Research article

Evaluation of Maternal and Neonatal Outcomes of 523 Pregnant Women with Covid-19 in a Single-Centre

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Abstract
Objective: To evaluate the maternal, perinatal and neonatal outcomes for pregnant women having tested positive for COVID-19 with the reverse transcription polymerase chain reaction (RT-PCR) technique.

Methods: PCR tests were administered to the women presenting with clinical complaints indicative of suspected COVID-19, or admitted to the hospital for obstetric reasons. The present study used clinical records to collect data such as general characteristics, clinical signs and symptoms, laboratory findings and radiological imaging results of the pregnant women, as well as the types of delivery and RT-PCR data of the newborns from the women who gave birth. Data related to the courses of pregnancy, maternal symptoms, types of delivery, and neonatal outcomes.

Results: 523 pregnant women tested positive for COVID-19 with RT-PCR technique. Of these pregnant women, 411 had asymptomatic while 112 women showed at least one symptom. Of the 523 pregnant women in total, 384 maintained their pregnancies. Eventually, 135 women gave birth. Twelve pregnant women (2.2%) in total were treated in the intensive care unit, and three (0.6%) died with COVID-19. All the newborns tested with the RT-PCR technique. All the test results were negative.

Conclusion: The existing data show that pregnant women with COVID-19 infection may need to be admitted to intensive care, and they may even be under a serious risk of maternal morbidity which may result in maternal death.

Keywords: Covid-19; Pregnancy; Rt-Pcr; Cesarean Section; Perinatal and Neonatal Outcomes.

1. Introduction

By December 2020, the number of cases of COVID-19, which has created a global public health crisis, has reached 80 million. 1 700 000 people have died from the pandemic since February 2020 [1]. While many studies focused on the effects of COVID-19 on the general population, enough evidence relating to its effects on vulnerable populations such as pregnant women has yet to be created [2-4]. It is known that pregnant women have an increased risk of contracting viral infections, severe respiratory tract infections, and pneumonia owing to the physiological changes in their immune and cardiopulmonary systems [5,6]. During pregnancy, changes in the anatomy of the pulmonary system, increase in the horizontal thoracic diameter, and elevated diaphragm levels increase the maternal sensitivity to hypoxia [7]. Changes in the pulmonary capacity and an increased vasodilatation may result in an increased secretion in the upper respiratory tract, and mucosal oedema. With the changes in the cellular immunity during pregnancy, susceptibility to viral infections such as COVID-19 increases [8]. Furthermore, newborns are under high risk of viral infections with their immature innate and acquired immune systems [9]. Irregularities of some factors such as complement cascade and cytokines may entail detrimental consequences for the brain development and function [10].

With the spread of coronavirus, some concerns have been raised as to intrauterine transmission from the mother to the baby in pregnant women [11,12,13]. Viral pneumonia is one of the prominent causes of pregnancy-related deaths around the world [14]. There have been some important questions raised with the spread of COVID-19: Are the symptoms of pneumonia different in pregnant women compared to non-pregnant women? What is the likelihood of maternal and neonatal death? Does it cause pregnancy-related complications or preterm birth? How much of COVID-19 is transmitted to the baby? [12,15].

The present study aims to contribute to the existing literature on maternal, perinatal, and neonatal outcomes for pregnant women testing positive for COVID-19 with the reverse transcription polymerase chain reaction (RT-PCR) test.

2. Materials and Methods

Five hundred and twenty-three pregnant women who presented to the Department of Obstetrics and Gynaecology of the Adana City Training and Research Hospital from 01.03.2020 to 01.01.2021 and tested positive for COVID-19 with the RT-PCR testing were entered into the present study. Following the ethics committee approval, hospital records were reviewed retrospectively and systematically, and demographics of the pregnant women having tested positive for COVID-19 with RT-PCR testing were recorded. Being a descriptive study, the present study analysed parameters such as age, date of presentation, pregnancy characteristics, type of delivery, accompanying diseases, symptoms (fever, cough, fatigue, dyspnoea, myalgia, sore throat, and diarrhoea), blood type, laboratory findings (haemoglobin, lymphopenia, platelet count, C-reactive protein, procalcitonin, ferritin, D-dimer, troponin I, AST, ALT, PT, and fibrinogen), radiological imaging results (chest radiograph, chest computed tomography), vertical transmission, maternal and foetal complications, and hospital stay. PCR tests were administered to the women presenting with clinical complaints indicative of suspected COVID-19, or admitted to the hospital for obstetric reasons.

Oropharyngeal and nasopharyngeal swab specimens taken both from asymptomatic pregnant women with indications for admission for suspected COVID-19 or various other reasons and from newborns were analysed in public health laboratories with the reverse transcription polymerase chain reaction (RT-PCR) technique and all the positive results were included in the present study.

