Research Article

Maternal and perinatal outcomes of sars-cov-2 infection in unvaccinated and vaccinated pregnant patients

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Abstract

The objective of this study is to evaluate maternal and fetal outcomes of Covid-19 in vaccinated compared with unvaccinated pregnant patients. The study included 244 pregnant patients with COVID-19 infection confirmed by a positive SARS-CoV-2 polymerized chain reaction (PCR) test. Two hundred-four patients were not unvaccinated, and 40 patients were vaccinated. The clinical, biochemical, and radiological results and maternofetal outcomes of the pregnant patients were recorded. All the data were evaluated statistically. The pregnant patients included in the study had a mean age of 31.4 in the vaccinated group and 28.3 years in the unvaccinated group. Comorbidities were determined in 25% of the patients, and the most common symptom was fever in 65.5% of cases. Sore throat, loss of taste sensation, and loss of smell sensation were detected significantly more in the unvaccinated group (p<0.01). Most of the patients were in third-trimester pregnancy in both groups. No patient in the vaccinated group needed intensive care due to covid. A significant difference was found between the two groups in terms of neonatal intensive care requirements.This study determined that intensive care requirement is increased for both mother and newborn, covid symptoms could be prolonged, and hospital stay is longer in the unvaccinated group. Considering these data, the covid-19 vaccine should be offered to all pregnant women.

Keywords: COVID-19, vaccine, pregnancy, cesarean, intensive care

1. Introduction

The severe acute respiratory syndrome coronavirus 2 virus (SARS-CoV-2), an agent of viral pneumonia, has resulted in a global pandemic (1). The disease caused by this virus has been named coronavirus 2019 (COVID-19), yet no effective treatment has been found (2). Different disease conditions of COVID-19 are seen in different populations. Therefore, prioritization for inpatient treatment can be made by determining different risk groups (3). Pregnancy is accepted worldwide as a risk factor for COVID-19 (4). Although pregnant women were excluded from the first trials of COVID-19 vaccines, the urgent need to protect this group, vaccines were offered to them before clinical trials were completed (5). However, current data presented the safety and effectiveness of vaccines in pregnant women as well (6).

Throughout pregnancy, biochemical, physiological, and immunological changes occur (7). Therefore, almost all diseases require different treatment strategies from the non-pregnant population (1). Previous studies have shown no difference in mortality between pregnant and non-pregnant women (8). However, when the same groups were compared in terms of the length of stay in the hospital, pregnant women had a more extended stay in the hospital than non-pregnant women (9). The effects of COVID-19 infection in pregnancy are also seen in the fetus (9).

Previous studies have shown vertical transfer of the SARS-CoV-2 virus (10). Although various studies have been conducted to date, reports of the effects of COVID-19 on pregnant patients are still limited. The aim of this study was to analyze COVID-19 in vaccinated versus unvaccinated pregnant patients and to compare clinical and biochemical results and fetal effects.

2. Materials and Methods

This single-center study included pregnant patients diagnosed with COVID-19 who presented at the Adana City Training and Research Hospital between February 2020 and June 2022. The study was approved by the Institutional Review Board (decision no:1191/301220) and the Turkish Ministry of Health (T01-21-35) and carried out in accordance with the Helsinki Declaration principles.

Given the high frequency of COVID-19 infection in Turkey and the fact that our institution is one of the major pandemic hospitals in the area, every pregnant woman who applied was given a COVID-19 PCR test. A SARS-CoV-2 PCR test was performed on nasopharyngeal and oropharyngeal smear samples to diagnose COVID-19 infection (9). The patients'

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demographic, laboratory, and follow-up characteristics were obtained. Patients with SARS-COV-2 infection were the subject of the study, and hence, patients with negative PCR results were excluded. If women with severe COVID-19 disease were at or near term, delivery was considered for increasing oxygen requirements. The patients were divided into two groups, group 1: vaccinated and group 2: unvaccinated. The vaccinated group included patients with at least one dose vaccinated with Covid 19 vaccine before or during pregnancy.

