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Pregnancy Outcomes in Pregnant Women with Symptoms of Covid-19 Admitted to Ayatollah Mousavi Hospital in Zanjan in 2019-2020

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Abstract

Background: Following the spread of Covid-19 worldwide and the increase in the percentage of pregnant women suffering from the disease, it will be very important to investigate its consequences in pregnancy.
Objectives: The present study was conducted to determine pregnancy outcomes in pregnant women with symptoms of covid-19 admitted to Ayatollah Mousavi Hospital in Zanjan in 2019-2020.
Methods: In this study, the pregnancy outcomes in 89 pregnant women with symptoms of covid-19 admitted to Ayatollah Mousavi Hospital in Zanjan were investigated with document review and file reading. The sampling method was complete enumeration. Maternal and neonatal outcomes were collected using a checklist and analyzed with descriptive statistics in SPSS version 22 Software.
Results: The most common symptoms in hospitalized pregnant women were cough (51.7%) and dyspnea (40.4%). In the laboratory results of pregnant women, leukocytosis, fasting hyperglycemia, increased CRP and alkaline phosphatase were evident. In terms of maternal outcomes, 27% of women had more than one of the examined outcomes. 13.5% had gestational diabetes and 11.2% of mothers had a premature delivery. Regarding neonatal outcomes, fetal heart rate disorder, hospitalization in the neonatal intensive care unit (37.5%), and the need for resuscitation in the first minute (28.1%) were the most reported outcomes.
Conclusion: Considering the increase in adverse maternal and neonatal outcomes in pregnant women with symptoms of covid-19, it is suggested to plan for access to special care to improve the outcomes and implement awareness programs to prevent pregnant mothers from this infection.

Keywords: pregnancy outcomes, pregnant women, Covid-19

Introduction

The COVID-19 pandemic was first identified in China in December 2019 and has grown to unprecedented proportions in the world [1]. The virus can be transmitted to all people through direct contact with the respiratory droplets of patients, especially people with weak immune systems, pregnant women, elderly people, and patients with other underlying diseases [2]. The primary effect of this virus is on the lungs, which can lead to damage to type I and II pneumocytes, inflammation, and bleeding [1]. Lower respiratory tract infection with covid-19 is characterized by pneumonia and respiratory distress syndrome. Manifestations associated with upper respiratory tract infection include fever, cough, and changes in chest radiography [3] Extra pulmonary manifestations of this disease include neurological, renal, hepatic, digestive, cardiac, thromboembolic, endocrine, and dermatological

symptoms. Many tissues seem to be sensitive to the cellular entry of SARS-CoV-2 according to the expression patterns of the angiotensin-converting enzyme-2 (ACE-2) receptor [4].

A variety of clinical symptoms of Covid-19 have been reported during pregnancy. A study reported that fever, cough, dyspnea, myalgia, and fatigue are the most common, and expectoration, headache, hemoptysis, and diarrhea are the least early symptoms of covid-19 in pregnant women [3]. Based on a systematic review of published articles, the clinical manifestations of pregnant women infected with COVID-19 were similar to non-pregnant infected people [5]. Based on preliminary evidence, pregnant women may be more susceptible to SARS-CoV-2 due to adaptation to physiological and immunological changes [3]. Another factor that increases the incidence of Covid-19 is the transfer of the virus to cells through the ACE2 receptor protein. Changes in ACE-2 regulation in the placenta and fetus during pregnancy make the placenta a potential site for SARS-CoV-2 infection [6]. Currently, the consequences of infection with COVID-19 in pregnant women are not fully understood [1]; However, the increased susceptibility to SARS-CoV-2 in pregnant women may increase the risk of adverse pregnancy outcomes in them [7]. Among these consequences, we can mention the increased risk of premature birth, low birth weight, perinatal death, and spontaneous abortion [2]. In addition, SARS-CoV-2 can cause hypoxic damage to the placenta, thereby contributing to the development of preeclampsia [8]. Adverse pregnancy and neonatal outcomes are more common, especially among those with more severe disease [9]. Intrauterine transmission of SARS-CoV-2 is rare, and this is probably related to the low levels of SARS-CoV-2 viremia and the reduced co-expression of ACE2 and TMPRSS2 required for entry of SARS-CoV-2 into host cells [9]; However, existing research suggests that even if the virus is not transmitted to the fetus, maternal infection and inflammation occurring in response to viral infection can affect the developing fetus [10]. Early diagnosis and intervention in the treatment of COVID-19 may reduce potential pregnancy complications such as abortion, intrauterine growth retardation, and preterm delivery, and may be beneficial in improving pregnancy outcomes [10].

