SARS-CoV-2 infection among preterm deliveries: frequency, determinants, effects. A retrospective cohort study in 2022

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Abstract. – OBJECTIVE: Pregnant women infected with SARS-CoV-2 are more likely to have obstetric complications, particularly preterm births, increasing the likelihood of maternal and neonatal morbidity and mortality. We tested the hypothesis by using a multivariable logistic regression analysis to take into account the effects of known confounding variables.

PATIENTS AND METHODS: A retrospective cohort study targeted a random sample of 89 preterm deliveries at the Obstetrics and Gynecology Department, Zagazig University Hospital, from January 2022 to April 2022, who fulfilled the selection criteria using a pretested, well-structured questionnaire that was composed of three main parts. The collected data were coded and analyzed using appropriate statistical methods.

RESULTS: This retrospective cohort study included 89 participants with a mean age of 26.6 years, 44.9% were middle-educated, 73% were not working, and the majority were not smoking or abusing substances. Regarding the frequency of COVID-19, dividing the studied participants into two groups, 22.5% had been infected, and there was no statistically significant difference between the two groups as regards the demographic characteristics, but smoking statistically increased the smoking (*p*-value = 0.034). Regarding the relationship between the history of COVID-19 and the past and present obstetric histories, there was no statistically significant difference between them. Even though the SARS-CoV-2 infection is significant (*p*-value = 0.037), pregnant women who are COVID-19 positive are more likely to have a cesarean section (16/80) than pregnant women who test positive.

CONCLUSIONS: Pregnant and preterm women were more likely to get SARS-CoV-2 if they smoked, had comorbidities, or were overweight or obese. Among COVID-19 preterm pregnancies, substance misuse and comorbidity were risk factors for a poor neonatal outcome, while women who had a previous history of PPH, were smokers, or had comorbid illnesses had a significantly increased risk of having a poor maternal outcome.

Key Words:
SARS-CoV-2 infection, COVID-19, Preterm deliveries, Neonatal outcomes, Maternal outcomes.

Abbreviations

American Academy of Pediatrics (AAP). Antepartum hemorrhage (APH). Body Mass Index (BMI). Cesarean Section (CS). Coronavirus Disease 2019 (COVID-19). Deep Vascular Thrombosis (DVT). In vitro fertilisation (IVF). Institutional Review Board (IRB). New York (NY). Polymerase-chain reaction (PCR). Premature rupture of the membranes (PROM). Preterm birth (PTB). Preterm labor (PTL). Primary postpartum hemorrhage (PPH).
Respiratory distress syndrome (RDS). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The American College of Obstetricians and Gynecologists (ACOG). The World Health Organization (WHO).

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-caused Coronavirus Disease 2019 (COVID-19) was declared a pandemic by the World Health Organization (WHO) on March 12, 2020[1]. It caused a nearly universal lockdown that had an impact on all fields of medi-

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cine. In Egypt, there were more than 387 thousand cases in January 2022, and there were 21,000797[2] deadly COVID-19 cases. Infected pregnant women may or may not show symptoms. Furthermore, there is an increased risk of developing severe COVID-19 sequelae, some pregnancy complications (including preterm birth), and in utero transmission[3].

According to the WHO, the American Academy of Pediatrics (AAP), and the American College of Obstetricians and Gynecologists (ACOG), preterm labor (PTL) is the labor that occurs during the delivery of a newborn before the completion of 37 weeks of gestation and can lead to preterm birth (PTB)[4]. Furthermore, it delays the hepatic bilirubin conjugation pathway[5]. PTB is a leading cause of neonatal deaths and different forms of neonatal morbidities, such as neurodevelopmental impairments, cerebral palsy, retinopathy, and bronchopulmonary dysplasia[6]. Preterm birth has become a global health problem. It affects 11% of babies born around the world, and 85% of those babies are born in Africa[7]. During the pandemic, many countries reported different rates of preterm birth. Ireland and Denmark have reported[8] a drastic reduction, while this is not found in the United Kingdom.

