

The Severity of Covid- 19 Among Pregnant Women and The Risk of Adverse Maternal Outcome

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ABSTRACT

Background and Aim: The obstetrical complications of pregnant women might elevate to a severe stage due to ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Limited study focused on association between COVID-19 and pregnant women adverse outcomes. The present study was carried out to evaluate the severity of COVID-19 among pregnant women and risk of adverse maternal outcome.

Materials and Methods: This cross-sectional study was carried out on 242 pregnant women of confirmed COVID-19 cases hospitalized in Aziz Fatimah Hospital, Faisalabad and Holy Family hospital Rawalpindi for six months duration from 5th December 2020 to 5th May 2021. Pregnant women demographic details, obstetric characterizations, adverse maternal outcomes, and laboratory findings were noted. Positive tested pregnant women through RT-PCR regardless of clinical symptoms and signs were enrolled as confirmed cases while negative tested pregnant women were excluded. Hypertensive disorders, preexisting pulmonary, obesity, renal, nulliparity, and cardiovascular disease were the maternal risk factors. Different variables were assessed through fisher's test and regression logistics model.

Results: Of the total 242 pregnant women, the prevalence of mild to moderate symptoms, and severe disease were 187 (77.3%) and 43 (17.7%) respectively. About 12 (5%) had a critical stage of the disease. During this study period, about 31 (12.8%) were admitted to the intensive care unit (ICU) and 9 (3.7%) died. Mode of delivery, maternal age, underlying conditions, parity, and admission to ICU were the important demographic factors in severe COVID-19 disease. Other severe maternal outcomes were fever, cough, breath shortness and anosmia. Increase ICU admission and cesarean section delivery were significantly associated with disease severity.

Conclusion: Our study founds a mortality rate of 3.7% among pregnant women with COVID-19. A higher prevalence of intensive care admission and cesarean delivery were reported in acute and severe COVID-19 disease. The obstetrical and neonatal outcomes significantly affected by the severity of maternal disease; neonatal prematurity, ICU admission, and cesarean sections complications.

Keywords: COVID- 19, Pregnant women, Adverse maternal outcomes

INTRODUCTION

The coronavirus disease has emerged as a major epidemic for human health globally since 2019 [1, 2]. COVID-19 pandemic is a novel virus causing illness spectrum from asymptomatic to severe acute respiratory diseases [3, 4]. Pregnant women could be exposed to higher risk complications such as reduced respiratory capacity, hemodynamic changes, altered immunity, and vascular changes. Though, a study conducted on pregnant women with COVID-19 infection suggested similarities about the clinical courses for the general population and pregnant women [5]. However, recent studies reported that additionally 8% to 11% severe outcomes were observed in pregnant women within equivalent age general population [6, 7]. Preexisting health conditions such as hypertension, pulmonary pathologies, and diabetes had a significant association with severe outcomes in the general population [8]. Pregnant women maternal disease advancement and pregnancy risk factors contributed by determinant impacts are still patchy but the evidence-based study suggested a significant contribution to the disease severity [9]. Additionally, a high prevalence of preterm birth

deliveries among coronavirus-infected pregnant women has been reported [10].

The obstetrical complications of pregnant women might elevate to a severe stage due to ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The limited study focused on the association between COVID-19 and pregnant women's adverse maternal outcomes. Clinical manifestations such as mild to severe pneumonia illness, mortality, and asymptomatic disease are significantly correlated with COVID-19. The severe complications of coronavirus among pregnant women could be sepsis shock, respiratory failure, septic shock, multiple organs failure like kidney, and heart, acute respiratory distress syndrome, and thromboembolism [10]. Another study reported an overall mortality rate of 2.3% [11]. The spectrum of COVID-19 disease varies from mild 95.6% to severe 3.6% and critical 0.8% among pregnant women [12]. One study found that the COVID-19 clinical spectrum could be varied and be affected by hypertension, chronic lung disease, diabetes, cancer, and heart disease. The risk of severe disease and mortality was found in COVID-19 patients with disproportional underlying conditions disease [13].

