

Comparison of clinical, laboratory, and imaging findings in pregnant and non-pregnant women with COVID-19: a case-control study

Asfa Zawar, Memuna Sohaib, Komal Ali

**Abstract:**

**Background:** Clinical, radiological, and laboratory findings characteristic of the coronavirus disease 2019 (COVID-19) infection have already been investigated and identified; however, data on pregnant women infected with COVID-19 are limited. This study aims to examine the clinical, radiological, and laboratory characteristics of pregnant women compared to non-pregnant women with COVID-19 disease.

**Method:** This hospital-based retrospective age-matched case-control study included two groups, pregnant and non-pregnant women, each consisting of 51 patients hospitalized with COVID-19 in Ejaz Hospital Lalamusa, Pakistan. Demographic, clinical, and laboratory information was extracted from medical records using a predefined checklist.

**Results:** Except for cough, there were no statistically significant differences in clinical signs and symptoms between pregnant and non-pregnant women. Although hemoglobin oxygen saturations are statistically significant among the two groups, this difference is not clinically significant (95% vs 93%). There were no statistically significant differences between pregnant and non-pregnant women in the pattern of pulmonary involvement in chest CT findings. Laboratory factors such as serum hemoglobin, red blood cell count, absolute lymphocyte count, prothrombin time and partial thromboplastin time, serum creatinine, serum potassium, and lactate dehydrogenase had statistically significant differences between the two groups. However, these differences were not clinically significant.

**Conclusion:** In a few aspects, the clinical characteristics and laboratory test results of COVID-19 in pregnant patients seem to be distinctive from their nonpregnant controls. We believe our findings can guide the prenatal and postnatal considerations for COVID-19 pregnant patients.

**Keywords:** Clinical features; Imaging; COVID-19; Laboratory tests; Pregnancy

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Correspondence:

Dr Asfa Zawar  
Consultant Gynecology  
Ejaz Hospital Lalamusa, Pakistan  
Email: Dentistnadia38@gmail.com

**Introduction**

In December 2019, in the city of Wuhan, the center of Hubei in China, a case of pneumonia without a known reason and usual presentation was found, and the symptoms were attributed to the coronavirus disease 2019 (COVID-19) after the virus was isolated and cultured. Clinical manifestations in patients with COVID-19 have a wide range, including asymptomatic infection, upper respiratory tract infection, severe viral pneumonia, respiratory failure, and even death, of which only a percentage of patients will require hospitalization (1-9)

In imaging findings, common findings in patients' computed tomography (CT) scans include bilateral patchy shadows, interstitial abnormalities, and focal glass opacity. Lymphopenia, neutropenia, and thrombocytopenia have also been found in the laboratory criteria, and lymphopenia is seen especially in patients with a very severe condition. Other laboratory parameters such as erythrocyte sedimentation rate (ESR), serum lactate dehydrogenase (LDH), creatinine (Cr), C-reactive protein (CRP), and D-dimer show an increase (10). Since no definitive treatment or optimal vaccination method has been found for this disease, quick diagnosis of sick people in the early stages of the disease and isolation of these patients from society is essential (11). One

way to diagnose the disease is to use a CT scan. The use of CT scans to diagnose the disease is controversial, and on the other hand, imaging findings may be unusual in patients and thus confuse the medical staff (12-14). Another suggested way to diagnose this disease is the use of cellular-molecular diagnostic tests, a real-time reverse transcription polymerase chain reaction (RT-PCR) method that is used for this purpose having sufficient sensitivity and specificity, hence, is the most widely used method (15,16). Maternal mortality is one of the important indicators for evaluating the social and economic development and shows the efficiency of a country's health system. Improving maternal health is one of the main priorities of the World Health Organization. Many causes that can lead to maternal death are avoidable and preventable, including infectious diseases, like COVID-19. Pregnant women who are infected with this disease are more likely to die due to infection or undergo premature birth, fetal growth restriction, and fetal distress; therefore, pregnant women should be considered as an at-risk population in strategies focused on the prevention and management of this infection. Considering that pregnant women are among the vulnerable groups in society, early diagnosis of the disease in pregnant mothers is of vital importance (17, 18). Ozer et al.

