

# Pregnancy Outcome after COVID-19 Infection in Different Trimesters

**Original Article** *Ahmed Kamel Sadek<sup>1</sup>, Alaa El-Din Nageeb El-Ebrashy<sup>2</sup>, Abobaker Hesham Negm<sup>3#</sup>, Ahmed Rizk El-Zayat<sup>4</sup>*

*Departments of Obstetrics & Gynecology, <sup>1,3</sup>Armed Forces College of Medicine, <sup>2,4</sup>Faculty of Medicine, Cairo University, Cairo, Egypt.*

## ABSTRACT

**Background:** Coronavirus disease of 2019 (COVID-19) infection during pregnancy could lead to worse pregnancy outcomes, whether maternal or fetal. Studies have associated COVID-19 with an increased risk of premature birth, premature membrane rupture (PROM), and cesarean section (CS) delivery, together with preterm delivery. Given the paucity of studies on the effect of COVID-19 on pregnancy outcomes, this study was conducted to determine the pregnancy outcomes among pregnant COVID-19 women in an Egyptian population.

**Patients and Methods:** This retrospective study was conducted at Masr El Gedida Military Hospital on 100 pregnant women with confirmed COVID-19 infection from March of 2020 to December of 2021. Women had been followed through their medical records and investigations for the different pregnancy outcomes (maternal or fetal).

**Results:** Sixty-two percent of COVID-19 pregnant women delivered by elective CS, 19% by emergency CS, and 12% by normal vaginal delivery. The mean GA at delivery was 35.7 weeks. Moreover, 70% of pregnant COVID-19 women continued their pregnancy; 7% had an abortion; 8% had intrauterine growth restriction; 5% had intrauterine fetal demise; 5% had preterm labour and PROM; 4% had preterm labour; and 1% had antepartum hemorrhage. The mean APGAR scores at 1 and 5 minutes were 8.5 and 9.5, respectively. The mean birth weight was 3054 grams. It was noticed that 22 neonates were COVID-19 positive, and 18 neonates needed NICU admission.

**Conclusion:** Women who had COVID-19 at any point during their pregnancies might be more likely to experience adverse maternal and newborn outcomes.

**Key Words:** COVID-19, maternal outcomes, pregnancy outcomes, preterm birth.

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**Corresponding Author:** Abobaker Hesham Gamal Negm, MSc, Departments of Obstetrics & Gynecology, Armed Forces College of Medicine, Cairo, Egypt. **Tel.:** 01555928259, **E-mail:** enas.ali.omar@kasralainy.edu.eg

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## INTRODUCTION

There are worries that the COVID-19 pandemic may have had a negative impact on pregnancies, as demonstrated in different contexts worldwide<sup>[1]</sup>. Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is more likely to cause severe symptoms in pregnant women<sup>[2]</sup>. COVID-19 infection during pregnancy has been linked to an increased risk of premature birth, PROM, and CS delivery<sup>[3]</sup>. As the pregnancy progressed, maternal infection after 20 weeks was linked to an increased risk for bad obstetric outcomes, and infection after 26 weeks was linked to an increased risk for severe neonatal outcomes, but infection before these timeframes did not raise these risks<sup>[4]</sup>. Preterm delivery, placenta previa, fetal pain, and stillbirth could be all associated with SARS-CoV-2 because of the inflammatory state it induces in the placenta<sup>[5]</sup>. Preterm birth rates during the COVID-19 pandemic have been documented with varying outcomes, with some studies reporting a drop<sup>[6]</sup>, others indicating no change in preterm birth rates or stillbirths<sup>[7]</sup>, and another study reporting an increase<sup>[8]</sup>. Changes to the mode of delivery

have also been reported with mixed findings<sup>[8,9]</sup>. Given the paucity of studies on the effect of COVID-19 on pregnancy outcomes, this study was conducted to determine the pregnancy outcomes among pregnant COVID-19 women in an Egyptian population.