Physiological cardiopulmonary and immunological changes such as increased oxygen consumption, diaphragm elevation, and respiratory tract mucosal edema of pregnancy are the severe pneumonia risk factors [14]. However, pregnant women are vulnerable to infectious disease and other major challenges. Another study associated pregnancy in coronavirus pandemic with increased morbidity, adverse pregnancy outcomes, and mortality [15]. It was found that the prevalence of vaginal and cesarean deliveries was 30.6% and 69.4% respectively. Of the total 256 neonates, reverse polymer chain reaction tested four coronavirus positives, one neonatal death, and two stillbirths [16]. About 14% of pregnant women suffered from severe pneumonia as a maternal complication. During the COVID-19 pandemic, validated recommendations for pregnant women treatment is a need of an hour for prevention of severe coronavirus disease impacting childbirth, mode of deliveries, and pregnancy. Therefore, the present study tends to evaluate the association of severe COVID-19 disease with pregnancy and adverse maternal outcomes.

MATERIALS AND METHODS

This cross-sectional study was carried out on 242 pregnant women of confirmed COVID-19 cases hospitalized in Aziz Fatimah Hospital, Faisalabad and Holy Family Hospital, Rawalpindi for six months duration from 5th December 2020 to 5th May 2021. Pregnant women demographic details, obstetric characterizations, adverse maternal outcomes, and laboratory findings were noted. Positive tested pregnant women through RT-PCR regardless of clinical symptoms and signs were enrolled as confirmed cases while negative tested pregnant women were excluded. Hypertensive disorders, preexisting pulmonary, obesity, renal, nulliparity, and cardiovascular disease were the maternal risk factors. Ethical approval was taken from the respective hospital ethical committee. A polymer chain reaction confirmed positively infected coronavirus pregnant women of 5-42 weeks gestational age were enrolled in this study. Based on the patient’s medical records, demographic details of COVID-19 positive infected pregnant women such as age, body mass index, chronic hypertension, liver disease, chronic diabetes, pre-eclampsia, gestational diabetes, cancer, and liver disease were noted. An ultrasound report was used for gestational age calculation. Azithromycin, hydroxychloroquine, and ceftriaxone were the drugs used for coronavirus disease treatment. Additionally, thrombocytopenia, the concentration of C- reactive protein (CRP), lymphopenia, alanine aminotransferase, leukopenia, white blood cell count, sedimentation rate, and hemoglobin concentration were noted as laboratory findings. Maternal outcomes such

as mode of delivery (vaginal or cesarean deliveries), rate of abortion, and prolong labor during COVID-19 were recorded. In addition, placental abruption, hematoma, and post hemorrhage were the postpartum complications. Furthermore, ICU and hospital stay and mortality rates were recorded from patients’ medical records.

Based on Maternal association, the COVID-19 severity was classified in pregnant women as follows; fever, cough, and fatigue like COVID-19 least common features were grouped as a mild illness; tachypnea (respiration rate >30 bpm), and >50% lung involvement on imaging or hypoxia was severe illness and shock, respiratory failure, and dysfunction of organs were grouped as critical. Different variables were assessed through fisher’s test and regression logistics model. The association between COVID_19 severity and demographics, obstetrics, and laboratory findings were assessed through Fisher test and one-way variance analysis. Adverse pregnancy outcomes predictions were examined through a regression logistics model. The COVID-19 severity, underlying disease, and maternal age were associated. SPSS version 20 was used for statistical analysis with <0.05 as the level of significance.

RESULTS

Of the total 242 pregnant women, the prevalence of mild to moderate symptoms, and severe disease were 187 (77.3%) and 43 (17.7%) respectively. About 12 (5%) had a critical stage of the disease as shown in Table/Figure 1. during this study period, about 31 (12.8%) were admitted to the intensive care unit (ICU) and 9 (3.7%) died. Mode of delivery, maternal age, underlying conditions, parity, and admission to ICU were the important demographic factors in severe COVID-19 disease as shown in Table 2. Increase ICU admission and cesarean section delivery were significantly associated with disease severity. Of the total COVID-19 infected pregnant women, 88 (36.4%) gave birth; out of which 54 (61.4%) had cesarean section while 34 (38.6%) had vaginal deliveries as shown in Figure 2. The COVID-19 infected pregnant women common reported symptoms were breath shortness 152 (62.8%), dry cough 162 (66.9%), headache 58 (24%), fever 89 (36.8%), and muscle aches 65 (26.9%) as shown in Table/Figure 3.

Table 1. Prevalence of mild to moderate, severe and critical cases among COVID-19 infected pregnant women (242)

Disease Symptoms	Frequency n	Percentage %
Mild to Moderate	187	77.3
Severe	43	17.7
Critical	12	5
Total	242	100

Figure 1. Prevalence of mild to moderate, severe and critical cases among COVID-19 infected pregnant women (242).

