



Clinical Profiles, Demographic Features, and Maternal Outcomes among Coronavirus Disease Positive Pregnant Women: A Cross-sectional Study

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Abstract

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BACKGROUND: Pregnant women are susceptible to coronavirus infection due to physiological changes in the circulatory and immunological parameters.

AIM: The current study aimed to determine the demographic factors, clinical symptoms, and fetal-maternal outcomes and also compare the blood parameters and chest X-ray results among coronavirus disease 2019 (COVID-19) positive and negative pregnant women.

MATERIALS AND METHODS: Complete blood count and Chest X-rays were performed as a routine in all pregnant women. Polymerase chain reaction for COVID-19 was performed for all women and the newborn.

RESULTS: The blood parameters revealed that a significantly greater proportion of COVID-19 positive pregnant women had abnormal hemoglobin, total leukocyte count, neutrophil count, lymphocyte count, monocyte count, bilirubin, aspartate aminotransferase, alanine aminotransferase, and urea.

CONCLUSIONS: The present study provided crucial insights into epidemiological and clinical features during the perinatal period. Chest X-rays and blood routine examination are reliable findings to prevent COVID-19 complications among pregnant women.

Introduction

In December 2019, a novel coronavirus was identified in China, causing multiple pneumonia cases. Globally, there was rapid spread, and the number of cases has increased. The World Health Organization designated the disease as coronavirus disease 2019 (COVID-19) in February 2020 [1]. Among the vulnerable group of the population, pregnant women are susceptible to coronavirus infection due to physiological alterations in the circulatory and immunological parameters [2].

During pregnancy, physiological changes occur, such as a decrease in the residual functional capacity of the lung, the height of the diaphragm, and changes in cellular immunity that lead to increased susceptibility to viral infections and more severe consequences in pregnant women [3]. Recently, severe sickness among pregnant women in the antenatal period has been reported in the previous studies. A study by Ellington *et al.* reported that approximately one-third of pregnant women were hospitalized compared with (5.8%)

non-pregnant women [4]. Similarly, Badr *et al.* reported a higher risk of complications and decompensation in the later trimesters of the pregnancy [5]. Yu *et al.* found that women who were receiving obstetrical care were asymptomatic; however, they developed symptoms within 2–3 days of their postpartum. The majority of the infections in their study were mild [6]. Apart from postpartum transmission (horizontal), multiple routes of transmission, including transplacental and immediate peripartum period through fetoplacental bleed, amniotic fluid, and breast milk, have been postulated. However, there is a lack of evidence for vertical transmission in pregnancy [7].

According to the Centers for Disease Control and Prevention (CDC), there is a paucity of information about the effects of Coronavirus on pregnancy and neonatal outcomes [8]. Therefore, during the COVID-19 pandemic, it is essential to acquire knowledge of pregnancy outcomes, including the severity of symptoms, potential complications during pregnancy, and the neonate's health conditions born to an infected mother, and the possibility of vertical

transmission. However, there is limited comprehensive data regarding its side effects on pregnancy. The disease remains significantly heterogeneous both in its demographic characteristics and clinical features. Hence, the current study aimed (1) to determine the demographic factors, clinical symptoms, fetal-maternal outcomes among pregnant women; and (2) to compare the blood parameters and chest X-ray results among COVID-19 positive and negative pregnant women.

Materials and Methods

An observational study was conducted at Sir Ganga Ram Hospital, Lahore, Pakistan. The hospital was the tertiary referral care center for COVID-19 cases in that region. A total of 94 pregnant women suspected of COVID-19 from April 2020 to May 2020 were referred to this center for medical facilities. The patients presented within 2–3 days of their onset of symptoms.

Patients' information was extracted from records and included age, address, gestational age, comorbidities, signs, and symptoms at onset, and information about neonates including birth weight, appearance, pulse, grimace, activity, and respiration (APGAR) score, neonatal intensive care unit (NICU) admissions, perinatal complication, and outcomes of pregnancy. The data were entered into an Excel Sheet directly. Only the electronic pro forma was used, and no paperwork was involved. The device used for data collection (iPad-device) was kept inside the data collecting zone (ward) and not removed from the ward at any time, and data were transferred through the internet to the department's main computer for analysis.

Testing policy

It was a hospital policy to perform complete blood count, blood sugar level, and comprehensive examination of urine as a routine in all pregnant women. Normal values for blood parameters are included in Table 1.