## PATIENTS AND METHODS:

### *Research design and setting:*

This retrospective study was conducted between March 2020 and December 2021 at the Obstetrics and Gynecology department of Masr El Gedida Military Hospital.

### *Participants*

Pregnant women with confirmed COVID-19 in Masr El Gdida Military Hospital in the period between March 2020 and December 2021. The inclusion criteria were adult pregnant women aged 18 to 37 who got infected with COVID-19 during pregnancy and had full medical records. Exclusion criteria were: pregnant women with any other

pre-existing co-morbidity with COVID-19 in pregnancy as: hypertension, diabetes mellitus, cancer, cardiac disease, and kidney disease. Also, pregnant women with an obstetric complication at the time of infection, such as pre-eclampsia were excluded, as were women with a detected congenital fetal malformation before COVID-19 infection.

### Data Collection

Records of subjects were retrieved, along with their follow-up sheets and laboratory findings, from the lab archive (including the polymerase chain reaction swab for COVID-19). Women had been followed through their medical records for the development of respiratory complications and pregnancy outcomes. Maternal data collected included maternal age, gravidity, parity, and GA at delivery. Laboratory tests included CBC; serum alanine transaminase, and aspartate aminotransferase; kidney function tests; a coagulation profile; inflammatory markers; and other lab tests. Moreover, chest X-ray reports were retrieved.

The retrieval of pregnancy outcomes included mode of delivery and miscarriage defined as pregnancy loss before 28 weeks of gestation. Maternal complications of COVID-19 infection were retrieved, including the requirement of oxygen therapy, invasive mechanical ventilation, and intensive care unit (ICU) admission. Neonatal outcomes such as birth weight, APGAR score, neonatal intensive care unit (NICU) admission, and NICU

length of stay were also retrieved. The main outcome was to assess the pregnancy outcomes of COVID-19 pregnant women.

### Statistical analysis

Data were entered into a Microsoft Excel spreadsheet for Windows and analysed with SPSS version 26 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Categorical variables were presented as frequency (n) and percentage (%) and analysed using the chi-square test. Whereas as quantitative variables were presented as mean, standard deviation (SD), median and interquartile range (IQR). Nonparametric data were analysed with the Mann-Whitney U test. A level of significance of 5% was set for all statistical analyses ( $\alpha = 0.05$ ).

### RESULTS:

One hundred pregnant women with confirmed COVID-19 infection were included in this retrospective study at Masr El Gdida Military Hospital. The age of the studied women ranged from 18 to 39 years, with a mean  $\pm$  SD of  $29.91 \pm 6.998$  years and a median age of 33 years. The mean parity was  $2.11 \pm 0.99$ ; 45% of them were para 3, 32% were para 2, 13% were para 1, and 10% were nullipara. The GA at the time of infection ranged from 5 weeks to 37 weeks, with a mean of  $22.43 \pm 11.69$  weeks. (Table 1)

**Table 1:** Baseline characteristics in the pregnant COVID-19 women (N = 100).

Parameters		Studied women (No.=100)
Age (years)	Mean $\pm$ SD	$29.91 \pm 6.998$
	Median	33.0
	Range	18.0- 39.0
Parity	Mean $\pm$ SD	$2.11 \pm 0.99$
	Median	2.0
	Range	0.0- 3.0
	0	10 (10%)
	1	13 (13%)
	2	32 (32%)
GA at infection	3	45 (45%)
	Mean $\pm$ SD	$22.43 \pm 11.69$
	Median	24.0
	Range	5.0- 37.0

SD: Standard deviation; GA: Gestational age

Regarding trimesters, 40% were in the 3<sup>rd</sup> trimester, 30% in the 2<sup>nd</sup> trimester, and 30% in the 1<sup>st</sup> trimester. (Figure 1).

