The Association Between COVID-19 Infection and Preterm Complications in Salah Al-Din General Hospital

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Abstract

Background: The release of inflammatory cytokines is considered to have a role in COVID-19's pathogenesis. However, irregularities in the formation of blood clots may have also had a role in the fatal outcome Aim: To determine if COVID-19 infection is linked to preterm birth, premature membrane rupture, admission to the neonatal intensive care unit, stillbirth, placental abruption, or maternal mortality. Patients and methods: In the months between October 2021 and March 2022, researchers in the Department of Gynecology and Obstetrics at the Salah Al-din Teaching Hospital in the Iraqi province of Salah Al-din conducted a cross-sectional study. Women who presented to the Gynecology and Obstetrics Department with symptoms suggesting a COVID 19 infection and premature birth difficulties made for a convenient sample. Fifty females participated in the research. Characteristics of the participants were reported as both raw numbers and percentages. The Chi-square test and Fisher's exact test were used to evaluate the differences in clinical features and complications between the infected and healthy pregnant women groups. For statistical significance, a p value of less than 0.05 was used. Results: Fifty pregnant patients were evaluated during the study. There were 17 (34.6%) confirmed cases of COVID-19 infection and 33 (66.6%) cases where the RT-PCR result was negative. Statistically, both IgG and IgM were significant (p 0.05). Participants averaged 33.06 years old (7.43). Significant statistical correlation between older age group and exposure to the virus, with the majority of cases occurring in the age range (35-49 years). There is no clear correlation between the mother's health and COVID-19 infection. Fatigue (90%), dyspnea (80%), cough (70%), headache (64%), sore throat (40%) and a loss of taste and smell (26%), were the next most prevalent symptoms after fever. Fever, dyspnea, and a loss of taste and smell were significantly correlated with the group that was exposed to the disease. C-reactive protein, E-selectin, and S. ferritin are all significantly correlated with COVID-19 infection exposure (p values 0.05). Most of the pregnant women in the study had normal levels of both platelets and white blood cells, with 90% and 60%, respectively, having normal Plt and WBC. Approximately 52% of the pregnant women in the study gave birth to premature babies, with a mean gestational age (GA) of 31 weeks + 2 days. A strong correlation between a maternal history of GDM and increased S. Ferritin and premature births exposed to COVID-19 was discovered. Significant correlation was established between premature vaginal delivery and exposure to COVID-19, with 16 instances (32% of total) compared to 10 cases (20% of total). Statistics also show that there was a considerable increase in the rate of preterm prolabor membrane rupture (PPROM) from the previous term, with 19 instances (38%). Occurrences of obstetric problems such as antepartum haemorrhage (APH) and severe postpartum haemorrhage (PPH) were documented, although there was no statistically significant link between them (p value > 0.05). However, the incidence of these side effects is greater in COVID-19 patients than in those who were not exposed to the virus. There were no maternal deaths observed, however the rate of stillbirths was significantly greater among individuals with COVID-19 compared to those who had not been exposed during pregnancy. Babies of mothers infected with COVID-19 are more likely to be admitted to the Neonatal Intensive Care Unit (NICU) for care than those of moms without the virus.Pregnant women with COVID-19 are at increased risk for premature delivery and preterm prelabor rupture of membranes, and the condition also affects NICU admissions. The aim of our study was to determine if COVID-19 infection is linked to preterm birth, premature membrane rupture, admission to the neonatal intensive care unit, stillbirth, placental abruption, or maternal mortality.

Keywords: COVID-19; preterm birth; premature membrane rupture; stillbirth; placental abruption.