Even yet, it is still not clear what impact the COVID-19 viral infection during pregnancy will have. The COVID-19 pandemic has an impact on reproductive, maternal, and perinatal health, both directly through infection and indirectly as a result of modifications to social policies, health services, or economic and social conditions. Direct and indirect consequences are interconnected, as are direct and indirect causes[4,9-17].

Numerous studies[18-21] have been conducted to compare the rate of preterm birth during the COVID-19 pandemic to earlier cohorts and to identify risk factors. But no studies were conducted in Egypt, and they do not compare pregnancy outcomes with those of individuals without infection from the same demographics and time periods, which is a limitation of these and other big registry studies[22].

Thus, we carried out this research in this study. We evaluated these variables to determine the frequency of COVID-19 cases and their related maternal outcomes (including antepartum hemorrhages, post-partum hemorrhages, and mother's Hb level at delivery) and neonatal-related outcomes, including gestational age and birthweight (gm), and their key risk factors among preterm births during the pandemic COVID-19 era.

Patients and Methods

Study Design

A retrospective cohort study was carried out at the Obstetrics and Gynecology Department, Zagazig University Hospital, for three months from February to April 2022.

Participants and Sampling

The number of preterm deliveries admitted to the Obstetrics and Gynecology Department at Zagazig University Hospital each month determines the number of subjects and sample size. The sample was convenient (89 women in six months).

Inclusion and exclusion criteria: women who gave birth at less than 34, less than 32, or less than 28 weeks at the start of the study were included in the study. Women who were already at 37 weeks of gestation or greater and *in vitro* fertilization (IVF) cases were excluded.

The preterm pregnant women were later classified into two main groups according to the history of SARS-CoV-2 infection during pregnancy into two main groups:

- Group (A): COVID-19 preterm pregnancy cases; positive polymerase-chain reaction (PCR) results from nasopharyngeal swabs were utilized to diagnose SARS-CoV-2 infection at any point during pregnancy in every pregnant patient admitted to the delivery unit during the trial, excluding severe and hospitalized cases. The WHO classification for adults was used to classify the clinical manifestations of SARS-CoV-2 infection in those cases, which included septic shock, severe pneumonia, severe-moderate pneumonia, and mild symptoms[5].
- Group (B): preterm pregnancies who had not been diagnosed with COVID-19.

Data Collection Instrument

A) Shared standard data set was matched up with comparable international data collection methods. Research staff members for each patient from relevant clinical records and hospital records[33], the following sociodemographic and medical data were extracted:
   1. Demographic data: age, education level, occupation, smoking, substance abuse, BMI (kg/m^2), medical history (diabetes, hypertension, anemia).
   2. Past history of infection with the SARS-CoV-2 virus.
   3. Past obstetric history: parity, mode of previous delivery, previous history of APH or PPH.

4. Laboratory reports for maternal Hb at delivery and infant SARS-CoV-2 testing.

B) Follow up (at delivery, 24 h after delivery, 6 weeks after delivery):
   1. Natal outcomes: mode of delivery (NB: as a free public university hospital, the provided modality of delivery was only vaginal or cesarean, while others, such as water birth to feel less pain, were not available), fetal birth weight, still birth, neonatal death.
   2. Maternal outcomes, mode of current delivery, APH, and PPH either primary or secondary.

Study Variables

- Antepartum hemorrhage (APH) is defined as bleeding from or into the genital tract that occurs between 24+0 weeks of pregnancy and the baby's birth[16].
- Postpartum hemorrhage (PPH) is defined as blood loss of more than 500 mL after vaginal delivery or more than 1,000 mL after cesarean delivery[17].
- Anemia: a condition in which the number of red blood cells or the hemoglobin concentration within them is lower than normal[18].
- Body Mass Index (BMI) is a person's weight in kilograms (or pounds) divided by the square of their height in meters[15].

Statistical Analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 22 (IBM Corp., Armonk, NY, USA). Categorical variables were described using their absolute frequencies. A Chi-square test was used to analyze qualitative data. An independent sample *t*-test was used to analyze the quantitative data. A paired *t*-test was used to analyze paired quantitative data. The level of statistical significance was set at 5% (*p*-value < 0.05.