All those above, the normal range is considered abnormal. Polymerase chain reaction (PCR) for COVID-19 for all women and the newborn was performed.

The qualitative COVID-19 PCR test was performed on VERSANT K PCR (SIEMENS) fully automated PCR System Extraction Siemens-Amplification Logix Smart (FDA Approved) using nasopharyngeal swabs. This test directly detects the viral RNA.

Due to the highly infectious nature of the disease, all precautions were ensured to keep the safety of data collectors in accordance with guidelines provided by the government of Pakistan [9]. According to the recommendations, all the health-care staff followed the doffing and donning sequence of total personal protective equipment, which included double layer gloves, goggles, head caps, N95 masks, and shoe covers. When aerosol-generating procedures were performed, face shields were used.

Ethics

The study was approved by the Institutional Review Board of the hospital. Informed consent was obtained from each pregnant woman. For the newborn infants, proxy written informed consent was obtained from the parent or legal guardian. Confidentiality of the data was maintained by keeping data anonymous in line with Helsinki's declaration.

Statistical analysis

The recorded data were compiled and entered into a spreadsheet computer program (Microsoft Excel 2010) and then exported to the data editor page of IBM SPSS version 22.0 (SPSS Inc., Chicago, Illinois, USA). Bivariate analysis was performed using the Chi-square test for the association of COVID-19 status of pregnant women with independent variables. For all tests, confidence interval and p-value were set at 95% and ≤ 0.05 , respectively.

Results

Table 2 shows the comparative evaluation of COVID-19 status in pregnant women according to demographic variables.

There was no significant association of age group (years) ($p = 0.713$), education ($p = 0.11$), and parity ($p = 0.891$) with COVID-19 status. When compared according to the occupation, the majority of COVID-19 positive patients were housewives (97.9%) followed by doctors (2.1%), and the association was statistically significant ($p = 0.002$) (Table 2).

Table 3 shows the fetomaternal outcome among COVID-19 and non-COVID-19 pregnant women.

There was no significant association of maternal death ($p = 0.162$), maternal complications

Table 1: Normal hematology parameters in pregnancy

Hematology parameters	1 st trimester	2 nd trimester	3 rd trimester
Hemoglobin (g/dL)	11.6–13.9	9.7–14.8	9.5–15.0
Total leukocyte (*103/mm ³)	5.7–13.6	5.6–14.8	5.9–16.9
Neutrophil count (*103/mm ³)	3.6–10.1	3.8–12.3	3.9–13.1
Lymphocyte count (*103/mm ³)	1.1–3.6	0.9–3.9	1.0–3.6
Monocyte count (*103/mm ³)	0.1–1.1	0.1–1.1	0.1–1.4
Platelet count (*109/L)	174–391	155–409	146–429
Bilirubin (mg/dL)	0.1–0.4	0.1–0.8	0.1–1.1
AST (U/L)	3–23	3–33	4–32
ALT (U/L)	3–30	2–33	2–25
Urea (mg/dL)	7–12	3–13	3–11
Creatinine (mg/dL)	0.4–0.7	0.4–0.8	0.4–0.9

AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase.

Table 2: Comparative evaluation of COVID-19 in pregnant women according to demographic variables

Demographic variables	COVID-19 positive n (%)	COVID-19 negative n (%)	p-value	Total n (%)
Age group (years)				
<30	32 (66.7)	29 (63)	0.713	61 (64.9)
More than 30	16 (33.3)	17 (37)		33 (35.1)
Education			0.11	
Uneducated	13 (27.1)	5 (10.9)		18 (19.1)
Primary School	6 (12.5)	6 (13)		12 (12.8)
Secondary School	15 (31.2)	13 (28.3)		28 (29.8)
College Level	13 (27.1)	16 (34.8)		29 (30.9)
University Level	1 (2.1)	6 (13)		7 (7.4)
Occupation			0.002*	
Housewife	47 (97.9)	30 (65.2)		77 (81.9)
Schoolteacher	0	5 (10.9)		5 (5.3)
Nurse	0	1 (2.2)		1 (1.1)
Doctor	1 (2.1)	6 (13)		7 (7.4)
Housemaid	0	4 (8.7)		4 (4.3)
Source of infection				
Family	10 (21.3)	–	–	10 (21.3)
Workplace	0	–		0
Not known	37 (78.7)	–		37 (78.7)
Parity			0.891	
≤2	37 (77.1)	36 (78.3)		73 (77.7)
More than 2	11 (22.9)	10 (21.7)		21 (22.3)
Total	48 (51.1)	46 (48.9)		94 (100)

The test applied: Chi-square test, (*): Indicates statistically significant results, COVID-19: Coronavirus disease 2019.

