

Clinical characteristics in pregnant women with COVID-19 infection in a hospital in Iran

Maryam Nikpour¹, Mehdi SepidarKish², Mahboobeh Darzipoor³, Mahmoud Sadeghi Haddad Zavareh⁴, Rahele Mehraeein⁵, Zeinab Pahlavan⁶, Fereshteh Behmanesh^{7,*}

¹Non-Communicable Pediatric Disease Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

²Department of Biostatistics and Epidemiology, Babol University of Medical Sciences, Babol, Iran

³Clinical Research Development Center, Shahid Yahyanezhad Hospital, Babol University of Medical Sciences, Babol, Iran

⁴Infectious Diseases and Tropical Medicine Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

⁵Radiology department of Rohani university hospital, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

⁶Department of Obstetrics and Gynecology, Ayatollah Rouhani Hospital, Babol University of Medical Sciences, Babol, Iran

⁷Department of Midwifery, Nursing and Midwifery Faculty, Babol University of Medical Sciences, Babol, Iran

Received: 3 Nov 2021 Accepted: 20 Dec 2021

Abstract

Background: Pregnant women have supposedly been among the most vulnerable groups since the onset of COVID-19 crisis. Some of the complications of COVID-19 are expected to be more severe in pregnant women, which could be attributed to physiological changes occurring during pregnancy. The aim of this study was to determine the clinical as well as laboratory characteristics of pregnant women with COVID-19 infection.

Methods: In this retrospective study, the medical records of all pregnant women with COVID-19, who were admitted in a tertiary hospital in Iran over the period between March and November 2020, were meticulously reviewed. The clinical and laboratory characteristics of 42 pregnant women with RT-PCR confirmed COVID-19 infection were assessed. Statistical analyses were performed on Stata 16.0. All statistical tests were two-tailed at the significance level of $P < 0.05$.

Results: At the time of the study, 42 pregnant women had the symptoms of COVID-19 and were hospitalized. The most common clinical signs of COVID-19 were: fever (69.0%), fatigue (31.0%), dyspnea (28.6%), and pharyngalgia (23.8%). In addition, the most common laboratory symptoms were: an increase in C-reactive protein (CRP) (69.0%), leukocytosis (66.7%), and lymphocytopenia (66.7%). Ground glass opacity (GGO) was a common (83.33%) finding in long computed tomography (CT scan).

Conclusion: The finding of this study indicated that most common clinical symptoms and laboratory parameters in pregnant women with COVID-19 were similar to those of non-pregnant women with COVID-19 infection as reported by other researchers.

Keywords: COVID-19, Pregnancy, laboratory test, pulmonary manifestations

Introduction

Coronaviruses (COVID-19) are a family of viruses that involve vital organs such as the respiratory system, the digestive system, the nervous system, hematology, and kidneys (1). However, the virus has the greatest impact on the respiratory system with a wide range from colds to acute respiratory syndrome

(2, 3). COVID-19 infection can affect people of all ages, and pregnant mothers are no exception in this regard. Pregnant women have been identified as a vulnerable group compared to the general population since the onset of COVID-19 crisis (4). The positive screening rates for pregnant women with COVID-19 infection have been reported to be 0.03% in Japan (5),

*Correspondence author: Dr. Behmanesh, Babol University of Medical Sciences, Ganjafruz Street, Babol, Iran Babol, Iran

Tel: +98-11-32360714

Email: f.behmanesh2015@gmail.com

3.4% in India (6) and 1.5% in the United States (4). Pregnant women tolerance to hypoxia decreases due to the weakened immune system and physiological changes in the respiratory system (7). Pneumonia, respiratory problems, and the risk of death are also expected to be high in pregnant women with COVID-19 infection (7).

Clinical manifestations and complications associated with COVID-19 infection are not exactly known in pregnant women (9), and the results of research studies in this regard have been contradictory, too (10). Most pregnant women with COVID-19 infection experience mild to moderate symptoms, about 10 to 15 percent experience severe symptoms, and less than three percent require intensive care (8, 9). Mirbeyk et al. (2021), in a systematic review of 37 studies, showed that the commonest symptoms for pregnant women with COVID-19 infection were: fever, cough, and myalgia (8). In another study, the Centers for Disease Control and Prevention (CDC) compared the symptoms of 8207 pregnant women with those of 83025 non-pregnant women with COVID-19 infection. The finding of their study illustrated that the need for hospitalization and intubation was higher in pregnant women (10-12). Other studies, nonetheless, did not report any differences in the symptoms of pregnant and non-pregnant women with COVID-19 infection (8, 13). Some researchers reported that acute syndrome and sever symptom were higher in non-pregnant women.