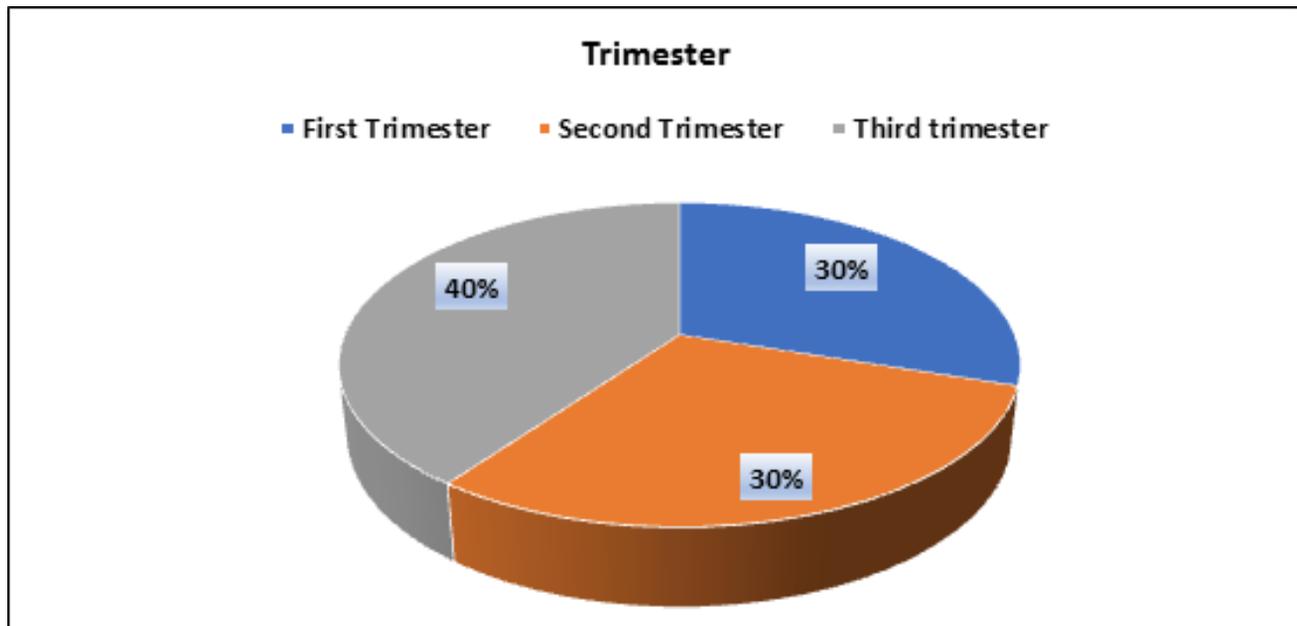


Fig. 1: Distribution of the studied women regarding trimester (N = 100).

Fever was the most common presenting symptom found in our studied patients (69%), followed by myalgia (34%), cough (24%), sore throat (14%), and loss of smell in 10% of pregnant COVID-19 women. GIT manifestations

were reported in 8% of women, including diarrhea and abdominal pain. It was noticed that 23% of women were asymptomatic. (Figure 2).