Emergency cesarean sections were performed on patients who required intubation or whose oxygen saturation did not increase after intensive oxygen treatment. COVID-19 patients who were asymptomatic and non-severe were monitored for the development of severe illness, and self-isolation was indicated. The timing of the patients' deliveries was determined by obstetric/medical indications. If there is no additional indication for cesarean section and there is no emergency, the patients were delivered by vaginal delivery.

Age, number of pregnancies, history of miscarriages, type of delivery of previous pregnancies, gravida, parity, pregnancy complications, pregnancy outcome, comorbidities, smoking status, length of hospital stay, need for intensive care, gestational age at birth, and continuing COVID-19 symptoms at 1 and 6 weeks after the birth were all recorded for each patient. The presence of COVID-19, birth weight, neonatal intensive care requirement, and APGAR scores at 1 and 5 minutes were all recorded for the neonates. All the patients were treated according to the national COVID-19 guidelines. According to vaccination status, patients were compared.

2.1. Statistical Analysis

Statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS version 16.0; SPSS Inc., Chicago, IL, USA). The variables were tested using visual and analytical methods (Shapiro–Wilk's test) to determine whether they were normally distributed or not. Comparative analyses were made using Fisher's exact test for categorical variables, the independent samples t-test for normally distributed continuous variables, and the Mann–Whitney U test for abnormal distributions. Descriptive analyses were presented using mean ± SD, and propriety data were shown as median and min–max values. A p-value of <0.05 was considered significant.

3. Results

Two hundred forty-four pregnant women with a positive SARS-CoV-2 PCR test were followed up during the study period. The demographic and clinical characteristics of the pregnant women in the study are shown in Table 1. The mean age of the patients was 28.3 years (range 18-43 years), BMI was calculated as a mean of 26.7 (range 22-35), and the mean gestational age at the time of diagnosis was 36.6 weeks. A total of 200 (98%) cases were diagnosed in the third trimester. Median gravida was two, parity was one, and the median

number of living children was one in two groups. The median length of hospital stays of the patients admitted for treatment was 11(± 10.2) days for the unvaccinated group and 4±8.4 for the vaccinated group. The duration was found to be significantly shorter in the vaccinated group (p<0.01).

Table 1. The demographic and clinical characteristics of pregnant women with COVID-19 infection

Parameter	Vaccinated (n:40)	Unvaccinated (n:204)	p-value
Age (years)	31.4± 4.6	28.3 ± 5.9	<0.01
BMI (kg/m²)	27.2±4	26.7 ± 2.3	0.35
Gestational age at the time of Covid-19 diagnosis (weeks)	36.2±2.9	36.6±3.8	0.54
Gravidity	2±3.2	2 ± 3.1	0.38
Parity	1±3,9	1± 4.5	0.42
Number of living child	1±3.2	1± 3.4	0.37
Previous miscarriages	1±2.3	1±2.4	0.62
Time from COVID-19 diagnosis to delivery (days)	10± 1.4	7± 82.3	0.14
Length of hospital stay (days)	4± 8.4	11±24.2	<0.01
Smoker (current/history)	6 (15.6)	54(26.4)	0.27
Admission to hospital			
Emergency Department	14(35.2)	100(49.3)	0.13
Covid-19 Outpatient Clinics	12(30.1)	52(25.4)	0.62
Obstetric Outpatient Clinics	16(40.0)	50(24.5)	0.54
COVID-19 case in the family	22 (55)	117(57.3)	0,61
Covid 19 infection Findings on Chest X-Ray	2(5)	23(11.2)	0.23
Covid 19 infection Findings on Pulmonary CT	1 (2,5)	17(8,3)	**0.02**
Comorbid disease			
Hypertension	1(2.5)	16(7.8)	<0.01
Diabetes Mellitus	1(2.5)	5(2.4)	0.21
Thyroid Gland Diseases	0(0)	2(0.9)	NA
Pulmonary Diseases	3(7.5)	3(1.4)	0.067
Liver Diseases	0(0)	1(0.4)	NA
Symptom			

