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The Effects and Outcomes of the COVID-19 Pandemic on Pregnant Women in Kuwait

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Highlights of the Study

- We compared obstetric outcomes in pregnant women infected with COVID-19 and an uninfected control group.
- The most frequent presenting complaints in pregnant women were dry cough and fever. Tachycardia was the most common sign at admission. ICU admission and respiratory failure were significantly higher in the COVID-19 group. Cesarean section rate was higher in this group, with obstetric and maternal complications being the most common indications.

Keywords
COVID-19 · Pregnancy · Obstetrical outcomes

Abstract
Objectives: This retrospective study reports the effects of COVID-19 among hospitalized pregnant women infected with COVID-19 and compares them to a control group. ***Methods:*** We performed a multicenter retrospective cohort study, in which data of pregnant women with COVID-19, admitted to five different hospitals in Kuwait, were collected. Two groups were included; the first group was women with COVID-19 who were admitted between March 22, 2020, and December 31, 2020. The second (control) group included pregnant women without COVID-19 who were admitted between March 1, 2019, and March 21, 2020. Data were collected using a standardized data collection survey, entered using Excel software, and analyzed using analysis of variance. ***Results:*** We compared 764 patients, with confirmed COVID-19 with 765 uninfected control subjects. The majority of pregnant women were diagnosed with COVID-19 infection during the third trimester. Tachycardia was the most frequent sign at admission, and dry cough and fever were the most common presenting symptoms. ICU admission and respiratory failure were significantly higher in the COVID-19 group. Cesarean section (CS) rate was higher in the COVID-19 group, with obstetric and maternal complications being the most common indications in comparison to fetal indications in the control group. ***Conclusions:*** This study was conducted to identify the effects of COVID-19 in pregnancy. Most patients were asymptomatic. The rate of normal vaginal delivery was higher in the control group. The

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main indications for CS in the COVID-19 group were obstetrical and maternal complications compared to fetal complications in the control group.

Introduction

A novel coronavirus, SARS-CoV-2, was initially identified in December 2019 in Wuhan, China, among a cluster of cases of pneumonia, which later spread rapidly to become a global pandemic as declared by the World Health Organization in March 2020 [1, 2]. Data are limited regarding the impact of SARS-CoV-2 infection on pregnant women, and it is not clear whether or not the infection increases the risk of pregnancy-related complications [1–3]. It is well known that the immune system and response to infection during pregnancy change due to reduced immunity, and this may explain why SARS-CoV-2 presentation is more severe during pregnancy [1]. This is supported by initial data, which showed that other forms of infection, such as H1N1 influenza virus and other coronavirus infections such as Middle East respiratory syndrome (MERS), can present in pregnant women with more severe manifestations, morbidity, and mortality compared to nonpregnant women [1]. The Center for Disease Control and Prevention (CDC) reported that hospitalization and rates of ICU admission among pregnant women with COVID-19 are higher than those in nonpregnant women [2]. However, it has been shown that the mortality rates are similar among the two groups [2]. We conducted this study to better understand this apparent discrepancy.

The risk of vertical transmission of COVID-19 infection seems to be very low, based on the fact that COVID-19 is a respiratory virus [1]. No cases of vertical transmission have been detected with other members of the coronavirus family (SARS and MERS); this is supported by a study which concluded that 18 pregnant women infected with COVID-19 during the third trimester gave birth to 19 infants, with no identified laboratory evidence of vertical transmission [1]. Current data suggest that the majority of neonates born to infected mothers are asymptomatic with only limited evidence of vertical transmission [3]. The risk of perinatal transmission of the infection is not well established [1]. A case series from Brazil reported five stillbirths in mothers with COVID-19, which might be secondary to chorioamnionitis [3]. A population-based descriptive study from Israel reported an increase in the rate of stillbirth of 2.5-fold during the pandemic period [3]; this is supported by a study from the United Kingdom, which showed similar findings [3]. A systematic review described the effect of stress on pregnancy outcomes, and it concluded an association between maternal exposure to stress and miscarriage [2]. Furthermore, some studies concluded that pregnant women with COVID-19 were generally at higher risk of life-threatening or critical illness, especially during the third trimester, and preterm cesarean section (CS) delivery for maternal indications [3]. This study was aimed at ascertaining the effect of COVID-19 infection on maternal outcomes.

Methodology

Study Design

We performed a multicenter retrospective cohort study, in which we studied data of pregnant women with COVID-19 admitted to five hospitals in Kuwait. The hospitals included Jaber Al Ahmad Hospital, Maternity Hospital, Al-Adan Hospital, Farwaniya Hospital, and Al Jahra Hospital. COVID-19 infection was confirmed using polymerase chain reaction assay from a nasopharyngeal swab. The study was approved by the Institutional Ethics Committee of the Ministry of Health of Kuwait (2020/1494).

Study Population

We studied two groups of pregnant women; one group included pregnant women with COVID-19 infection admitted between March 22, 2020, and December 31, 2020, while the second (control) group comprised pregnant women without COVID-19 infection admitted between March 1, 2019, and March 21, 2020, for various indications.

Data Collection

Data were collected by five researchers using a standardized data collection survey. We included ten main questions (patient identification, nationality, hospital, parity, gestational age, maternal comorbidities related to pregnancy such as hypertensive diseases in pregnancy, and gestational diabetes mellitus, and maternal comorbidities unrelated to pregnancy such as obesity, maternal age above 35 years, and respiratory diseases). Presenting symptoms and signs at the time of admission, as well as laboratory results, were collected. Laboratory results were categorized as low, normal, or high (according to the laboratory reference ranges). The tests included complete blood count with differential, coagulation studies, ferritin, lactate dehydrogenase (LDH), C-reactive protein (CRP), troponin, and alanine aminotransferase (ALT). Obstetric ultrasound scan parameters and positive findings related to COVID-19 on chest imaging (X-ray or CT) were included.