(p = 0.513), baby's weight (p = 0.249), APGAR score (p = 0.161), and NICU admission (p = 0.24) with COVID-19 status. However, the mode of delivery was significantly (p = 0.001) associated with COVID-19 status. The majority of COVID-19 positive subjects (80%) had lower segment caesarean section delivery, while the majority of COVID-19 negative subjects (63%) had an spontaneous vaginal delivery type of delivery (Table 3).

Table 3: Comparative evaluation of fetomaternal outcome among COVID-19 and non-COVID-19 pregnant women

Independent variables	COVID-19 positive n (%)	COVID-19 negative n (%)	p-value	Total n (%)
Maternal death				
No	46 (95.8)	46 (100)	0.162	92 (97.9)
Yes	2 (4.2)	0		2 (2.1)
ICU admission				
Yes	7 (14.9)	0	–	7 (14.9)
No	40 (85.1)	0		40 (85.1)
Maternal Complications			0.513	
Renal failure	0	0		0
Cardiac failure	0	0		0
HELLP syndrome	0	0		0
Preeclampsia	0	0		0
Preterm labor	1 (2.1)	0		1 (1.1)
PPROM	1 (2.1)	2		3 (3.2)
Cord Prolapse	0	0		0
No complication	46 (95.8)	44 (95.7)		90 (95.7)
Mode of delivery			0.001*	
SVD	5 (20)	29 (63)		34 (47.9)
LSCS	20 (80)	17 (37)		37 (52.1)
Baby's weight			0.249	
<2.5	7 (28)	7 (16.3)		14 (20.6)
More than 2.5	18 (72)	36 (83.7)		54 (79.4)
APGAR score			0.161	
Below 6	2 (8)	1 (2.2)		3 (4.3)
6–9	6 (24)	5 (11.1)		11 (15.7)
Ten and above	17 (68)	39 (86.7)		56 (80)
NICU admission			0.24	
Yes	3 (12)	2 (4.4)		5 (7.1)
No	22 (88)	43 (95.6)		65 (92.9)
Fetal PCR				
Positive	–	–	–	–
Negative	24 (100)	–		24 (100)

NICU: Neonatal intensive care unit, PCR: Polymerase chain reaction, COVID-19: Coronavirus disease 2019, LSCS: Lower segment Caesarean section, SVD: Spontaneous vaginal delivery, APGAR: Appearance, pulse, grimace, activity, and respiration.

When blood parameters were compared among COVID positive and COVID negative subjects, significant differences were observed in hemoglobin, total leukocyte count (TLC), neutrophil count,

lymphocyte count, monocyte count, bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and urea levels among the COVID-19 positive group than COVID-19 negative group (Table 4).

Table 4: Comparative assessment of blood parameters among COVID-19 and non-COVID-19 pregnant women

Independent variables	COVID-19 positive n (%)	COVID-19 negative n (%)	p-value	Total n (%)
Hemoglobin				
Normal	40 (83.3)	46 (100)	0.004*	86 (91.5)
Not normal	8 (16.7)	0		8 (8.5)
TLC			0.003*	
Normal	26 (54.2)	38 (82.6)		64 (68.1)
Not normal	22 (45.8)	8 (17.4)		30 (31.9)
Neutrophil count			0.023*	
Normal	1 (2.1)	7 (15.2)		8 (8.5)
Not normal	47 (97.9)	39 (84.8)		86 (91.5)
Lymphocyte count			0.001*	
Normal	4 (8.3)	43 (93.5)		47 (50)
Not normal	44 (91.7)	3 (6.5)		47 (50)
Monocyte count			0.001*	
Normal	2 (4.2)	41 (89.1)		43 (45.7)
Not normal	46 (95.8)	5 (10.9)		51 (54.3)
Platelet count			0.55	
Normal	42 (87.5)	42 (91.3)		84 (89.4)
Not normal	6 (12.5)	4 (8.7)		10 (10.6)
Bilirubin			0.045*	
Normal	44 (91.7)	46 (100)		90 (95.7)
Not normal	4 (8.3)	0		4 (4.3)
AST			0.001*	
Normal	28 (58.3)	41 (89.1)		69 (73.4)
Not normal	20 (41.7)	5 (10.9)		25 (26.6)
ALT			0.001*	
Normal	24 (50)	44 (95.7)		68 (72.3)
Not normal	24 (50)	2 (4.3)		26 (27.7)
Urea			0.001*	
Normal	3 (6.2)	18 (39.1)		21 (22.3)
Not normal	45 (93.8)	28 (60.9)		73 (77.7)
Creatinine			0.505	
Normal	37 (77.1)	38 (82.6)		75 (79.8)
Not normal	11 (22.9)	8 (17.4)		19 (20.2)
Total	48 (51.1)	46 (48.9)		94 (100)

The test applied: Chi-square test, (*): Indicates statistically significant difference, COVID-19: Coronavirus disease 2019, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, TLC: Total leukocyte count.