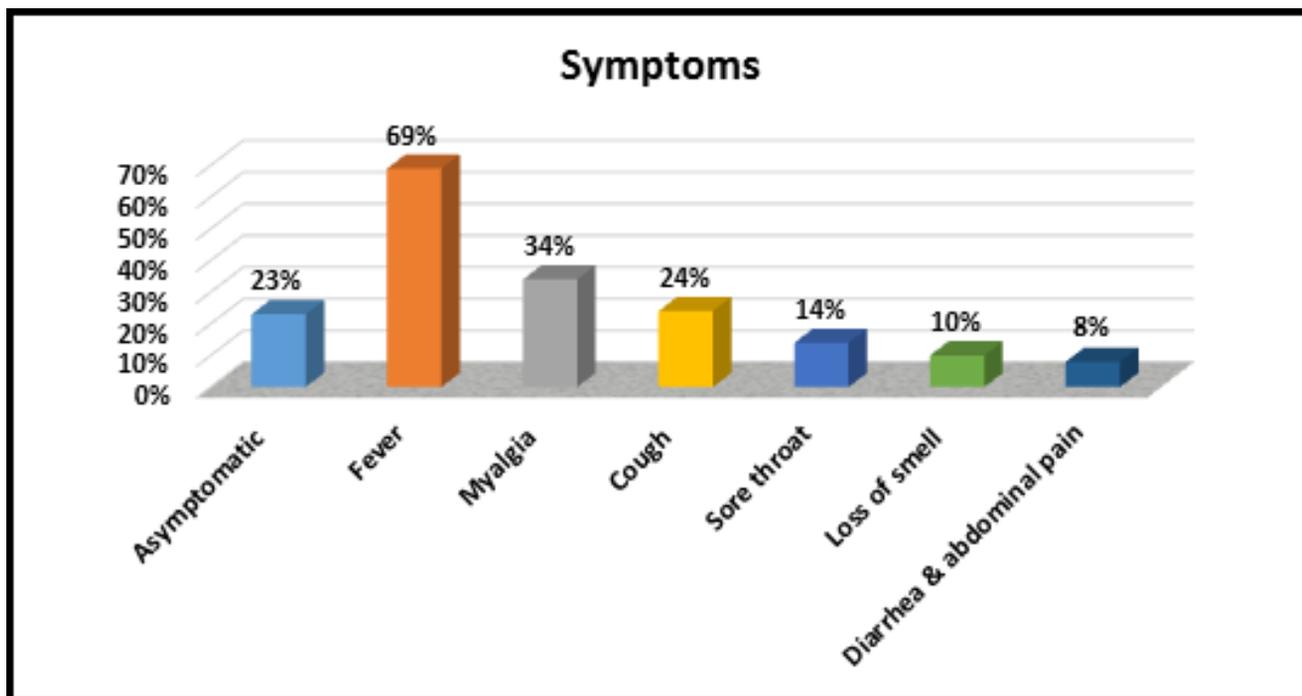


Fig. 2: Distribution of COVID-19 women (N = 100) regarding symptoms.

Regarding vaccination, 15% women had one dose of vaccine and 18% of women had two or more doses of vaccine. 30% of women were vaccinated by Pfizer

BioNTech (BNT162b2) vaccine while 13% of women were vaccinated by Moderna (mRNA-1273) vaccine. Error! Not a valid bookmark self-reference.)

**Table 2:** Distribution of the studied pregnant COVID-19 women regarding vaccination (N = 100).

Parameters	Studied women (No.=100)		
	No.	%	
Vaccination	No	67	67.0%
	1 dose	15	15.0%
	≥ 2 doses	18	18.0%
Type of vaccine	Pfizer BioNTech (BNT162b2)	30	30.0%
	Moderna (mRNA-1273)	13	13.0%

The mean Hb level was  $12.13 \pm 1.88$  g/dl, while the mean red cell count was  $4.76 \pm 0.43$ . The mean WBCs was  $9222.24 \pm 9880.15 \times 10^3/L$  while the platelet count

was  $214.86 \pm 62.24 \times 10^9/L$ . The mean neutrophils and lymphocytes were  $3.26 \pm 0.96$  and  $2.95 \pm 1.33$ , respectively. (Table 3)

**Table 3:** Complete blood count parameters among pregnant COVID-19 women (N = 100).

	Studied women (N= 100)				
	Mean	±SD	Median	Minimum	Maximum
Hb (gm/Dl)	12.13	1.88	11.90	9.90	16.10
WBCs ( $10^3/L$ )	9222.24	9880.15	7896.0	3800.0	76857.0
Red cell count	4.76	0.43	4.90	4.00	5.30
Platelets ( $10^9/L$ )	214.86	62.24	213.0	131.0	324.0
Neutrophil	3.26	0.96	3.20	2.0	5.10
Lymphocyte	2.95	1.33	3.35	0.82	4.70

**Hb:** hemoglobin; **WBCs:** white blood cells

The mean globulin level was  $44.06 \pm 7.23$  g/L while the mean albumin level was  $34.26 \pm 8.01$  g/L. The mean alanine transaminase and aspartate aminotransferase of studied cases was  $38.92 \pm 12.72$  U/L and  $32.75 \pm 11.12$