Maternal outcomes such as antepartum hemorrhage, preterm labor, preterm delivery, threatened miscarriage, missed miscarriage, incomplete miscarriage, intrauterine fetal demise, cardiac disease, preeclampsia, respiratory complications, multiple organ failure, sepsis, venous thromboembolism, ICU admission, gestational hypertension, and maternal death were reported. Mode of delivery was categorized into spontaneous vaginal delivery, assisted vaginal delivery, and CS. Those who underwent CS were divided according to the indication (obstetrical, fetal, maternal, COVID-19-related, and unspecified).

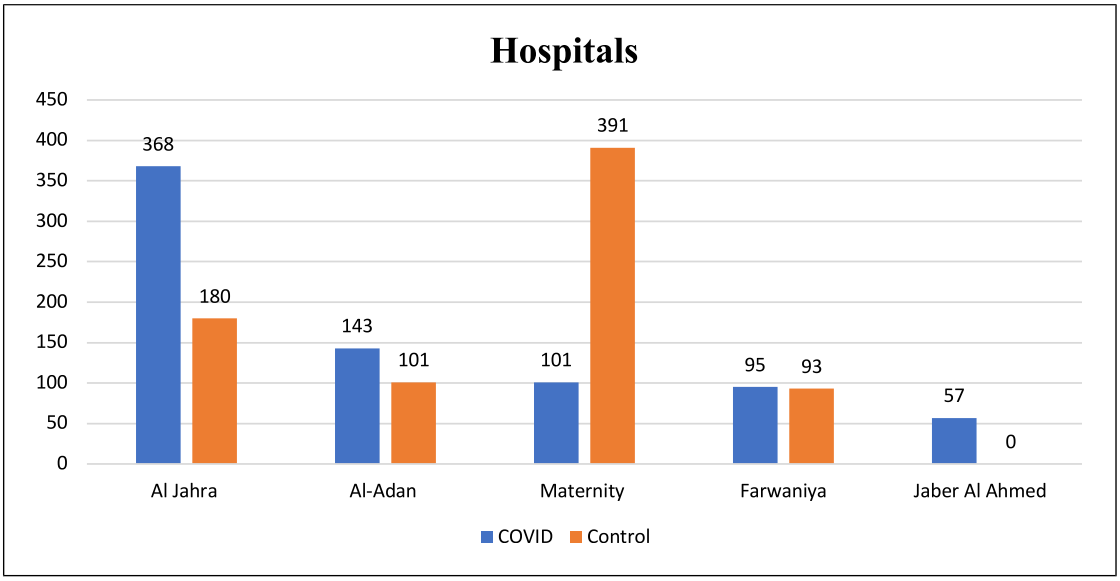

Fig. 1. Graph depicting the number of pregnant women (both COVID and control groups) admitted to five different government hospitals in Kuwait. No controls were admitted in Jaber Al Ahmed Hospital as only pregnant women with COVID infection were admitted during the study period.

Statistical Analysis

Data were entered in Excel software and analyzed using analysis of variance. The descriptive statistics are reported as mean ± standard deviation. The categorical variables were reported as numbers and percentages. The threshold for statistical significance was considered as $p < 0.05$.

Results

Subjects

We compared 764 pregnant subjects with confirmed COVID-19 to 765 pregnant uninfected control subjects admitted to five government hospitals. No control subjects were available at Jaber Al Ahmed Hospital as there were no admissions for non-COVID pregnant patients during the study period. The largest number of patients were from Al Jahra Hospital (368 patients, 48.2%) as it was a referral center for pregnant COVID-19 patients during part of the study period (Fig. 1). The majority of COVID-19 cases were 31–40 years old ($n = 378$, 49%). On the other hand, most controls were 21–30 years old ($n = 367$, 48%) (Fig. 2).

Parity

Primiparity was more common among controls. There were 142 cases (19.1%) and 227 (29.7%) controls ($p \leq 0.0001$). The majority of COVID patients and control subjects were multiparous with previous one or two pregnancies (322 COVID cases compared to 360 control cases). Grand multiparas (five and above) accounted for the least number of patients. There were 84 (11.3%) cases and 38 (5%) controls, $p \leq 0.0001$ (Fig. 3).

Gestational Age

The majority of patients were in the third trimester (24 + 1–42 weeks), with 575 (75.3%) in the COVID-19 group and 669 (87.5%) in the control group ($p \leq 0.0001$). The first trimester of pregnancy (1–12 weeks) accounted for the least number of patients for the COVID-19 group, 72 (9.4%), and only 54 (7.1%) patients for the control group ($p = 0.11$). For the second trimester (12 + 1–24 weeks), there were 117 (15.3%) from the COVID-19 group and 42 (5.5%) patients from the control group ($p \leq 0.0001$).

Pregnancy-Related Maternal Comorbidities

These include hypertensive disorders in pregnancy (COVID-19 group $n = 28$, 3.7% vs. control group $n = 47$, 6.2%, $p = 0.038$), gestational diabetes mellitus (COVID-19 group $n = 96$, 12.7% vs. control group $n = 76$, 10%, $p = 0.10$), placenta previa (COVID-19 group $n = 7$, 1% vs. control group 4, 0.5%, $p = 0.4$), placental abruption (COVID-19 group $n = 2$, 0.3% vs. control group $n = 3$, 0.4%, $p = 1.00$), rupture of membrane (preterm premature rupture of membranes, premature rupture

