

Feto-Maternal Outcomes of Pregnant Women Infected with COVID-19: A Single-Center Observational Study

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ABSTRACT

Introduction: World health organization (WHO) declared COVID-19 a pandemic on 11th March 2020 but the outbreak of this infection was first reported in December 2019 in China and spread to other countries all over the world. This virus is a single-stranded RNA virus that was spread from wild animals sold at Huanan Seafood Market in Wuhan. COVID-19 affects all segments of the population including pregnant women. Pregnant women and their newborns are at high risk due to physiological changes in their immune and cardiopulmonary. The objective of this study was to explore the Feto-maternal outcome of infected pregnant women during the pandemic of COVID-19 virus infection.

Material and Methods: This is a single-center cross-sectional observational study that was carried out in the Government Hospital at Salmaniya Medical Complex (SMC). All laboratory-confirmed COVID-19-positive pregnant women (341) were included in this study during the period from December 2019 until February 2021. The Feto-maternal outcomes were recorded in a data sheet.

Results: 341 women were included. The age ranged between 17 and 45 years. (77.1% were multigravida and (22.9%) were primigravida. Most patients infected with COVID-19 were in their first and second trimesters. Most subjects (81.5%) do not have any comorbidities. Fever (47.2%), cough (47.2%), and dyspnea (36%) were the most common symptoms. Forty-four percent of the patients had a vaginal delivery, (17. 2%). underwent emergency section and early pregnancy loss was (3.8%). Among the (341) live births, 77.1% were term and 22% were preterm, small for gestational age were (59.8%)

Conclusion: Although this study shows that pregnant women infected with COVID-19 are at risk of poor Feto-maternal outcomes, further study with the control group will be an asset to the management and counseling of those patients.

Keywords: Coronavirus disease 2019 (COVID-19); Feto-maternal outcome; Fetal death; Maternal mortality; Preterm birth; Severe acute respiratory distress.

INTRODUCTION

World health organization (WHO) declared COVID-19 a pandemic on 11th March 2020^{1,2}, but the outbreak of this infection was first reported in December 2019 in China and spread to other countries all over the world³. This virus is a single-stranded RNA virus⁴, that is a member of a Coronavirus family responsible for severe acute respiratory syndrome and called coronavirus 2 (SARS-CoV-2)². The virus was tested genetically and found to have close similarity to bat coronavirus which is believed that it is the source of infection⁵. Investigations into this matter revealed that the virus spread from wild animals sold at Huanan Seafood Market in Wuhan (ibid).

Reviewing the literature, it was gathered that COVID-19 affects all segments of the population and particularly affects people with low socio-economic status, elderly people, individuals with comorbidities, as well as pregnant women. Pregnant women and their newborns are at high risk of acquiring viral infection and severe pneumonia due to physiological changes in their immune and cardiopulmonary systems^{5,6}.

The objective of this study was to explore the Feto-maternal outcome of infected pregnant women during the pandemic of COVID-19 virus infection.⁷⁻⁹ concluded that fever was associated with adverse maternal and neonatal outcomes especially maternal mortality.

In terms of the mode of delivery and based on search studies, normal vaginal delivery was the most common mode of delivery^{10,11}. Among those women infected with COVID-19 who went for cesarean, the common reason was either worsening of respiratory symptoms (respiratory indicated CS)^{3,11-13}, or related to geographic practice pattern^{7,14}, or undeclared reason^{4,15-17}.

Comorbidities including obesity, diabetes mellitus, hypertension, cardiovascular disease, etc were strongly linked to maternal morbidities and mortalities^{1,3,7,10,13,14,17,18,19}.

The aim of this study is to investigate the Feto-maternal outcomes of pregnant women infected with COVID-19 during the pandemic, with

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a focus on assessing the impact of the viral infection on pregnancy outcomes and maternal health.

We hypothesize that pregnant women infected with COVID-19 are at a higher risk of adverse Feto-maternal outcomes, including an increased incidence of preterm birth, fetal death, and maternal mortality, compared to non-infected pregnant women.

