

Maternal and Fetal Outcome in Women with First Trimester COVID-19 Infection

Original Article

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) is an international public health emergency that is attributed to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Aim: To assess maternal and fetal results in women with COVID-19 infection in the 1st trimester.

Patients and Methods: This prospective observational and analytical research was performed on eighty pregnant females infected with COVID-19 in the 1st trimester at the Obstetrics and Gynecology Department, Kasr Al-Ainy Hospital Maternity Hospital, Cairo University.

Results: The main pregnancy-associated complications were bleeding in 24 cases (30%), abortion in 20 cases (25%), hyperemesis gravidarum in 1 case (1.3%), hospital admission in 3 cases (3.8%), hypertension/preeclampsia in 10 cases (12.5%), gestational DM in 1 case (1.3%) and preterm premature rupture of membranes (PPROM) in 16 cases (20%). Postpartum hemorrhage occurred in 1 case (1.3%), and 2 cases were admitted to ICU (2.5%). There were 15 preterm neonates (25%) and 45 full-term (75%). The mean birth weight was 2734±797.07 grams, and the median birth weight was 2975 grams (range: 550–4000 grams). The neonatal complications included congenital anomalies in 1 case (1.7%), intrauterine fetal death (IUFD) in 3 cases (5%), neonatal intensive care unit (NICU) in 12 cases (20%), and fetal morbidity in 8 cases (13.3%).

Conclusion: During pregnancy, COVID-19 infection is linked to severe maternal and fetal complications. The adverse impacts of COVID-19 through the 1st trimester of pregnancy, where fewer researches have been performed compared to other trimesters, should not be disregarded.

Key Words: Acute respiratory syndrome, COVID-19, congenital anomalies, preterm.

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INTRODUCTION

On December 31, 2019, Chinese authorities notified WHO regarding a succession of patients resembling pneumonia that had been reported in the city of Wuhan^[1]. On January 7, 2020, the Chinese Center for Disease Control and Prevention classified this infection as a novel coronavirus infection. Subsequently, on February 11, 2020, the WHO designated the pandemic disease as COVID-19. The infection causes respiratory distress, fever, malaise and dry cough, in addition to shortness of breath^[2].

More than three million people have been infected globally as of May 2, 2020^[3], COVID-19 is an international public health emergency that is attributed to SARS-CoV-2^[4]. Many cohort investigations have concentrated on assessing the impacts of COVID-19 on the general population; however, a lack of evidence has been found about its effects on vulnerable groups like pregnant women^[5].

Pregnant females are more vulnerable to viral respiratory infections and severe pneumonia because of alterations in their immune and cardiopulmonary systems^[6]. Pregnant females are especially prone to negative outcomes, such as requiring endotracheal intubation, being admitted to the ICU, experiencing renal failure and death^[7].

The initial study investigated the clinical characteristics and possible vertical transmission of SARS-CoV-2 in nine pregnant women diagnosed with COVID-19. COVID-19 severity in pregnant women was found to be comparable to that in non-pregnant persons. Six cases showed no vertical transmission of SARS-CoV-2 as the virus was absent in amniotic fluid, cord blood, and newborn throat swab tests^[8].

The Royal College of Obstetrics & Gynecology advises that the decision for delivery in COVID-19 individuals should be based on obstetric reasons and discourages the automatic separation of infected women and their infants^[9].

This research aimed to assess maternal and fetal results in females with COVID-19 infection in the 1st trimester.

PATIENTS AND METHODS

This prospective observational and analytical research was performed on eighty pregnant females infected with COVID-19 in the 1st trimester at the Obstetrics and Gynecology Department, Kasr Al-Ainy Hospital Maternity Hospital, Cairo University.