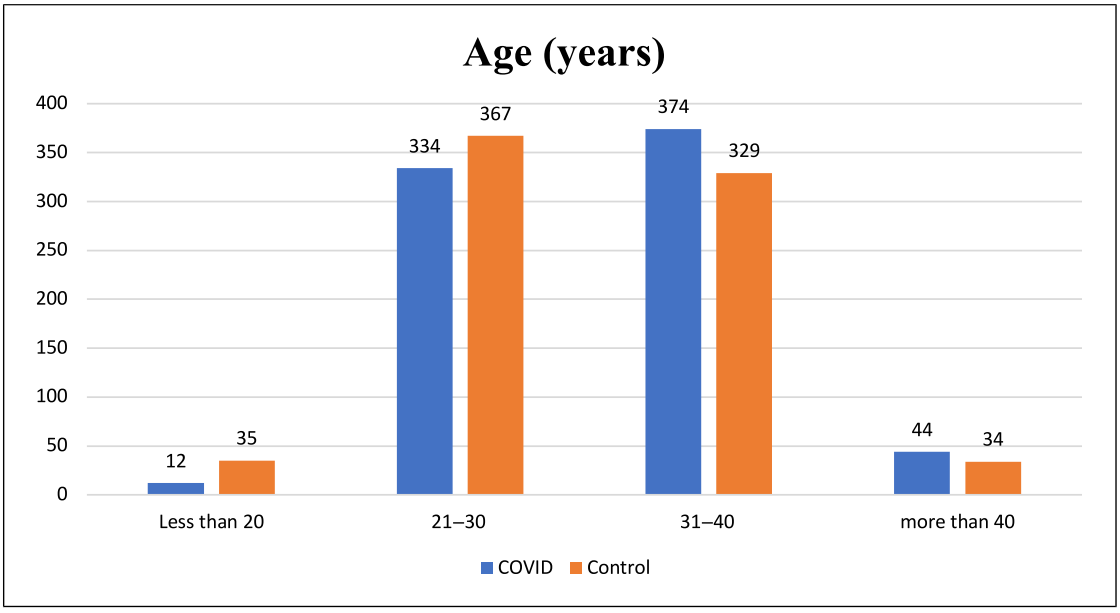

Fig. 2. Graph showing four main age group categories.

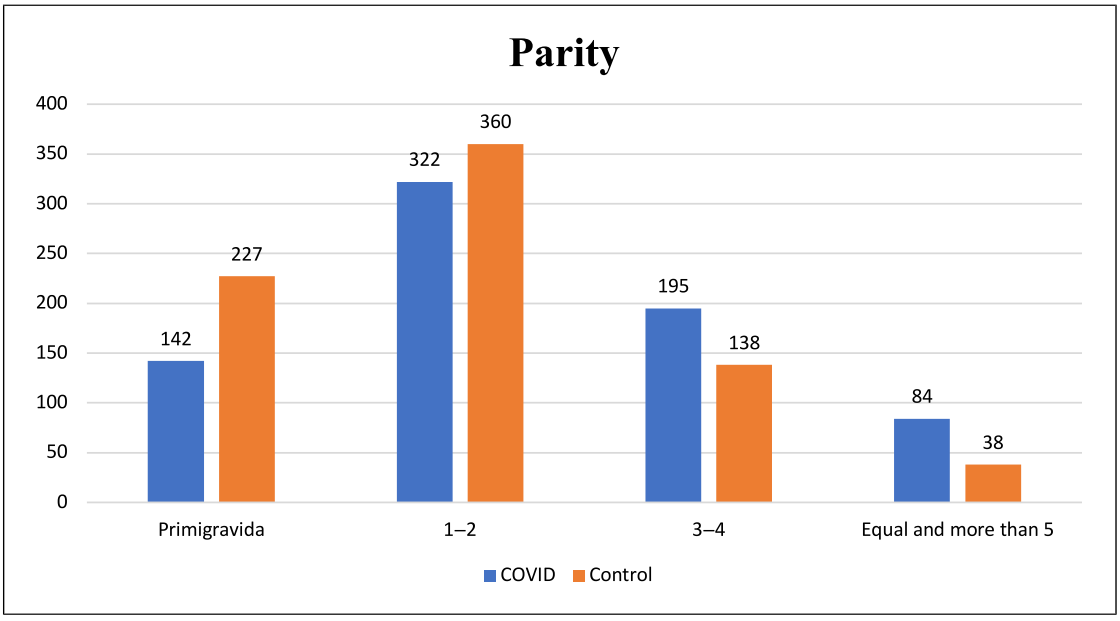

Fig. 3. Graph presenting four main parity categories.

of membranes, spontaneous rupture of membranes) (COVID-19 group $n = 23$, 3.1% vs. control group $n = 60$, 7.9%, $p \leq 0.0001$), and others (COVID-19 group $n = 7$, 0.9% vs. control group $n = 18$, 2.4%, $p = 0.041$). No pregnancy-related maternal complications were seen in 612 (81.2%) and 571 (75.2%) for the COVID-19 group and control groups, respectively, $p = 0.003$ (Fig. 4).

Non-Pregnancy-Related Maternal Comorbidities

Maternal obesity, defined as BMI >25 kg/m^2 (COVID-19 group $n = 5$, 0.7% vs. control group $n = 10$, 1.3%, $p = 0.29$), maternal age above 35 years (COVID-19 group $n = 115$, 15.4% vs. control $n = 105$, 13.8%, $p = 0.43$), pre-existing diabetes (COVID-19 group $n = 24$, 3.2% vs. control $n = 32$, 4.2%, $p = 0.37$), chronic hypertension