MATERIAL AND METHODS

Study Design

This study is a cross-sectional observational study that was conducted in Government Hospital (Salmaniya Medical Complex). All laboratory-confirmed COVID-19-positive pregnant women were included in this study during the period from December 2019 until February 2021. Other patients who had clinical symptoms of COVID-19, but PCR negative were excluded. These women were recruited consecutively over time till the desired sample was reached.

Adverse outcomes of interest/ variables definition:

Pregnancy outcomes: (e.g., ectopic pregnancy, miscarriage, delivery mode, preterm birth, fetal growth restriction, antepartum hemorrhage, maternal morbidity, and mortality).

2. Perinatal outcomes: related to the fetus/neonate that occurs after 22 weeks gestation and within 7 days after birth (e.g., intrauterine fetal death (IUFD), admission to the neonatal intensive care unit (NICU), neonatal morbidity or mortality within 7 days of life).

Statistical analysis was carried out using the Statistical Social Sciences version (IBM SPSS 28) where the categorical variables (dichotomous and ordinal) were summarized calculating the categories' frequencies and percentages. Continuous variables were summarized by calculating the mean and the standard deviation (Mean(±SD)). The significance of the difference between any categories were examined by the Chi square test or the Fisher's exact test (An extension of Chi square test for 2x2 tables). the set significance level was 0.05.

RESULTS

The sample consisted of 341 women who contacted COVID-19 during their pregnancy or during childbirth., the vast majority are between 19 to 35 years old. More than two-thirds of them are Bahrainis (239(70.1%)) whereas the rest (102(29.9%)) belong to at least 15 other nationalities.

The sample is dominated by the multigravida group representing 77.1% whereas the primigravidae formed less than the quarter (22.9%).

Patients with gestational age between 28 to 42 weeks accounted for most of the sample 235 (68.9%). The great majority of the patients did not have any obstetric history 291(85.3%) though those who had cesarean section one or more were the most prevalent category 33(9.7%). See the table 1 for obstetric descriptive results.

Table 1. Obstetric descriptive results

Obstetric variable	Categories	Count	Percentage
Gravidity-Parity	Primi	78	22.9%
	Multigravida	263	77.1%
	Gestational age (Weeks)		
	<=13+6	37	10.9%

	14-27	69	20.2%
	28-42	235	68.9%
Obstetric history			
	1 Cesarean section	23	6.7%
	2 Cesarean sections	7	2.1%
	IUFD/Fetal/Neonatal death	5	1.5%
	3 Cesarean sections or more	3	0.9%

Among pregnant women with covid-19 it was observed that those who do not have any comorbidities represented the dominant proportion of the sample with 81.5%. Hypothyroidism and bronchial asthma were the more prevalent chronic illness found in the patients reported with medical history. See the table 2 for obstetric Antenatal complications results.

Table 2. Antenatal complications results

Antenatal complications			
	GDM	21	6.2%
	Other complications	21	6.2%
	IVF	9	2.6%
	Twins or more	8	2.3%
	Placenta previa	6	1.8%
	PROM	5	1.5%
	Nil	271	79.5%
Medical history			
	DM	5	1.5%
	SCD	7	2.1%
	Bronchial asthma	10	2.9%
	Hypothyroidism	11	3.2%
	Other comorbidities	29	8.5%

It was observed that Only 7 patients were vaccinated representing 2.1% of the sample. Interestingly, most of these patients got COVID-19 in their first or second trimesters with as significantly less proportion of them had it in their third trimester (3.0(88%) vs. 12%, p=0.0002). this finding suggests a relationship between the gestational phase and the chance of contracting COVID-19 infection. See the table 4 for obstetric COVID-19 vaccination and onset status results.

See Table 3 .

Table 3. Obstetric COVID-19 vaccination and onset status results

	Count	Percentage	p-value
Vaccination status			
	Not vaccinated	334	97.9%
	Vaccinated	7	2.1%
First positive COVID-19			
	First trimester	153	44.9%
	Second trimester	147	43.1%
			0.0002*

The patient reported many symptoms during COVID-19 infection; however, the most prevalent symptoms were fever (47.2%), cough (47.2%), and shortness of breath (36.1%) respectively. The rest of the

symptom were reported by 10% or less of the patients. See the table 4 for COVID-19 symptomatology results.