1. Introduction

COVID19 is the term given to the sickness caused by the severe acute respiratory syndrome coronavirus 2 (SARSCoV2) (1). By the end of the year 2021, the global total of confirmed cases is expected to reach

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262,430,000, with over 5,204,683 fatalities. Several instances of pneumonia with an unknown origin were reported in December 2019 in Wuhan City, and the WHO China regional office was notified. The World Health Organization (WHO) designated the COVID19 outbreak a public health emergency of worldwide concern on January 30, 2020. SARS-CoV-2 is the third coronavirus to cause serious illness in humans and spread globally in the last two decades (1). In a previous study published in the American Journal of Obstetrics and Gynecology. Young et al. found that IL-6, IL-12, IFN-, and TNF levels in the maternal sera were elevated during uncomplicated pregnancies compared to nonpregnant controls, with IL12 levels remaining elevated into the postpartum period (2,3). Women who are already physiologically fragile due to pregnancy may be even more at risk when IL-6 levels rise in SARS-CoV-2 infection. Given this context, one could wonder whether COVID19 has any harmful effects during pregnancy. We hypothesised that exposure to COVID19 during pregnancy would increase infection-related obstetric morbidity due to an inflammatory body response, such as preterm birth and premature prelabour rupture of membranes, which would lead to an increase in NICU admissions, stillbirths, placental abruption due to a drop in serum fibrinogen and platelet levels, and maternal mortality (4,5,6) The aim of this study was to determine if COVID-19 infection is linked to preterm birth, premature membrane rupture, admission to the neonatal intensive care unit, stillbirth, placental abruption, or maternal mortality.

2. Patients and Methods

Cross-sectional study was done From October 2021 to March 2022, researchers from the Department of Gynecology and Obstetrics at the Salah Al-Din Teaching Hospital in the Iraqi province of Tikrit. This study included a convenience sample of pregnant women who reported to the Gynecology and Obstetrics Department with symptoms that would indicate a COVID-19 infection and its associated preterm problems. Fifty women participated overall in the research. Information was gathered through questionnaires, in-person interviews, and medical history, examination, and test findings. Women aged 18-49 who were pregnant and who's nasopharyngeal and/or oropharyngeal swabs were positive for SARSCoV2 were included. The gestational age ranged from 24 weeks to 36 weeks+6 days. Specifically, with symptoms consistent with COVID-19. Rejection happened if the patient had history of preterm labour in previous pregnancies, known case of cervical incompetence, she used a pessary or cerculage, or she didn't want to get checked out. The Gynecology and Obstetrics department of the College of Medicine at Tikrit University made this questionnaire after looking at papers from the past. It was then revised by the department's supervisors and an expert panel. In the first part: factors like age, number of births, and smoking status were taken into account. Second part: Preexisting conditions, such as diabetes, hypertension, chronic heart failure, chronic obstructive pulmonary disease (COPD), chronic renal disease, liver illness, and medication use. In the third section, we talked about current obstetrical history. We talked about things like GDm, PIH, multiple pregnancies, IVF, IUGR, and stillbirth. In the fourth section, we looked at the patient's clinical signs, which included things like temperature, cough, sore throat, headache, exhaustion, myalgia, dyspnea, diarrhoea, a lack of taste or smell, and examination findings like oxygen saturation (SPO2) and respiratory rate (RR). Real-time polymerase chain reaction (RT-PCR), haemoglobin (Hg), serum ferritin, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), platelet count, white blood cell count, immunoglobulin (Ig) G, immunoglobulin (Ig) M, and D-dimer were all tested in the lab. Describing obstetrical outcome, gestational age (GA), type of preterm delivery, premature prelabour rupture of membrane (PPROM) , and obesity were all factors in the sixth section.Intrauterine growth restriction (IUGR), preeclampsia (PE), antepartum haemorrhage (APH), and severe preeclampsia are all complications that may arise during pregnancy and childbirth. The seventh focused on newborn outcomes such as APGAR scores, NICU stays, and stillbirths. Mild, moderate, and severe cases of COVID19 infection were defined according to WHO criteria. The presence of respiratory symptoms without evidence of pneumonia or hypoxia is characteristic of a mild COVID-19 infection, whereas the presence of such evidence is characteristic of a moderate or severe infection. Moderate cases were those with a SpO2 of 90% on room air, and severe cases were those with a breathing rate of more than 30 breaths per minute or a SpO2 of 90% on oxygen supplementation (6,7).