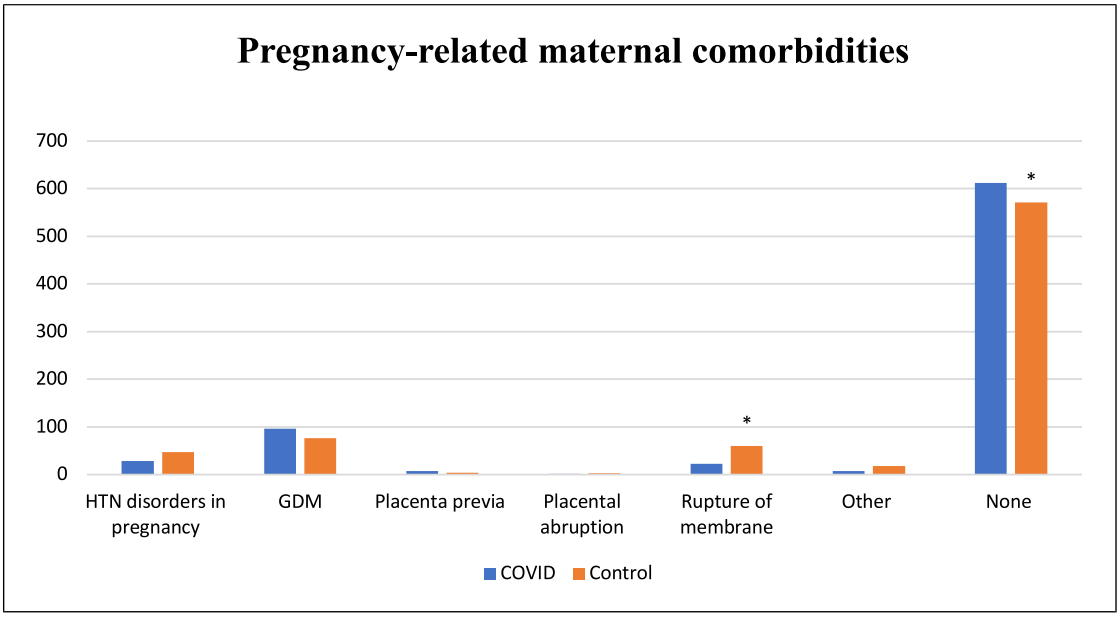

Fig. 4. Graph depicting pregnancy-related maternal comorbidities in COVID and control groups. *Indicates statistically significant *p* values.

(COVID-19 group $n = 13$, 1.9% vs. control group $n = 12$, 1.6%, $p = 0.81$), infection (COVID-19 group $n = 4$, 0.5% vs. control group $n = 2$, 0.3%, $p = 0.45$), hematological disorders (COVID-19 group $n = 12$, 1.6% vs. control group $n = 26$, 3.4%, $p = 0.036$), respiratory conditions (COVID-19 group $n = 43$, 5.7% vs. control group $n = 21$, 2.8%, $p = 0.006$), cardiovascular diseases (COVID-19 group $n = 11$, 1.5% vs. control group $n = 3$, 0.4%, $p = 0.003$), and other comorbidities (COVID-19 group $n = 10$, 1.3% vs. control group $n = 8$, 1.1%, $p = 0.64$). No comorbidities were found in 559 (74.6%) and 571 (75.1%) patients from the COVID-19 and control groups, respectively, $p = 0.87$ (Fig. 5).

Vital Signs

The majority of patients were admitted with vital signs within the normal range, 512 patients (67%) and 603 patients (78.8%) from the COVID-19 and control groups, respectively, $p \leq 0.0001$. Hypertension, defined as blood pressure equal to or more than 140/90 mm Hg, was found in 35 patients (4.6%) from the COVID-19 group and 43 patients (5.6%) from the control group, $p = 0.42$. On the other hand, hypotension, defined as blood pressure equal to or less than 90/60 mm Hg, was found in 7 patients (0.9%) from the COVID-19 group and in 3 patients (0.4%) from the control group, $p = 0.22$. Tachycardia, defined as maternal heart rate of more than 100 beats per minute, was found in 159 patients (20.8%) and 118 patients (15.4%) from the COVID-19 and control groups, respectively, $p = 0.008$. Bradycardia, maternal heart rate of less than 60 beats per minute, was found in 2 patients (0.3%) in the COVID-19 group and none of the patients in the control group, $p = 0.25$. Low oxygen saturation, less than 95%, was seen in 23 patients (3%) from the COVID-19 group, and none of the patients from the control group had low oxygen saturation, $p \leq 0.0001$. Fever, body temperature of more than 37.5°C, was seen in 127 patients (16.6%) and 14 patients (1.8%) from the COVID-19 and control groups, respectively, $p \leq 0.0001$ (Fig. 6).

Presenting Symptoms

Upon presentation, most patients admitted were asymptomatic ($n = 405$, 53% vs. $n = 686$, 89.8% in the COVID-19 and control groups, respectively, $p \leq 0.0001$). Fever was more common in the COVID-19 group ($n = 177$, 23%) as compared to the control group ($n = 12$, 1.6%), $p \leq 0.0001$. Dyspnea was also more common in the COVID-19 group ($n = 111$, 27.1%) as compared with the control group ($n = 1$, 0.1%), $p \leq 0.0001$. Chest pain ($n = 28$, 3.7% vs. $n = 1$, 0.1%, $p \leq 0.0001$), headache ($n = 41$, 5.4% vs. $n = 13$, 1.7%, $p = 0.0002$), and gastrointestinal symptoms ($n = 64$, 8.4% vs. $n = 14$, 1.9%, $p \leq 0.0001$) were also more commonly seen with the COVID-19 group. Dry cough was reported by 207 (27.1%) and 9 (1.2%) patients from the COVID-19 and control