(2021) concluded that laboratory findings and imaging studies might be different in pregnant and non-pregnant mothers (19). Mohr-Sasson et al. (2021) found that the laboratory characteristics of pregnant women with COVID-19 did not differ from that of the non-pregnant, although the trend of decreasing the number of lymphocytes was observed in the group of pregnant women (20). Also, Asghar et al. (2022) concluded that COVID-19 does not show a significant risk of disease severity for pregnant women compared to non-pregnant women in the same age group (21). The pathogenic mechanisms and adverse consequences of COVID-19 have attracted the attention and focus of many researchers. However, limited information is available on its management during pregnancy. Some reports showed that the clinical characteristics of COVID-19 are the same in pregnant and non-pregnant patients (20). However, the potential of the virus to cause severe complications for mothers and infants requires careful screening during pregnancy and long term follow-up. Although existing studies provide critical knowledge, research in this area is limited and results are confusing. Therefore, due to the high prevalence of this disease and its high mortality, as well as the insufficiency and inconsistency of the studies, it is important to examine laboratory findings and imaging in pregnant and non-pregnant women. Consequently, the present study was conducted to compare clinical, laboratory, and imaging findings in pregnant and non-pregnant women with COVID-19.

### Methods

**Design, settings, and participants** The present retrospective case-control study was conducted at Ejaz Hospital Lalamusa, Pakistan, a tertiary care hospital located in southern Iran from 20/03/2020 to 19/02/2022. The case group includes all hospitalized pregnant with COVID-19 with a positive PCR molecular test result. The control group were age-matched non-pregnant women hospitalized simultaneously (within one month) at the same time frame as the case group, having a positive RT-PCR molecular test result (confirmed COVID-19 cases), and providing consent to participate. Patients who were hospitalized due to medical impressions other than COVID-19 were excluded from the study. This study was reviewed and approved by the ethics committee of Ejaz Hospital Lalamusa, Pakistan and has the code of ethics "IR.IHLPAK.1400.113". Also, informed consent was taken from patients on admission papers that explained to them that the hospitalization record may be used for research purposes with confidentiality, without their names and surnames. In addition, informed consent was obtained from the participants based on the Helsinki Declaration.

#### 2.2. Data Collection:

A researcher-made checklist, including demographic, clinical, and laboratory information, was used to collect data. The data was collected by expert nurses who received prior training for this task. Throughout the data gathering process, they are closely supervised by a general practitioner. Demographic information included age, smoking, pregnancy characteristics of pregnant women, the history of hypertension, asthma, diabetes, chronic kidney disease, chronic liver disease, and other underlying conditions. Clinical information included the number of hospitalization days, systolic and diastolic blood pressure, respiratory rate, heart rate, body temperature, blood oxygen percentage, fever symptoms, cough symptoms, shortness of breath symptoms, digestive symptoms, headache symptoms, and muscle pain symptoms. The types of pulmonary involvement were assessed by a radiologist: the different types of pulmonary involvements were Multi-Focal, Nodular, Alveolar, ground-glass opacification/opacity (GGO), Consolidation, and Pleural effusion. Finally, laboratory findings were collected from patients' files.

#### 2.3. Data analysis

In this study, quantitative variables were described using mean and standard deviation, and qualitative variables were described using frequency and percentage. Normality and skewness were assessed with the Shapiro–Wilk test and visual inspection of P-P plots, Q-Q plots, and histograms. Collinearity between variables was assessed with the variance inflation factor. To analyze the data and compare the averages between two groups of pregnant and non-pregnant women, the independent t-test was used if the distribution of data was normal, and the Mann-Whitney U test was used if the data were non-normal. Also, the chi-square test was used to check the relationship between qualitative variables. Statistical analyses were performed using SPSS v.23 software, and in all cases, the significance level was considered less than 0.05

### Results

**3.1. Baseline Characteristics** A total of 102 women with COVID-19, including 51 pregnant and 51 non-pregnant women in the control group, with an age range of 20 to 42 years old and an average age of  $31.6 \pm 5.27$  ( $P = 0.104$ ) years, were included in the study. Regarding hospitalization, 3 pregnant women and 2 non-pregnant women were hospitalized in ICU and the rest were hospitalized in non-ICU wards. However, we found a statistically significant higher tobacco consumption in non-pregnant women ( $n = 8$ ; 15% vs  $n = 1$ ; 2%) than in pregnant women ( $P = 0.031$ ). There were no statistical significances between pregnant and non-pregnant women in the history of hypertension, asthma, diabetes, chronic kidney disease, chronic liver disease, and other underlying conditions.

