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Evaluation of epidemiology, clinical signs, and laboratory factors in pregnant patients with COVID-19 admitted to Valiasr Hospital in Birjand from 2020 to 2021

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Abstract

Pregnant women are considered a high-risk group during the coronavirus crisis. Due to the physiological and immune system changes that occur during pregnancy, they may be more susceptible to SARS-CoV-2 infection and experience more severe clinical outcomes. A cross-sectional study was conducted on all pregnant women with COVID-19 who were hospitalized at Valiasr Hospital in Birjand. Participants were selected through a consus method, with a total sample size of 250 individuals. The research tool consisted of a researcher-developed checklist that includ demographic information, clinical symptoms, medical examinations, and paraclinical results. The average age of the mothers was 30.48 ± 5.32 years. The most common underlying conditions were hypothyroidism (12.7%), gestational diabetes mellitus (9.3%), hypertension (2.0%) and diabetes mellitus (1.5%). Common clinical symptoms observed in pregnant women with COVID-19 included cough (39.5%), myalgia (25.9%), shortness of breath (24.4%), fever (21.5%), and nausea (14.6%). Inflammatory markers such as ESR and CRP were reported as 14.88 ± 30.52 mm/h and 27.62 ± 34.30 mg/L, respectively. The average hospitalization duration for pregnant women with COVID-19 was 3.05 ± 3.17 days. The mortality rate among pregnant women with COVID-19 was only 1 person (0.5%). Hypothyroidism was identified as the most prevalent underlying condition among the pregnant women in this study. It is important to implement measures to manage this condition and prevent any negative impacts on both the mother and the fetus.

Keywords: COVID-19, Pregnancy, Epidemiology, Clinical signs

Introduction

The coronavirus disease (Covid-19) first emerged in December 2019 in Wuhan, China. It quickly spread worldwide and was officially declared an epidemic by the World Health Organization (WHO) (1, 2). Subsequent studiesidentified a new type of coronavirus as the cause of the disease, which the WHO named SARS-CoV-2 and the disease itself was named Covid-19 (3). Most patients experience mild symptoms such as fever, cough, sore throat and muscle pain, although some develop severe conditionsacute conditions like multiple organ failure, acute respiratory distress syndrome, pulmonary edema and pneumonia (4, 5).

During an epidemic of infectious diseases, pregnant women and their fetuses are considered part of the high-risk population. It should be noted that a corona infection in pregnant women may be associated with severe complications and even death (6).Pregnant women, fetuses, and newborn babies are exposed to more risks during outbreaks of infectious diseases than other populations. Studies have shown that some viral diseases can lead to unwanted complications in pregnant women, their fetuses or babies (7, 8). Most studies have focused on patients with the novel coronavirus in the general population, so limited details are available on pregnancy outcomes in women infected with Covid-19. Pregnant women are relatively immunocompromised or immune-suppressed, theoretically making them more at risk of contracting the virus (9).Therefore, it is necessary to prevent the infection of pregnant women during an epidemic or pandemic such as Covid-19 (10).

Reports have shown a high prevalence of maternal death (11, 12) and a higher frequency of maternal and perinatal problems in patients with Covid-19. However, the data is still insufficient and further investigation of laboratory and clinical tests is necessary in this group of women (13). In order to effectively manage this crisis, a detailed report on the prevalence of the disease in pregnant women, the rate, and causes of death is nessasary. While many articles have described hemocytometric and hematological changes in Covid-19 patients, there are still few studies in this field in pregnant women highlighting the need for more research (10, 14, 15).

Given the high risk of the disease in pregnant women, the novelity of this epidemic globally, and the lack of similar studies in Birjand, the present study was conducted to investigate the epidemiology, clinical symptoms and laboratory factors in pregnant patients with Covid-19 who were hospitalized in Valiasr Hospital in Birjand.