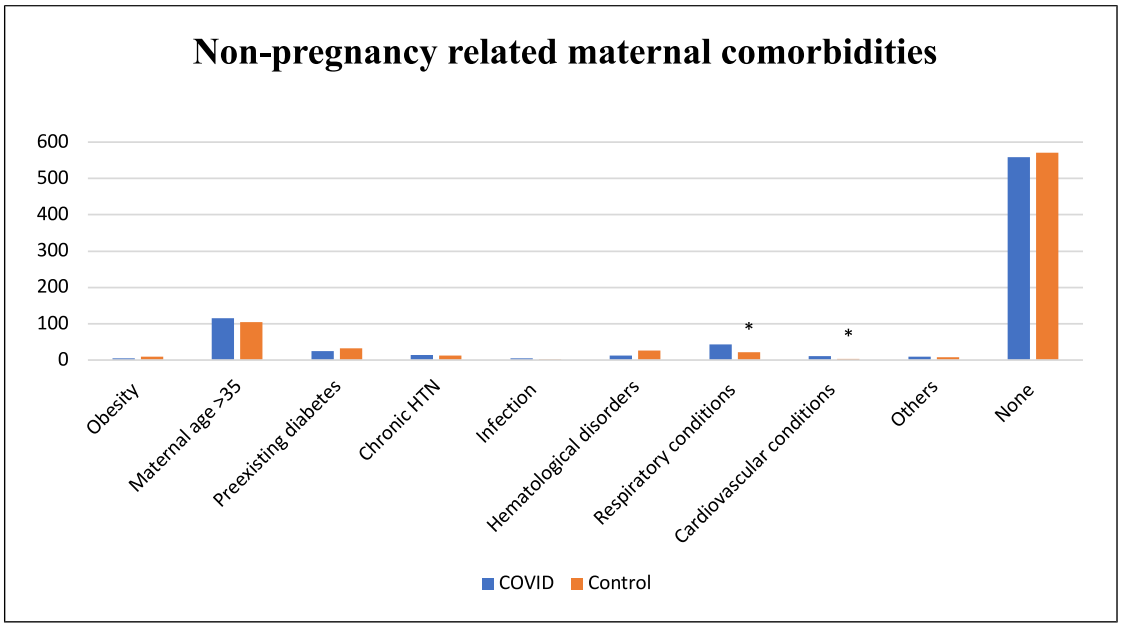

Fig. 5. Graph presenting non-pregnancy-related maternal comorbidities in COVID and control groups. *Indicates statistically significant *p* values.

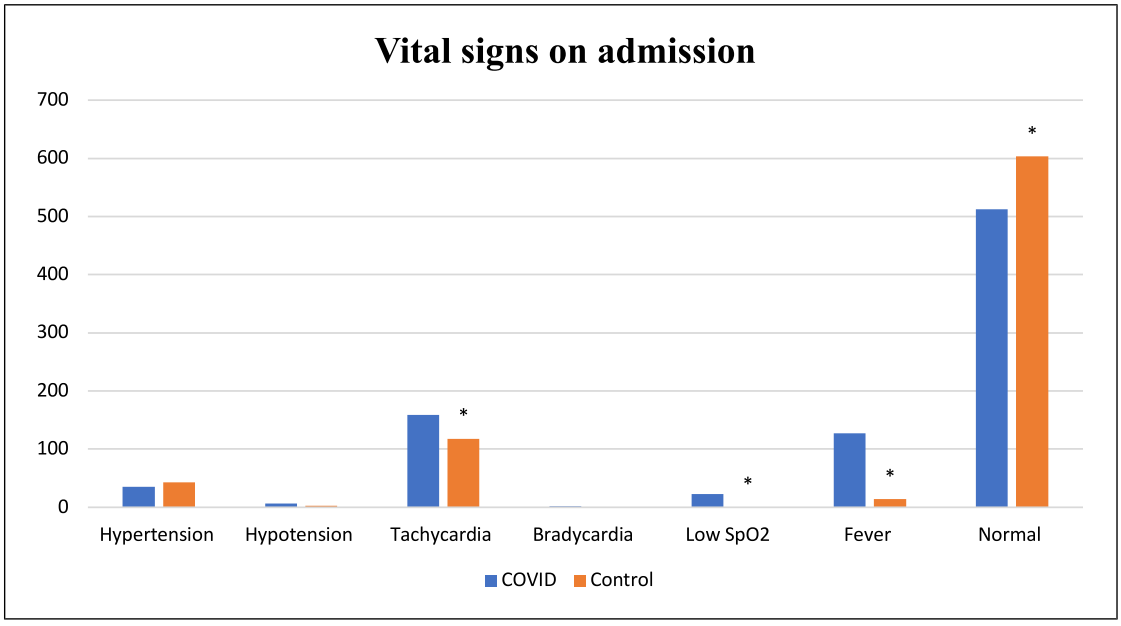

Fig. 6. Graph showing vital signs upon admission for COVID and control groups. *Indicates statistically significant *p* values.

groups, respectively, $p \leq 0.0001$. On the other hand, productive cough was less prevalent and was seen in 9 (1.2%) and 2 (0.3%) patients from the COVID and control groups, respectively, $p = 0.027$ (Table 1).

Laboratory Results

The white blood cell count was elevated in 202 (26.9%) and in 302 (39.9%) patients and decreased in 40 (5.3%) and 5 (0.7%) patients from the COVID-19 and control

Table 1. Presenting symptoms in COVID-19 and control groups

Presenting symptoms	COVID-19 group, *n* (%) (*N* = 764)	Control group, *n* (%) (*N* = 765)	OR (CI)	*p* value
Asymptomatic	405 (53)	686 (89.7)	0.13 (0.10–0.17)	<0.0001*
Dry cough	207 (27.1)	9 (1.2)	31.22 (15.87–61.40)	<0.0001*
Fever	177 (23.2)	12 (1.6)	19 (10.44–34.29)	<0.0001*
Dyspnea	111 (14.5)	1 (0.1)	129.9 (18.07–93.14)	<0.0001*
GI symptoms	64 (8.4)	14 (1.8)	4.90 (2.72–8.82)	<0.0001*
Sore throat	49 (6.4)	3 (0.4)	17.4 (5.40–56.11)	<0.0001*
Myalgia	48 (6.3)	0 (0)	103.6 (6.37–16.9)	<0.0001*
Headache	41 (5.4)	13 (1.7)	3.28 (1.74–6.17)	0.0002*
Chest pain	28 (3.7)	1 (0.1)	29.1 (3.94–21.27)	<0.0001*
Runny nose	21 (2.8)	4 (0.5)	5.37 (1.84–15.74)	0.0005*
Fatigue	19 (2.5)	2 (0.3)	9.73 (2.26–41.93)	0.0001*
Anosmia	15 (2)	0 (0)	31.7 (1.89–53.47)	<0.0001*
Ageusia	11 (1.4)	1 (0.1)	11.2 (1.44–86.70)	0.003*
Productive cough	9 (1.2)	2 (0.3)	4.55 (0.97–21.13)	0.037*
Nasal congestion	6 (0.8)	2 (0.3)	3.02 (0.61–15.02)	0.18

Most patients were asymptomatic upon presentation in both groups. *Statistically significant.

groups, respectively. D-dimer was higher in the COVID-19 group (n = 355, 74.4%) than the control group (n = 3, 21.4%). An elevated C-reactive protein was also more prevalent in the COVID-19 group (n = 289, 70.2%) than the control group (n = 26, 65%) (Table 2).