3. Results

Mean age of the participants 33.06 years (±7.43). Most of them 20 case (40%) in the age group (35-49) years, and 10 cases from this (58.8%) were infected with COVID-19. Preterm prelabour rupture of membranes (PPROM) reported in 19 cases (38%), 10 cases (58.82) were among diseased group and statistically significant, p value of 0.029. Obestetrical complications like antepartum haemorrhage (APH), severe PE, were recorded during the study, 4 (8%) , 5 (10%) respectively , without significant association (p value > 0.05) . But these complications being higher in patients with COVID-19 than in the non-exposed ones (11.76% vs 6.06%, p=0.481) and (11.76% vs 9.09%, p=0.765).

As shown in the Table 1, significant statistical association between the older age group and exposure to the infection, p value =0.002.

Regarding maternal comorbidities, medical history with pulmonary disease in 12 case (24%) , 10 cases (2%) were asthmatic and 2 cases (4%) with COPD (chronic bronchitis) , while obesity (BMI >30) reported in 6 cases (12%) , Dm in 4 cases (8%) ,

without significant association with COVID-19 infection (p value 0.955 , 0.378 , 0.071 respectively) . Obstetrical history of GDm found in 15 case (30%), 5 cases (29.4) were infected , without statistical association , Table 1.

Table 3.1 Patient demographic characteristics, comorbidities and current obstetric history in a pregnancy cohort screened for COVID-19.

Maternal characteristic	Total No =50	%	COVD-19 +VE		COVID-19 -VE		P value
			N0=17	%	N0=33	%	
Maternal demographics							
Age range 18 – 24 year 25 - 34 year 35 – 49 years	15 15 20	30 30 40	3 4 10	17.64 23.5 58.8	12 11 10	36.36 33.33 30.3	0.171 0.473 0.002
Parity primiparous	22	44	5	29.41	17	51.51	0.136
Smoking	7	14	2	11.76	5	15.15	0.744
Maternal comorbidities							
Obesity BMI>30	6	12	3	17.64	3	9	0.378
CVS CHFCHT	- 2	- 4	- 1	- 5.88	- 1	- 3.03	- 0.626
Pulmonary disease Asthma COPD	12 10 2	24 20 4	4 3 1	23.5 17.64 5.88	8 7 1	24.24 21.21 3.03	0.955 0.765 0.626
Kidney disease	-	-	-	-	-	-	-
Liver disease	3	6	2	11.76	1	30.30	0.218
Diabetes	4	8	3	17.76	1	30.30	0.071
Current obstetrical history							
GDm	15	30	5	29.4	10	30.30	0.948
PIH	3	6	1	58.82	2	6.06	0.980
Multiple pregnancy	12	24	4	23.52	8	24.24	0.955
IVF	-	-	-	-	-	-	-
IUGR	21	42	8	47	13	39.39	0.903

CVS (cardiovascular system), CHF (congestive heart failure), CHT (chronic hypertension), COPD (chronic obstructive pulmonary disease) , GDm (gestational diabetes mellitus) , PIH (pregnancy induced hypertension) , IVF (invitro fertilization) , IUGR (intrauterine growth retardation) , IUD (intrauterine death) .

Clinical presentations of the pregnant women enrolled in the study shown in Table (2). All cases had fever and the other most common presentations in decreasing order were fatigue 45 (90%), dyspnea 40 (80%), cough 35 (70%), headache 32 (64%), sorethroat 20 (40%) , loss of taste and smell 13 (26%) . Significant association found between fever, dyspnea, loss taste and smell and the group exposed to disease, p value < 0.05 (0.0001, 0.011, 0.00001 respectively). At examination respiratory rate (RR) >30 in 46 case (92%) and SpO2 >90 in 47 case (97%) without statistical significance.

Table 2: Clinical manifestations of participants.