Methods

In this retrospective descriptive study, all pregnant women with COVID-19 who were admitted to Valiasr Hospital in Birjand from the beginning of 2020 to the end of 2021 were included. Sampling was conducted using a census method, with a sample size estimated to be 205 individuals. Inclusion criteria required a positive PCR test for COVID-19, while exclusion criteria included a lack of access to the patients' medical records or inaccurate documentation. Ptient files and their contents were utilized as the promary data sources for the study. A researcher developed checklist was used to collectd emographic characteristics, clinical symptoms, medical examinations and paraclinical results. Following approval from the university's ethics committee, basic information such as demographics, parity, birth weight, gestational age, history of abortion or premature birth, underlying diseases, clinical symptoms (fever, fatigue, cough, runny nose, nasal congestion, headache, sore throat or gastrointestinal symptoms like diarrhea) and oxygen saturation were extracted from the patients' files. All gathered data was recorded in Excel and analyzed using SPSS 19. Descriptive statistics including number, percentage, mean and standard deviation were used for reporting. The study was conducted in compliance with the university's ethics committee under the

reference number IR.BUMS.REC.1401.190. Patient confidentially was maintained throughout data collection and analysis ensuring the independence of patient identities.

Results

The average age of the mothers included in the study was 30.48 ± 5.32 years. Additionally, gestational age based on the time of the last menstrual period (LMP) and ultrasound, was reported as 37.69 ± 2.07 and 37.50 ± 2.16 weeks, respectively. The average number of pregnancies or the patients was 1.35 ± 1.12 and the average weight of the babies was 2985.98 ± 583.12 grams.

The most common underlying diseases reported in the studied pregnant mothers were hypothyroidism (12.7%), gestational diabetes mellitus (9.3%), high blood pressure (2.0%) and diabetes mellitus (31.5%). Additionally, dyslipidemia, seizures, chronic obstructive pulmonary disease (COPD) and irritable bowel syndrome (IBS) each had the lowest frequency among underlying diseases with a frequency of 1 person (0.5%).

29 people (32.6%) of the mothers included in the study experienced preterm delivery (below 37 weeks). In terms of pregnancy complaints, labor pain and vaginal discharge were the most commonly reported complaints among the study subjects with frequencies of 26 (12.7%) and 16 (7.8%) respectively. Preeclampsia, convulsions, placental abruption, absence of fetal heartbeat (FHR), intrauterine fetal death (IUFD), and hydrops fetalis each had the lowest frequency among pregnancy-related complaints with a frequency of 1 case (0.5%). The frequency of other pregnancy records in the studied subjects can be seen in Table 1.

The prevalence of clinical symptoms observed in pregnant mothers with COVID-19 was reported in 16 cases (8.1%), 36 cases (18.2%) and 146 cases (73.7%) in the first, second and third trimesters, respectively. The most clinical symptoms observed were cough (81 people, 39.5%), myalgia (53 people, 25.9%), shortness of breath (50 people, 24.4%), fever (44 people, 21.5%) and nausea (30 people, 14.6%). Less common symptoms included flushing, convulsions, joint pain, loss of consciousness, and blood sputum, each with 1 case (0.5%). The frequency of other clinical symptoms in the studied subjects can be seen in Table 2.

The average blood oxygen saturation level (SpO2) was 93.96% ± 3.88%. Additionally, the white blood cell count and platelet count were 6.98 ± 2.37 and 196.30 ± 58.06 thousand per cubic millimeter of blood, respectively. The average hemoglobin level was 12.07 ± 1.41 g/dL and the average hematocrit level was 35.13 ± 3.62%. The average results of the PTT, PT, and INR tests were 12.39 ± 1.18 seconds, 32.37 ± 5.07 seconds, and 1.02 ± 0.19 units, respectively. The average levels of liver enzymes ALT and AST were reported as 27.09 ± 28.63 and 35.33 ± 18.82 units per liter, respectively. The average results of LDH, CRP, ESR and ferritin inflammatory indices were reported as 30.52 ± 14.88 mm/hour, 34.30 ± 27.62 mg/liter, 523.70 ± 211.44 units/liter, and 145.91 ± 132.71 ng/dL. In total, data related to the D-dimer test was available for 20 of the people studied. In 7 cases (35.0%), the test result was below 1000 nanomol per liter, in 6 cases (30.0%) the test result was between 1000 and 2000 nanomol per liter, in 4 cases (20.0%) the test result was between 2000 and 7000 nanomol per liter and in 3 cases (15.0%) the test result was above 7000 nanomol per liter (Table 3).