Results

As Regards the General Characteristics of Preterm Pregnancies

As regards the demographic and clinical characteristics, this prospective study included 89 participants with a mean age of 26.266.189. 44.9% were middle-educated, 73% were not working, and the majority were not smoking or abusing substances. By calculating BMI, 18% of them were > 30 kg/m^2, and 32.6% were between 18 and 32.4 kg/m^2. Nearly half of the included participants had a medical history of anemia, and 1.1% of them had a medical history of renal failure, rheumatoid arthritis, DVT, and rheumatic heart disease (Table I). Cases with hypertension were treated with methyl dopa and then continuously monitored.

In terms of previous obstetric history, 41.6% and 9% of participants had 1-3 and > 3 previous pregnancies, respectively. 42.22% of them had a previous cesarean section. The majority had no previous history of APH and PPH (97.8%, and 96.6%) and they were treated with ecbolic and uterine massage; one case required a blood transfusion but did not require surgical intervention.

Regarding the present obstetric history, most of the recruited preterm women underwent cesarean section (60.7%) with a decrease in the incidence of PPH (1.1%), while 10.1% had APH (Table II).

Relationship Determinants of SARS-CoV-2 Infection in Preterm Pregnancies

By dividing the study participants into two groups based on the incidence of COVID-19, 22.5% had been infected (Table I). There was no statistically significant difference between the two groups with respect to demographic characteristics such as education, medical history, and occupation, but there was a statistically significant difference with respect to special habits such as smoking (*p*-value = 0.034) (Table I).

Regarding the relationship between the history of COVID-19 and the past obstetric history, there was no statistically significant difference between them (Table II).

Regarding the relationship between the history of SARS-CoV-2 infection and neonatal and maternal outcomes, preterm pregnant COVID-19 cases were significantly (p-value = 0.037) associated with a higher frequency of caesarean sections (16, 80%) compared to non-infected preterm pregnant females (Table III).

In Terms of SARS-CoV-2 Infection Predictors

When compared to nonsmokers, smoking significantly (*p*-value = 0.02) increases the OR (95% CI) of catching SARS-CoV-2 infection by 1.22 (1.00-1.49). Comorbidities increase the risk of contracting SARS-CoV-2 infection by 3.7 (1.9-11.7) times (*p*-value = 0.001*). While overweight and obese, they increase the OR (95% CI) of catching the SARS-CoV-2 infection by 1.97 (0.99-3.11) (Table IV).

Table I. Socio-demographic characteristics of the studied participants (T = 89).

Characteristics	F	%	Group (A) T=20 F (%)	Group (B) T=69 F (%)	*p*-value
Education					
Illiterate	30	33.7	5 (25.0)	25 (36.2)	0.226
Middle education	40	44.9	8 (40.0)	32. (46.4)	
High education	19	21.3	7 (35.0)	12. (17.4)	
Age (Y) Mean ±SD	26.26 ±6.189		26.20 ±6.645	26.28 ±6.10	0.955
Occupation					
Not working	65	73	13 (65.0)	52 (75.4)	0.397
Working	24	27	7. (35.0)	17. (24.6)	
Smoking					
Yes	4	4.5	3 (15.0)	1 (1.4)	0.034*
No	85	95.5	17. (85.0)	68. (98.6)	
Substance abuse					
Yes	2	2.2	1 (5.0)	1 (1.4)	0.401
No	87	97.8	19 (95.0)	68. (98.6)	
BMI(Kg/m^2)					
< 18 (Underweight)	28	31.5	6 (30.0)	22 (31.9)	0.726
18- 24.9 (Normal)	29	32.6	8. (40.0)	21. (30.4)	
25-30 (Overweight)	16	18	3 (15.0)	13 (18.8)	
> 30 (Obese)	16	18	3 (15.0)	13 (18.8)	
Medical History					
Diabetes	10	11.2	4 (20.0)	6 (8.7)	0.223
Hypertension	9	10.1	2 (10.0)	7 (10.1)	0.675
Anemia	48	53.9	10 (50.0)	38 (55.1)	0.800
Renal failure	1	1.1	0. (0.0)	1 (1.4)	0.775
Autoimmune disease	4	4.5	1. (5.0)	3 (4.1)	0.775
DVT (Deep Vascular Thrombosis)	1	1.1	0 (0.0)	1 (1.4)	0.775
Rheumatic heart disease	1	1.1	0 (0.0)	1 (1.4)	0.775

**p*-value < 0.05 shows statistical significant difference. T= total number of cases. F=Frequency. BMI=Body Mass Index.

Table II. Past obstetric history of the studied participants (T = 89).