Understanding the clinical course of COVID-19 during pregnancy is essential for maternal and child health providers to provide standard care for the mother and her fetus [5]. Due to the inconsistency of published results in this field [11], and to reach a clear view of the effects of this disease on pregnancy outcomes, the present study was conducted to determine the pregnancy outcomes of pregnant women with symptoms of covid-19 admitted to Ayatollah Mousavi Hospital in Zanjan in 2019-2020.

Methods

The current research is a descriptive study of document review and file reading type conducted on 89 pregnant women with symptoms of covid-19 who were admitted to the delivery room of Ayatollah Mousavi Hospital in Zanjan between March 2019 and February 2020. The current research has been registered with the code of ethics (IR.ZUMS.REC.1399.413) in the Ethics Committee of Zanjan University of Medical Sciences. The sampling method was full count. The inclusion criteria included pregnant women hospitalized in the maternity and elective departments with complaints of covid-19 disease. The exclusion criteria were lack of access to file information or incomplete data recording. The criterion for Covid-19 diagnosis was a positive Polymerase chain reaction (PCR) test or lung involvement based on the CT scan report of the lung. The data was collected by a researcher using a checklist made by the researcher in accordance with the objectives of the research and by referring to the files of patients hospitalized in the delivery room and the elective department of Ayatollah Mousavi Zanjan Hospital, and the mother and baby information registration system (Iman System). The information registration checklist included demographic characteristics, laboratory findings reports, clinical manifestations of the disease, the status of performing PCR test or CT scan for the diagnosis of Covid-19 disease, and the report of neonatal and maternal outcomes. The answers to the questions were yes or no. Demographic characteristics included age (years), education (illiterate, elementary school, middle school, diploma, university), place of residence (city, village), obstetric characteristics including

termination of pregnancy–(natural birth, cesarean delivery, discharge from the hospital without termination of pregnancy), causes Cesarean delivery, number of pregnancies and parity.
Clinical manifestations included average systolic and diastolic blood pressure, having or not having symptoms of fever and chills, cough, diarrhea, nausea, vomiting, headache, fatigue, body pain, sore throat, runny nose, phlegm, impaired sense of smell or taste, dyspnea and chest pain; And laboratory findings included hemoglobin, hematocrit, alkaline phosphatase, white blood cell, platelet count, fasting blood sugar, liver enzymes, increased CRP and PCR test for covid-19 diagnosis. In case of a negative result of the PCR test, CT scan imaging was used. The content validity of the checklist was checked and approved by the opinion of faculty members (5 persons). Data analysis was done with SPSS software version 22 (SPSS Inc., Chicago, IL, USA) using descriptive statistics (frequency, percentage, mean and standard deviation).

Results

The results showed that at the time of admission, the average age of people was 30.34±7 years (with an age range of 14-45 years), gestational age was 31.85 weeks (with a range of 6 to 41 weeks), systolic blood pressure was 114.84±12.41 mm Hg, and the average diastolic blood pressure was 71.50±11.22 mm Hg. The highest percentage of hospitalized women with covid-19 were in the age group of 31 to 35 years (27 percent), with elementary education and illiterate (29.2 percent), gravid 2 (37.1 percent), parity 1 (40.4 percent), and city residents (58.4 percent). In this study, 62.9% of women were discharged after recovery without termination of pregnancy. Cesarean delivery had the highest percentage among the women who gave birth (22.5%). In terms of causes of cesarean section, the highest percentage of cesarean sections was related to fetal distress (40%) (Table 1). Hospitalized women had a wide range of clinical manifestations of Covid-19. Nearly 60% of women had more than one of the clinical symptoms reported in Table 2. Also, the most common symptoms included cough (51.7%) and dyspnea (40.4%). Chest pain and throat phlegm had the lowest percentage (1.1%) (Table 2).