The average length of hospitalization due to COVID-19 in pregnant mothers was 3.17 ± 3.05 days (Table 4).

In the study, 17 pregnant mothers (8.3%) were admitted to the Intensive Care Unit (ICU) due to COVID-19. Additionally, 2 individuals (1.0%) required a ventilator. The mortality rate among pregnant mothers in this study was only 1 (0.5%) (Table 5).

Discussion

Maternal and fetal health is now considered one of the most important health indicators in any society. With the onset of the COVID-19 pandemic, pregnant women were also at risk

Table 1. Frequency of pregnancy records among pregnant mothers studied

Assessment / Parameter	Number	Percentage
Preterm delivery	29	32.6%
Labor pain	26	12.7%
Vaginal discharge	16	7.8%
History of previous caesarean section	9	4.4%
Reduction of fetal movements	7	3.4%
Vaginal bleeding	7	3.4%
Spotting	4	2.0%
Itching	4	2.0%
History of preterm delivery	3	1.5%
Decrease in amniotic fluid	3	1.5%
HEELP syndrome	2	1%
Increase in blood pressure	2	1%
Preeclampsia	1	0.5%
Seizure	1	0.5%
Placental abruption	1	0.5%
Absence of FHR	1	0.5%
Intrauterine fetal death (IUFD**)**	1	0.5%
Total	117	77.8%

Abbreviations: HEELP: Hemolysis, Elevated Liver enzymes and Low Platelets syndrome; FHR: Fetal heart rate; IUFD: Intrauterine fetal death

Table 2. Distribution of the frequency of clinical symptoms related to COVID-19 in the pregnant mothers studied

Assessment / Parameter		Number	Percentage
Trimester	**first Trimester**	16	8.1%
	second Trimester	36	18.2%
	third Trimester	146	73.7%
Cough		81	39.5%
Myalgia		53	25.95
Shortness of breath		50	24.4%
Fever		44	21.5%

Nausea	30	14.6%
Headache	25	12.2%
Vomiting	21	10.2%
Abdominal pain	20	9.8%
Lethargy	15	7.3%
Sore throat	14	6.8%
Anorexia	8	3.9%
Disorder in the sense of smell	7	3.4%
Diarrhea	6	2.9%
Back pain	6	2.9%
Disorder in the sense of taste	4	2.0%
Runny nose	4	2.0%
flank pain	3	1.5%
Dizziness	3	1.5%
Increase in blood pressure	2	1.0%
Hoarseness	2	1.0%
Flushing	1	0.5%
Seizure	1	0.5%
Joint pain	1	0.5%
Decreased consciousness	1	0.5%
Hemoptysis	1	0.5%
Total	578	

Table 3. Average levels of laboratory indicators in the pregnant mothers studied.

Assessment / **Parameter**	**Mean ± standard deviation**	**median (Q1-Q3)**
oxygen saturation (%SpO2)	93.96 ± 3.88	95.00 (7.00)
White blood cell count ($\times 10^3/mm^3$)	6.98 ± 2.37	6.58 (3.00)
Hemoglobin (g/dl)	12.07 ± 1.41	12.10 (2.00)
Hematocrit (%)	35.13 ± 3.62	34.50 (3.00)
Platelet count ($\times 10^3/mm^3$)	196.30 ± 58.06	201.00 (80.00)