Table 5 shows a comparative assessment of clinical presentations among COVID-19 and non-COVID-19 pregnant women.

Table 5: Comparative assessment of clinical presentations among COVID-19 and non-COVID-19 pregnant women

Clinical presentation	COVID-19 positive n (%)	COVID-19 negative n (%)	p-value	Total n (%)
Flu	26 (54.2)	1 (2.2)	0.001*	27 (28.7)
Cough	27 (56.2)	1 (2.2)	0.001*	28 (29.8)
Fever	27 (56.2)	1 (2.2)	0.001*	28 (29.8)
Aches and pains	24 (50)	1 (2.2)	0.001*	25 (26.6)
Sore throat	19 (39.6)	1 (2.2)	0.001*	20 (21.3)
Shortness of breath	12 (25)	0	0.001*	12 (12.8)
Red eyes	2 (4.2)	0	0.162	2 (2.1)
Loose motion	1 (2.1)	0	0.325	1 (1.1)
Cyanosis	3 (6.2)	0	0.085	3 (3.2)
No symptoms	21 (43.8)	45 (97.8)	0.001*	66 (70.2)

The test applied: Chi-square test, (*): Indicates statistically significant difference, COVID-19: Coronavirus disease 2019.

Flu, cough, fever, aches and pains, sore throat, and shortness of breath occurred with significantly high prevalence among COVID-19 positive subjects than among COVID-19 negative subjects.

Table 6 shows Chest X-ray before and after delivery among COVID-19 positive subjects.

Table 6: Comparative assessment of imaging parameters before and after delivery among COVID-19 women

Chest X-ray	Before delivery n (%)	After delivery n (%)	p-value
Not done	39 (83)	42 (89.4)	0.083
Mild changes	6 (12.8)	3 (6.4)	
Severe infiltrates	2 (4.3)	2 (4.3)	

COVID-19: Coronavirus disease 2019.

Only two subjects had severe infiltrates before as well as after delivery. The proportion of those with mild changes before delivery (12.8%) reduced after delivery (6.4%), but the difference was statistically significant ($p = 0.083$).

Discussion

The study revealed that pregnant women diagnosed as COVID-19 positive were housewives under 30 years of age. The most common symptoms included flu, cough, fever, aches and pains, sore throat, and shortness of breath. Chest X-ray demonstrated mild and severe infiltrates in 6 (12.8%) and 2 (4.3%) pregnant women before delivery. The majority of the neonates was delivered through cesarean section and was above 2.5 kg weight with an Apgar score above 10. Only 3 (12%) neonates born to COVID-19 positive mothers were admitted to NICU. The blood parameters revealed that a significantly more proportion of COVID-19 positive pregnant women had abnormal hemoglobin, TLC, neutrophil count, lymphocyte count, monocyte count, bilirubin, aspartate aminotransferase, alanine aminotransferase, and urea levels.

A systematic review by Panahi *et al.* on 37 pregnant mothers with COVID-19 reported that the age range of mothers was between 23 and 40 years. Babies were delivered through the cesarean section in 29 women, and eight women had a normal delivery. Preterm labor was reported in seven women at 30–33 weeks of gestational age, and the remaining women had a delivery in the third trimester (between 34 and 40 weeks gestation) [10]. Similarly, a case series report by Perrone *et al.* evaluated four convalescent mothers with COVID-19 and found that all three babies were above 2.5 kg with an APGAR score above 9 [11]. Another study reported 4.1% preterm delivery and 2.2% miscarriage [12].