Clinical manifestation	No=50	%	With COVID 19 (n=17)		Without COVID 19 (n=33)		P value
			No.	%	No.	%	
Fever	50	100	17	100	33	100	0.00001
Fatigue	45	90	17	100	28	84.84	0.091
Cough	35	70	15	88.23	20	60.60	0.043
Dyspnea	40	80	17	100	23	69.69	0.011
Sorethroat	20	40	10	58.82	10	30.30	0.051
Loss taste and smell	13	26	12	70.58	1	3.03	0.00001
Headache	32	64	12	70.58	20	60.60	0.486
Diarrhea	10	20	5	29.41	5	15.15	0.232
RR < 30 >30	46	92	15	88.23	31	93.93	0.481
	4	8	2	11.76	2	6.06	
SPO2 >90 <90	47	94	15	88.23	32	96.96	0.217
	3	6	2	11.76	1	3.03	

Fifty patients were analyzed, all of them symptomatic and screened for COVED-19 infection. 17 (34%) case of confirmed COVID-19 infection and 33 (66%) case negative RT- PCR test. IgG was positive in 20 case (40%) of the participants and only 3 (17.64) cases of them were infected. IgM was positive in 14 case (28%) of the participants, 12 (70%) of them were infected. Both IgG and IgM were statisticaly significant with p value < 0.05 (0.021 and 0.00001 respectively), Table 3

Laboratory investigations of the participants are shown in the Table 3. Most paricipants with elevated D-dimer, 46 case (92%), and all exposed group were with elevated D-dimer, without significant association (p value > 0.05 (0.2855) . CRP was elevated in half of the participants, ESR in 30 cases (60%), S.Ferritin found elevated in only 12 case (24%). There is significant association between CRP, ESR, S.Ferritin and exposure to COVID-19 infection , p values < 0.05 .

Both platelet count (Plt) and white blood cell count (WBC) found normal in most of the pregnant women in the study, 45 (90%) and 30 (60%) respectively. Elevated WBC in 12 case (24%), 8 cases were exposed to COVID-19 infection with statistical

significance, p value was 0.0001.

When the possible associations of preterm outcomes and neonatal data with COVID-19 infection were analysed, about half of the preterm pregnant women in the study had delivered, 26 case (52%) preterm births with mean gestation age (GA) of 31 weeks+ 2 days. 13 (76.47) preterm births from the infected group, with significant association, p value=0.012. Among preterm births who exposed to COVID-19 significant association found with obstetrical history of GDm and elevated S.Ferritin , p value was 0.022 , 0.0294 , respectively . Table (3.5).

The number of preterm births who deliverd vaginally was higher than those who delivered by cesarean section, 16 case (32%) vs 10 cases (20%), respectively. Significant association found between preterm vaginal delivery with exposure to COVID-19, p value=0.0227.

Table 3: laboratory findings of the participants.

characteristics		Total No=50	%	COVID-19 +VE		COVID-19 -VE		P value
				No.17	%	No.33	%	
PCR	Positive	17	34	17	100	0	-	*
	Negative	33	66	0	-	33	100	
Hg	Anemia	10	20	2	11.76	8	24.24	0.296
	Normal	40	80	15	88.23	25	75.75	
ferritin	Decreased	3	6	2	11.76	1	3.03	0.006
	Normal	35	70	7	41.11	28	84.84	
	Elevated	12	24	8	47.05	4	12.12	
WBC	Decreased	8	16	6	35.29	2	6.06	0.0001
	Normal	30	60	3	17.64	27	81.81	
	Elevated	12	24	8	47.05	4	12.12	
CRP	Normal	25	50	1	5.88	24	72.72	0.0001
	Elevated	25	50	16	94.11	9	27.27	
D_dimer	Normal	4	8	0	-	4	12.12	0.2855
	Elevated	46	92	17	100	29	87.87	
PLT	Decreased	2	4	1	5.88	1	3.03	0.888
	Normal	45	90	15	88.23	30	90.9	
	Increased	3	6	1	5.88	2	6.06	
ESR	Elevated	30	60	16	94.11	14	42.42	0.0004
	Normal	20	40	1	5.88	19	57.57	
IgG	Positive	20	40	3	17.64	17	51.51	0.021
	Negative	30	60	14	82.35	16	48.48	
IgM	Positive	14	28	12	70.85	2	6.06	0.00001
	Negative	36	72	5	29.41	31	93.93	

RT-PCR (Real time-polymerase chain reaction), Hg (haemoglobin) , WBC (white blood cells) , CRP (C-reactive protein) , PLT (platlets) , ESR (erythrocyte sedemintation rate)

No maternal deaths were recorded in the study, but there were stillbirths, the proportion of these being higher in patients with COVID-19 than in the non-exposed ones (5.88% vs 3.03%, p= 0.626) (Table 4).