PT (s)		12.39 ± 1.18	12.20 (1.10)
PTT(s)		32.37 ± 5.07	32.00 (7.00)
INR		1.02 ± 0.19	1.00 (0.20)
ALT(U/L)		28.63 ± 27.09	20.00 (26.00)
AST(U/L)		35.33 ± 18.82	31.00 (19.00)
ESR (mm/h)		30.52 ± 14.88	27.00 (23.00)
CRP(mg/L)		34.30 ± 27.62	37.00 (57.00)
LDH(U/L)		523.70 ± 211.44	490.00 (177.00)
Ferritin(ng/dl)		145.91 ± 132.71	111.90 (159.30)
Parameter	**Assessment**	**Number**	**Percentage**
D-Dimer (nmol/L)	<1000	7	35.0%
	1000-2000	6	30.0%
	2000-7000	4	20.0%
	>7000	3	15.0%

Abbreviations: PT: Prothrombin time; PTT: Partial thromboplastin time; INR: International normalized ratio; ALT: Alanine transaminase; AST: Aspartate transaminase; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; LDH: Lactate dehydrogenase

Table 4. Determining the average duration of hospitalization in the studied pregnant mothers

Parameter / **Assessment**	**Mean ± standard deviation**	**median (interquartile range)**
Duration of hospitalization (days)	3.17 ± 3.05	2.00 (3.00)

Table 5: Frequency of hospitalization in the ICU, need for a ventilator, and mortality rate among the pregnant mothers studied

Parameter / **Assessment**	**Number**	**Percentage**
Hospitalization in the intensive care unit (ICU)	17	8.3%
Need for a ventilator	2	1.0%

mortality	1	0.5%
Total	20	9.8%

of infection, similar to the general population. However, pregnant women have a relatively reduced immune system, which theoretically puts them at higher risk of contracting the virus (9). Dealing with SARS-CoV-2 during pregnancy poses a serious threat to both pregnant women and their fetuses (16). The management of COVID-19 in pregnant women is also presenting challenges and problems (17).Therefore, this study was conducted to investigate the epidemiology, laboratory factors and clinical symptoms of COVID-19 in infected pregnant patients.

According to the results of the current study, the majority of mothers with COVID-19 were in their third trimester of pregnancy. Consistent with these findings, a study by Vousden and colleagues in Britain in 2022 in found that 36.7% of pregnant mothers with COVID-19 who visited health centers were at term (37 weeks and above) (18). Several studies have indicated that, similar to other viral diseases, such as influenza and chickenpox, pregnant mothers are at an increased risk of developing a severe form of the disease compared to non-pregnant individuals, particularly if they are infected during the third trimester of pregnancy (19, 20).

For example, a study conducted in 2020 by Antoun and colleagues, showed that the severity of Covid-19 infection was higher in the third trimester of pregnancy. All individuals who required invasive ventilation were in the third trimester (21). Similarly, research has demonstrated that the severity and rate of influenza in the second and third trimesters of pregnancy are higher compared to the first trimester (22). In the current study, it was also found that the highest incidence of clinical symptoms among pregnant mothers with COVID-19 occurred in the third trimester at 73.7%.

In support of this issue, we can refer to the study by Kraus et al. in 2011, which showed that the number and function of natural killer (NK) cells and T cells significantly decrease in towards the end of the second trimester and into the third trimester. This indicates a changes in inflammatory Th1 responses and interferon gamma production. Additionally, the number of peripheral B cells decreases in the third trimester (23).

According to the results of the present study, the most common underlying disease reported in the studied pregnant mothers was hypothyroidism (12.7%) Gestational diabetes mellitus (GDM) was recorded in 19 people (9.3%), high blood pressure in 2.0%, and diabetes mellitus in 1.5%. In a study conducted by Antoun and colleagues in 2020 with the aim of investigating the epidemiology of covid-19 in pregnant women, diabetes mellitus, acute kidney failure, asthma and hypothyroidism were reported as the most common underlying diseases in pregnant women with COVID-19 (21).