Table 1: Frequency Distribution of Demographic Characteristics of Pregnant Women with Symptoms of Covid-19 Admitted to Ayatollah Mousavi Hospital, Zanjan

Variable		frequency	Percentage	Causes of termination of pregnancy, caesarean section	Variable		frequency	Percentage
Age (n=89)	14-20	9	10.1		Fetal distress (n=20)	No	12	60.0
	21-25	13	14.6			Yes	8	40.0
	26-30	20	22.5		Abnormal presentation (n=20)	No	19	95.0
	31-35	24	27.0			Yes	1	5.0
	36-40	17	19.1		High blood pressure (n=20)	No	17	85.0
	41-45	6	6.7			Yes	3	15.0
Education (n=89)	Illiterate and elementary school	26	29.2		Maternal respiratory distress (n=20)	No	16	80.0
	Middle school	18	20.2			Yes	4	20.0
	Diploma	24	27.0		Multifetal gestation (n=20)	No	19	95.0
	University	21	23.6			Yes	1	5.0
Gravida (n=89)	1	26	29.2		Placental abruption (n=20)	No	19	95.0
	2	33	37.1			Yes	1	5.0
	3	22	24.7		Premature rupture of the amniotic	No	19	95.0
	≥4	8	9.0			Yes	1	5.0

				sac (n=20)			
parity (n=89)	0	29	32.6	macrosomia (n=20)	No	19	95.0
	1	36	40.4		Yes	1	5.0
	2	17	19.1	More than one cause (n=20)	No	13	65.0
	>3	7	7.9		Yes	7	35.0
Residence (n=89)	City	52	58.4				
	Village	37	41.6				

Table 2: Distribution of the Frequency and Percentage of Clinical Manifestations of Covid-19 in Pregnant Women During Hospitalization in Ayatollah Mousavi Zanjan Hospital

Variable		Frequency	Percentage	Variable		Frequency	Percentage
Fever	No	67	75.3	Diarrhea	No	86	96.6
	Yes	22	24.7		Yes	3	3.4
Cough	No	43	48.3	Nausea/ vomiting	No	84	94.4
	Yes	46	51.7		Yes	5	5.6
Fatigue	No	86	96.6	Rhinorrhea	No	87	97.8
	Yes	3	3.4		Yes	2	2.2
Dyspnea	No	53	59.6	Headache	No	83	93.3
	Yes	36	40.4		Yes	6	6.7
Throat phlegm	No	88	98.9	Sore throat	No	87	97.8
	Yes	1	1.1		Yes	2	2.2
Body pain	No	63	70.8	Chest pain	No	88	98.9
	Yes	26	29.2		Yes	1	1.1
Impaired sense of smell	No	83	93.3	Fever and Chill	No	84	94.4
	Yes	6	6.7		Yes	5	5.6
Impaired sense of taste	No	87	97.8	More than one	No	36	40.4
	Yes	2	2.2		Yes	53	59.6