Despite the global spread of the disease, the epidemic and clinical patterns, and the risks associated with COVID-19 infection for pregnant women are not vividly known yet. The signs and symptoms of this infection vary according to living conditions, the availability of medical facilities and care as well as people's knowledge of this disease. Studies on the effect of COVID-19 infection on pregnant women in Iran are also limited in scope. Therefore, this study was performed to determine the clinical and laboratory manifestations of pregnant women with COVID-19 infection, who referred to Rouhani Hospital in Babol in 2020.

Materials & Methods

This retrospective study was approved by the Institutional Review Board of Babol University of Medical Sciences (ID: IR.MUBABOL.HRI.REC.

1399.010). The underlying study included all pregnant women who were admitted in a tertiary hospital in Iran over the period between March and November 2020. In our hospital, at admission, sputum and throat swab specimens were obtained from all pregnant women who were suspected of having COVID-19 and were also willing to participate in the study. The real time polymerase chain reaction (RT-PCR) test for SARS-Cov-2 RNA was also performed according to the guidelines of the World Health Organization (WHO). In addition, five mL of intravenous blood was taken from each patient for laboratory tests including a complete blood count and serum biochemistry if necessary. Moreover, a lung Computed tomography (CT) scan was performed on pregnant women with Covid-19 infection. Pregnant women were covered with a lead blanket before undergoing an abdominal and pelvic CT scan, and were exposed with a low radiation dose (mean $\pm$ SD, 4.1 ± 0.9 mGy). Pulmonary involvement was assessed by criteria such as consolidation, ground glass opacity (GGO) and mixed GGO. All imaging features were evaluated by two experienced radiologists and an infectious diseases specialist. From March to Nov, 2020, 42 pregnant women with Covid-19 were admitted in our hospital. Medical records of all 42 pregnant women with polymerase chain reaction (PCR) test confirmed that COVID-19 infection had thoroughly been assessed. Then, all the data regarding maternal age, reproductive data (gestational age, gravidity, history of miscarriage, and history of previous section), comorbidities, clinical characteristics including fever, fatigue, dry cough, myalgia, dyspnea, pharyngalgia, vomiting, diarrhea, and radiologic characteristics (white blood cell count, lymphocyte count, C-reactive protein, and lung CT scan) were extracted.

Statistical analysis

Continuous and categorical variables were described by mean $\pm$ standard deviation (SD) and counts (percentages), respectively. Statistical analyses were performed on Stata 16.0 (Stata Corp, College Station, TX, USA). All statistical tests were two-tailed at the significance level of $P < 0.05$.

Results

42 pregnant women with COVID-19, 37 (88.1%) were at ≥ 38 week of gestation at admission. The remaining women (11. 9%) had been infected by COVID-19 in the first or second trimester. The mean

gestational age of patients was 27.5 ± 6.1 years. At least one comorbid disease was observed in 42.9% ($n = 18$) of the pregnant women with COVID-19 (Table 1).

Table 1. Demographic and reproductive characteristics of women with COVID-19 infection in a hospital in Iran ($n=42$)

Variables	N (%)
Age (year), Mean (SD)	27.5 (6.1)
Gestational age (weeks), Mean (SD)	35.8 (5.9)
Gravidity*	
<2	18 (42.9)
≥ 2	24 (57.1)
History of abortion	
No	31 (73.8)
Yes	11 (26.2)
Comorbidities	
No	24 (57.1)
Yes	18 (42.9)
History of previous C-section *	
No	14 (60)
Yes	6 (30)

*C-section: cesarean section

The commonest symptoms in hospitalized pregnant women with COVID-19 were: fever (69.1%), fatigue (31.0%), dry cough (42.9%), myalgia (19.0%), and dyspnea (28.6%). The commonest laboratory symptoms in pregnant women with COVID-19 were: an increase in blood CRP (69.0%), leukocytosis (white blood cell count $>11 \times 10^9/L$) and lymphocytopenia (Lymphocyte count $<1.0 \times 10^9/L$). According to chest computed tomography, 15 (83.3%) patients showed ground-glass opacity (GGO) (Table 2).