U/L respectively. Regarding kidney function tests, the mean creatinine and urea nitrogen of studied cases was  $0.85 \pm 0.28$  mg/dl and  $7.43 \pm 1.92$  mmol/L respectively. (Table 4)

**Table 4:** Liver and kidney function tests among pregnant COVID-19 women (N = 100).

	Studied women (N= 100)				
	Mean	SD	Median	Minimum	Maximum
Globulin (g/L)	44.06	7.23	46.0	31.0	54.0
Albumin (g/L)	34.26	8.01	34.0	20.0	47.0
AST (IU/L)	38.92	12.72	39.0	12.0	55.0
ALT (IU/L)	32.75	11.12	34.0	16.0	65.0
Serum creatinine (mg/dl)	0.85	0.28	0.74	0.50	1.40
Urea nitrogen (mmol/L)	7.43	1.92	6.80	4.80	10.29

**P-value < 0.05:** significant; **P-value < 0.01:** highly significant; **SD:** standard deviation.

The mean prothrombin time was 20.42 seconds, while the mean INR was 1.28. The mean activated partial thromboplastin time and D-dimer of the studied cases

were 32.7 seconds and 2.41 ng/ml, respectively. The mean fibrinogen level was 5.13 g/L. (Table 5)

**Table 5:** Coagulation profile among pregnant COVID-19 women (N = 100).

	Studied women (N= 100)				
	Mean	SD	Median	Minimum	Maximum
PTs	20.42	3.06	19.0	17.0	27.0
INR	1.28	1.12	1.10	1.0	12.2
APTT	32.7	5.31	34.0	24.0	39.0
D-dimer (ng/ml)	2.41	2.82	1.10	0.90	13.2
Fibrinogen (g/L)	5.13	0.92	5.0	4.0	7.2

**PT:** prothrombin time; **INR:** international normalized ratio; **APTT:** activated partial thromboplastin time; **SD:** standard deviation

The mean LDH was 428.64 u/l, while the mean CRP was 33.33 mg/l. The mean ferritin level was 873.99 ng/mL. (Table 6)

**Table 6:** Inflammatory markers among pregnant COVID-19 women (N = 100).

	Studied women (N= 100)				
	Mean	SD	Median	Minimum	Maximum
LDH, u/l	428.64	221.31	412.0	176.0	876.0
CRP, mg/L	33.33	29.03	20.0	8.0	98.0
Ferritin (ng/mL)	873.99	432.99	678.0	498.0	2111.0

**SD:** standard deviation.

Chest X-ray results showed that more than half of the women (56%) had a “ground glass” appearance, 20% had pneumonia, and 24% had a normal chest X-ray.

All cases showed normal ultrasonography findings. Error! Not a valid bookmark self-reference.)

**Table 7:** Distribution of the studied pregnant COVID-19 women as regard chest x-ray findings

	Parameters	Studied women (No.=100)	
		No.	%
Chest X-ray	Normal	24	24.0%
	Ground glass appearance	56	56.0%
	pneumonia	20	20.0%
Ultrasonography	Normal	100	100.0%

All the studied women showed positive SARS-CoV-2 RT-PCR results in the first trimester. In the second

trimester, five (16.67%) cases became negative, but they returned positive in the third trimester. (Table 8)

**Table 8:** The SARS-CoV-2 RT-PCR results among pregnant COVID-19 women according to trimesters

First trimester		Second trimester		Third trimester	
Positive	Negative	Positive	Negative	Positive	Negative
30 (100%)	0 (0.0%)	25 (83.33%)	5 (16.67%)	30 (100%)	0 (0.0%)

**RT-PCR:** The reverse transcription-polymerase chain reaction test

Out of the 100 studied women, 7% were reinfected by SARS-CoV-2. (Table 9)