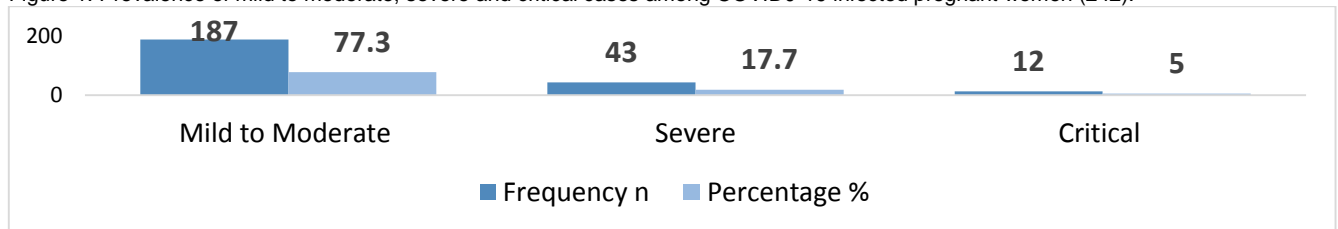


Table 2. Association of COVID-19 severity and demographic details, laboratory and obstetric findings

Features	Mild to Moderate n= 187	Severity N=43	Critical N=12
Maternal Age (years)	27.61±3.45	29.43±4.9	28.32±3.6
Gestational Age (Weeks)	28.2±8.5	29.9±6.9	31.8±3.9
Body Mass Index (BMI)			
Normal	155 (82.9%)	27 (62.8%)	7 (58.3%)
Overweight	14 (7.4%)	5 (11.6%)	1 (8.4%)
Obese	18 (9.6%)	11 (25.6%)	4 (33.3%)
Parity			
Nulliparity	51 (27.3%)	7 (16.3%)	5 (41.7%)
Multiparous	136 (72.7%)	36 (83.7%)	7 (58.3%)
Underlying conditions			
No Medical Treatment	161 (86.1%)	21 (48.8%)	7 (58.3%)
Hypertension	13 (7%)	13 (30.2%)	4 (33.3%)
Diabetes	3 (1.6%)	7 (16.3%)	0 (0.0%)
Liver disease	2 (1.1%)	0 (0.0%)	0 (0.0%)
Anemia	4 (2.1%)	0 (0.0%)	0 (0.0%)
Renal disease	0 (0%)	0 (0.0%)	0 (0.0%)
Heart disease	3 (1.6%)	1 (2.3%)	1 (8.3%)
Severe pre- eclampsia	2 (1.1%)	1 (2.3%)	1 (8.3%)

Figure 2. Prevalence of Vaginal and Cesarean deliveries among 88 pregnant women given birth