According to the prescriptions, the pregnant women with COVID-19 received painkillers, antibiotic, and antiviral treatment. Additionally, pregnant women with dyspnea received lung inhale such as combivent respimat (every 6h, with nebulizer). None of the patients required intubation and invasive ventilation in the disease course. 39 patients (92.9%) had decreased oxygen saturation. The mean duration of hospitalization was 4.9 ± 2.5 days. Finally, 39 pregnant women were discharged in good general condition. However, three pregnant women were transferred to the intensive care unit (ICU) between the 16 and 24 gestational weeks due to their severe dyspnea.

Table 2: Clinical and laboratory characteristics of women with COVID-19 infection in a hospital in Iran ($n=42$)

Signs and symptoms	N (%)
Fever	29 (69.1)
Fatigue	13 (31.0)
Dry cough	18 (42.9)
Myalgia	8 (19.0)
Dyspnea	12 (28.6)
Pharyngalgia	10 (23.8)
Vomiting	7 (16.7)
Diarrhea	7 (16.7)
Laboratory characteristics	
WBC ¹ ($\times 10^9/L$), Mean (SD)	15.0 (4.7)
WBC ($\times 10^9/L$)	
< 11.0	14 (33.3)
≥ 11.0	28 (66.7)
LYM ² ($\times 10^9/L$), Mean (SD)	1.0 (0.9)
LYM ($\times 10^9/L$)	
<1.0	28 (66.7)
≥ 1.0	14 (33.3)
CRP ³ (mg/L), Mean (SD)	44.38 (34.55)
CRP (mg/L), (mg/L)	
0.5 – 10	13 (31.0)
10 – 116	29 (69.0)
Long CT⁴	
GGO ⁵	38 (90.5)
Normal	4 (9.5)

¹WBC: White blood cell count, ²LYM: Lymphocyte count, ³CRP: C-reactive protein, ⁴CT: Computerized tomography, ⁵GGO: Ground-glass opacity

Discussion

The commonest symptom in pregnant women with COVID-19 was fever, followed by cough. A systematic review of 37 studies also reported fever and cough as the commonest symptoms in pregnant women with COVID-19 (8). Other researchers such as Kuzan et al. in Turkey (14), Vizheh et al. in Iran (13), and Chen et al., in China (15) also reported fever as the commonest symptom. Fever was also reported as the commonest symptom in non-pregnant women (16). Fever is normally the body's first defense system against infection and virus (20). It is a complex cytokine-mediated physiological response that drives both the innate arms and the adaptive immune arm, including adrenergic pathways (17). Guan et al., reported fever in 42.8% of COVID-19 patients at admission and 88.7% during hospitalization (18). High fever (above 39 °C) was associated with a higher probability of acute respiratory distress syndrome (17).

In addition, the finding of this study has shown that the commonest problem with laboratory parameters was an increase in blood CRP. Blood CRP level is commonly used as a nonspecific marker of inflammation. CRP is usually normal in mild viral infections but is significantly increased in patients with COVID-19 infection. CRP testing is probably useful in the initial evaluation of COVID-19 patients (19). A study of 140 patients with COVID-19 showed that CRP level increased in 91 patients at the time of admission. They found CRP in severe cases of 41.8 mg / L and suggested that high CRP levels could effectively predict respiratory deterioration (20). Similarly, in a meta-analysis, Saho et al., compared CRP in 849 deceased cases with COVID-19 and 1896 patients recovering from COVID-19. They reported high concentrations of CRP in deceased patients and further showed that CRP could effectively predict the prognosis of COVID-19 (21). A retrospective multicenter study of 3,219 patients also showed an

association between high CRP levels and in-hospital deaths (22).

Furthermore, out of 42 pregnant women with COVID-19 in this study, 11 had pulmonary involvement. The predominant pattern of lung injury due to COVID-19 infection was pure GGO, which was in line with Line et al's study (23). GGO is described as a weak reduction in the lung parenchyma while maintaining the visual margin (24). GGO is one of the main findings of lung CT scan in COVID-19, but its presence is not specific to viral pneumonia. In fact, GGO is a radiological sign of various pathologies with acute and chronic clinical manifestations of lung. In evaluating an issue with a GGO or diffuse focus, the radiologist must know the patient's medical history to make a valid diagnostic hypothesis (25). The long CT scan findings in asymptomatic patients with COVID-19 were often peripherally and predominantly round GGO (24).

