

Covid-19: Possible Vertical Transmisson and Inreased Still Birth Ratio

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Abstract: The coronavirus disease 2019 (Covid-19), that was later declared pandemic by World Health Organization, had led to panic and fear worldwide. Like many outbreaks caused by viruses, in chief reason for fear was the infectious agent's potential to be transmitted from pregnant women to their fetuses and newborns. In our study, the hospital records of 117 pregnant women who delivered stillbirths in our clinic between 01.01.2015 and 31.12.2020 were examined. The pregnancy characteristics and perinatal outcomes were examined by making retrospective analysis of the records. Considering six year of the study data, it was observed that the stillbirth rates increased in the pandemic period. One hundred seventeen stillbirth cases that occurred in the last six years were analyzed. The mean age of the pregnant women was 29.64 ± 6 (18-44) and parity was 2.54 ± 1.58 (1-8). Body mass index was calculated as 21.36 ± 3.40 (16-27) average and smoking consumption rate was 9.40% (11/117). Maternal diabetes was detected in 8.54% of the patients (10/117) and pregnancies were complicated by maternal hypertension in 5.12% of the patients (6/117). The average birth weight was 1597 ± 1038 (500-4700) gram. Sixty percent of the deliveries (n=71) were performed by vaginally. Fetal sex was 52.1% male (n=61). The number of deliveries in the past six years was 11780. Almost 1% of the deliveries occurred as stillbirths (117/11780). The unusual stillbirth ratio during the pandemic was 3.1 times higher than the average of pre-pandemic period (2.5vs0.80). In our study, we investigated stillbirth rates before and during the pandemic. Although vertical transmission of Covid-19 has not been reported, the adverse pregnancy and neonatal outcomes have been provided in many studies. Undoubtedly, in obstetrical practice stillbirth is one of the most destructive consequences for pregnant women. Considering the increase in stillbirth rates, we think that pregnant women with adverse perinatal outcomes should be routinely tested for Covid-19, especially during the outbreak.

INTRODUCTION

Coronavirus, and also named Orthocoronavirinae, is an enveloped, positive-sense, single-stranded ribonucleic acid (RNA) virus belonging to the Nidovirales order. Coronaviruses contain the largest genomes of all RNA viruses. Coronaviruses derive their name from the crown-shaped glycoprotein structures on their surface which seen in the electron microscope examination ¹. The most striking feature of this group of viruses is that they have human and animal hosts. Coronaviruses is generally causing respiratory infections range from self-limiting respiratory symptoms to simple organ dysfunction (i.e. respiratory failure linked viral pneumonia) and then multiple organ failure, even death².

There are seven types of coronavirus that cause human diseases. Three of them are highly pathogenic: Severe acute respiratory syndrome coronavirus (SARS-CoV or SARS-CoV-1), Middle East respiratory syndrome-related coronavirus (MERS-CoV) and Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). SARS-COV-1 infected 8098 people in its epidemic in 2003 with a approximately 10.5% fatality rate ³. Then, in 2013, MERS-CoV caused an epidemic, infecting 2519 people in 21 countries with a mortality rate of 34.4% ⁴. Finally In late 2019, a new mutation belonging to the coronavirus family was identified called SARS-CoV-2 ⁵.

The SARS-CoV-2 epidemic was declared a public health emergency of international concern by World Health Organization (WHO) on 30 January 2020 due to its rapid spread from human to human. As a consequence that reported on February 28 2020, WHO has raised the assessment to very high level globally ⁶. And eventually by 11 March 2020 it was described as a pandemic because of the 118.223 confirmed cases and 4.291 deaths in 114 countries ⁷. On the first anniversary of the pandemic announcement, the number of cases of Covid-19 exceeded 116 million worldwide with 2.2% fatality rate ⁷. As of the same date 2.835.989 confirmed cases and 29.290 deaths have been reported in Turkey⁸.

One of the questions tried to be answered in every outbreak that especially caused by viruses, is whether the infectious agent transmitted to the unborn fetuses. This path is generally defined as

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‘intrauterine vertical transmission’ and many microbial pathogens have been proved to cause fetal infection for many years ⁹.

On the other hand, physiological maternal adaptations during pregnancy can cause more severe respiratory diseases such as viral pneumonia in pregnant women. Accordingly, maternal and fetal morbidity and even mortality may increase. However, according to current data, it is still unclear to what extent this new viral infection can lead to maternal and fetal complications ⁹.

In our study, we aimed to investigate the effect of pandemic on stillbirths due to possible vertical transmission.