Sample size:

For sample size calculations, the "Ostend, Belgium"-based MedCalc® version 12.3.0.0 program was utilized, along with a statistical calculator that reported a 95% confidence interval and 80% power of the research with a 5% margin of error. Based on a prior investigation by Shanes *et al.*, it was revealed that the maternal vascular mal-perfusion formal diagnosis in pathology by cases group [$n=2$ (13.33%)] compared to control group [$n=1$ (0.47%)] had a significant p -value of 0.012 and an odds ratio of 32.9. As a result, it is possible to conclude that a minimum sample size of 76 cases was sufficient to detect this distinction in the present research, which was calculated using this assumption as its foundation. The sample size for individuals with COVID-19 infection in the 1st trimester was eighty, assuming a five percent dropout coefficient^[10].

Inclusion criteria:

First trimester pregnancy, BMI between 18.5-29.9 kg/m², confirmed COVID-19 infection: Positive PCR by nasopharyngeal swab, symptoms including fever, cough, fatigue, loss of taste or smell, bone aches, diarrhea, vomiting, and sore throat, labs (D-dimer, serum ferritin, LDH, and CRP), and CT chest showed a ground-glass appearance, a single viable fetus, and no history of congenital anomalies.

Exclusion criteria:

Multifetal pregnancy, pregnant women with medical comorbidities (HTN, DM, epilepsy, thyroid disorder, autoimmune disease, chronic heart disease, COPD, asthma, CKD, chronic liver disease), previous history of preeclampsia, eclampsia, HELLP syndrome, GDM in previous pregnancies, multiple fibroid uterus, blood coagulopathy, and bleeding disorder, and previous history of PTL or PROM in previous pregnancies.

Patients involved in the investigation were subjected to the following: full history taking, clinical examination, investigations, and ultrasonography.

Primary outcomes:

Bleeding in early pregnancy, incidence of abortion, incidence of hyperemesis gravidarum, and need for hospital admission.

Secondary outcomes:

Maternal morbidity

Incidence of pregnancy-induced hypertension or preeclampsia, gestational DM, DVT, or pulmonary embolism; severe antepartum hemorrhage; incidence of CS elective or emergency, or vaginal delivery; gestational age at time of termination; need for ICU admission; and postpartum hemorrhage.

Fetal and neonatal outcomes

Full-term and preterm neonates Incidence of fetal morbidity as an incidence of congenital anomalies, IUFD, fetal weight at birth, need for NICU admission and low APGAR score.

Statistical analysis and data interpretation

In accordance with SPSS (Statistical Package for the Social Sciences) version 27 for Windows® (IBM SPSS Inc., Chicago, IL, USA), the gathered data were coded, processed, and analyzed. In order to evaluate the normality of the data, the Shapiro Walk test was applied. In contrast to parametric quantitative data, which were represented as mean $\pm$ standard deviation (SD), non-parametric quantitative data were presented as median (range) (SD). In order to represent qualitative data, frequencies and relative percentages were utilized.

Ethical consideration

The study was conducted following the Helsinki Declaration and with the agreement of the local ethics committee at Cairo University, Faculty of Medicine. Every patient provided written informed consent.

RESULTS

Average age of the included cases was 28.27 $\pm$ 6.18 years and the median age was 27 years, with range of 18 and 42 years. The average BMI was 33.98 $\pm$ 3.99 kg/m² and the median was 34kg/m² with a range between 26 and 42kg/m². There were 23 primigravidas (28.8%) and 57 multigravidas (71.3%) (Table 1).

Table 1: Demographic data and obstetric history in examined cases:

Items	examined cases N= 80	
	Mean $\pm$ SD	Median (min-max)
Age (years)	28.27 $\pm$ 6.18	27(18-42)
	Mean $\pm$ SD	33.98 $\pm$ 3.99
BMI (Kg/m ²)	34(26-42)	
	Median (min-max)	
	Number	Percent
Gravidities		
Primigravida	23	28.8
Multigravida	57	71.2

Continuous data expressed as mean $\pm$ SD and median (range), categorical data expressed as number (%).