More than 60% of women hospitalized with Covid-19 had a positive PCR test, and nearly 16% had not had a PCR test despite having symptoms. Chest CT scan was not performed in 77.5% of cases. Lung involvement was reported in 19.1% of people who had a chest CT scan. In terms of paraclinical findings, the average hemoglobin and hematocrit, liver enzymes, and platelets were in the normal range. Leukocytosis, fasting hyperglycemia, increased CRP and alkaline phosphatase were the most important clinical pathological findings in the laboratory results (Table 3). Regarding maternal and neonatal outcomes, the results showed that the mean (standard deviation) weight of the Newborns at birth was 2901.33±791.09 grams, the mean head circumference of the newborns was 34.29±2 cm, and the mean length was 47.44±4.44 cm. 59.4% of the babies were male. 40.6% of babies had more than one of the consequences mentioned in table 4. The highest percentage of outcomes was related to fetal heart rate disorder, hospitalization in the neonatal intensive care unit (37.5%), and the need for resuscitation in the first minute (28.1%). Stillbirth and infant death had the lowest percentage (3.1%) (Table 4). In terms of maternal outcomes, 27% of women had more than one of the outcomes listed in Table 4. 13.5% had gestational diabetes, and 11.2% had premature delivery (Table 4).

Table 3: Mean and Frequency of Paraclinical Findings of Pregnant Women with Covid-19 at the Time of Admission to Ayatollah Mousavi Hospital in Zanjan

Variable	Mean ± standard deviation	Percentage (prevalence)
Hemoglobin g/dL	11.63±1.45	
Hematocrit (%)	34.47±3.56	
Alkaline phosphatase U/L	264.70±112.86	
WBC (×1000) count per cubic millimeter	22.06±90.59	
Platelet (×100000)	198.53±69.09	
Fasting blood sugar (mg/dL)	133.44±41.49	
ALT	29.68±29.74	
AST	36.19±25.02	
Increased CRP	No	50(56.2)
	Yes	39(43.8)
PCR	Positive	54(60.7)
	Negative	21(23.6)
	Not performed	14(15.7)
Chest CT scan	Normal	3(3.4)
	lung involvement	17(19.1)
	Not performed	69(77.5)

Table 4: Distribution of the Frequency and Percentage of Maternal and Neonatal Outcomes in Pregnant Women with Covid-19 at the Time of Admission to Ayatollah Mousavi Hospital in Zanjan

Maternal outcome variable		Frequency	Percentage	Neonatal outcome variable		Frequency	Percentage
Placental abruption	No	87	97.8	Neonatal outcome	Prematurity	No	24	75.0
	Yes	2	2.2			Yes	8	25.0
Preterm delivery	No	79	88.8		Intrauterine growth retardation	No	30	93.8
	Yes	10	11.2			Yes	2	6.3
Preeclampsia	No	81	91.0		Underweight	No	24	75.0
	Yes	8	9.0			Yes	8	25.0
Gestational Diabetes	No	77	86.5		Admission in NICU	No	20	62.5
	Yes	12	13.5			Yes	12	37.5
Emergency cesarean section	No	88	98.9		Need to resuscitate in the first minute	No	23	71.9
	Yes	1	1.1			Yes	9	28.1
Blood transfusion	No	88	98.9		Covered with meconium	No	30	93.8
	Yes	1	1.1			Yes	2	6.3
Need for ICU admission	No	78	87.6		Abnormal changes in fetal heart rate	No	20	62.5
	Yes	11	12.4			Yes	12	37.5
Abortion	No	88	98.9		Stillbirth	No	31	96.9
	Yes	1	1.1			Yes	1	3.1
Type of delivery	Normal vaginal delivery	13	14.6		Infant with a positive PCR test for Covid-19	No	31	96.9
	Cesarean section	20	22.5			Yes	1	3.1
	Discharge without termination of pregnancy	56	62.9		Death of infant	No	31	96.9
						Yes	1	3.1
More than one adverse outcome	No	65	73.0		More than one	No	19	59.4
	Yes	24	27.0			Yes	13	40.6

Discussion

The results of the present study regarding the clinical manifestations and maternal and neonatal outcomes of pregnant women with symptoms of covid-19 admitted to Ayatollah Mousavi Hospital in Zanjan between March 2018 and Bahman