3. Statistical Analysis

SPSS 23.0 software package was used for statistical analysis of the data. Categorical measurements were given as numbers and percentages while continuous measurements were shown as mean values and standard deviation (where necessary as median and minimum–maximum values).

4. Results

Tables 1 and 2 show the demographics, maternal characteristics at the time of presentation, perinatal outcomes, laboratory values, and radiological imaging results of the 523 pregnant women having presented to our clinic from 01.03.2020 to 01.01.2021 and tested positive with RT-PCR technique. Birth outcomes of the pregnant women who were not admitted to the hospital but treated as outpatients and discharged with medical advice are unknown.

Parameters		Number (n)	Percent (%)
Pregnancy Outcomes	Abort	4/523	0,8
	Delivery	135/523	25,8
	IU ex fetus	0	0
	Continuing Pregnancy	384/523	73,4
Delivery Method	Cesarean section	96/135	71.1
	Vaginal delivery	39/135	28.9
Medical History	Asthma, Diabetes Mellitus, Preeclampsia etc.	30/523	5.7
Symptoms	Asymptomatic	411/523	78.6
	Symptomatic	112/523	21.4
	Cough		
	Fatigue	112/523	21.4
	Fever	66/523	12.6
	Dyspnea	63/523	12
	Sore throat	46/523	8.8
	Myalgia	31/523	5.9
	Diarrhea	26/523	4.9
		5 /523	1
Blood Types	Unknown	83	15,8
	0 rh -	15	2,8
	0 rh +	109	20,8
	A rh -	20	3,8
	A rh +	176	33,6
	AB rh +	26	4,9
	AB rh -	2	0,3

	B rh -	8	1,5
	B rh +	84	16
Torax CT	Radiological Imaging	109/523	20.8
	Ground-glass opacifications-Ground-glass opacifications with mixed consolidation Pleural effusion	73/109	70
		3/109	2.8
PA Chest X-ray	Radiological Imaging	44/523	8.4
Intensive Care Support		12/523	2.1
Mechanical Ventilator		12/523	2.1
Preterm Birth	Delivery <37 weeks of gestation	4/135	3
Maternal Death		3/523	0.6

Table 1. Clinical courses, maternal symptoms and medical imaging results of the women testing positive for COVID-19 with PCR testing

	mean values ±sd
Age	28,3±5,8
Gestation Weeks	27,1±9,9
Gravidity	2,52±1,62
Parity	2,02±1,42
Hemoglobin (g/dL)	11,6±1,4
Lymphocyte (103/µl)	1,57±0,91
Platelet (10^3/ml)	224,3±68,1
C-RP turbidimetric (mg/L)	21,7±31,6
Ferritin (µg/L)	30,6±60,9
D-Dimer (µg/L)	2,23±6,91
Procalcitonin (ng/mL)	0,07±0,33
Troponin-I (ng/L)	3,7±6,3
AST (U/L)	28,8±42,3
ALT (U/L)	21,1±23,6
PT (sec)	12,3±5,8
APTT (sec)	25,16±2,77
Fibrinogen (mg/dL)	445,6±120,6
Treatment Time (days)	5,54±4,25

Table 2. Demographics and laboratory results of the women testing positive for COVID-19 with PCR testing

During the present study, 411 of the 523 pregnant women testing positive for COVID-19 with RT-PCR technique had no symptoms (asymptomatic) while the other 112 women showed at least one symptom (cough, fatigue, fever, shortness of breath, sore throat, muscle pain, or diarrhoea). Of the 523 pregnant women, 256 (48.9%) were admitted to and monitored in hospital while 267 (51.1%) were followed up as outpatients. Age range of the women was 15-46 and the mean maternal age was found to be 28.3. While the mean gestational age was 27 weeks, the most common gestational week at which pregnant women presented to the hospital was the week 38 with a ratio of 8%. Of the 523 women with COVID-19 infection in total, 384 maintained their pregnancies. Eventually, 135 women gave birth. 96 (72%) of these women delivered their babies by caesarean section while 39 (28%) gave birth by vaginal delivery. Analysis of the existing data revealed that the most common indication for caesarean section was foetal distress. When the parities of the pregnant women with COVID-19 infection were reviewed, 166 women (32%) were primigravid while 357 women (68%) were multigravid.

Review of the blood types of the pregnant women showed that the most common blood type was A positive (33.6%) while the least common was AB negative (0.3%). Blood types of 83 women (15%) were not reviewed.

When we review the records of the patients having presented to our clinic since WHO's declaration of the pandemic in March

2020, we see that there have been 2 peaks in the number of presentations, i.e. one in September 2020 and the other one in November 2020. Having analysed these 10-month data, we found that September 2020 had seen the highest number of presentations with 162 patients.