Fetal Imaging

Fetal imaging findings were obtained for 480 (62.9%) and 390 (51%) patients from the COVID-19 and control groups, respectively. Intrauterine growth restriction/small for gestational age fetuses were seen in 12 (2.6%) from the COVID-19 group as compared to 40 (11%) fetuses from the control group. Oligohydramnios, defined as amniotic fluid index of less than 5 cm or deepest vertical pocket of less than 2 cm, was also more prevalent in the control group (n = 27, 7.1%) than the COVID-19 group (n = 16, 3.4%). Decreased umbilical artery flow by Doppler complicated more pregnancies from the control group (n = 8, 2.2%) than the COVID-19 group (n = 4, 0.9%). Congenital anomalies were found in 5 (1.5%) fetuses from the control group and in only 1 (0.2%) fetus from the COVID-19 group (Table 3).

Maternal Outcomes

Data on maternal outcomes were gathered for 723 (94.6%) patients from the COVID-19 group and 644 (84.2%) patients from the control group. The majority of pregnancies were delivered without adverse outcomes in both groups, 605 (83.9%) and 496 (77%) from the COVID-19 and control groups, respectively, p = 0.002. Preterm labor was seen in 17 (2.4%) patients from the COVID-19 group and 21 (3.3%) patients from the control groups, p = 0.39. Preterm delivery was higher in the control group with 44 (6.8%), and only 33 (4.56%) COVID-19 patients had a preterm delivery, p = 0.08. Missed and incomplete miscarriages were also higher in the control group (59, 9.2% control patients compared to 24, 3.3% COVID-19 group, $p \leq 0.0001$). The number of pregnancies that ended with intrauterine fetal death was equal in both groups, 6 (0.8%) and 6 (0.9%) patients from the COVID-19 and control groups, respectively, p = 1.00. Preeclampsia was higher in the COVID-19 group, 12 (1.7%) patients, when compared to the control group, 9 (1.4%) patients, p = 0.83. The number of patients admitted to the ICU was higher in the COVID-19 group, 12 (1.7%) patients, than the control group, 2 (0.3%) patients, p = 0.0006. There were no maternal deaths in either group (Table 4).

Mode of Delivery

A total number of 440 (57.6%) patients were delivered from the COVID-19 group and 637 (83.3%) patients from the control group. Spontaneous vaginal deliveries accounted for 210 (47.7%) and 416 (65.3%) from the total number of deliveries from the COVID-19 and control groups, respectively ($p \leq 0.0001$). CS was higher among the COVID-19 group (224 [51%] patients than the control group, compared to 197 [31%] patients, [$p \leq 0.0001$]). Six (1.4%) patients had an assisted vaginal delivery from the COVID-19 group and 24 (3.8%) patients from the control group (p = 0.022) (Fig. 7).

Table 2. Laboratory results in COVID-19 and control groups

Parameters	COVID-19 group			Control group			*p* value
	low, *n* (%)	normal, *n* (%)	high, *n* (%)	low, *n* (%)	normal, *n* (%)	high, *n* (%)	
WBC	40 (5.3)	510 (67.8)	202 (26.9)	5 (0.7)	450 (59.5)	302 (39.9)	0.001
Lymphocytes	240 (32)	494 (65.8)	17 (2.3)	82 (11)	649 (87.2)	13 (1.8)	<0.0001
Neutrophils	21 (2.8)	421 (56.1)	310 (41.3)	4 (0.5)	441 (59.5)	296 (40)	0.40
Eosinophils	454 (60.8)	288 (38.6)	5 (0.7)	283 (38.5)	447 (60.8)	5 (0.7)	<0.0001
Platelets	65 (8.8)	668 (89.9)	10 (1.4)	57 (7.6)	689 (91.4)	8 (1.1)	0.18
INR	12 (1.7)	695 (95.7)	19 (2.6)	6 (0.8)	699 (95.1)	30 (4.1)	0.95
PT	106 (14.5)	576 (79)	48 (6.6)	10 (1.4)	686 (93.6)	37 (5.1)	<0.0001
APTT	25 (3.5)	628 (86.6)	72 (9.9)	19 (2.6)	689 (93.6)	28 (3.8)	<0.0001
Fibrinogen	2 (1.6)	72 (57.1)	52 (41.3)	0 (0)	55 (53.9)	47 (46.1)	0.13
D-dimer	4 (0.8)	119 (25)	355 (74.4)	0 (0)	11 (78.6)	3 (21.4)	<0.0001
Ferritin	38 (14.5)	192 (73.3)	32 (12.2)	0 (0)	15 (100)	0 (0)	<0.0001
LDH	1 (0.2)	226 (61.9)	164 (38.1)	0 (0)	20 (80)	5 (20)	<0.0001
CRP	0 (0)	123 (29.9)	289 (70.2)	0 (0)	14 (35)	26 (65)	<0.0001
Troponin	5 (4)	114 (84.4)	16 (11.9)	0 (0)	9 (90)	1 (10)	<0.0001
ALT	49 (7.1)	588 (84.6)	58 (8.4)	223 (30.9)	488 (67.6)	11 (1.5)	<0.0001

p values were calculated for the percentage of normal results.

Table 3. Imaging findings in COVID-19 and control groups

Parameters	COVID-19 group, *n* (%), (*N* = 480)	Control group, *n* (%), (*N* = 390)	*p* value
X-ray/CT chest positive findings	18 (6.3)	0 (0)	<0.0001
Oligohydramnios	16 (3.4)	27 (7.1)	0.02
IUGR/SGA	12 (2.6)	40 (10.5)	<0.0001
Abnormal placental location±implantation	9 (2)	3 (0.9)	0.24
Abnormal Doppler	4 (0.9)	9 (2.3)	0.09
SCH	3 (0.7)	7 (1.9)	0.12
Polyhydramnios	2 (0.4)	4 (1.1)	0.42
LGA	1 (0.2)	4 (1.1)	0.18
Congenital anomaly	1 (0.2)	5 (1.5)	0.09

IUGR, intrauterine growth restriction; SGA, small for gestational age; SCH, subchorionic hematoma; LGA, large for gestational age; UMA, umbilical artery Doppler.

