

Effects of COVID-19 Infection on the Fetus

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ABSTRACT

Objectives: The aim of this study is to evaluate the effects of COVID-19 infection on fetal Doppler indices and ultrasound parameters in women confirmed with the infection.

Methods and Materials: This retrospective case-control study was conducted at Queen Alia Hospital, Amman, Jordan, between January 1 and March .2022 ,31 Eighty pregnant women confirmed with the COVID-19 infection were compared to eighty pregnant women who were negative .Foetalbiometry ,fetal anomaly scan, amniotic fluid index, umbilical artery Doppler, middle cerebral artery Doppler ,and cerebro-placental ratio were investigated and compared between the groups.

Results: A total of 160 patients were evaluated in this study. 80 confirmed Covid-19 cases were matched to 80 controls and ultrasound findings were compared. There was no increase in the risk of SGA (P = 0.99), oligohydramnios (P = 0.99), polyhydramnios (P = 0.99), anomalies (P = 0.99), or IUFD. There was no difference between both groups regarding UA-PI (P = 0.62), MCA-PI (P = 0.65), or CPR (P = 0.109). No significant differences were found between the positive and negative groups regarding fetal biometry and fetal Doppler parameters.

Conclusion: COVID-19 infection during pregnancy seems to have no impact on fetal well-being.

Keywords : COVID ,19-pregnancy ,fetal Doppler

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Introduction

COVID 19-was declared a pandemic by the WHO on March 11, 2020, and has become the most serious medical issue of the modern era in a short time .The prevalence of COVID-19 among pregnant women has been reported to be ⁽¹⁾ %10 Physiological and immunological changes in pregnancy increase susceptibility to infections in general and respiratory infections in particular. Pregnant women are at an increased risk of developing severe diseases if they are infected compared to nonpregnant women of a similar age ⁽²⁾ The hematologic and pulmonary effects of COVID 19-might affect maternal and fetal circulation with the added risk of the hypercoagulable state of pregnancy ⁽³⁾ Decreased maternal oxygen saturation, cytokine storm, and placental thrombosis contribute to possible obstetric complications that have been reported among pregnant women with COVID 19-infection, such as IUGR and stillbirth ⁽⁴⁾ In this study ,our aim was to investigate the relationship between COVID 19-infection and possible fetal consequences by ultrasound examination and Doppler parameters.

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Methods

This was a retrospective case-control study conducted in the obstetrics and gynecology department of Queen Alia Hospital, Amman, Jordan, between January 1 and March 31, 2022. The positive cases included in this study (80 women) were either patients who were admitted for delivery and tested positive for COVID-19 or who were admitted due to symptomatic infection. 47 patients (59%) were asymptomatic or 33 patients (41%) were symptomatic. All patients were diagnosed by polymerase chain reaction using nasopharyngeal swabs. The control group patients (80 women) were recruited from the antenatal care clinic at Queen Alia Hospital, where a rapid antigen test was performed on all patients prior to ultrasound examination. Inclusion criteria: maternal age 18–44 years, gestational age 24–40 weeks, and singleton pregnancy. Exclusion criteria: severe cases of COVID-19 infection that required intensive care unit (ICU) admission, multiple gestations, patients known to have fetal anomalies prior to the study, and patients receiving medications that may affect the fetus, such as anti-epileptics.

Fetal biometry, amniotic fluid index (AFI), and Doppler studies were performed on all patients by a fetal medicine specialist following the guidelines of the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG)⁽⁵⁾. An ultrasound examination was done as soon as the infection was confirmed. Sonographic parameters: Biparietal diameter (BPD), head circumference (HC), femur length (FL), and abdominal circumference (AC) were used to estimate the fetal weight. An estimated fetal weight (EFWT) < 10th percentile for gestational age was considered as small for gestational age (SGA). An AFI < 5 or > 25 was considered abnormal.