Laboratory specimens analysed at the time of presentation to the hospital revealed that 131 (25%) of the 523 pregnant women had lymphocytopenia (lymphocyte count <1500/microL). Similarly, 397 (75%) of the 523 pregnant women had increased concentrations of C-reactive protein (> 5 mg/L). One hundred and twenty-two pregnant women (23%) had anaemia (<10.8 g/dL). Six pregnant women (1%) had high ferritin levels (>307 μg/L) while 385 women (73%) showed high D-dimer levels (>654 μg/L). Certain liver enzyme values were above the normal range, namely AST in 81 pregnant women (15%) and ALT in 70 pregnant women (13%).Of the 523 pregnant women having presented to our clinic and tested positive for COVID-19 with the PCR technique, 256 (48%) were admitted, treated and monitored for various clinical preliminary diagnoses, and the average duration of hospital stay was five days across the whole population of these pregnant women. Twelve pregnant women (2.2%) in total were treated in the intensive care unit, and unfortunately, three (0.6%) died with COVID-19. The underlying pathology in all the pregnant women requiring intensive care treatment was respiratory problems.

Thoracic CT was performed, mostly postnatally, on 109 pregnant women in total, and PA chest radiograph was performed on 44 pregnant women including some of the women from the above-mentioned 109-pregnant women group. Seventy-three (70%) of the thoracic CT images showed findings consistent with COVID-19 infection, particularly peripheral multiple consolidations, increased ground-glass opacity, and nodular densities.

Four pregnant women (0.8%) had an abortion within the course of observation. Four other pregnant women (3%) had preterm births before the 37 weeks of gestational age. In our clinic, 135 pregnant women having tested positive for COVID-19 with the PCR technique delivered their babies under special contact precautions, and oropharyngeal and nasopharyngeal swab specimens were taken from all the newborns and tested with the RT-PCR technique. All the test results were negative and no vertical transmission was detected in any of the newborns. It is believed that indications for admission of the newborns to the intensive care unit originated from perinatal obstetric reasons. In accordance with the World Health Organization's recommendations, healthy newborns were taken to their mothers immediately after birth and it was ensured that mothers breastfed the babies.

5. Discussion
In our study, we found that one-fifth of pregnant women positive for RT-PCR were symptomatic. Cough was detected in all of our symptomatic patients. While the rate of admission to intensive care unit of pregnant women infected with Covid-19 was 2.1%, we determined 3 maternal mortalities. In our cases who gave birth, we found that cesarean section was applied more frequently as the mode of delivery.All newborn babies were scanned by RT-PCR. There was no RT-PCR test positivity in any newborn.

While other coronaviruses – SARS and MERS – have important adverse maternal outcomes with maternal mortalities of 25.8% and 28.6%, respectively, a recent systematic review has found the COVID-19-related maternal mortality to be 0.6% [16,17]. Consistent with the literature, our study similarly found three maternal deaths (0.6%). Furthermore, the Centers for Disease Control and Prevention (CDC) COVID-19 Response Pregnancy and Infant Linked Outcomes Team Report states that maternal mortality is higher than the mortality among non-pregnant women of reproductive age [18].

When clinical symptoms and findings of the pregnant women in the present study were reviewed, 78.6% of the women showed no symptoms (asymptomatic) while 21.4% had at least one symptom. The literature review revealed that 59%-75% of the pregnant women testing positive for COVID-19 with the PCR technique were asymptomatic [17,19]. In the present study, the most common symptom was cough among symptomatic pregnant women, which accompanied all the other symptoms in these women. Across all patients with COVID-19, cough is the most common symptom for both pregnant women and other adults [18,19]. In the present study, the symptoms of fatigue and fever were present in more than half of the pregnant women. The PRIORITY (Pregnancy Coronavirus Outcomes Registry) study found cough to be the most common symptom as well, followed by sore throat (16%), body aches (12%), and fever (12%) [20]. Another issue to take into consideration is that some symptoms that may manifest during a normal pregnancy (e.g. fatigue, shortness of breath, nasal congestion, nausea/vomiting) are consistent with some clinical symptoms of COVID-19. This should be considered in assessing pregnant women.

It was found that the ratio of intensive care admission for COVID-19 was higher among pregnant women than in non-pregnant women of reproductive age [18]. In the present study, the ratio of pregnant women admitted to intensive care was 2.1%. A recent systematic review reported that the ratio of admission to intensive care was 4% for pregnant women [17].

While the most common laboratory anomalies were elevated levels of C-reactive protein and reduced lymphocyte count among pregnant women testing positive for COVID-19, leucocytosis was rarely seen among these women. These findings are generally similar to those seen in non-pregnant adult women with COVID-19 [21]. The present study found the elevated CRP levels to be 75% while lymphocytopenia was 25%. Abnormal liver chemistries were found to be 13-15%.