**Table 9:** Reinfection status among pregnant COVID-19 women (N = 100).

Parameters	Studied women (No.=100)	
	No.	%
SARS-CoV-2 Re-Infection	No	93
	Yes	7

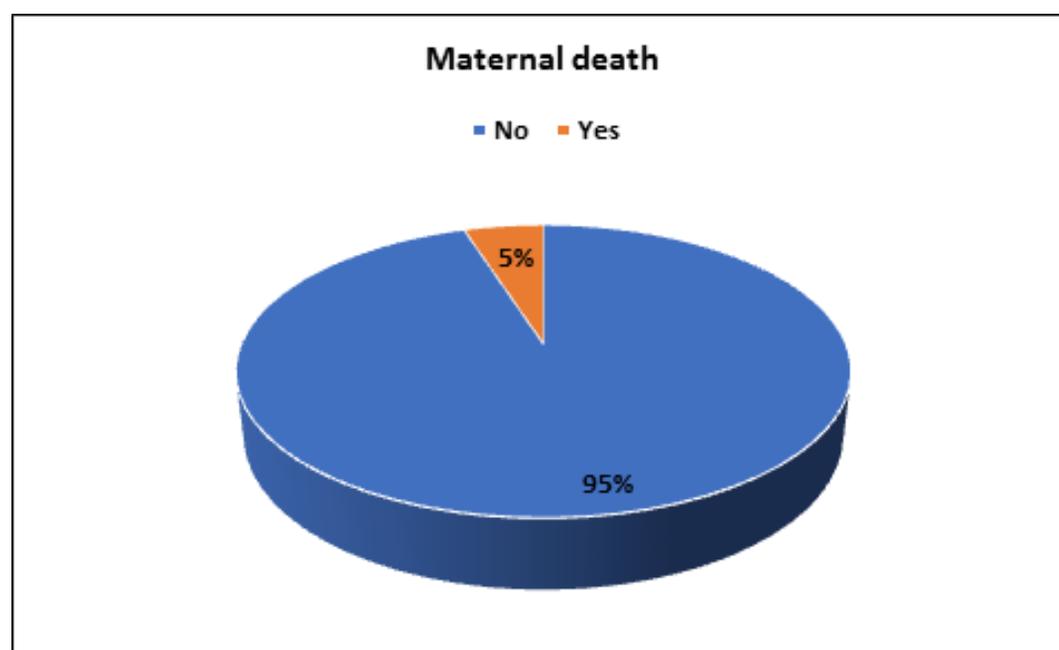
Out of 100 women, 25% needed hospitalization, with 9% on the medical floor and 18% in the ICU. Twenty-four percent of the women needed oxygen therapy, while 13% needed ventilation.

Regarding management, 41% of women were treated by antibiotic therapy and corticosteroids; 12% by antibiotic therapy, corticosteroids, and antivirals; 42% by antibiotic therapy and symptomatic treatment; and 5% were treated by Actemra. (Table 10)

**Table 10:** Need for ventilation between pregnant COVID-19 women treated with anticoagulant early and late

Parameters		Studied women (No.=100)	
		No.	%
Hospitalization	No	75	75.0%
	Yes	25	25.0%
Medical floor	No	91	91.0%
	Yes	9	9.0%
ICU	No	82	82.0%
	Yes	18	18.0%
Ventilation	No	87	87.0%
	Yes	13	13.0%
Treatment given	Antibiotic therapy& corticosteroids	41	41.0%
	Antibiotic therapy, corticosteroids & antiviral	12	12.0%
	Antibiotic therapy& symptomatic treatment	42	42.0%
	Actemra	5	5.0%
Oxygen therapy	No	76	76.0%
	Yes	24	24.0%

Out of the 100 women, five died (5%). (Figure 3)

**Figure 3:** Distribution of maternal death among pregnant COVID-19 women (N = 100).

Out of 100 women, 70% continued their pregnancy, 7% had an abortion, 8% had intrauterine growth restriction, 5% had intrauterine fetal demise, 5% had preterm labour and

premature rupture of membranes, 4% had preterm labour and 1% had antepartum hemorrhage. (Table 11)