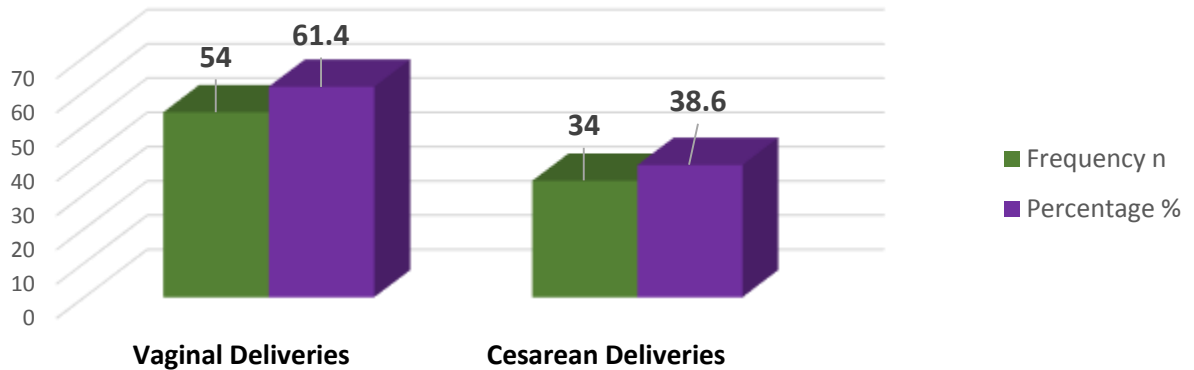
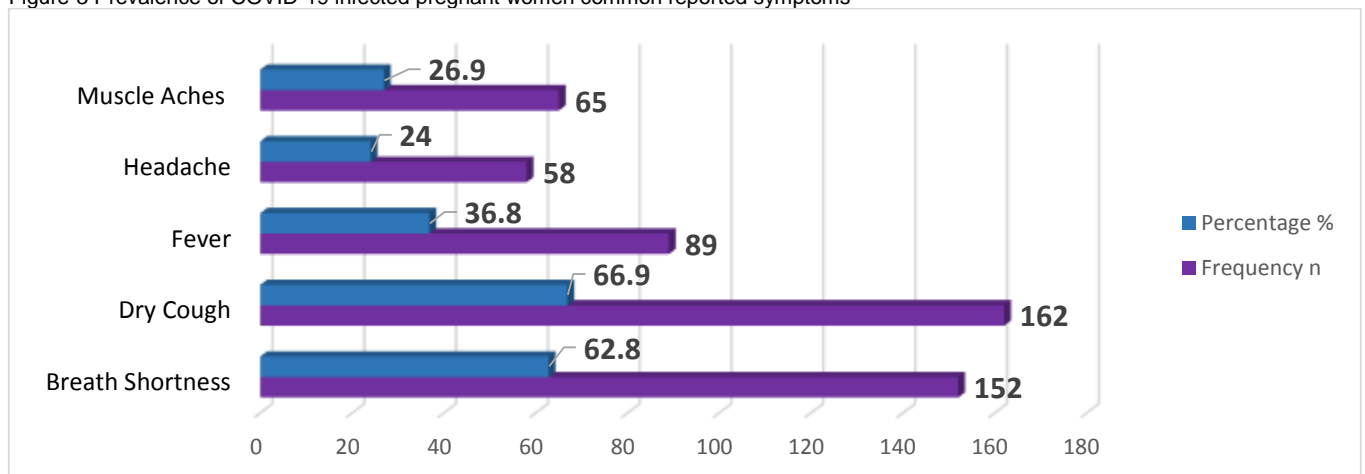


Table 3. Prevalence of COVID-19 infected pregnant women common reported symptoms

Symptoms	Frequency n	Percentage %
Breath shortness	152	62.8
Dry cough	162	66.9
Fever	89	36.8
Headache	58	24
Muscle Aches	65	26.9

Figure-3 Prevalence of COVID-19 infected pregnant women common reported symptoms



Laboratory findings details such as Hemoglobin levels, Lymphopenia, Thrombocytopenia, and ESR (mm/h), and CRP (mg/L) are shown in Table 4.

Table 4. Association between laboratory findings of pregnant women and COVID- 19 severity

Laboratory Findings	Mild to Moderate Cases n=187	Severe Cases n=43	Critical Cases n=12
Hemoglobin levels	10.86±2.1	11.6±1.5	10.43±1.1
Lymphopenia (Yes, No)	51 (27.3%), 136 (72.7%)	7 (16.3%), 36 (83.7%)	7 (58.3%), 5 (41.7%)
Thrombocytopenia	40 (21.4%), 147 (78.6%)	9 (20.9%), 34 (79.1%)	4 (33.3%), 8 (67.7%)
ESR (mm/h) [Normal, Increased]	7 (3.7%), 180 (96.3%)	5 (11.6%), 38 (88.4%)	5 (41.7%), 7 (58.3%)
CRP (mg/L)	23 (12.3%), 164 (87.7%)	6 (14%), 37 (86.1%)	2 (16.7%), 10 (83.3%)

Adverse maternal outcomes such as Hospital length of stay, mode of delivery, prolonged labor, and postpartum compliance among pregnant women were associated with COVID-19 positive infected patients as shown in Table 5.

Table-5. Correlation of adverse maternal outcomes in pregnant women with COVID19 infection.