Doppler velocimetry included umbilical artery Doppler (UAD), middle cerebral artery Doppler (MAD), and cerebroplacental ratio (CPR). The umbilical artery pulsatility index (UA-PI) > 95th percentile for gestational age was considered abnormal. The middle cerebral artery pulsatility index (MCA-PI) and CPR < 5th percentile for gestational age were considered abnormal⁽⁶⁾.

Co-morbidities (DM, HTN, hypothyroidism, anemia, and asthma) were reported and compared between both groups.

Data were analyzed statistically using SPSS software. Measured variables were expressed as mean ± standard deviation or as a percentage. The statistical significance of the variables was tested using the P-value. P-values were considered significant only if they were less than 0.05.

Ethical approval was obtained from the ethical committee of Royal Medical Services before starting the study.

Results

Data collected from 80 positive cases and 80 negative controls were analyzed and compared.

The clinical characteristics of the patients are shown in Table I.

Table I: Clinical characteristics of the patients

Characteristic	Positive (n=80)		Negative (n=80)		Mean Difference	P Value
	Mean	Std. Deviation	Mean	Std. Deviation		
Age	29.55	5.61	30.46	5.53	0.912	0.302
Parity	2.99	1.56	2.65	1.59	-0.338	0.178
GA at u/s exam	32.75	3.83	29.79	3.55	-2.963	0.000

According to the independent sample T-test

The mean age in the positive group was 29.55 years compared to 30.46 years in the negative group (P=0.302). The mean parity in the positive group was 2.99 compared to 2.65 in the negative group (P=0.178). Gestational age at ultrasound examination was higher in the positive group (32.75 weeks compared to 29.79 weeks in the negative group), P=0.000.

The associated co-morbidities are shown in Table II.

Table II: Associated Morbidities

Characteristic	Positive (n=80)		Negative (n=80)		P Value
	Count	Percentage	Count	Percentage	
DM	13	16.3%	11	13.8%	0.825
HTN	10	12.5%	9	11.3%	0.999
Hypothyroidism	3	3.8%	2	2.5%	0.999
Anemia	12	15.0%	11	13.8%	0.999
Asthma (or other respiratory diseases)	3	3.8%	1	1.3%	0.620

According to the Chi-squared test

The prevalence of DM was higher in the positive group (16.3%) compared to (13.8%) in the negative group but not significant, P= 0.825. Prevalence of HTN wasn't significantly different between positive patients (12.5%) and controls (11.3%), P= 0.999. 3.8% of positive patients had Hypothyroidism compared to 2.5% in the negative group, P = 0.999. Anemia was comparable

between positive and negative groups (15%, 13.8%) respectively, $P = 0.999$. Respiratory diseases were more prevalent in the positive group (3.8%) compared to (1.3%) in the negative group, $P = 0.62$ but not statistically significant.

Doppler indices are shown in Table III.

Table III: Doppler indices.

Characteristic	Positive (n=80)		Negative (n=80)		Mean Difference	P Value
	Mean	Std. Deviation	Mean	Std. Deviation		
UA_PI	1.06	0.16	1.05	0.16	-0.013	0.628
MCA_PI	1.50	0.24	1.48	0.22	-0.016	0.654
CPR	1.45	0.32	1.45	0.33	0.007	0.900
AFI	13.84	4.32	13.36	4.39	-0.489	0.479

UA-PI: uterine artery pulsatility index

MCA -PI: pulsatility index

CPR: Cerebroplacental ratio

AFI: Amniotic fluid index

According to the independent sample T-test

The mean UA-PI was 1.06 in the positive group compared to 1.05 in the controls, $P = 0.628$. And the mean MCA-PI was 1.5 in the positive group and 1.48 in the negative group, $P = 0.654$. No difference in CPR between both groups (1.45, 1.45) respectively, $P = 0.900$.

Ultrasound Findings are shown in Table IV.