<b>Table 1: The characteristics of pregnant women infected with COVID-19 in the third trimester of pregnancy</b>	
<b>Subgroup</b>	<b>Number</b>
<b>Trimester</b>	
First trimester	4(8.0)
Second trimester	24(48.0)
Third trimester	22(44.0)
<b>Late termination of pregnancy*</b>	
Yes	10(19.6)
No	41(80.4)
<b>Number of pregnancies</b>	
1 time	22(44.9)
2 times	13(26.5)
3 times	8(16.3)
4 times	6(12.2)
<b>Number of births</b>	
Never	22(44.9)
1 time	13(26.5)
2 times	9(18.4)
3 times	5(10.2)
<b>Type of labor</b>	
Cesarean section	7(70)
Normal vaginal delivery	3(30)
<b>Vaginal bleeding</b>	
Yes	0(0)
No	51(100)
<b>Rupture of water bag</b>	
Yes	4(7.8)
No	47(92.2)
<b>Premature labor pain</b>	
Yes	6(11.8)
No	45(88.2)
<b>Preclampsia</b>	
Yes	3(5.9)
No	48(94.1)

### 3.2. Clinical Characteristics

Table 1 shows the characteristics of pregnant women infected with COVID-19 and its consequences. The average gestational age in them was  $26.78 \pm 8.17$  weeks. Also, most of the pregnant women were in their first pregnancy and a low percentage of them suffered from ruptured water sacs, premature labor pain, and pre-eclampsia. Also, vaginal bleeding was not observed in any of the Causes.

**Table: 2 Comparison of clinical characteristics and laboratory findings between pregnant women with COVID-19 and non-pregnant patients**

Characteristics	Pregnant	Non-pregnant	p-value
<b>Hospitalization days</b>	5.31±2.61	6.14±3.72	0.048
<b>Vital sign</b>			
Systolic blood pressure	116.67±12.87	116.98±10.21	0.495*
Diastolic blood pressure	71.12±9.31	74.45±9.0	0.65*
Respiratory rate per minute	20.4± 11.58	19.29± 11.73	0.226*
Heart rate per minute	99.92± 18.26	97.60± 13.15	0.307*
Temperature	37.05±1.08	37.38±0.75	0.051*
Blood oxygen Saturation on admission	95.08±3.68	93.21±5.3	0.025
<b>Clinical sign and symptoms</b>			
Fever	11(22.0)	15(29.4)	0.394
Cough	25(49.0)	35(68.6)	0.044
Shortness of breath	36(72.0)	39(76.5)	0.607
Gastrointestinal symptoms	7(13.7)	11(21.6)	0.299
Headache	11(21.6)	7(13.7)	0.299
Muscular pain	20(39.2)	20(39.2)	0.999
<b>Laboratory findings</b>			
White blood cell count(*10 <sup>3</sup> )	7.72±5.09	7.12±6.91	0.102*
Absolutely mphocyte count	1158.04±575.13	1991.34±3567.70	0.039*
Hemoglobin(mg/dl)	10.75±1.47	12.19±1.55	<0.0001
Red blood cell count(*10 <sup>6</sup> )	3.93±0.5	4.7±.52	>0.0001
Platelet count (perdL)	195.72±79.96	225.02±94.15	0.137*
Prothrombintime(second)	11.48±1.56	12.81±2.46	0.007*
Partial thrombo plastintime(second)	38.65±5.76	26.45±3.33	0.001*
International normalized ratio	1.03±0.14	1.08±0.16	0.007*
Erythrocytes edimentation rate(mm/hr)	43.40± 21.25	38.53± 27.21	0.094*
C-reactive protein(mg/L)	37.26± 29.92	47.73± 44.12	0.605*
Blood urea nitrogen(mg/dL)	8.09±3.79	12.05±4.67	0.0001
Creatinine (mg/dL)	0.83±0.15	0.97±0.25	0.0001
Na (mEq/L)	138.26±1.95	137.42±2.78	0.077*
K(mEq/L)	3.84±0.36	4.08±0.4	0.008*
As partateamino transferase(IU/L)	41.14± 25.55	41.59± 23.25	0.866*
Alkaline phosphatase(IU/L)	249.45±115.13	212.88±88.53	0.122*
Creatine phosphokinase(IU/L)	193.88±152.27	252.51±271.32	0.898*
Lactated ehydrogenase(U/L)	433.22±164.21	584.20±346.36	0.061*
Total bilirubin(mg/dL)	0.57±0.27	0.63±0.76	0.562*
Data were presented as mean ± standard deviation or frequency (%). According to Mann-Whitney U test			

cases. Tables 2 show the comparison of clinical findings in patients with COVID-19 in pregnant women with the control group. The average length of stay in pregnant women was less than in non-pregnant women (p =0.048). Although the difference between the average

Percentage of blood oxygen between two groups of pregnant and non-pregnant women was significant, this difference was clinically non-significant (95% vs 93%). Also, in comparing clinical symptoms in pregnant women and the non-pregnant control, the findings indicate that none of these variables were statistically significant except for cough (p = 0.044).