2019, in relation to maternal outcomes, showed that 27% of pregnant mothers had more than one of the investigated pregnancy outcomes. 13.5% of mothers had gestational diabetes and 11.2% had premature birth. Also, 12.4% of mothers needed hospitalization in the intensive care unit. Pregnancy modifies the immune system. Gonadotropin and progesterone inhibit the T1 lymphocyte proinflammatory pathway through downregulation of tumor necrosis factor-alpha, and it is hypothesized that this modulated immune system may protect pregnant women against cytokine storm syndrome and associated mortality. Probably, for this reason, the mortality rate in pregnant mothers has been reported low [12], and the results of our study were in line with this evidence. The prevalence of maternal diabetes in the study subjects was 13.5%. Gestational diabetes (GDM) is the most common medical complication of pregnancy, the prevalence of which ranges from 5.8% in Europe to 12.9% in the Middle East and North Africa [13]. In a study conducted by Bayat et al., in 2020, they investigated gestational diabetes in Zanjan and reported its prevalence to be 4.7% [14]. The difference can be due to the difference in the volume of samples and the non-identity of the diagnosis method of gestational diabetes. It seems that gestational diabetes may play a significant role in weakening the body's immune system, which may increase pregnant mothers' susceptibility to covid-19 infection [15].

A review of the findings of 24 studies conducted by Matar et al showed a high rate of premature birth (37.7%) in mothers with covid-19, which is higher than the percentage of the present study (11.2%) [16]. Among the differences between these two studies, we can point out the difference in the gestational age of the affected mothers at the time of admission to the hospital, because in the study of Matar et al., studies were reviewed in which mothers in the third trimester of pregnancy were included in the study, but in the present study mothers were included in the study without limitation on gestational age; Therefore, the range of gestational age in the present study was 6 to 41 weeks and finally 37.1% of the samples gave birth and 62.9% of the mothers were discharged without termination of pregnancy, after treatment, so the observed difference can be due to the difference in the gestational age of pregnant women.

In a meta-analysis study in 2021, Di Toro et al reported that the rate of maternal admission to the ICU was 8%, preeclampsia was 7%, and preterm delivery was 23% [17]. In the present study, 12.4% of pregnant mothers needed hospitalization in the ICU, and 9% had preeclampsia, which was not much different from the results of Di Toro et al.'s study. The only difference was in the prevalence of preterm delivery, which was reported much higher than in our study. The reason for this can be due to the difference in the type of study. In the above study, the overall prevalence of premature birth was 23%, while its prevalence varied from 5% in several European countries to 18% in some African countries. The higher prevalence of premature birth in some countries can be due to poor maternal and fetal health services and lack of health facilities. In a meta-analysis, Dobi et al. found that 27% of pregnant women with covid-19 had adverse pregnancy events such as premature delivery, impaired vascular perfusion of the fetus, and premature rupture of the fetal membrane [18]. In the current study, 27% of women with covid-19 have experienced more than one adverse pregnancy outcome, which is consistent with the results of the above study. CDC conducted a surveillance analysis of 598 pregnant women with laboratory-confirmed COVID-19 from March to August 2020 and found that 12.6 percent of deliveries were preterm (less than 37 weeks). This is higher than the preterm birth rate observed in the United States, which was estimated at 10 percent in 2018. In addition, according to CDC estimates, preterm delivery was three times higher in pregnant mothers with symptomatic than those with asymptomatic COVID-19 [19], which is consistent with the results of the present study.

Also, regarding the termination of pregnancy, in this research, 22.5% of pregnant mothers had cesarean delivery; On the other hand, 6.14 mothers had normal vaginal delivery. In the study of Di Tu et al., the rate of cesarean delivery was different from the present study, so according to their report, 85% of women underwent cesarean section [17]. Although a high cesarean section rate was reported in this study, no clinical evidence supports this delivery method. In fact, in most cases, the disease does not threaten the

mother, and vertical transmission is not clearly indicated. Therefore, COVID-19 should not be considered as an indication for elective cesarean section. The reason for the low rate of cesarean section in our study may be due to the discharge without indication of termination of pregnancy, which accounted for the highest percentage compared to the total number of hospitalizations.