Table 4. COVID-19 symptomatology results

COVID-19 symptom	No n(%)	Yes n(%)
Fever	180 52.8%	161 47.2%
Cough	180 52.8%	161 47.2%
SOB	218 63.9%	123 36.1%
Body ache	306 89.7%	35 10.3%
Loss smell	312 91.5%	29 8.5%
Headache	317 93.0%	24 7.0%
Sore throat	322 94.4%	19 5.6%
Run nose	323 94.7%	18 5.3%
Pneumonia	328 96.2%	13 3.8%
Vomiting	331 97.1%	10 2.9%
Other symptoms	337 99%	34 1.3%

Nearly 8% of the patients required Oxygen therapy during their COVID-19 infection whereas the significant majority did not need it (27(7.9%) vs. 314(92.1%), p<0.0001). The most used Oxygen delivery device for those who needed Oxygen therapy was mechanical ventilation (11(40.7%)), nasal cannula (6(22.2%)), and non-rebreathing mask (5(22.2%)). Like the proportion who need oxygen therapy, those who needed ICU admission account for 7.6% of the whole sample with a significantly higher proportion did not need to receive care in this setting (26(7.6%) vs. 315(92.4%), p<0.0001). See the table 5 for COVID-19 therapy results.

Table 5. COVID-19 therapy results

Oxygen	Categories	Count	Percentage	p-value
Need for oxygen	No	314	92.1%	<0.0001*
	Yes	27	7.9%	
Oxygen delivery device	Ventilator	11	40.7%	0.792
	Nasal cannula	6	22.2%	
	Non-rebreathing mask	5	18.5%	
	ECMO/INTUBATED	2	7.4%	
	Face mask	2	7.4%	
	BIPAP	1	3.7%	
	Need for ICU admission	Admitted to ICU	26	
	Not admitted to ICU	315	92.4%	

*Statistically significant differences with Chi square Goodness of fit test at Alpha 0.05

The overall mortality is among age group 31 years and above. They were five times more likely to die compared to their 30 years and less counterparts (5.1% vs. 1.2%, p=0.038). On the contrary, the patient's nationality showed no association with her chance for mortality. Although the non-Bahraini chance for mortality was two times higher than their Bahraini counterparts, however, this difference was not statistically significant (5.9% vs. 2.5%, p=0.138).

None of the obstetric characteristics was found to be associated with mortality except for the gestational age. The mortality rate among those gestational age between 14-27 weeks is at least ten times higher than the other two groups (11.6% vs. 1.7% and 0%). This finding suggests an association between gestational age and patients' chance for mortality. Neither the presence of comorbidities nor the period the patient got COVID-19 were found to be associated with their chance for mortality. See the table 6 for results based on obstetric characteristics.

Table 6. Results based on obstetric characteristics

Variable	Categories	Mortality n(%)	p-value
Gravidity-Parity	Primipara	3(3.8%)	0.860
	Multipara	9(3.4%)	
Gestational age	<=13+6 weeks	0(0%)	<0.001*
	14-27 weeks	8(11.6%)	
	28-42 weeks	4(1.7%)	
Obstetric history	No	11(3.8%)	0.449
	Yes	1(2%)	
Antenatal complications	No	11(4.1%)	0.241
	Yes	1(1.4%)	
Past medical history	No	10(3.6%)	0.889
	Yes	2(3.5%)	
Trimester when first positive	First trimester	4(2.6%)	0.980
	Second trimester	8(5.4%)	
	Third trimester	0(0%)	

*Statistically significant difference with Chi-square test at Alpha 0.05

The development of certain COVID-19 manifestations (fever, cough, shortness of breath, and loss of smell) were found to be significantly associated with the patients' chance for mortality. The mortality rate among those had fever was more than seven time higher than patients who did not develop this symptom (7.5% vs. 0%, p<0.001). The same observation is true for the other three symptoms. See the table 7 for results based on COVID-19 symptoms.