Fever	12 (30)	111 (54)	0.236
Cough	5 (12.5)	75(36.7)	0.728
Sore Throat	2(5)	26(12.7)	<0.01
Loss of taste sensation	1(2.5)	14(6.8)	<0.01
Loss of smell sensation	2(5)	20(10.2)	<0.01
Tiredness	7(17.5)	37(18.1)	0.652
Loss of appetite	16(40)	57(27.9)	0.523
Tiredness continuing in the 6th week postpartum	12(30)	59(29)	0.865

Abbreviations: BMI: body mass index, CT: computed tomography, Data are mean standard deviation or n (%) unless otherwise specified Values are given as a number (percentage), mean ± standard deviation (range), or median (interquartile range, range).

There was no difference between the groups in terms of BMI, gravida, parity, time from Covid -19 diagnosis to delivery, smoking status, and the unit to which they applied to the hospital (emergency department, Covid-19 outpatient Clinics, Obstetric Outpatient Clinics). Seventy-five percent (n:184) of the pregnant women in the study population were a non-smoker. In 114 (46,7 %) of patients, admission to the hospital occurred through the emergency department. In order to determine the origin of COVID-19 transmission, it is necessary to identify the vectors that could have carried it; the patients were questioned about the existence of positive family members; 57.3% (n=117) of the unvaccinated group and 55% (n=22) of the vaccinated group had a positive family history (p: 0.61).

A total of 41 patients refused all methods of radiological imaging. Radiological imaging revealed no lung findings on Chest X-ray (CXR) examination of 72,9% (n:178) of the patients. Pulmonary computed tomography was not performed in 61.0% (n:149) of patients. Findings were determined in 7.3 percent of individuals to whom tomography was performed (n:18).

All the pregnant patients were clinically evaluated in respect of comorbid diseases. Comorbidities were identified in 25% (n:51) of patients, and the most common condition was hypertension. Laboratory tests were performed for all the patients for diagnostic and treatment purposes. Twelve (5.8%) patients had anemia, and 4 (1.9%) had thrombocytopenia. The most common hematological abnormality was neutrophilia. Only 8 (4.5%) patients had elevated liver enzymes; one was HELLP syndrome. The blood levels of urea and creatinine were within the normal limits, except for three patients who died owing to multiorgan failure. C-reactive protein was found to be increased in 87% of the patients. Procalcitonin levels were similarly high. In addition, no significant difference was found between the groups in terms of laboratory tests. The symptoms seen in pregnant patients during COVID-19 infection are shown in Table 1. There was no difference

between the groups in terms of symptoms. Nasal oxygen was administered to 36.9% of the patients, and 2.9% received mechanical ventilator support in the unvaccinated group.

Table 2. Pregnancy characteristics and maternal, fetal outcomes of patients with COVID 19 infection

	Vaccinated (n:40)	Unvaccinated (n:204)	P value
Trimester of the pregnancy at the time of diagnosis	n (%)	n (%)	
1st trimester	0	1(0.4)	
2nd trimester	4(10)	3(1.4)	0.456
3rd trimester	36(90)	200(98)	
Cesarean indication	n (%)	n (%)	
History of previous cesarean	8(20)	70(51.9)	0.742
Maternal-related problems	1(2.5)	26(19.3)	0.264
Cephalopelvic disproportion	1(2.5)	3	0.438
Fetal distress	1(2.5)	36(17.6)	0.842
Delivery type	n (%)	n (%)	
Vaginal birth	29(72.5)	37(33)	0.082
Cesarean section delivery	11(27.5)	136(67)	
Pregnancy outcome	n (%)	n (%)	
Abortus	0	1(0.5)	
Premature birth	1(2.5)	37(18.2)	0.475
Stillbirth	0	1(0.5)	
Term live birth	39(97.5)	165(81.3)	
Pregnancy complications	n (%)	n (%)	
Intrahepatic cholestasis of pregnancy	0	2(1.1)	
Pre-eclampsia	0	8(3.9)	
Placenta previa	0	3(1.4)	0.658
HELLP Syndrome	0	1(2)	
No pregnancy complications	40(100)	191(93.6)	
Nasal Oxygen	8(20)	73(36.9)	0.261
Admitted to the intensive care unit	0	13(5.3)	NA
Mortality due to Covid-19 infection	0	4(1.6)	NA