Several studies have shown that having diabetes mellitus increases the risk of contracting COVID-19 and its severe forms, both in pregnant individuals and in the general population (24). One possible reason for the lower prevalence of diabetes in the society being studied is that individuals may not have been adequately screened. Because pregnant women are typically younger or middle-aged, and complications related to diabetes may not manifest at this age, leading individuals to be unaware that they have the condition.

According to the results of the present study, Kazemi Aski and his colleagues found hypothyroidism to be the most common underlying disease in pregnant women with COVID- 19 in a study conducted in the north of Iran in 2020, with a frequency of 15.0% (25). In contrast, a systematic review and meta-analysis reported a prevalence of 1.8% in

developing countries and 0.8% in developed countries for hypothyroidism in pregnant women with COVID-19 (26). However, in our study, 12.7% of pregnant women with COVID-19 were found to have hypothyroidism. The overall estimated prevalence of hypothyroidism during pregnancy is 2% (71). Research has shown that hypothyroxinemia is more likely to occur in pregnant women with COVID-19 (72), which may explain the higher prevalence of hypothyroidism observed in our study.

The results of the present study show that labor pain and vaginal discharge were the most common complaints reported. A study conducted by Mayopoulos and colleagues in 2020 found that pregnant women with COVID-19 reported significantly more labor pain compared to pregnant women without the virus. This trend persisted even when after adjusting for factors such as childbirth complications, pain medication, and delivery. The study also revealed the approximately 50% of pregnant women suspected or confirmed to have COVID-19 exhibited clinical symptoms of acute stress during childbirth. These women were twice as likely to experience acute stress compared to pregnant women without COVID-19 (27).

In this study, cough (39.5%), myalgia (25.9%), shortness of breath (24.4%), fever (21.5%), and nausea (14.6%) were the most common clinical symptoms observed in pregnant mothers with COVID-19. A study conducted by Zambrano et al. in 2020 reported that cough, headache, myalgia, and fever were the most common clinical symptoms among pregnant mothers with COVID-19 (28). Another study by Navai et al. from the beginning of the COVID-19 pandemic on all patients admitted to hospitals in South Khorasan province found that the most common clinical symptoms were fever, cough, shortness of breath, weakness and lethargy (29). It appears that there is no significant difference between the symptoms caused by COVID-19 in pregnant mothers and the general population. However, higher clinical symptoms such as nausea and headache in pregnant mothers, may be related to pregnancy complications (30, 31). Pregnancy can exacerbate shortness of breath in the context of COVID-19 infection (78) due to the pressure it exerts on the diaphragm. Studies have also indicated that symptoms like shortness of breath and cough are more prevalent in pregnant women with COVID-19 in the third trimester compared to the first and second trimesters (32).

In the present study, the average level of blood oxygen saturation (SpO2) in pregnant mothers was 93.96% ± 3.88%. Aside from the complications caused by COVID-19, the lower SpO2 level in the studied pregnant women can be attributed to a decrease in the diffusion capacity of the lungs and an exacerbation of shortness of breath during pregnancy (78). It is important to note that changes in physiological adaptation during pregnancy, such as an increase in the level of the diaphragm and oxygen consumption, can lead to hypoxia intolerance in pregnant women with COVID-19 (33).

In the present study, no leukocytosis or leukopenia was observed in pregnant women with COVID-19. The results of measuring the levels of hemoglobin, hematocrit, platelets, PT, INR, PTT, liver enzymes ALT and AST, as well as the inflammatory index of ferritin, showed that these indicators were within the normal range. However, the levels of CRP, ESR and LDH indices were higher than normal. This is expected, as COVID-19 is an inflammatory disease that leads to an increase in inflammatory indicators. The increase in these inflammatory indices is directly related to the severity and prognosis of the disease (34, 35). According to the results of the present study, Kazemi Aski and colleagues reported in a 2020 study in the north of Iran that the LDH index was disturbed in 90% of pregnant women with COVID-19(25). Some studies have reported normal levels of CRP in pregnant women and leukocytosis in pregnant women (36).