Discussion

This is a retrospective study describing the clinical characteristics and maternal outcomes of COVID-19-infected pregnant women with noninfected pregnant women. During the COVID-19 pandemic, most of the cases in Kuwait were admitted to Al Jahra Hospital as it was a designated COVID-19 center. Jaber Al Ahmad Hospital also received only COVID-19 patients [4].

In this study, maternal comorbidities were identified in both COVID-19 and control groups. Hypertensive disorders in pregnancy were recognized more in the control group (6.2%) compared to the COVID-19 group (2.3%). In contrast, gestational diabetes was found to be higher in the COVID-19 group (12.7%) compared to the control group (10%). This finding is in accordance with a study done by Zanardo et al. [5], which identified an association between gestational diabetes and COVID-19, with 13.5% of pregnant women with COVID-19 having gestational diabetes compared to (9%) control group.

The majority (90%) of patients in both groups were 21–30 years old with only 5% more in the COVID-19 group being 31–40 years old. Regarding gestational age, most of the patients were in their third trimester. However, the number of second trimester pregnant patients was higher in the COVID-19 group (117, 15.3%)

Table 4. Maternal outcomes in COVID-19 and control groups

Maternal outcomes	COVID-19 group, *n* (%) total *N* = 723	Control group, *n* (%) total *N* = 644	OR (CI)	*p* value
None	605 (83.7)	496 (77)	1.53 (1.16–2.00)	0.002*
APH	9 (1.2)	8 (1.2)	1.00 (0.38–2.61)	1.00
Primary PPH	5 (0.7)	5 (0.8)	0.90 (0.26–3.08)	1.00
Preterm labor	17 (2.4)	21 (3.3)	0.71 (0.37–1.37)	0.39
Preterm delivery	33 (4.6)	44 (6.8)	0.65 (0.41–1.03)	0.08
Threatened miscarriage	3 (0.4)	9 (1.4)	0.29 (0.8–1.09)	0.078
Missed, incomplete miscarriage	24 (3.3)	59 (9.2)	0.34 (0.21–0.55)	<0.0001*
IUFD	6 (0.8)	6 (0.9)	0.89 (0.29–2.77)	1.00
Cardiac disease	2 (0.3)	0 (0)	4.47 (0.21–93.28)	0.50
Preeclampsia	12 (1.7)	9 (1.4)	1.19 (0.49–2.85)	0.83
Gestational HTN	4 (0.6)	1 (0.2)	3.58 (0.39–32.11)	0.38
Respiratory	9 (1.2)	1 (0.2)	8.11 (1.02–64.18)	0.02*
MOF	2 (0.3)	0 (0)	4.46 (0.21–93.28)	0.50
Sepsis	1 (0.1)	0 (0)	2.68 (0.11–65.86)	1.00
VTE	1 (0.1)	0 (0)	2.67 (0.11–65.86)	1.00
ICU admission	12 (1.7)	2 (0.3)	22.65 (1.34–38.5)	0.0006*
Maternal death	0 (0)	0 (0)	–	–
Others	8 (1.1)	5 (0.8)	1.43 (0.47–4.39)	0.59

APH, antepartum hemorrhage; PPH, postpartum hemorrhage; IUFD, intrauterine fetal death; MOF, multi-organ failure; VTE, venous thromboembolism; ICU, intensive care unit. *Statistically significant.

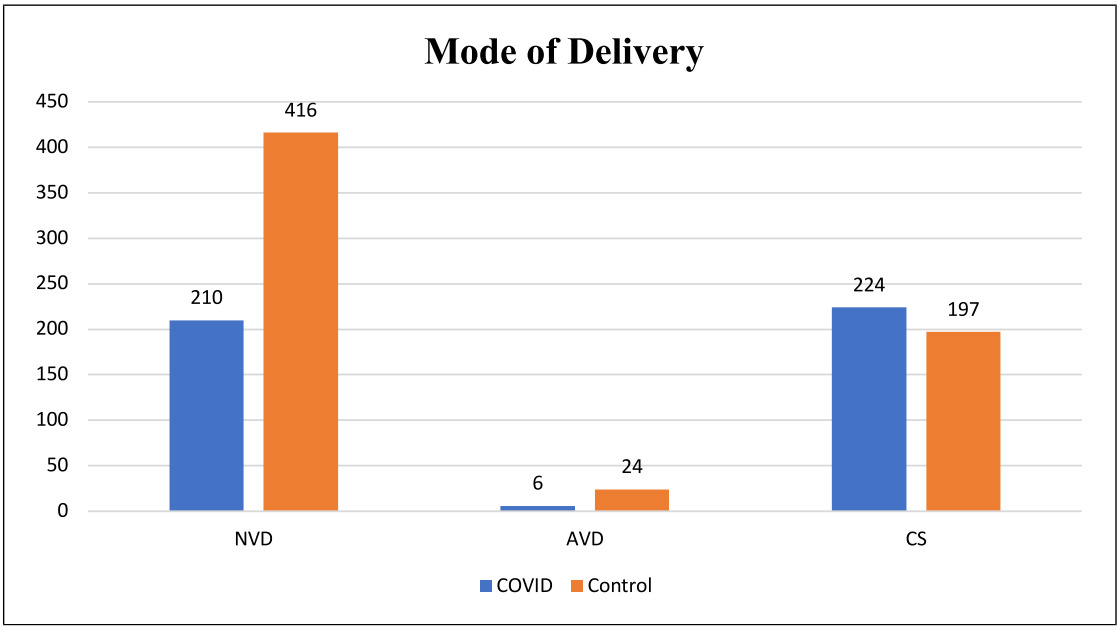

Fig. 7. Graph demonstrating mode of delivery for COVID and control groups.

compared to the control group. This is similar to the finding of a prospective cohort study using UK Obstetric Surveillance System (UKOSS) in which most women were admitted in late second or third trimester of pregnancy [2].