Data are mean standard deviation or n (%) unless otherwise specified Values are given as a number (percentage), mean ± standard deviation (range), or median (interquartile range, range).

Pregnancy characteristics and maternal and fetal outcomes of patients with COVID-19 infection were summarized in table 2. Ninety-six percent (n:236) of the patients were in the third trimester at the time of diagnosis. There was no difference between the two groups regarding the delivery type, cesarean indications, pregnancy prognosis, and pregnancy complications. In the unvaccinated group, 13(5.3%) patients needed intensive care. Mortality due to COVID-19 was in 4 (1.6%) patients.

The median birthweight of the newborns was 3200 gr (range, 620-4900) in the unvaccinated group and 2940 (2100-3190) in the vaccinated group. The median 1-min APGAR score was 8 (range, 0-9), and the median 5-min APGAR score was 9 (range, 0-10). Nutrition of the newborns was started with maternal breastfeeding in 63.5% (n:155) of cases. A SARS-CoV-2 PCR test was applied to all the infants; in the unvaccinated group, 5.4% (n = 11) were found to have a positive result. There were no newborns with positive test results in the vaccinated group. The number of cases admitted to the neonatal intensive care unit was found to be higher in the unvaccinated group by 14.9% (n:29). Neonatal outcomes of newborns are shown in Table 3.

Table 3. Neonatal outcomes of newborns

	Vaccinated (n=40)	Unvaccinated(n=204)	P value
Parameter	Min-Max	Min-Max	
Birthweight of term newborn (gr)	2100-3190.0	620-4900	NA
1-min Apgar	4-8	1-9	
5-min Apgar	8-9	3-9	
Requirement for neonatal intensive care	**n(%)**	**n(%)**	
Admitted to intensive care unit	1(2.5)	29(14.9)	<0.01
Intensive care not required	39(97.5)	166(85.1)	0.647
COVID-19 positivity in the newborn	**n(%)**	**n(%)**	
Not tested	0	11(5.4)	
Negative	40(100)	192(94.6)	NA
Positive	0	1(0.49)	

Data are mean standard deviation or n (%) unless otherwise specified Values are given as a number (percentage), mean ± standard deviation (range), or median (interquartile range, range).

4. Discussion
The physiological and immunological changes that occur in women during pregnancy lead to complications related to respiratory tract infections, maternal and fetal mortality, or increased morbidity (11, 12). COVID-19 infection in pregnant women leads to higher mortality rates and more negative outcomes associated with the disease course than the general population (13, 14). In a recent meta-analysis of 111 papers, researchers found that SARS-CoV-2 infection significantly increased the risks of premature delivery, pre-eclampsia, stillbirth, neonatal mortality, and maternal mortality compared to uninfected pregnant patients (15). Therefore, the protection of pregnant women against COVID-19 is of great importance in preventing adverse outcomes of the disease (15).

Vaccinating pregnant women against COVID-19 is crucial because of the increased risk of poor outcomes following SARS-CoV-2 infection during pregnancy. In a population study with many cases, it was emphasized that the vaccination acceptance rate of pregnant women was less than the normal population (16). Consistent with this information, our study was conducted on 244 pregnant women with SARS-CoV-2 PCR test positivity, and during the study, the number of vaccinated pregnant women was only 40. This finding demonstrates that the vaccination acceptance rate among pregnant women is relatively low.