In the current study, the average length of hospital stay due to COVID-19 in pregnant mothers was 3.17 days. A study conducted by

Qeadan and colleagues in 2021 on pregnant women with COVID-19 reported that the length of hospital stay for pregnant women with COVID-19 was significantly different compared to non-pregnant women. Pregnant women with Covid-19 had an average hospital stay of 2.55 days while non-pregnant women had an average stay of 6.59 days (37). In 2009, pregnant women were at a higher risk of complications due to the H1N1 pandemic influenza virus infection. The duration of their hospitalization was four times longer than that of non-pregnant individuals (38). However, this pattern was not observed in pregnant women with COVID-19 (39). The differences in these patterns can be attributed to variations in the type and pathogenesis of each virus, as well as the advancements in therapeutic available during the COVID-19 pandemic outbreak.

It can be noted that pregnant patients receive special care according to government policies. As a result, the risk of contracting a severe form of the disease and the length of hospitalization for pregnant women with COVID-19 are reduced in the hospital (37, 40, 41).

The percentage of pregnant women hospitalized in the ICU in this study was 8.3%, and the percentage needing a ventilator was 1.0%. Consistent with the results of the present study, Kazemi Aski and colleagues conducted a study in 2020 in northern Iran and reported the frequency of ICU hospitalization in pregnant women with COVID-19 as 2% (25).

In a study conducted in 2020 in 13 American states, 16.2% of pregnant women were admitted to the ICU and 8.5% required invasive mechanical ventilation (42). Several factors may account for the discrepancies between the statistics of the aforementioned study and our own study, including differences in geographical location, timing of the study, and variation in the prevalent strain of COVID-19 in the two countries at the time of data collection.

In this study, the mortality rate of pregnant mothers with COVID-19 was reported as 0.5%. A study conducted by Zambrano and colleagues in the United States in 2020, reported a mortality rate of 1.5% in pregnant women with COVID-19 and 1.2% in non-pregnant women with the disease (28). Another study conducted by Qeada and colleagues in 2021 on pregnant women with COVID-19 found a mortality rate of 0.2% in pregnant women and 0.5% in non-pregnant women with the disease (37).

One of the reasons for the lower mortality rate in pregnant women with COVID-19, as found in this study, compared to the general population, may be related to the age of these individuals. Most pregnant women fall within the young to middle-age range, which means they may experience fewer complications from COVID-19 compared to older individuals. However, it is important to note that pregnant women may still face more complications from the disease compared to individuals of the same age due to a weakened immune system (23).

Conclusion

Based on the results of the current study, hypothyroidism was identified as the most common underlying disease among the pregnant women examined. It is crucial to implement measures to manage this condition and prevent its negative impacts on both the mother and the fetus. Interestingly, the prevalence of diseases like diabetes, which are relatively common in society, was lower in this study. Additionally, symptoms such as cough, myalgia, shortness of breath, fever, and nausea were the most frequently reported clinical symptoms in pregnant mothers with COVID-19, mirroring trends in the general population. Moreover, the prevalence of these symptoms was higher in the third trimester compared to the first and second trimesters of pregnancy. One limitation of this study was its retrospective nature, as it relied on information extracted from patient files. Those responsible for recording information on these forms may not have considered the research objectives.

Ethical Approval

The present study was approved by the Ethics Committee of Birjand University of Medical Sciences with the code of ethics IR.BUMS.REC.1401.190

Consent to participate

Informed consent was obtained from the participant enrolled in the study.

Consent to publish

The patient has given her written informed consent for the case report and any accompanying images to be published.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

N.J and M.Z contributed to the conception, acquisition of data, analysis, and interpretation of data and agreed to be responsible for all aspects of the work. F.B and N.J were actively involved in searching the literature, and drafting the manuscript. S.B approved the final version to be published and agreed to be responsible for all aspects of the work. We ensure that all authors have read and approved the final manuscript.

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Availability of data and materials

The datasets used during the current study are available from the corresponding author upon reasonable request.

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