**Table 11:** Pregnancy outcomes among pregnant COVID-19 women (N = 100).

Parameters	Studied women (No.=100)		
	No.	%	
Pregnancy outcome	Continued	70	70.0%
	Abortion	7	7.0%
	Antepartum hemorrhage	1	1.0%
	IUFD	5	5.0%
	IUGR	8	8.0%
	preterm labour	4	4.0%
	preterm labour& PROM	5	5.0%

**IUFD:** Intrauterine fetal demise; **IUGR:** Intrauterine growth restriction; **PROM:** premature rupture of membranes

Most women (62%) delivered by elective cesarean section, 19% by emergency cesarean section, and 12% by normal vaginal delivery. The mean GA at delivery was  $35.68 \pm 5.13$  weeks. (Table 12)

**Table 12:** Delivery characteristics among COVID-19 pregnant women (N = 100).

Parameters	Studied women (No.=100)		
	No.	%	
Mode of delivery	Elective CS	62	62.0%
	Emergency CS	19	19.0%
	Normal vaginal	12	12.0%
GA at delivery (weeks)	Mean $\pm$ SD	$35.68 \pm 5.13$	
	Median	37.0	
	Range	21.0- 38.0	

**CS:** cesarean section; **GA:** gestational age; **NVD:**

The mean APGAR scores at 1 and 5 minutes were 8.51 and 9.5, respectively. The mean birth weight was 3054 grams. It was noticed that 22 neonates showed positive viral status. 18 neonates needed NICU admission. (Table 13)

**Table 13:** Birth outcomes among pregnant COVID-19 women (N = 93)

Parameters	Studied Birth (No.=93)		
	No.	%	
APGAR score (1 minute)	Mean $\pm$ SD	$8.51 \pm 0.68$	
	Median	9.0	
	Range	7.0- 9.0	
APGAR score (5 minute)	Mean $\pm$ SD	$9.5 \pm 0.68$	
	Median	10.0	
	Range	8.0- 10.0	
Birth weight (grams)	Mean $\pm$ SD	$3054.09 \pm 308.7$	
	Median	3100.0	
	Range	2100.0- 3456.0	
Positive Viral status	22	23.66%	
NICU Admission	18	19.35%	

**SD:** standard deviation

## DISCUSSION

The effects of COVID-19 on the health of pregnant mothers and their babies are still unclear. There was a strong association between severe COVID-19 and adverse maternal and infant outcomes (Wei *et al.*, 2021). Those infected with SARS-CoV-2 during the third trimester of pregnancy had a higher risk of preterm birth compared to women without the virus, whereas neonates born to infected mothers early in their pregnancies were unharmed<sup>[10]</sup>.

The current observational study was carried out retrospectively in Masr El-Gededa military hospital in the period between March 2020 and December 2021 to explore the pregnancy outcomes after COVID-19 infection in different trimesters of pregnancy.

In the current study, the age of the studied women ranged from 18 to 39 years, with a mean age of 29.9 years and a median age of 33 years. Also, the mean parity was 2.11, with para 3 being the most reported, followed by para 2, para 1, and nullipara. In agreement with these results, the Piekos *et al.* (2022) study showed that patients in the SARS-CoV-2 positive cohort were more likely to have higher parity compared with the SARS-CoV-2 negative cohort<sup>[11]</sup>.

Forty percent of pregnant COVID-19 women in the study were in the third trimester, 30% were in the second, and 30% were in the first trimester of pregnancy. Infection occurred between 5 and 37 weeks of pregnancy, with a median of 22.4 weeks. These results overlapped with Fallach *et al.*, (2022) study results, which revealed that 48.4% of infections were in the third trimester, 34.3% in the second trimester, and 17.4% in the first trimester<sup>[10]</sup>.