Table (2) showed that the main presenting signs among the patients included fever in 40 cases (50%), cough in 46 cases (57.5%), sore throat in 49 cases (61.3%), dyspnea in 42 cases (52.5%), diarrhea in 24 cases (30%), loss of taste in 29 cases (36.3%), loss of smell in 39 cases (48.8%), bone ache in 48 cases (60%), and fatigue in 46 cases (57.5%).

Table 2: Symptoms of COVID-19 in examined cases:

Items	examined cases N= 80	
	Number	Percent
Fever	40	50
Cough	46	57.5
Sore throat	49	61.3
Dyspnea	42	52.5
Diarrhea	24	30
Loss of taste	29	36.3
Loss of smell	39	48.8
Bone ache	48	60
Fatigue	46	57.5

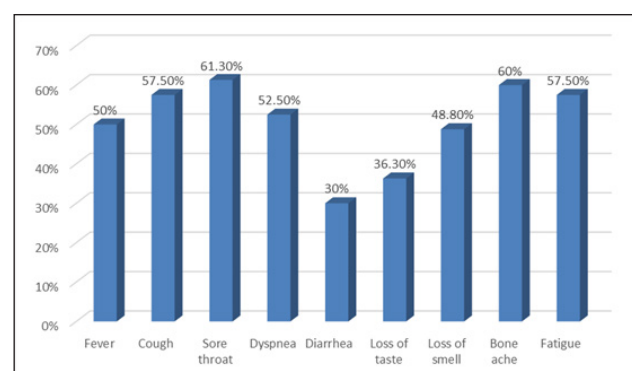


Fig. 1: Symptoms of COVID-19 in the cases of the study.

The mean percent of lymphocytes in the included patients was $16.41 \pm 8.21\%$, and the median percent was 15% (lymphopenia), with a range between 2 and 40%. The mean CRP was $58.62 \pm 35.88 \text{ mg/L}$, and the median was 55 mg/L, with a range between 3 and 142 mg/L. The PCR was done for 32 cases (40%), but the CT chest wasn't done at all (Table 3).

Table 3: Analysis of investigations in examined cases:

Items	examined cases N= 80	
	Number	Percent
Lymphocytes (%)	Mean $\pm$ SD	16.41 $\pm$ 8.21
	Median (min-max)	15(2-40)
CRP (mg/L)	Mean $\pm$ SD	58.62 $\pm$ 35.88
	Median (min-max)	55 (3-142)
PCR		
Not done	48	60.0
Done	32	40.0
CT chest		
Not done	80	100
Done	0	0

Table (4) showed that the main pregnancy-associated complications were bleeding in 24 cases (30%), abortion in 20 cases (25%), hyperemesis gravidarum in 1 case (1.3%), hospital admission in 3 cases (3.8%), hypertension/preeclampsia in 10 cases (12.5%), gestational DM in 1 case (1.3%), and PPROM in 16 cases (20%). Regarding the mode of delivery, 43 pregnant females (53.8%) had normal vaginal delivery, while the incidence of cesarean delivery was 46.3%. Postpartum hemorrhage occurred in 1 case (1.3%), and 2 cases were admitted to the ICU (2.5%).

Table 4: Pregnancy complications in examined cases:

Items	examined cases N= 80	
	Number	Percent
Bleeding	24	30
Abortion	20	25
Hyperemesis gravidarum	1	1.3
Hospital admission	3	3.8
Hypertension/preeclampsia	10	12.5
Gestational DM	1	1.3
DVT or pulmonary embolism	0	0
PPROM	16	20
Mode of delivery		
Normal vaginal delivery	43	53.8
Caesarean delivery	37	46.3
ICU admission	2	2.5
PPH	1	1.3

There were 15 preterm neonates (25%) and 45 full term (75%). The mean birth weight was 2734 ± 797.07 grams, and the median birth weight was 2975 grams, with a range between 550 and 4000 grams. The mean APGAR score was 8 ± 3.56 , and the median APGAR score was 9, with a range between 0 and 12. The neonatal complications included congenital anomalies in 1 case (1.7%), IUFD in 3 cases (5%), NICU in 12 cases (20%), and fetal morbidity in 8 cases (13.3%) (Table 5; Figure 1, 2).