Another finding of this study was that out of 42 pregnant women, only 5 were hospitalized in the first and second trimesters of pregnancy, but the rest were in the third trimester. In two reports examining 18 pregnancies with COVID-19 disease, all mothers became infected in the third trimester (26, 27). In a study conducted by Delahoy et al. among 596 women with COVID-19, 2.3% were in the first trimester, 10.2% were in the second trimester, and 87.4% were hospitalized in the third trimester. The commonest reason for hospitalization in the third trimester was obstetric symptom (26).

This study has several limitations. First, we examined hospitalized pregnant women only in a single center, and outpatient treatment cases were not included in the study. Also, limited laboratory tests were evaluated in this study. We were not able to assess all related laboratory tests used for COVID-19 patients.

Conclusion

In the present study, the commonest clinical symptoms, laboratory parameters and pulmonary involvement in pregnant women with COVID-19 were: fever, increased CRP, and GGO. This finding is similar to the results of studies on non-pregnant women with COVID-19 infection, as reported by other researchers.

Acknowledgements

We would like to thank Shabnam Mehdinia, Fatemeh Shafizadeh, Dr. Bozari and Dr. Mahsa Adnani, the gynecologists in Rohani hospital, Babol, Iran. We are also thankful to the Institutional Review Board of Babol University of Medical Sciences and Rohani hospital, Babol, Iran for their approval and support of the study.

Conflicts of Interest

None declared.

References

1. American Diabetes A. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010 Jan;33 Suppl 1:S62-69.
2. Xiong X, Saunders LD, Wang FL, Demianczuk NN. Gestational diabetes mellitus: prevalence, risk factors, maternal and infant outcomes. *Int J Gynaecol Obstet*. 2001 Dec;75(3):221-228.
3. Hirst JE, Tran TS, Do MA, Morris JM, Jeffery HE. Consequences of gestational diabetes in an urban hospital in Viet Nam: a prospective cohort study. *PLoS Med*. 2012;9(7):e1001272.
4. Deierlein AL, Siega-Riz AM, Chantala K, Herring AH. The association between maternal glucose concentration and child BMI at age 3 years. *Diabetes Care*. 2011 Feb;34(2):480-484.
5. Aulinas A, Biagetti B, Vinagre I, Capel I, Ubeda J, Maria MA, et al. [Gestational diabetes mellitus and maternal ethnicity: high prevalence of fetal macrosomia in non-Caucasian women]. *Med Clin (Barc)*. 2013 Sep 21;141(6):240-245.
6. Katon J, Reiber G, Williams MA, Yanez D, Miller E. Antenatal haemoglobin A1c and risk of large-for-gestational-age infants in a multi-ethnic cohort of women with gestational diabetes. *Paediatr Perinat Epidemiol*. 2012 May;26(3):208-217.
7. Fuchs F, Bouyer J, Rozenberg P, Senat MV. Adverse maternal outcomes associated with fetal macrosomia: what are the risk factors beyond birthweight? *BMC Pregnancy Childbirth*. 2013;13:90.
8. Parhofer KG, Hasbargen U, Ulugberdiyeva A, Abdullayewa M, Melebayewa B, Annamammedov A, et al. Gestational diabetes in Turkmenistan: implementation of a screening program and first results. *Arch Gynecol Obstet*. 2014 Feb;289(2):293-298.
9. Di Cianni G, Volpe L, Lencioni C, Miccoli R, Cuccuru I, Ghio A, et al. Prevalence and risk factors for gestational diabetes assessed by universal screening. *Diabetes research and clinical practice*. 2003 Nov;62(2):131-137.
10. M KN, S AA, B L. A review on the prevalence of gestational diabetes mellitus (GDM) in different regions of Iran. *Journal of Diabetes and Metabolic Disorders*. 2009.
11. Crete JE, Anasti JN. Diagnosis of gestational diabetes mellitus: can we avoid the glucose challenge test? *J Am Assoc Nurse Pract*. 2013 Jun;25(6):329-333.
12. Corrado F, Pintaudi B, Di Vieste G, Interdonato ML, Magliarditi M, Santamaria A, et al. Italian risk factor-based screening for gestational diabetes. *J Matern Fetal Neonatal Med*. 2014 Sep;27(14):1445-1448.
13. Godwin M, Muirhead M, Huynh J, Helt B, Grimmer J. Prevalence of gestational diabetes mellitus among Swampy Cree women in Moose Factory, James Bay. *CMAJ*. 1999 May 4;160(9):1299-1302.
14. Esmaeilzadeh S, Delavar MA, Amiri M, Khafri S, Pasha NG. Polycystic ovary syndrome in Iranian adolescents. *Int J Adolesc Med Health*. 2014;26(4):559-565.
15. Kulshreshtha B, Arora A, Pahuja I, Sharma N, Pant S. Menstrual cyclicity post OC withdrawal in PCOS: Use of non-hormonal options. *J Obstet Gynaecol*. 2016 Mar 16:1-6.
16. Haver MC, Locksmith GJ, Emmet E. Irregular menses: an independent risk factor for gestational diabetes mellitus. *Am J Obstet Gynecol*. 2003 May;188(5):1189-1191.

