234187.
- Metz TD, Collier C, Hollier LM. Maternal mortality from coronavirus disease 2019 (COVID-19) in the United States. *Obstet Gynecol* 2020;136:313-6.
- Nakamura-Pereira M, Andreucci CB, Menezes M, Knobel R, Takemoto ML. Worldwide maternal deaths due to COVID-19: A brief review. *Int J Gynecol Obstet* 2020;151:148-50.