	F	%	Group (A) T=20 F (%)	Group (B) T=69 F (%)	*p*-value
Parity					
Nulliparous	44	49.4	8 (40.0)	36 (52.2)	0.478
1-3 Multi-para	37	41.6	9 (45.0)	28 (40.6)	
> 3 Multi-para	8	9.0	3 (15.0)	5 (7.2)	
Mode of previous deliveries **(T=45)					
Vaginal	17	37.78	4 (33.3)	13 (40.6)	0.306
Cesarean	19	42.22	4 (33.3)	15 (46.9)	
Both	9	20	4. (33.3)	5. (12.5)	
History of APH					
Yes	2	2.2	1 (5.0)	1 (1.4)	0.401
No	87	97.8	19 (95.0)	68 (98.6)	
History of PPH					
Yes	3	3.4	1 (5)	2 (2.9)	0.539
No	86	96.6	19 (95)	67 (97.1)	

T= total number of cases. **Multiple answers were allowed. F=Frequency. APH=Antepartum hemorrhage.

Table III. Current maternal and neonatal outcomes among the studied groups (T=89).

	F	%	Group (A) T=20 F (%)	Group (B) T=69 F (%)	*p*-value
a) Maternal outcomes					
Mode of delivery					
Vaginal	35	39.3	4 (20.0)	31 (44.9)	0.037*
Cesarean-section	54	60.7	16 (80.0)	38 (55.1)	
PROM	60	67.4	18 (90.0)	38 (55.1)	0.02*
Maternal infection	0	0.0	0 (0.0)	0 (0.0)	—
Presence of APH					
Yes	9	10.1	2 (10)	7 (10.1)	0.675
No	80	89.9	18 (90)	62. (89.9)	
Presence of PPH#					
Yes	1	1.1	1 (5)	0 (0)	0.227
No	88	98.9	19 (95)	69 (100)	
Hb level at delivery (g/dL)	Mean ± SD =10.0 ±1.297		9.51 ±1.244	10.16 ±1.28	0.049*
Post-partum Sepsis	0	0.0	0 (0.0)	0 (0.0)	—
Maternal death	0	0.0	0 (0.0)	0 (0.0)	—
b) Neonatal outcomes					
Gestational age (w)	Mean ± SD =29.752 ±3.736		28.90 ±1.24	30 ±3.857	0.249
Birthweight (gm)	Mean ± SD =1717.93 ±349.56		1640 ±267.83	1740.5 ±368.48	0.260
Still birth	0	0.0	0 (0.0)	0 (0.0)	—
Neonatal death	0	0.0	0 (0.0)	0 (0.0)	—

**p*-value < 0.05 shows statistical significant difference. T= total number of cases. F=Frequency. PROM =Premature rupture of the membranes. APH=Antepartum hemorrhage. #PPH (primary and secondary PPH).

As Regards the Predictors of Bad Maternal and Neonatal Outcomes Among SARS-CoV-2 Following Correction for the Confounding Variable

Substance abuse (OR 7.1), comorbid mothers (OR 95% CI) 1.3 (1.04-3.74), and educated mothers were considered non-significant protective factors. COVID-19-infected mothers had a significantly higher risk of poor maternal outcome than smokers [2.2 (1.3-3.9)], comorbidity [1.7 (0.99-1.16)], and those with a history of PPH [OR (95% confidence interval), 1.34 (1.02-2.1)] (Table V).