Table IV: Ultrasound findings

Characteristic	Positive (n=80)		Negative (n=80)		P Value
	Count	Percentage	Count	Percentage	
SGA	3	3.8%	2	2.5%	0.999
Oligohydraminos	3	3.8%	2	2.5%	0.999
Polyhydraminos	1	1.3%	2	2.5%	0.999
IUFD	0	0.0%	0	0.0%	-

According to the Chi-squared test

Three cases of SGA were encountered in the positive group (3.8%); two of them were associated with pre-eclampsia toxemia and were managed according to obstetric protocols. The third case was an isolated SGA with normal AFI and Doppler studies. Two cases of SGA were encountered in the negative group (2.5%), $P = 0.999$.

Three cases of oligohydramnios were encountered in the positive group (3.8%); one for a case of preterm premature rupture of membrane (PPROM) and two cases were associated with hypertensive disorders of pregnancy. Two cases of oligohydramnios were encountered in the negative group (2.5%), $P = 0.999$.

One case of polyhydramnios in the positive group (%1.3) was associated with uncontrolled DM. Two cases of polyhydramnios in the negative group, (%2.5) $P.0.999 =$

No cases of IUFD were found in both groups.

Discussion

This study was conducted to address the possible consequences of COVID-19 infection on fetal well-being. After analyzing our data, we found that both positive and negative groups were comparable in all parameters with no significant differences except in the gestational age which is considered a limitation of this study.

E. Soto-Torres et al in a retrospective case-control study released in Jul 2021 showed that no significant differences in fetal ultrasound and Doppler findings between pregnant women who were positive for Covid-19 and the controls ⁽⁷⁾.

Another study that was published in the International Journal of Medical Sciences in Jan 2021 by Chiu-Lin Wang et al concluded that Covid-19 infection in pregnant women doesn't increase the risk of intrauterine deaths or IUGR ⁽⁸⁾.

However, Shu Qin Wei et al in a systematic review published in Canadian Medical Association Journal in April 2021 showed that Covid-19 infection in pregnancy was associated with low birth weight and increased risk of preeclampsia and other adverse pregnancy outcomes ⁽⁹⁾.

Another study by Vincenzo Berghella published in the American Journal of Obstetrics and Gynecology in Nov 2020 showed that in-utero transmission is rare and rates of miscarriages and congenital anomalies are not increased in pregnancies affected by Covid-19, and the neonatal outcome is generally good ⁽¹⁰⁾.

Mehreen et al in a systematic review published in April 2020 found that one of 75 newborns tested was positive for Covid-19 but this baby did well clinically ⁽¹¹⁾.

Currently, there is not enough evidence of vertical transmission of the COVID 19-virus during pregnancy. ⁽¹²⁾ Apart from the vertical transmission of the disease, excessive inflammation, vascular injury, and impaired perfusion may affect the fetomaternal circulation in the absence of direct fetal infection. Histopathological examination of the placentae obtained from COVID-19-positive women showed an increased prevalence of microcalcification and fibrin thrombi, which may reflect an underlying hypercoagulable state induced by the infection. ⁽¹³⁾ Pathological processes that interact with the vascular structure of the placenta and maternal hypoxia have been reported to cause impaired Doppler findings. Placental endothelial injury and hypoxemia cause high resistance in fetal circulation, which can be measured non-invasively by Doppler indices. ^(15,14)

Despite our initial assumption, we didn't find significant differences in UA-PI, MCA-PI, and CPR between both groups. COVID 19-infection may affect the microscopic structures of the placenta without clinical significance. However, more studies are needed to confirm these findings

Conclusion

According to our results, there were no significant differences in fetal ultrasound findings and fetal Doppler indices between positive and negative pregnant women. COVID-19 infection seems to have no adverse effects on fetal well-being. However, the full impact of infection on pregnancy remains to be determined by further studies.

Limitations of this study are the small number of cases and the difference in the gestational age between both groups. Also, the ultrasound examination was done soon after the infection so the study evaluates only the immediate changes of Covid-19 on the amniotic fluid and fetal Doppler's.

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