Table 5: Analysis of fetal outcomes in examined cases:

Items	examined cases N= 60	
	Number	Percent
Maturity		
Preterm	15	25
full term	45	75
Birth weight (gm)	Mean $\pm$ SD	2734 $\pm$ 797.07
	Median (min-max)	2975(550-4000)
APGAR score	Mean $\pm$ SD	8 $\pm$ 3.56
	Median (min-max)	9(0-12)
Neonatal complications		
	Number	Percent
Congenital anomalies	1	1.7
IUFD	3	5
NICU admission	12	20
Fetal morbidity	8	13.3

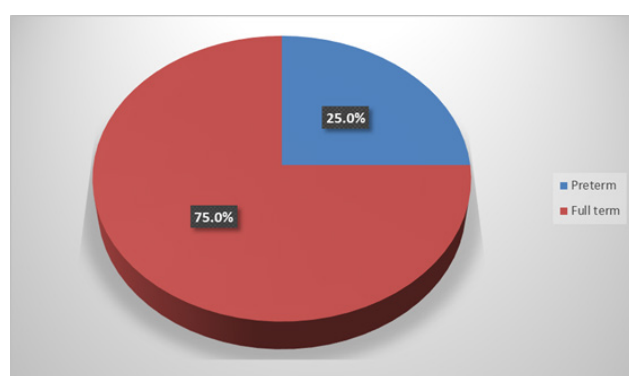


Fig. 2: Maturity of the neonates.

DISCUSSION

In current research, the mean age of the included cases was 28.27 ± 6.18 years, the mean BMI was $33.98 \pm 3.99 \text{ kg/m}^2$ and the median was 34 kg/m^2 . There were 23 primigravidas (28.8%) and 57 multigravidas (71.3%).

The current finding aligns with Ibrahim *et al.*, indicating that COVID-19 prevalence is higher in women under 30 years old, multigravida, and with a high body mass index^[11].

In the current study, the main presenting symptoms among the cases included fever in 40 cases (50%), cough in 46 cases (57.5%), sore throat in 49 cases (61.3%), dyspnea in 42 cases (52.5%), diarrhea in 24 cases (30%), loss of taste in 29 cases (36.3%), loss of smell in 39 cases (48.8%), bone ache in 48 cases (60%), and fatigue in 46 cases (57.5%).

This agreed with Ibrahim *et al.*, who reported that the predominant symptoms seen in confirmed pregnant instances of COVID-19 were fever, cough, dyspnea and exhaustion^[11]. In a similar vein, fever and cough emerged as the prevailing signs among pregnant females diagnosed with COVID-19, as indicated by a systematic review^[12].

These outcomes vary from those of Allotey *et al.*, who found that an analysis of 11,432 newly pregnant women showed a higher likelihood of remaining asymptomatic versus non-pregnant. Pregnant females are less likely to report signs of fever and myalgia in comparison to non-pregnant females^[13].

In the current research, abortion was reported in 20 cases (25%). This study closely matched Kiremitli *et al.*, study, which involved 52 individuals with SARS-CoV-2 infection identified by RT-PCR and 53 individuals with negative RT-PCR tests in samples obtained with a nasopharyngeal swab during the 1st trimester from March 1 to December 31, 2020. The study authors discovered that the percentage of pregnancy loss in individuals infected with SARS-CoV-2 during the 1st trimester was 28.8 percent^[14].

Conversely, Cosma *et al.*, found that SARS-CoV-2 does not serve as a risk factor for preterm birth during the initial trimester of pregnancy. Nevertheless, it was stated that the study cohort consisted solely of individuals who sought medical attention at the facility. They claimed that miscarriages that happen early in pregnancy might not require obstetric care; as a result, the research may have overlooked this finding^[15].