Most patients in our study presented with fever, followed by myalgia, then a cough, sore throat, or loss of smell, and finally a gastrointestinal manifestation such as diarrhea or abdominal discomfort. 23% of women were found to have no symptoms. Vivanti *et al.*, (2020) study showed that at diagnosis, all but a woman experienced symptoms compatible with SARS-CoV-2 infection: 80% had cough, 62% had fever, 30% had dyspnea, 26% had myalgia, 16% had anosmia, and 10% had gastrointestinal symptoms<sup>[12]</sup>.

The current study showed that the mean prothrombin time was 20.4 and the mean INR was 1.3. The mean activated partial thromboplastin time and D-dimer of the studied cases were 32.7 seconds and 2.4 ng/mL, respectively. The mean fibrinogen level was 5.1 g/L. In a case report conducted by Vlachodimitropoulou Koumoutsea *et al.*,<sup>[13]</sup> D-dimers were significantly greater in COVID-19 pregnant women, which may

point to an association between perinatal COVID-19 infection and rapid maternal deterioration, shown by coagulopathy.

In the current study, 25% of women needed hospitalization with a mean hospital stay of 11.9 days, while 9% were on the medical floor, 18% needed ICU, 24% needed oxygen therapy, and 13% needed ventilation. In the Vivanti *et al.*, (2020) study, following an initial examination, 48% of patients got outpatient follow-up alone, while 52% were hospitalized 19% in ICUs, and 80.9% in regular wards<sup>[12]</sup>. Among all patients, 32% needed oxygen treatment. Five women out of 100 died, which was more than the zero maternal deaths reported in the Adhikari *et al.*,<sup>[14]</sup> study.

In the present study, most women delivered by elective CS, followed by emergency CS and normal vaginal delivery. On the contrary, Piekos *et al.*,<sup>[11]</sup> study results showed that the mode of delivery of COVID-19 patients included caesarean section in 31.8% and vaginal delivery in 68.2%<sup>[11]</sup>.

Among deliveries in the Vivanti *et al.*,<sup>[12]</sup> study, COVID-19 was the cause of 36% of the cesarean sections, whereas maternal respiratory distress and significant coagulopathy both accounted for 48% of cesarean sections, while 51.5% of the births were vaginal<sup>[12]</sup>. Though there was no significant difference in the mode of delivery between women in the COVID-19 group and normal controls in the Wilkinson *et al.*, (2022) study, women with COVID-19 had more emergency caesareans for maternal sickness than controls. Also, COVID-19 women were more likely to have iatrogenic (caesarean or induced) preterm deliveries<sup>[15]</sup>.

In our study, the mean GA at delivery was 35.6 weeks, which was much lower than Fallach *et al.*,<sup>[10]</sup> study (39 weeks). The mean APGAR scores at 1 and 5 minutes were 8.5 and 9.5, respectively, and a mean birth weight was 3054 grams. Moreover, 7% of women had abortions, 5% had intrauterine fetal demise, 8% had intrauterine growth restriction, 5% had preterm labour and premature rupture of membranes, 4% had preterm labour and 1% had antepartum hemorrhage. It was noticed that 22 infants showed positive viral status and 18 infants needed NICU admission. Compared with our study, Fallach *et al.*,<sup>[10]</sup> study revealed that there was preterm birth and pregnancy loss including spontaneous, induced, and stillbirth in 3.8%, 15.9%, 1.0%, and 1.3%, respectively, of pregnant COVID-19 women<sup>[10]</sup>. In the Piekos *et al.*,<sup>[11]</sup> study, 0.8% of the babies were stillbirth, and 13.3% were small for GA.

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## CONCLUSION

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The current study indicated that pregnant women who had SARS-CoV-2 in any trimester of their pregnancies might have an increased rate of intrauterine growth restriction, preterm delivery, and NICU hospitalization, as well as other negative maternal and neonatal outcomes.

## ABBREVIATIONS

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**COVID-19:** coronavirus disease of 2019

**CS:** cesarean section

**GA:** gestational age

**ICU:** intensive care unit

**INR:** international normalized ratio

**NICU:** neonatal intensive care unit

**PROM:** premature membrane rupture

**SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2

## CONFLICT OF INTEREST

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There are no conflicts of interest.

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