Examining the research that evaluates the progression of the infection reveals the following: The cumulative incidence of infection in vaccinated women was significantly lower than in unvaccinated women (17). The hospitalization rate was found to be higher in vaccinated pregnant women than in unvaccinated pregnant women, and the severe covid rate was reported more in unvaccinated pregnant women (5). In our study, consistent with these data, the length of hospital stay was found to be significantly higher in the unvaccinated group.

The results obtained in the current study are similar to the most commonly seen COVID-19 symptoms defined in the literature. According to data from the Centre for Disease Control (CDC) in the USA, the most common symptoms of COVID-19 patients were cough (84%) (18). Aktaş et al. determined fever (70%) most often in the first presentations at the hospital of pregnant women with COVID-19 and reported that the findings of persistent dry cough (34%) and weakness (13%) were seen less often (19, 20). Similarly, in the current study, the most frequently seen symptom was fever at the rate of 65.5%, followed by cough (39.4) and myalgia (12.8%). There was no difference between the groups in terms of these symptoms.

In a surveillance report of pregnant and non-pregnant women with laboratory-confirmed COVID-19 published by the CDC in the USA, it was stated that there was a higher probability of admission to the Intensive Care Unit for mechanical ventilation (0.5% vs.0.3%) for pregnant women compared to non-pregnant women (1.5% vs. 0.9%) (21). In our study, 13 patients in the unvaccinated group were admitted to the intensive care unit. None of the patients in the vaccinated group were admitted to the intensive care unit. However, it should be noted that our study's number of vaccinated patients

is very low. Therefore, based on these data alone, it may not be possible to say that the vaccine reduces the need for intensive care. However, similar results were found in many comprehensive studies (18-21).

Previous studies have reported high rates of obstetric complications such as premature birth and cesarean section delivery in women infected with SARS-CoV-2 (22). Blakeway et al. reported similar stillbirth rates, fetal abnormalities, postpartum hemorrhage, cesarean delivery, small for gestational age, and high maternal dependency unit or ICU or NICU admission rates in vaccinated and unvaccinated pregnant women in their study (19). Morgan et al. reported in their comprehensive study with 10,092 cases that severe coronavirus disease was higher in the unvaccinated group (5). According to the World Perinatal Medical Association COVID-19 Working Group data, 26.3% of pregnancies affected by COVID-19 infection result in premature birth and 4.1% in perinatal death (23). In the current study, 18.2% of the cases resulted in premature birth and 0.5% in stillbirth. According to this data, cesarean section delivery was performed in 54.2% of pregnant women with COVID-19, and this rate was 67% in the current study. The study group report stated that 27.5% of the newborns received intensive care support (24), whereas this rate in the current study was 14.9%.

The main limitation of the study is the small sample size. In addition, the fact that it is a retrospective design study is a disadvantage. However, its major value is that it provides comparison data on a highly significant topic. This issue will become clearer as the number of immunized pregnant women increases if clinicians are provided with more actionable information about vaccination. On this topic, prospective studies with more cases are required.

As efforts continue to improve vaccine acceptance, obstetricians and gynecologists should inform pregnant women of the potential benefits of the SARS-CoV-2 vaccine in preventing serious or critical illnesses.

Conflict of interest
The authors declared no conflict of interest.

Authors' contributions
Concept: S.S., C.A.,S.B., Design: S.S., S.A., Data Collection or Processing: M.A.N, C.A., Analysis or Interpretation: S.S., S.A., R.N., Ş.G.G., Literature Search: S.S., C.A., Writing: S.S., C.A., S.B.

Ethical Statement
The study was approved by the Institutional Review Board (decision no:1191/301220) and the Turkish Ministry of Health (T01-21-35), and it was carried out in accordance with the Helsinki Declaration principles.

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