In the current study, no cases reported DVT or pulmonary embolism.

Comparably, a recent comprehensive analysis that included 1630 pregnant females with confirmed COVID-19 found that 0.9% of the women had a diagnosis of disseminated intravascular coagulopathy, thromboembolic illness, coagulopathy, or deep vein thrombosis^[16].

A different study found a greater incidence of venous thromboembolism and myocardial infarction in pregnant females with COVID-19 compared to those without COVID-19 (myocardial infarction: 0.1 percent vs. 0.004 percent; VTE: 0.2 percent vs. 0.1 percent)^[17]. The difference could be explained by the efficient prophylactic antithrombotic regimen encountered among the included cases.

In the current study, the rate of CS was 46.3%. This aligns with Ayed *et al.*, findings that 47.8 percent of neonates born to SARS-CoV-2-positive pregnant females were delivered via CS^[18].

In the current research, there were 15 preterm neonates (25%) and 45 full-term neonates (75%).

According to a match with Ayed *et al.*, 26.6 percent of the neonates born to pregnant mothers who tested positive for SARS-CoV-2 had premature deliveries^[18]. A further investigation found that 27 percent of newborns born to pregnant mothers who tested positive for SARS-CoV-2 were born prematurely^[19].

In the current study, the mean birth weight was 2734 ± 797.07 grams, and the median birth weight was 2975 grams, with a range between 550 and 4000 grams.

A large study by Wilkinson *et al.*, analyzed the data of 43,802 pregnancies of COVID-19-affected mothers in the first trimester. The authors reported that, in comparison to the WHO fetal growth tables, the average birth weight was $3,284 \pm 577 \text{ g}$ ^[20], which corresponds to an average birth weight z-score of -0.46 ± 1.10 ^[21].

In the current study, the mean APGAR score was 8 ± 3.56 and the median APGAR score was 9, with a range between 0 and 12. The neonatal complications included

congenital anomalies in 1 case (1.7%), IUFD in 3 cases (5%), NICU in 12 cases (20%), and fetal morbidity in 8 cases (13.3%).

Within the same context, Ibrahim *et al.*, reported that the predominant newborn results were NICU hospitalization for treatment (31.25%), necessitated mechanical breathing (12.5 percent), low birth weight (18.75 percent), ARDS (2.6 percent) and mortality (6.25 percent). The mean $\pm$ standard deviation of the Apgar score at one minute was 8.93 ± 1.913 , and after five minutes it was 9.06 ± 1.691 , indicating normal values^[11].

The current study found that twenty percent of cases resulted in NICU hospitalization. Martinez-Perez *et al.*, found that pregnant females with confirmed COVID-19 had a greater incidence of neonatal critical care unit hospitalizations^[22].

In disagreement with our result, An investigation in the UK revealed that 88 percent of the few newborns who tested positive for SARS-CoV-2 were sent home after treatment^[23].

In the present research, the frequency of IUFD was 5%.

In disagreement with our result, Wilkinson *et al.*, reported that there were 116 newborn deaths and 179 stillbirths, representing 0.26 percent & 0.41 percent of the total, respectively^[21].

In the current study, congenital anomalies were reported in only 1 case (1.7%).

Our results align closely with those of research conducted by Khan *et al.*, which found that small case researches have documented defects as congenital pulmonary airway malformation, cleft palate, & features of Down syndrome linked to maternal COVID-19^[24].

Although findings were obtained, the current research has limitations. The investigation had a limited sample size, and the patients were recruited exclusively from a single site.

CONCLUSION

The COVID-19 infection has significant impacts on both maternal and fetal outcomes throughout pregnancy. It is important not to overlook the adverse impacts of COVID-19 on pregnancies during the first trimester, as there has been less research performed on this compared to later trimesters.

CONFLICT OF INTERESTS

There are no conflict of interests.

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