Data relating to the ratio of preterm births among pregnant women diagnosed with COVID-19 are unclear [17,22]. Some studies have found increased preterm birth ratios while others have reported reduced ratios. The present study found the prevalence of preterm births to be 3%. Although it has been stated that COVID-19 was not an indication for change of the

planned method of delivery, a recent study found an increase in the prevalence of caesarean section among pregnant women with COVID-19 [23,24]. In the present study, 71.1% of the pregnant women delivered their babies with caesarean section. Indications for caesarean section given to prevent the poor prognosis of the COVID-19 infection may have had an impact on this. More studies on the stages of COVID-19 are needed to determine whether the type and timing of delivery have different effects on the course of maternal and foetal outcomes.

The uncertainty over the vertical transmission of COVID-19 from mother to the infant has yet to be resolved. Only a few studies have reported a probable vertical transmission so far [25-27]. In the present study, oropharyngeal and nasopharyngeal swab specimens were taken from all the newborns and tested with the RT-PCR technique. All the test results were negative and no vertical transmission was detected in any of the newborns.

Increased rates of obstetric complications, fetal distress, and cesarean delivery for pregnant women with COVID-19 infection have been reported in the literature (28,29). Rates for both spontaneous and iatrogenic preterm deliveries were found to be increased in pregnancies complicated by COVID-19. Furthermore, low oxygen saturation and subsequent impaired perfusion to the fetus may lead to fetal distress, resulting in increased rates of cesarean delivery [28,29]. There are also studies on the relationship between pregnancy loss, congenital anomalies and COVID-19 infection [30,31].

In our study,of the 523 women with COVID-19 infection in total, 384 maintained their pregnancies. Eventually, 135 women gave birth. 96 (72%) of these women delivered their babies by caesarean section while 39 (28%) gave birth by vaginal delivery. Analysis of the existing data revealed that the most common indication for caesarean section was fetal distress.And no congenital anomalies were associated with covid-19.
Another point discussed in the literature is the possibility of vertical transmission of the virus [32].Although isolation of the newborn from the mother during the active infection was recommended previously, encouraging breastfeeding with appropriate precautions is the usual approach at present [33]. There is no vertical transmission of the virüs to the babies in our study.

Developmental and reproductive toxicology studies, which typically use animals to assess the potential effects of a new medication or vaccine on the full spectrum of reproduction, have not yet been completed for any of the COVID-19 vaccines, except for the Moderna vaccine, which submitted results to the FDA on December 4, 2020; thus, pregnant persons have yet to be enrolled. A preliminary report of developmental and reproductive toxicology studies on the Pfizer–BioNTech vaccine is expected to be sent to the FDA in the near future. According to the VRBPAC briefing documents on the Moderna vaccine, a combined developmental and perinatal and postnatal study was conducted in rats and showed no adverse effects on female reproduction, fetal or embryonic development, or postnatal development [34].

Another issue to be discussed is the risks of COVID-19 illness to a pregnant person and the fetus. Current data suggest that pregnant persons are more likely to be admitted to an intensive care unit, to require invasive ventilation, to receive extracorporeal membrane oxygenation, and to die than nonpregnant women of reproductive age [35]. The effects on the fetus are not completely understood.

Given the vaccine reactogenicity, including fever, vaccination in the first trimester could increase the risk of neural tube and other congenital defects [36]. In addition, exposures earlier in pregnancy are more likely to cause adverse outcomes. However, the risks of vaccine reactogenicity on the pregnant person and the fetus need to be weighed against the risks of COVID-19 itself. Data collection on persons who received a COVID-19 vaccine during pregnancy will be needed to provide information to guide future vaccine recommendations regarding pregnancy.

One of the strengths of our study is that asymptomatic pregnant women with positive RT-PCR results for covid 19 who were admitted to the hospital with any obstetric indication were included. Thus, maternal and perinatal outcomes in pregnant women infected with Covid-19 were determined more accurately. In addition, the fact that it is one of the studies including the highest number of pregnant cases reported from a single center is another strength of our study. Since some of the pregnancies continued during the study period, the perinatal and neonatal outcomes of these cases could not be evaluated. This is one of the limitations of our study.

6. Conclusion
The existing data show that pregnant women with COVID-19 infection may need to be admitted to intensive care, and they may even be under a serious risk of maternal morbidity which may result in maternal death. In most of the reported cases, no maternal-foetal transmission of the SARS-CoV-2 virus has been detected. Further prospective studies are needed to reveal the real risks and identify the optimal management of COVID-19 in pregnancy.

Disclosure Of İnterests
The authors have no conflicts of interests to declare in relation to this article.

Details Of Ethics Approval
Our study approved by the University of Health Sciences, Adana City Training and Research Hospital
Ethics Committee (Date:22/04/2021, decision no: 1378). This study was performed in accordance with the Declaration of Helsinki.

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Presentation
This study has not been presented anywhere before.

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