Pregnancy Outcomes	Mild and Moderate (187)	Severity (43)	Critical (12)
Hospital Length	3.7±1.6	6.9±3.8	12.9±3.8
Prolong labor			
Yes	3 (1.6%)	5 (11.6%)	2 (16.7)
No	184 (98.4%)	38 (20.3%)	10 (83.3%)
Postpartum Complications			
No compliance	165 (88.2%)	37 (86%)	3 (25%)
Placental abruption	1 (0.53%)	1 (2.3%)	1 (8.3%)
Hematoma	2 (1.1%)	0 (0%)	0 (0%)
Postpartum hemorrhage	19 (10.2%)	5 (11.6%)	8 (66.7%)
Hospitalized in the ICU			
Yes	0 (0%)	19 (44.2%)	12 (100%)
No	187 (100%)	24 (55.8%)	0 (0%)
Mortality Rate			
Yes	0 (0%)	0 (0%)	9 (75%)
No	187 (100%)	43 (100%)	3 (25%)

DISCUSSION

The present study focused on the severity of coronavirus disease among pregnant women and evaluated the adverse maternal outcomes risk factors associated with COVID-19. Maternal mortality rate and ICU admission were the factors for defining the severe adverse outcomes. It has been found that hypertension, diabetes, and pulmonary comorbidities were significantly associated with adverse maternal outcomes. Regarding the live birth rate, no adverse complications patients and adverse complications pregnant women had similar results. Yet, preterm birth, neonate’s admission to ICU, and cesarean deliveries increased risks were perceived. Another study found similar results in terms of disease severity in maternal adverse outcomes while COVID-19 pregnant women estimated as 13% [17]. One study found a significantly higher prevalence of severe maternal outcomes in pregnant women compared to non-pregnant women [18].

The maternal disease severe risks observed have matched the previous study conducted on the general population. Diabetes mellitus, pulmonary pathology, and hypertension were the subsequent maternal disease outcomes [19]. Another study reported that pregnant women above 35 years had higher risks for severe disease along with other pre-existing diabetes, BMI, and chronic hypertension [20]. Remarkably, obesity was an insignificant risk factor of severe adverse outcomes. Obstetrical complications such as pre-eclampsia, elevated liver enzymes, low platelets, hemolysis, and gestational hypertension were well-known mechanisms for endothelial changes in pregnant women [21, 22]. These factors significantly contribute to complications of COVID-19

disease [23]. COVID-19 infected pregnant women’s frequent clinical symptoms were breath shortness, headache, fever, cough, and muscle aches. It has been observed that COVID-19 clinical manifestation overlapped with pregnancy symptoms such as vomiting, nausea, fatigue, nasal congestion, and breathe shortness which should be elevated among pregnant women [24].

Parity, underlying conditions, and maternal age were the key demographic details in our study. Increased lymphopenia and liver enzymes were the critical and severe laboratory findings. Additionally, ICU admission and cesarean deliveries increased significantly with severe disease as a maternal outcome. Other studies’ results matched our findings [25]. Gestational diabetes and postpartum complications were the common underlying conditions among COVID-19 infected positive tested pregnant women. Other studies also reported one-third of pregnant women were hospitalized with coronavirus underlying conditions accompanied by COVID-19 severity [26, 27].

Our study observed that body mass index and maternal age had a significant association with COVID-19 severity. The COVID-19 severity likelihood increased with BMI and maternal age. Another study found similar findings of BMI and maternal age contribution to the COVID-19 severity [28]. One study reported the prevalence of hospitalized coronavirus-infected pregnant women of age above 35 years to be 40% [29]. Our study associated the COVID-19 severity with laboratory findings with increased CRP and liver enzymes while decreased lymphocytes levels. Another study found about 35% of lymphocytes in COVID-19 infected pregnant women and increased CRP

[30]. Secondary lymphohistiocytosis is the syndrome caused by COVID-19 viral infections. The mortality rate among COVID-19 patients increased due to the development of hypercytokinemia, cytokine, and multiple organ failure [31].

About 31 (12.8%) pregnant women were admitted to the intensive care unit when the rate of hospitalization was associated with coronavirus disease severity. The risk of ICU admission increased to triple with underlying disease conditions. Another study found a prevalence of 13% regarding pregnant women admission to the intensive care unit [32]. The mortality rate of the positive tested coronavirus infected pregnant women was 3.7%. Various studies reported higher mortality rate among COVID-19 infected pregnant women compared to uninfected women [32, 33]. Another study reported 11.4% mortality rate among coronavirus infected pregnant women [34].

CONCLUSION

Our study finds a mortality rate of 3.7% among pregnant women with COVID-19. A higher prevalence of intensive care admission and cesarean delivery were reported in acute and severe COVID-19 disease. The obstetrical and neonatal outcomes significantly affected by the severity of maternal disease; neonatal prematurity, ICU admission, and cesarean sections complications.

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