Table 7. Results based on COVID-19 symptoms in relation to mortality rate

COVID-19 symptoms	Categories	Mortality n(%)	p-value
Fever	No	0(0%)	<0.001*
	Yes	12(7.5%)	
Cough	No	0(0%)	<0.001*
	Yes	12(7.5%)	

Shortness of breath		
No	0(0%)	<0.001*
Yes	12(9.8%)	
Loss of smell		
No	2(0.6%)	<0.001*
Yes	10(34.6%)	

*Statistically significant difference with Chi square test at Alpha 0.05

The need for oxygen therapy and ICU admission are strongly associated with patients' mortality rate. The mortality rate among those who required Oxygen therapy during their COVID-19 illness is more than 70 times higher than their counterparts (37% vs. 0.6%, $p < 0.001$) with a statistically significant difference. Worth mentioning that two patients required ECMO, one transferred to Bahrain Defensive Force Hospital and survived while the other one traveled abroad where she was bridged with ECMO before a lung transplant but unfortunately died before surgery. Likewise, those who required ICU admission had a significantly higher mortality rate than those who remained in the wards (46.2% vs. 0%, $p < 0.001$). See the table 8 for oxygen requirement in relation to mortality rate.

Table 8. Results based on COVID-19 oxygen requirement in relation to mortality rate

Categories	Mortality n(%)	p-value
Need Oxygen therapy		
No	2(0.6%)	<0.001*
Yes	10(37%)	
Admitted to ICU		
No	0(0%)	<0.001*
Yes	12(46.2%)	

*Statistically significant difference with Chi square test at Alpha 0.05

Most of these patients went through SVD (150(44%)) and had full-term babies (185(54.3%)). Babies who stayed with their mothers (166(48.7%)) with a weight (2.4(59.8%)).

DISCUSSION

In this study, we summarize the findings of 341 pregnancies with positive PCR tests for COVID-19 infection, with a focus on maternal symptoms, Feto-maternal outcomes, and the risk of mortality.

The mean age group was 31 years as Bahrain is one of the countries with a large youth population. About 47% of our COVID-19 infection pregnant women were asymptomatic. The most common symptoms that were observed in our study are fever, cough, malaise, and shortness of breath which are consistent with other studies^{9,10,18}. The age factor was not stressed in most of the studies. Yet, ^{1,3,7,19} reported that advanced maternal age is a risk factor for severe illness and a chance for intensive care unit (ICU) admission.

Based on the results, the majority of deliveries with COVID-19 infection were by vaginal delivery (44%) which is similar to the study¹¹, in which 57% of women had a spontaneous vaginal delivery. With regard to the adverse perinatal outcome of pregnancies infected with COVID-19 infection, low birth weight and preterm deliveries were the most significant perinatal adverse effect^{4,10,13}. Those who had iatrogenic preterm deliveries were mainly medically (respiratory indicated) to improve maternal medical status (3,13). Pregnant women infected by COVID-19 and more likely to have preterm labor, low birth weight babies, and more chances of admission to NICU in comparison to those pregnant without COVID-19,^{15,17,19}

In contrast to our findings, many studies show that women infected with COVID-19 infection had a relatively higher cesarean section rate^{15,16}. Few articles especially from China show that COVID-19 infection is an indication for delivery by a lower segment cesarean section²³. Those who have severe COVID-19 pneumonia, comorbidities, and advanced maternal age required ICU admission and oxygen support,^{3,7,8,12,13}. Retrospective review of medical records covering Wuhan- China hospitals, found no maternal deaths among the 38 pregnant women who were infected by COVID-19²⁰. A Cohort study performed on the outcomes associated with the COVID-19 of 118 pregnant women in Wuhan revealing that only 8% had hypoxemia, and from those only 1 woman was critically ill and required mechanical ventilation. No maternal deaths occurred,²¹. In another retrospective review of clinical records on 116 pregnant women from hospitals in China who were infected with COVID-19. His analysis revealed that 8 cases had severe pneumonia but not death,¹².

Similar to other research conclusions⁸, An interesting finding in this current study is that among pregnant women infected with COVID-19, 81.5% had no baseline comorbidities and it is explained that the study group was of younger age group mother.