Discussion

Pregnant women infected with SARS-CoV-2 are more likely to have obstetric complications[5] particularly preterm births, which increases the risk of maternal and neonatal morbidity and mortality. Thus, we carried out this research in this study and evaluated these variables to determine the frequency of COVID-19 cases, poor maternal and bad neonatal outcomes, and their key risk factors among preterm births during the pandemic COVID-19 era.

Table IV. Predictors of COVID-19 among preterm pregnancy.

Variables	Univariable Analyses	
Demographics	OR (95% CI)	*p*-value
Education	Reference	–
Illiterate		
Middle education	1.75 (0.64-10.3)	0.19
High education	2.89 (0.83-13.5)	0.08
Age (y)	1.63 (0.48-6.09)	0.71
Occupation		
Not working	Reference	0.45
Working	4.83 (3.72-6.97)	
Smoking		
No	Reference	–
Yes	1.22 (1.00-1.49)	0.02*
Substance abuse		
Yes	3.7 (1.34-6.74)	0.34
No	References	
BMI (Kg/m²)		
Underweight and normal	References	<0.001*
Overweight and obese	1.97 (0.99-3.11)	
Comorbidities	3.7 (1.9-11.7)	<0.001*

CI (confidence intervals). BMI (Body Mass Index). **p*-value < 0.05 shows statistical significant difference.

Table V. Predictors of bad neonatal outcome and bad maternal outcome among preterm pregnancy with SARS-CoV-2 infected mothers.

#Standard COVID-19 cases with good outcomes	Poor neonatal outcome		Poor maternal outcome	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Education				
Illiterate	Reference	–	Reference	
Middle or high education	0.75 (0.64-1.3)	0.19	0.1 (1-1.7)	0.30
Smoking				
No	Reference	0.08	Reference	
Yes	2.89 (1.8-5.6)		2.2 (1-3.9)	0.00*
Substance abuse				
No	Reference	<0.00*	Reference	
Yes	7.1		4.3	<0.00*
BMI (Kg/m²)				
Underweight and normal	Reference	0.11	Reference	
Overweight and obese	1.3 (0.18-2.1)		1.5 (0.87-1.9)	0.14
Comorbidities				
No	Reference		Reference	
Yes	1.3 (1.04-3.74)	<0.001*	1.7 (0.48-1.16)	0.01
Previous history of APH				
No	Reference	0.38	Reference	
Yes	1.0 (0.25-3.08)		1.33 (0.65-2.7)	0.06
Previous history of PPH#				
No	Reference			
Yes	0.81 (0.61-1.08)	0.159	1.34 (1.02-2.1)	0.03*

*p-value < 0.05 shows statistical significant difference. CI (confidence intervals). APH=Antepartum hemorrhage. #PPH (primary and secondary PPH). BMI (Body Mass Index).

As Regards the General Characteristics of Preterm Pregnancies

As regards the demographic and clinical characteristics, the prospective study included 89 participants with a mean age of 26.26 ± 6.18 y, 44.9% were middle educated, 73% were not working, and the majority were not smoking or abusing substances. By calculating BMI, 18% of them were > 30 kg/m², and 32.6% were between 18 and 32.4 kg/m². Nearly half of the included participants had a medical history of anemia, and 1.1% of them had a medical history of renal failure, rheumatoid arthritis, DVT, and rheumatic heart disease.

As Regards the Frequency and Determinants of SARS-CoV-2 Infection in Preterm Pregnancies

As regards the frequency of COVID-19 among recruited preterm pregnancies, it was 22.5%. The infection rates differ from one country to another and across different durations. For example, it was lower during the first wave in the United Kingdom (UK)[9] (March-April 2020): 4.9%, and it was 6.1% in Spain[10] in March 2020. In New York (NY) (March-April 2020)[23], 6.7% were confirmed positive for COVID-19. This may be attributed to the degree of adherence to the preventive measures and the local application of restriction measurements, the availability of the tests, the virus strain, and the availability and effect of the vaccine.