When the informations regarding the neonates were analyesd, Table (4 and 5) , preterm babies born to mothers with COVID-19 admitted to NICU significantly more often than those born to healthy mothers as p value=0.0072 . Unfortunately, none of those babies were screened for COVID-19 infection.

Table 4: Preterm complications and outcomes of the participants.

Preterm pregnancy outcome	Total No.50	%	COVID-19 +VE		COVID-19 -VE		P value
			No=17	%	No=33	%	
GA (Weeks + days) Mean/ range	31 wks+6ds (28wks+5ds - 36wks+2ds)	-	30 wks +5 ds	-	31wks+ 4 ds	-	0.630
PPROM	19	38	10	58.82	9	27.27	0.029
Preterm birth VD CS	26 16 10	52 32 20	13 9 4	76.4752.94 23.52	13 7 6	39.39 21.21 18.18	0.0129 0.0227 0.654
Obestetrical complication							
APH	4	8	2	11.76	2	6.06	0.481
Severe PE	5	10	2	11.76	3	9.09	0.765
Stillbirth	2	4	1	5.88	1	3.03	0.626
Neonatal data							
Apgar score < 7 in5 min.	8	16	5	29.41	3	9.09	0.063
NICU	10	20	7	47.17	3	9.09	0.0072

GA (gestational age), PPROM (preterm prelabor rupture of membranes) , VD (vaginal delivery) ,CS (cesarean section) , APH (antepartum haemorrhage) , PPH (postpartum haemorrhage) ,

PE (preeclampsia) , NICU (neonatal intensive care unit) .

Table 5: The association between preterm complications in pregnant women with COVID-19 infection.					
	PPROM	Preterm Birth	VD	CS	NICU
	No = 10 P value	No = 13	No = 9 P value	No = 4 P value	No = 10 P value
PCR	-	-	-	--	--
ESR	-	-	-	--	-
D-dimer	-	-	-	-	-
S.Ferritin	0.092	0.0294	0.052	0.082	0.627
PIH	-	-	-	-	-
GDm	0.308	0.022	0.079	0.824	-
Pulmonary disease Asthma COPD	0.452 - -	0.936 - -	0.892 0.599 -	0.481 0.569 -	0.622 0.937 -
Dm	0.977	0.659	0.599	-	0.210
Multiple pregnancy	0.681	0.151	0.20	0.936	0.622

4. Discussion

The purpose of this research was to determine whether being exposed to COVID-19 increased the risk of having an infection during pregnancy. Those who were exposed to COVID19 during pregnancy were more likely to have premature babies, prelabor prelabor rupture of membranes, higher CRP, ESR, S.Ferritin, and NICU hospitalizations compared to women who were not exposed. Since fewer patients presented with severe symptoms after a screening system was put in place, researchers were unable to fully assess the impact of symptomatic COVID-19. Obstetric complications such as severe preeclampsia, haemorrhage, pulmonary thromboembolism, and abruption were common in the years, before most centres implemented screening programmes. Patients diagnosed withCOVID19 were present in this study as they were at admission.