**Table 3 Comparison of pulmonary involvement in CT between pregnant women with COVID-19 and non-pregnant patients**

Pulmonary involvement	Pregnant (n=28)		Non-pregnant (n=51)	
	N	%	N	%
Multi-Focal	10	35.7	9	24.1
Nodular	3	10.7	5	10.1
Alveolar	1	3.6	6	8.9
Ground glass type	11	39.3	25	45.6
Consolidation	2	7.1	5	8.9
Plural Effusion	1	3.6	1	2.5

### 3.3. Laboratory Findings

The findings show that absolute lymphocyte count, hemoglobin level (Hb), red blood cell (RBC) count, prothrombin time (PT), partial thromboplastin time (PTT), blood urea nitrogen (BUN), Cr level, serum K, and LDH levels had a significant statistical difference between two groups of pregnant and non-pregnant ( $p < 0.05$ ). However, these differences were not clinically significant. An absolute lymphocyte counts of less than 1500 was considered lymphopenia, 39 (78.0%) and 32 (62.7%) of pregnant and non-pregnant women had lymphopenia, respectively, which was a non-significant statistical difference ( $p = 0.093$ ). Thrombocytopenia (platelet count less than 150000 per microliter) was in 14 (27.5%) and 9 (17.6%) of pregnant and non-pregnant patients, respectively, that was a non-significant statistical difference ( $p = 0.236$ ). Leukopenia (total white blood cell count of less than 4,000 per microliter) was observed in 6 (11.8%) and 14 (27.5%) of pregnant and non-pregnant patients respectively that was a significant statistical difference ( $p = 0.046$ ). Pregnancy is not an effective factor in the occurrence of certain types of renal complications (Table 2) 3.4. Imaging Findings

Table 3 shows the comparison of pulmonary involvement in CT scans between pregnant women and nonpregnant controls. The findings show that a total of 77% of pregnant and non-pregnant women had lung involvement, including multi-focal, nodular, alveolar, GGO, consolidation, and pleural effusion. Among the types of lung involvement in both groups, GGO lung involvement was the most frequent, and pleural effusion lung involvement was the least frequent. There were no statistically significant differences between pregnant and non-pregnant women in lung CT scan patterns ( $p = 0.462$ ).

### Discussion

The results of the present study show that clinical, laboratory, and radiological features do not significantly differ between pregnant and non pregnant women with COVID-19, and pregnancy is not an influential factor in the exacerbation of COVID-19. In general, clinical signs and symptoms were not different between pregnant and non-pregnant women except for cough. This result is in line with the results of previous studies, in the study of Mohr-Sasson et al., which was conducted in 2020 (20). Also, Liu et al. (22) reported 23% shortness of breath and 70% fever in a study with a population of 13 pregnant women infected with COVID-19. In another study with a larger population, Chen et al. (2020) (23) evaluated 122 pregnant women with COVID-19, in which fever was reported in 75%, cough in 73%, and shortness of breath in only 7% of the cases. The results of these two studies are inconsistent with the current research. The reason for the high prevalence of shortness of breath and low prevalence of fever in the present study in pregnant women with COVID-19 can be due to the increase in people's awareness of the symptoms of COVID-19 and their faster referral to health centers in case of the slightest respiratory problems. Therefore, the prevalence of respiratory symptoms at the time of admission to the health centers was higher than fever in this study. In addition, the number of hospitalization days of pregnant women with COVID-19 was significantly less than non-pregnant women, and this point is in line with the results of the study by Wang et al. (2020) (24) which was conducted on 30 pregnant and 42 non-pregnant women infected with COVID-19. This issue can be a sign of prioritization of pregnant patients to receive medical services and faster referral of pregnant