Respiratory conditions were noted more frequently in pregnant patients with COVID-19 (5.7%) in comparison to the control group (2.8%). Likewise, cardiovascular conditions were found to be greater in the COVID-19 group (11 cases) compared to the control group (three cases). One study reported that asthma was the most common risk factor associated with pregnant women infected with COVID-19 [6].

Vital Signs

We noted that pregnant patients with COVID-19 mostly presented with normal vital signs. The blood pressure was lower in the COVID-19 group, and maternal pulse was found to be higher in the COVID-19 group when compared to controls. Tug et al. [7] found that tachycardia was significantly more frequent in infected pregnant women compared to nonpregnant women (16% vs. 1.9%, respectively). Low oxygen saturation was noted in the COVID-19 group (3%). COVID-19 in pregnant women was found to be associated with the need for oxygen support and hence ICU admission [7]. In our study, 16.6% of COVID-19 patients had fever. A retrospective national-based analysis reported that 58% of infected cases presented with fever [2].

Clinical Manifestations

In our study, most pregnant patients with COVID-19 presented to the emergency department without symptoms (53%). This is supported by another study, which showed that almost three-quarters of pregnant women with COVID-19 were asymptomatic when compared to the nonpregnant counterparts [8]. Moreover, another study showed that the majority of pregnant women with COVID-19 infection (88.6%) were asymptomatic at the time of diagnosis [2]. Regarding patients who presented with symptoms, the most dominant symptoms in the COVID-19 group were dry cough (27.1%), fever (23.2%), and dyspnea (14.5%). Several other studies have reported similar findings [8–11].

Laboratory Tests

Despite the occurrence of leukocytosis and neutrophilia in both control and COVID-19 groups in almost similar proportions, low levels of lymphocytes and eosinophils were observed in the COVID-19 group. In addition, elevated levels of D-dimer and CRP were also observed. Eosinopenia has been reported to be associated with severe COVID-19 disease [12]. In addition, lymphocytopenia, elevated CRP, and elevated D-dimer have been reported in other studies [13, 14].

Fetal Imaging

Contrary to our expectations, the rate of IUGR/SGA, OH, abnormal fetal Doppler studies, and congenital anomalies were notably higher in the control group. This leads us to conclude that COVID-19 is not associated with adverse fetal outcome, as reported earlier [15]. A meta-analysis published estimates of the low incidence of IUGR (2.6%) in women infected with COVID-19 [16].

Maternal Outcomes

The majority of the COVID-19 patients had uneventful pregnancies without adverse maternal outcomes. Contrary to the published literature [17, 18], the rate of preterm labor and birth and miscarriages were all lower in the COVID-19 group, suggesting that COVID-19 has no significant impact on pregnancies. Other studies published in the literature confirm our findings [2, 19]. In contrast, respiratory complications and ICU admissions were significantly higher in the COVID-19 group because ultimately COVID-19 is a respiratory disease associated with high rates of ARDS and need for mechanical ventilation or ECMO [13, 17, 20].

Mode of Delivery

Significantly less vaginal deliveries and higher rates of CS were seen in the COVID-19 group. Majority of the CS were performed for obstetric indications. This was contrary to the published literature that higher rates of CS were observed in the COVID-19 pandemic due to maternal reasons [17, 18]. Vertical transmission was one of the leading concerns for CS; however, multiple studies published confirmed that the mode of delivery had no effect on vertical transmission nor the mortality rate on the mothers or the neonates [18, 21, 22]. The high rate of CS in our cohort may reflect an inherent high rate of CS in the general obstetrical population, in addition to higher rates of high-risk pregnancies requiring CS such as placenta previa.

COVID-19 virus is surrounded by a phospholipid bilayer membrane, which plays a crucial role in viral life cycle. It has been proposed that viral infection interferes with lipid metabolism and this includes the fusion of viral membrane to the host cell, replication, endocytosis, and exocytosis. Studies have shown that viral entry and replication could be blocked by targeting membrane lipid metabolism [23]. Multiple studies demonstrated

the role of statins in targeting and treating different infections [24]. Statins have the potential to suppress coronavirus infection, as shown in other viruses where cholesterol-lowering agents interfere with lipid composition and metabolism [24]. Other studies reported the beneficial effect of statin in reducing infection, the frequency of mortality related to infections and ventilator-associated pneumonia, and increasing the survival rates [25, 26]. Until now, no effective drug for SARS-CoV-2 has been made available except for supportive therapy. Therefore, more research needs to be focused on the viral life cycle in order to allow the identification of new drug targets.

Conclusions

COVID-19 infection has a negative impact on pregnant women. The majority were diagnosed during the third trimester. Most patients were asymptomatic, and if symptomatic, dry cough and fever were the most common presenting complaints with tachycardia being the most frequent sign. ICU admission and respiratory failure were significantly higher in the COVID-19 group. The rate of Caesarian section was higher in the COVID-19 group, with obstetric and maternal complications being the most common indications in comparison to fetal indications in controls.

Statement of Ethics

The study was approved by the Institutional Ethics Committee of the Ministry of Health of Kuwait (2020/1494).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Dr. Zahraa Akbar, Dr. Eman Al Azmi, Dr. Khalid AlMuzayen, Dr. Eelaf Husain, and Dr. Mariam Aldarweesh: data collection and manuscript preparation; Dr. Zahraa Akbar: submission and revision of the manuscript; Dr. Fatemah Alhadhoud: obtaining ethics approval and writing; and Dr. Jehad Al Harmi: revision of the manuscript content and publication.

Data Availability Statement

Data generated or analyzed during this study are included in this article and its supplementary material files. Further inquiries can be directed to the corresponding author.

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