As regards the determinants of SARS-CoV-2 infection, although there was no statistically significant difference between the two groups with the studied demographic characteristics except for smoking, smoking significantly increases (p-value = 0.02) the OR (95% CI) of catching SARS-CoV-2 infection by 1.22 (1.00-1.49). Comorbidities increase the risk of contracting SARS-CoV-2 infection by 3.7 (1.9-11.7) times (p-value = 0.001). While overweight and obese, they increase the OR (95% CI) of catching the SARS-CoV-2 infection by 1.97 (0.99-3.11), which is consistent with what was reported in the UK in 2020[9], as the majority of infected pregnant women were overweight or obese and a third had pre-existing comorbidities. Except for age, as in the UK, infection was more common among those over 35 or over 40%.

As Regards the Effect of SARS-CoV-2 Infection Among Preterm Pregnancies on the Fetal Outcomes

Preterm labor and other maternal problems were substantially more common during the COVID-19 pandemic. In women with COVID-19, premature births are thought to be caused by pro-inflammatory cytokines disrupting the equilibrium of cytokines at the maternal-fetal interface. We may therefore infer that SARS-CoV-2 may be linked to more prominent cytokine storms and inflammatory cascades, which may have resulted in preterm delivery in our instances[4].

As Regards Maternal Outcomes

HB level at delivery

Our results, which show that preterm infected women's Hb levels are significantly lower (*p*-value = 0.02) than those of non-infected mothers, are in line with a study from India[24] that discovered anemia to be the most prevalent comorbid disease linked to preterm birth rates and COVID-19 infection. This could be as a result of the several risk factors for premature birth, which include anemia throughout pregnancy. The extremely virulent and diverse SARS-CoV-2 infection in pregnant women[24]. This might be because anemia may result from acute immunological activation, a defense mechanism that takes advantage of low blood iron levels to prevent the virus from infecting the organs while enhancing cellular immunity. Reduced erythropoietin progenitor cell proliferation decreased erythropoietin stimulation, and a shorter erythrocyte half-life were all factors in the pathophysiology of severe anemia. The imbalance of iron homeostasis in inflammation is due to increased iron retention in the cells of the reticuloendothelial system. These patients have very high ferritin levels, which are an acute phase reactant[23-27].

Premature rupture of the membranes (PROM)

Our study's relationship between SARS-CoV-2 infection and premature rupture of the membranes (PROM) as 18 (90.0%) among preterm pregnancies is a unique and novel observation. The link is that the PROM and premature delivery activate a number of mediators and biochemical pathways of inflammation that are also present in SARS-CoV-2 infection, such as macrophages or IL-6[28]. The findings showing how IL-6 affects preterm delivery provide a solid foundation for further research[32]. In order to control inflammatory and immune reactions, cytokines are essential. Among them, IL-6 is crucial since research[29] has shown a strong correlation between circulating IL-6 levels and the severity of the SARS-CoV-2 infection, so that therapy is already recommended.

The frequency of cesarean sections (CS)

However, as the pandemic spreads and more scientific data becomes available, induced deliveries that depend only on maternal SARS-CoV-2 infection are increasingly prohibited[5]. The frequency of cesarean sections was considerably greater (*p*-value = 0.03) among infected preterm pregnancies[10] than 80.0%. The frequency varies across time and countries. For example, in NY (March-April 2020), it was 93%[18], and in a single-center hospital in NY, it was 44.4%[3]. This is in agreement with other studies[30-32] that found an increased rate of CS among pregnant women who were found to be positive for SARS-CoV2.

Maternal Outcomes

Among the recruited preterm pregnancies, the mean GA (W) COVID-19 cases were not significantly lower than non-infected cases (28.90 ± 1.24) according to our subset analysis based on gestational age. Our results were in agreement with research by Villar et al[33] that discovered greater rates of preterm delivery in a global cohort study, as well as research by Jering et al[34] that identified COVID-19 as being associated with increased risks of preterm birth. In contrast, research by Adhikari et al[35] found no difference between COVID-19-positive and COVID-19-negative women in terms of preterm birth rates.

The CDC research by Wood et al[13] stated that less than 10% of the cases in their sample were linked to asymptomatic SARS-CoV-2 infection in pregnancy, which may possibly account for our comparative findings on the maternal and neonatal outcomes. When utilizing universal diagnostic methods, numerous investigations[29,34,36-37] have revealed that the majority of pregnant people with SARS-CoV-2 infection are asymptomatic.