Many studies show that women with COVID-19 infection had a high prevalence of maternal comorbidities⁷. It was reported in one study, approximately one out of every three women infected with COVID-19 had a comorbid condition [14]. A systematic review of 108 pregnancies on perinatal outcomes with COVID-19 in Sweden, found that most pregnant women presented with COVID-19 were in their third trimester and had no major complications. Only three of them required intensive care with no maternal mortality, [22]. In another study, 9.3% of the cases required ICU admission, and 5.4% needed mechanical ventilation but there were no maternal deaths, [15]

The most reported adverse outcome of pregnancies with COVID-19 infection was low birth weight and increased prevalence of preterm deliveries [13]. A systematic review of many studies described the outcomes of 385 pregnant women with COVID-19 with a preterm birth of 15.2% [4]. In Bahrain, the Governmental hospitals recorded an average of 15% of preterm deliveries in 2019, which is less than the percentage of preterm deliveries during the pandemic period of COVID-19 (22%) in our study. This increase in preterm deliveries could be related to premature termination of pregnancies to have a better outcome for severely infected pregnant women. In our study, it was also noted that 59.8% of the babies have low birth weight (2.4 kg) which is similar to a study [13].

Maternal ICU admission was also one of the pregnancy outcomes. It was noticed that those who required ICU admission had significantly higher mortality rates than those who remained in the wards (46.2% vs. 0%, $p < 0.001$) [3]. Maternal mortality can occur even in the absence of comorbidities.

In contrast, a study conducted in the United Kingdom, stated that the UK Obstetric Surveillance System (UKOSS) launched; on 20 March 2020; a registry for all women admitted to UK hospitals with confirmed COVID-19 infection during pregnancy. This cohort study reported 427 cases of whom 9% required intensive care and <1% received extracorporeal membrane oxygenation. Five out of the 427 women died mounting the fatality rate to 1.2% and the maternal mortality rate of 5.6 per 100,000 maternities. Of the study population, it was noticed that the black, Asian, or minority ethnicities (BAME) have more ICU admissions and worse outcomes. According to the author, this could be related to factors of socioeconomic, genetic, or differences in response to infection [2]. Similarly, both studies [7,16] also reported maternal death in severe cases.

Regarding transmission from mothers to their fetuses, there was no confirmed evidence of intrauterine transmission of the virus [10]. Placentas and neonates of these cases were also swabbed for the virus and turned out to be negative [20]. Among those who continued their pregnancies, no intrauterine or neonatal fetal deaths were reported as well [21]. Negative results were also revealed when assessed for vertical transmission of Covid-19 virus by collecting samples from amniotic fluid, cord blood, and neonatal pharyngeal swabs [12]. Contrary to the above findings, one study found that vertical transmission of COVID-19 to the fetuses couldn't be excluded having one intrauterine and one neonatal death [22].

Two-thirds of the cases delivered around 38 weeks of gestation with 10% percent of the term babies required admission to the neonatal unit. 2.5% of these babies; some of whom were derived by elective cesarean; had positive tests for Covid-19 during the first 12 hours after birth. Two perinatal deaths occurred, and it wasn't clear whether it was related to Covid-19 infection or not. Nevertheless, the study believes there is no data suggesting an increased risk of miscarriage in relation to Covid-19. It also mentioned that currently there is no evidence to label the virus teratogenic [2]. Although some concluded that vertical transmission remains a probability but in small proportions [3].

Similar to another study [16], all cases of maternal death in this current study, are found to be five times higher in older individuals infected with COVID-19 virus.

The mortality rate among those who had a fever was more than seven times higher than patients who did not develop this symptom with $p < 0.001$. Other symptoms especially cough, shortness of breath, and loss of smell were also associated with a high mortality rate with $p < 0.001$. In accordance with these findings, in another systemic review, the most common symptoms at presentation were cough, fever, shortness of breath, and fatigue [7,16].

This study was a descriptive, single-center, in which all pregnant women infected with COVID-19 in our kingdom were reviewed in our center with no selection bias. The limitation of this study is that there was no control group to compare the results with.

CONCLUSION

Most common symptoms among pregnant women infected with COVID-19 in Bahrain and in other countries; as revealed in the literature; range between fever, cough, and shortness of breath. Similarly, Maternal infection with COVID-19 is associated with high morbidity and mortality rate.

Therefore, ICU facilities must be readily available for better Feto-maternal outcomes.

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