17. Heidari T, Kariman N, Afrakhteh M, Alavi Majd H. The study of relationship between menorrhagia and gestational diabetes. *koomesh*. 2008;9(2):147-154.
18. Weiss DJ, Charles MA, Dunaif A, Prior DE, Lillioja S, Knowler WC, et al. Hyperinsulinemia is associated with menstrual irregularity and altered serum androgens in Pima Indian women. *Metabolism*. 1994 Jul;43(7):803-807.
19. Solomon CG, Hu FB, Dunaif A, et al. Long or highly irregular menstrual cycles as a marker for risk of type 2 diabetes mellitus. *JAMA*. 2001;286(19):2421-2426.
20. Sreekanthan K, Belicita A, Rajendran K, Vijayakumar A. Prevalence of Gestational Diabetes Mellitus in a Medical College in South India: A Pilot Study. *Indian Journal of Clinical Practice*. 2014;24(4):341-347.
21. Roumain J, Charles MA, de Courten MP, Hanson RL, Brodie TD, Pettitt DJ, et al. The relationship of menstrual irregularity to type 2 diabetes in Pima Indian women. *Diabetes Care*. 1998 Mar;21(3):346-349.
22. Chen L, Li S, He C, Zhu Y, Buck Louis GM, Yeung E, et al. Age at Menarche and Risk of Gestational Diabetes Mellitus: A Prospective Cohort Study Among 27,482 Women. *Diabetes Care*. 2016 2016-01-22.
23. Seshiah V, Sahay B, Das A, Shah S, Banerjee S, Rao P, et al. Gestational diabetes mellitus-Indian guidelines. *Journal of the Indian Medical Association*. 2009;107(11):799.
24. Boriboonhirunsarn D, Talungjit P, Sunsaneevithayakul P, Sirisomboon R. Adverse pregnancy outcomes in gestational diabetes mellitus. *J Med Assoc Thai*. 2006 Oct;89 Suppl 4:S23-28.
25. Getahun D, Fassett MJ, Jacobsen SJ. Gestational diabetes: risk of recurrence in subsequent pregnancies. *Am J Obstet Gynecol*. 2010 Nov;203(5):467 e1-6.
26. Yang X, Hsu-Hage B, Zhang H, Yu L, Dong L, Li J, et al. Gestational diabetes mellitus in women of single gravidity in Tianjin City, China. *Diabetes Care*. 2002 May;25(5):847-851..
27. Kaaja R, Ronnemaa T. Gestational diabetes: pathogenesis and consequences to mother and offspring. *Rev Diabet Stud*. 2008 Winter;5(4):194-202.
28. Tabak AG, Tamas G, Peterfalvi A, Bosnyak Z, Madarasz E, Rakoczi I, et al. The effect of paternal and maternal history of diabetes mellitus on the development of gestational diabetes mellitus. *J Endocrinol Invest*. 2009 Jul;32(7):606-610.
29. Al-Rowaily MA, Abolfotouh MA. Predictors of gestational diabetes mellitus in a high-parity community in Saudi Arabia. *East Mediterr Health J*. 2010 Jun;16(6):636-641..
30. Zargar AH, Sheikh MI, Bashir MI, Masoodi SR, Laway BA, Wani AI, et al. Prevalence of gestational diabetes mellitus in Kashmiri women from the Indian subcontinent. *Diabetes research and clinical practice*. 2004 Nov;66(2):139-145.
31. Sivakumar V, Rajasekeran A, Arummugam A. Assessment of Risk Factors for the Early Detection of Gestational Diabetes Mellitus. *Int J of Pharma Sciences and Research*. 2014;5(3):114-118.
32. Hadaegh F, Tohidi M, Harati H, Kheirandish M, Rahimi S. Prevalence of gestational diabetes mellitus in southern Iran (Bandar Abbas City). *Endocr Pract*. 2005 Sep-Oct;11(5):313-318.