Regarding neonatal outcomes, this research showed that 40.6% of infants had more than one of the investigated outcomes. 37.5% of the fetuses, in the process of labor, experienced disturbances in their heartbeat, 28.1% of the newborns needed resuscitation measures in the first minute. Finally, 37.5% of them were admitted to the neonatal intensive care unit. One infant death and one stillbirth occurred in infants born during this period.

Marchand et al., in a meta-analysis, which examined neonatal outcomes during the Covid-19 era, reported that approximately 32.9% of newborns required NICU admission. The infant mortality rate was 3.0%, and the fetal death or stillbirth rate was 1.9% [1]. The results of another systematic review and meta-analysis that investigated the effects of Covid-19 on newborns and pregnancy also reported obstetric and neonatal outcomes as follows: fetal distress (13.5%), rupture of membranes before delivery (9.6%), prematurity (8.7%), fetal death (4.8%), and abortion (2.9%). There were no positive results of infant infection by RT-PCR [20]. Zhu et al. stated that Covid-19 infection in the perinatal period may have side effects for infants and cause problems such as fetal distress, premature birth, respiratory distress, thrombocytopenia with abnormal liver function, and even death [21]. The results of these studies did not show much difference with the present study.

In the present study, the most common symptoms and clinical manifestations in hospitalized mothers were cough with 51.7% and dyspnea with 40.4%. The least symptoms reported in these mothers included chest pain and phlegm (1.1%). In the laboratory results of these patients, leukocytosis, fasting hyperglycemia, increased CRP, and alkaline phosphatase was seen.

Al-Shafi et al. mentioned fever, cough, fatigue, dyspnea, chest pain,and some less common symptoms such as diarrhea and anorexia among the most common symptoms of mothers [12]. In the present study, diarrhea with 3.3% was one of the symptoms that appeared less in pregnant women. In a meta-analysis, Matar et al. examined twenty-four studies (136 women) in order to investigate the clinical manifestations and outcomes of pregnant women with covid-19. The most common symptoms were fever (62.9%) and cough (36.8%). Laboratory findings in Matar et al.'s study included increased CRP (57%) and lymphocytopenia (50%). There was one case of maternal death and two cases of fetus infected with Covid-19 [16].

In the current study, cough was one of the most common symptoms reported among pregnant mothers, and an increase in CRP was evident in the laboratory results of affected mothers. However, fever was less reported in these mothers. In the study by Delahoy et al., among symptomatic women, the most commonly reported symptoms were fever or chills (59.6%) and cough (59.2%) [22]. The results of a systematic review and meta-analysis showed that fever (58.6%) and cough (30.7%) were the most common symptoms. Other symptoms included dyspnea (14.4%), chest discomfort (3.9%), sputum production (1.0%), sore throat (2.9%), and nasal obstruction (1.0%). 52 patients (50.0%) finally showed abnormal chest CT. Cesarean section was the delivery method for half of the women (50.0%), although information was not available for 28.8% of cases [20].

In the present study, chest pain, phlegm, and sore throat were among the less common symptoms reported by affected mothers. In the present study, information was collected from birth documents; Therefore, the unavailability of individuals and the incompleteness of some files were among the limitations of the study, and an attempt was made to remove the mentioned sample in case of incomplete information.

Conclusion

According to the results of the study, gestational diabetes and premature birth were the most important adverse maternal outcomes, and fetal heart rate disorders and hospitalization in the neonatal intensive care unit (NICU) were the most common adverse outcomes for infants in mothers with covid-19 symptoms. This finding was almost similar to the results of other domestic and foreign studies. It seems that in addition to implementing

awareness programs to prevent pregnant mothers from infection, it is necessary to plan for access to special newborn care for pregnant women with symptoms of Covid-19 admitted to the hospital in order to improve maternal and newborn outcomes. It is suggested to conduct more studies to understand the relationship between the clinical manifestations of Covid-19 disease and the pathological and molecular characteristics of the virus with pregnancy outcomes.

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Conflict of interest
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