In the present study, the majority of the COVID-19 positive mothers had flu, cough, fever, aches and pains, sore throat, and shortness of breath. The present study was in line with the Yang *et al.* study conducted at a non-designated hospital of Wuhan on 13 pregnant women with Corona infection. Most of the women were asymptomatic and had milder symptoms of prenatal fever (15.4%), postpartum fever (61.6%), and coughing cases (15.4%) [13]. Similarly, a systematic review reported by Ashraf *et al.* revealed that the most common symptoms among pregnant women included cough ($n = 34$), fever ($n = 47$), and dyspnea. The temperatures were between 37°C and 38.8°C [14]. In a systematic review by Zaigham and Andersson on 108 pregnancies in the COVID-19 pandemic, they reported that most of the pregnant women had a fever, cough, and lymphocytopenia with elevated C-reactive

protein, and most of them delivered through cesarean section [15]. Another study reported that the high-risk pregnancy group had a significantly higher RT-PCR positivity rate compared with the low-risk pregnancy group (2.9 % vs. 0%, $p = 0.04$) [16].

When comparing hematological parameters, significant abnormal differences were observed in hemoglobin, TLC, neutrophil count, lymphocyte count, monocyte count, bilirubin, AST, ALT, and urea levels among the COVID-19 positive group compared with the negative group. In Yang *et al.* study, there were no differences in leukocyte count, neutrophil granulocytes, lymphocyte counts, and CRP between Corona confirmed group and control group before and after delivery [13]. The present study results are consistent with Chen *et al.* findings and might be related to persistent infection and prolonged hypoxia resulting in bone marrow hyperplasia to deliver more granulocytes [17]. The abnormal lymphocyte count may be caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continuous invasion and proliferation, causing the death or depletion of lymphocytes when they reach the spleen and other immune organs [18].

The X-ray findings in the current study found mild changes (12.8%) and severe infiltrates 2 (4.3%) before delivery. A systematic review by Turan *et al.* in 221 Chinese women with mild COVID-19 reported that they had abnormal X-ray and chest CT and findings (88.7%). Abnormal pulmonary findings among pregnant women included focal unilateral or bilateral ground-glass opacities, diffuse, bilateral ground-glass opacities with subpleural involvement, and pleural effusion. These X-ray findings help in evaluating the extent and severity of the disease and in the early screening of highly suspected patients [19].

In the present study, none of the neonates were COVID-19 positive. Whereas, in a study conducted by Zeng *et al.* in China, 33 women with COVID-19 infection delivered through cesarean section. Out of 33 newborns, only three acquired COVID-19, a postnatal transmission was postulated since PCR assays revealed that breast milk, cord blood, and amniotic fluid were all clear from the virus [20].

Women experience physiological and immunological changes during pregnancy, making them more prone to viral respiratory infections, such as influenza. High fevers in early pregnancy are connected with specific birth defects, such as neural tube defects [21]. Published studies to date seem to be reassuring that pregnant women with COVID-19 might not be at increased risk for severe complications or adverse reproductive health outcomes [10], [11], [13]. CDC stated that pregnant women should meticulously follow the safety measures that were recommended for health-care providers [22]. In addition, maintaining appropriate self-care and hygiene practice during pregnancy is crucial to reduce the morbidity and complications of the COVID-19 infection [23].

The available guidelines for the management of pregnant women with COVID are rapidly changing and getting updated with time. Due to the limited number of cases analyzed and the short duration of the study period, multiple strategies are required, including sentinel surveillance and seroprevalence studies to address the knowledge gaps on the effects of COVID-19 during pregnancy.

There are a few limitations to the study. First, the sample size was limited, and all of the pregnant women confirmed with COVID-19 were not classified based on mild, moderate, and severe symptoms. Second, the antibody titers and viral load kinetics were not determined in the study. Further large-scale, multi-centric studies with larger sample sizes are expected to determine the management protocols at the time of delivery to inhibit the transmission and complications of infection in the mothers and neonates.

Conclusions

Pregnant women and their infants are the most vulnerable cases in this COVID-19 outbreak because of their susceptibility to infections, altered physiology, and compromised immunological functions. The present study provided crucial insights into epidemiological and clinical features during the perinatal period. Chest X-rays and blood routine examination are reliable findings to prevent COVID-19 complications among pregnant women. None of the neonates were found to be COVID-19 positive, which mandates to explore reliable evidence on mechanisms of vertical transmission. Health-care professionals also need to formulate obstetric management principles to safeguard the fetus and pregnant women affected with COVID-19 infection.

Author contribution

Saadia, Z. and Farrukh, R. designed the experiment, analyzed the data, and wrote the manuscript; S.Z. analyzed the data; Kanwal. S. and Sumaira, Q. collected the data and helped in discussion writing.

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