patients with milder conditions due to concern about pregnancy. As a general report, the state of pulmonary and clinical involvement of pregnant women with COVID-19 was milder compared to non-pregnant women, and this result is in line with the study of Wang et al. (2020) (24). 55% of all pregnant women with COVID-19 in this study had CT scan, while all of non-pregnant women had it. The most common type of pulmonary involvement in pregnant and non-pregnant women was the ground glass type, and the least type of involvement in them was pleural effusion with a prevalence of less than 10% in both groups. The frequency of pulmonary CT scan patterns was similar in both groups, and this point is in line with the findings of the study by Wu et al. (2020) (25). Laboratory abnormalities indicative of coronavirus infection have been identified. Study results have shown that lymphopenia is the most common finding, observed in 83% of 1099 infected patients, followed by thrombocytopenia, which was observed in 36.2% of the patients. Leukopenia has also been reported in 33 % of the patients, and 60% of the patients have elevated CRP levels (12, 26) In the present study, lymphopenia in pregnant and non-pregnant women was found to be about 78% and 63%, respectively, which in both groups is lower than the average prevalence of lymphopenia in a normal society (26). Thrombocytopenia in pregnant and non-pregnant women was about 27% and 18%, respectively, and leukopenia was 12% and 27%, respectively, both factors of thrombocytopenia and leukopenia had a lower prevalence in both groups compared to a normal population. In the study by Mohr-Sasson et al. (2020) (20), the rate of lymphopenia in pregnant women was reported to be 44%, which is in line with our study. The mean lymphocyte count in pregnant women was significantly lower than in non-pregnant women and a similar result was obtained in the study by Cheng et al. (2019) (27). Concerning the severity of inflammation, no significant difference was observed in CRP between pregnant and non-pregnant women, and this point is inconsistent with the study of Cheng et al. (2019) (27) The reason is the lack of high specificity of the CRP kits used in the present study, as well as the use of highly sensitive CRP in similar studies. Highly sensitive C-reactive protein (h-CRP), procalcitonin, and interleukin-6 are three markers widely

used to detect the acute phase of systemic inflammation, while procalcitonin is specific for distinguishing bacterial and viral infections (28). Therefore, it is obvious that the changes and dispersion of CRP values in the present study are very high and this has caused the non-significance of this factor between the two groups. Creatine, BUN, and lactate dehydrogenase enzymes were significantly higher in non-pregnant women than in pregnant women, and these results are inconsistent with the studies of Cheng et al. (2019) (27). However; in the study by Mohr-Sasson et al. (2020) (20) similar to the results of the present study, creatinine, and BUN values were reported to be higher in non-pregnant women than in pregnant women with COVID-19. It is important to mention that despite the significant difference between the two groups of pregnant and non-pregnant women, all these values are within the normal range, so clinically the difference between these factors is not significant between the two groups.

#### 4.1. Limitations

This case-control study provides extensive information on pregnant and non-pregnant women with COVID-19.

Additionally, primary data can be used for a better understanding of laboratory results, immediate actions, pre-awareness, and diagnosis. Among the limitations of this study, a case-control design can be mentioned. While case-control studies are useful for investigating associations, they cannot establish causation. Moreover, the study was conducted in one referral hospital, potentially limiting the generalization of findings to other populations or regions. Although Hb varies during pregnancy trimesters, we analyzed it in total, since there was a low sample size in trimester subgroups. It is suggested that future studies on a wider population and also focusing on the consequences of COVID-19 infection in pregnancy will provide clearer information.

#### Conclusion

In general, it can be concluded that the clinical, laboratory, and radiological characteristics of COVID-19 are not different between pregnant and non-pregnant women. Our findings can guide the prenatal and postnatal considerations for COVID-19 pregnant patients.

## 6. Declarations

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- Dr Asfa Zawar  
MBBS , FCPS  
Consultant Gynecology  
Ejaz Hospital Lalamusa, Pakistan
- Dr. Memuna Sohaib  
MBBS , FCPS  
Senior Registrar  
Ejaz Hospital Lalamusa, Pakistan
- Dr Komal Ali  
MBBS , FCPS  
Lecturer  
SMBBMU Larkana

<b>Authors Contribution</b>	
<b>Dr Asfa Zawar</b>	<i>Conception of study design, acquisition, analysis, and interpretation of data.</i>
<b>Dr Memuna Sohaib</b>	<i>Drafting and methodology, data interpretation</i>
<b>Dr Komal Ali</b>	<i>Analysis and interpretation of data for work &amp; Data Collection</i>