Most of the recruited preterm women reported a decrease in the incidence of PPH (1.1%) in relation to their current obstetric history, while 10.1% had APH. Primary postpartum hemorrhage (PPH) is the main cause of death in mothers. At least 25% of deaths during pregnancy, childbirth, and the postpartum period are caused by PPH[27].

Strength and Limitation

The study's major strength is in the use of a common testing procedure to include all individuals who meet the eligibility requirements. In addition, the only and biggest public educational hospital in the third-largest governorate of Egypt is Zagazig University Hospital in Elsharkia Governorate. Because we conducted this study in a high-resource environment where access to healthcare was universally free, the results are generally applicable to environments with similar characteristics. Most women get a minor infection, which suggests that even in places with less developed health care systems, the outcome is likely to be good.

There are several limitations to the study, including its single-center design, the absence of testing for vaginal cytokines to identify intra-amniotic inflammation, and the lack of genome sequencing information on SARS-CoV-2 strains to definitively establish a direct link between SARS-CoV-2 infection and preterm birth. The retrospective design of the study and the unknown timing and severity of infection. Many women were excluded because they had severe infections or needed critical care. Moreover, all the disadvantages of retrospective studies.

Recommendations

1. Our results show that more research is needed to figure out how COVID-19 works in the body when a baby is born early.
2. More extensive research is needed to detect the connection between COVID-19 and uncommon occurrences such as the risk of neonatal death, pre-eclampsia, and placental abruption. Signals in these results may be easier to detect by pooling data in meta-analyses.
3. Large study sizes, multicenter studies, and control groups are recommended to prove that pregnant women with COVID-19 symptoms are more likely to experience negative outcomes than non-pregnant women.
4. To reach the sustainable development goals, the right health care policies need to be made, especially since the COVID-19 outbreak is causing more babies to be born early.
5. Pregnant women need to be informed about the disease's heightened severity and encouraged to take preventative measures to avoid getting sick. Primary care providers must strike a balance between managing women suspected of having COVID-19 infection, preferably through virtual antenatal clinics, and the need for routine multidisciplinary prenatal care.
6. If a pregnant woman gets COVID-19 before giving birth, she may need to be treated in a tertiary care facility with a NICU and a cesarean section suite to care for premature babies, babies with low Apgar scores, and babies in fetal distress.

Conclusions

If a pregnant, preterm woman smokes, has concomitant conditions, or is overweight or obese, she is more susceptible to having SARS-CoV-2. SARS-CoV-2 infection in preterm pregnant women increases the risk of PROM, CS, and a low maternal hemoglobin level at delivery and low birth weight. In COVID-19 preterm births, substance abuse and comorbidity were risk factors for a poor neonatal outcome, while those with a history of PPH, smoking, or concomitant illnesses had a significantly worse maternal outcome.

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Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request (dr_samar11@yahoo.com).

Conflict of Interest

The authors declare that they have no competing interests.

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Ethics Approval

Approval by an Institutional Review Board (IRB) for medical research ethics at Zagazig University, Faculty of Medicine, was obtained before implementation of the study (ZU-IRB 9041-24-10-2021). Prior to the study's implementation, official approval was obtained from the director of Zagazig University outpatient clinics to the Obstetrics and Gynecology Outpatient Department, Zagazig University Hospitals, after explaining the purpose of the research and obtaining permission for data collection.

Informed Consent

Before any data were collected, each participant signed a form that said they understood what was going on and that their participation in the study was completely voluntary.

Authors' Contributions

Conceptualization: Nahla A. Zaitoun (NAZ), Ahmed M. Abdalkader (AA). Methodology: Hala A.El Maghawry (HE). Formal analysis: NAZ, Samar A. Amer (SA). Data curation: Mohamed M. Zaitoun (MZ), AA. Writing, and preparation of the first draft; NAZ, SA, HE. Writing-review and editing: all authors. All authors have read and agreed to the published version of the manuscript.

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