Only 3 (17.64%) of the infected patients tested positive for IgG, whereas 12 (70% of the cases) tested positive for IgM, indicating a strong correlation between the two.The presence of IgG antibodies indicates that a person has generated,antibodies that prevent him from acquiring a serious COVID19 infection or being hospitalised, but the presence of IgM antibodies indicates that you may still be infected.However, Zullo et al.(7) note that the therapeutic utility of antibody testing has not yet been fully established, either in nonpregnant or, more importantly, in pregnant women. Even though Zambrano et al. (8) didn't find a statistically significant link between IgG levels and symptomatic women, they did not find a similar link between symptomatic women and their IgM levels. Twenty subjects (40%) were aged 35-49, and ten of them (58.8%) tested positive for COVID19. There was a statistically significant correlation between increasing age and exposure to the virus. Priyadharshini et al. (9) found similar outcomes to those seen in earlier research. However, Turan et al.'s contradict,these findings, showing that the vast majority of pregnant women with COVID19 across countries present with either no symptoms at all or only mild symptoms like fever and cough. This is likely due to the fact that the average age of infected pregnant women is not in line with the age group that is most affected by the severe form of COVID-19 (10). There was no evidence of an association between obesity (BMI >30) or Dm (recorded in 4 cases, 8%) in our study group and COVID19 infection, which contradicts a previous study suggesting that obesity may have contributed to the severity of the COVID-19 pandemic either directly or indirectly through its metabolic consequences, such as the development of type 2 diabetes (11). Fever was present in all 50 patients (100%), followed by exhaustion (90%) and dyspnea (80%) in terms of clinical presentation; nevertheless, fever was the most prevalent symptom among those studied by Di Mascio et al., followed by cough (57%) and dyspnea (27%) (12). The most frequent symptoms reported by Wu et al. are cough (8/9) and anosmia (7/9)(13). All of the exposed people (n = 46, or 92%) had D-dimer levels that were much higher thannormal.One possible explanation for this is that pregnancy makes women more prone to blood clots (14).Half of the people in this research had abnormally high levels of CRP, which is similar to the results of a study conducted in China (15), where CRP was increased in six out of nine people.According to Lapi et al., among laboratory tests used for evaluation of the acutephase response reflecting the inflammatory state, ESR is regarded as the least specific, occurring in 30 out of 60 instances (60%).There are several documented physiological and pathological circumstances that may have an effect on it(16).This finding is consistent with previous research by Kaushal K et al. (17), which suggests that serum ferritin levels may serve as an important biomarker that can aid in COVID-19 treatment.S.Ferritin was observed to be high in 12 cases (24%).Thewhiteblood cell (WBC) and platelet (Plt) counts were both found to be normal in the vast majority of pregnant women in the research.In twelve instances (24%), a significant portion of those exposed to COVID-19 had normal WBCs.This finding runs counter to otherresearch in which pregnant individuals showed significant lymphopenia(18). The correlation between PPROM, preterm births, and COVID19 was the most significant discovery of our research. We showed that a range of inflammatory mediators and biochemical pathways are activated in COVID-19, including macrophages and IL-6(19),

which may help explain the link between the two conditions. Controlling inflammatory reactions via cytokines is crucial.Among them, IL6 is particularly noteworthy because of the correlation between circulating IL-6 levels and the severity of COVID-19 infection(88). In contrast to what we found, Murphy et al. (17) looked at hospital records from five years and found no increased risk of preterm birth or admission to the neonatal critical care unit after a COVID-19 infection in the mother. Lombardi et al. disagreed with this finding and declared that D-dimer or ferritin are not reliable indicators of poor outcomes (20) among preterm newborns exposed to COVID-19. While one systematic review found that 32% of preterm births occurred when women gave birth vaginally, 82% of preterm births occurred when women gave birth by CS (18). However, we think they were most likely elective treatments performed for obstetric reasons.Prematurity is a major reason why infants born to moms with COVID-19 are more likely to be admitted to the NICU than babies delivered to mothers without the virus. A study by Murphy et al. (17) found that the health of the mother did not affect how the baby turned out.

5. Conclusions

1. Pregnant women between the ages of 35 and 49 make up the majority of those infected with COVID-19.
2. All of the patients had a fever, and they also felt tired, had trouble breathing, coughed, had a sore throat, couldn't taste or smell, and had a throbbing headache.
3. COVID-19 infection is linked to higher levels of C-reactive protein, Erythrocyte sedimentation rate, and serum ferritin.
4. COVID Pregnant patients are an increased risk for premature births, preterm prelabour rupture of membranes, and NICU hospitalizations.

Recommendations

1. More research is needed, preferably with a longer follow-up period and a larger sample size, to find out if pregnant women who are infected with COVID-19 have different obstetrical outcomes than pregnant women who are not infected.
2. Neonatal and long-term effects of COVID-19 infections should be evaluated with the use of prospective data gathering.
3. Babies born to moms with the COVID-19 virus should be tested for infection.
4. Social education emphasises topics such as avoiding crowds, using protective gear, and getting vaccinated.

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