MATERIALS and METHODS

In the present retrospective study, we investigated women whose pregnancy ended with stillbirth between January 2015 and December 2020 at Ordu University Medical Faculty. The data were evaluated in two groups: pre-pandemic period (from January 1, 2015, to February 28, 2020 - antecedent the first reported Turkey cases of Covid-19), and pandemic period (from March 1, 2020, to December 31, 2020). All stillbirths were investigated. Births with no fetal heartbeat, more than 20 gestational weeks and / or birth weight over 500 grams were accepted as stillbirths. Pregnancy terminations due to fetal anomalies were excluded from the study.

Pregnancy characteristics such as maternal age, body mass index, parity, smoking consumption, maternal diabetes, and maternal hypertension were compared between the groups.

Perinatal outcomes such as stillbirth ratio, birth weight, fetal sex, mode of delivery were also compared between the groups.

Group comparisons were made using Mann-Whitney and Fisher exact tests. SPSS program version 26 was used to make comparisons. Two sided P value less than 0.05 was defined as statistically significant.

Ethical approval

Ethics committee approval (2020-05-11T22_14_33) was received from the Republic of Turkey Ministry of Health Directorate General of Health Services.

RESULTS

There were 10.419 deliveries in the pre-pandemic period and 1.361 deliveries during the pandemic period. Almost 1% of the deliveries have occurred as stillbirths (117/11780) in the last six year period. Considering the study data, it was observed that the stillbirth rates increased in the pandemic period. While stillbirth was detected at a rate of 0.8% (83/10.419) in the pre-pandemic period, the stillbirth rate was calculated as 2.50% (34/1.361) during the pandemic period. In other words, the unusual stillbirth ratio during the pandemic was 3.1 times higher than the average of pre-pandemic period (2.5 vs 0.80) ($p < 0.001$) (Figure 1).

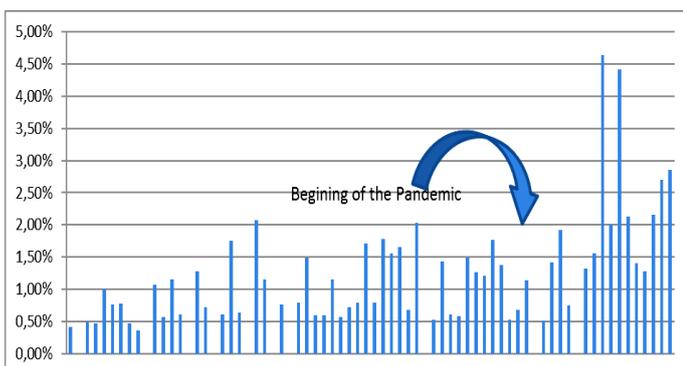


Figure 1: Stillbirth ratio by month

Pregnancy characteristics were analyzed and presented at Table 1. The mean age of the pregnant women was 29.64 ± 6 (18-44) and parity was 2.54 ± 1.58 (1-8). The groups were similar in terms of maternal age (29.89 ± 6.43 vs 29.05 ± 4.81). Parity was found to be higher in the pandemic period (2.31 ± 1.43 vs 3.11 ± 1.82). Body mass index was calculated as 21.36 ± 3.40 average and smoking consumption rate was 9.40% (11/117). Body mass index and smoking consumption data were also statistically similar in both groups (21.43 ± 3.44 vs 21.20 ± 3.37 and 9.6% vs 8.8%). Maternal diabetes was detected in 8.54% of the patients (10/117) and the pregnancies were complicated by maternal hypertension in 5.12% of the patients (6/117). The incidence of maternal diabetes and hypertension was similar in both pre-pandemic and pandemic groups (8.4% vs 8.8% and 4.8% vs 5.8%). Parity was found to be statistically significant higher in the pandemic period (2.31 ± 1.43 vs 3.11 ± 1.82) ($p = 0.01$). However, there were no significant differences in other pregnancy characteristics (maternal age, body mass index, maternal diabetes and maternal hypertension) (Table 1).

Table 1: Comparison of the pregnancy characteristics

	Pre-pandemic period	Pandemic period	P value
Maternal age	29.89+6.43	29.05+4.81	0.6
Parity	2.31+1.43	3.11+1.82	0.01*
Body mass index ^a	21.43+3.44	21.20+3.37	0.7
Cigarette consumption	8/83 (9.6%)	3/34 (8.8%)	0.5
Maternal diabetes ^b	7/83 (8.4%)	3/34 (8.8%)	0.4
Maternal hypertension ^c	4/83 (4.8%)	2/34 (5.8%)	0.5

^a BMI; weight in kilograms divided by height in meters squared.

^b Including pre-gestational and gestational diabetes mellitus

^c Including pre-gestational and gestational hypertension, preeclampsia

* statistically significant

Perinatal outcomes were compared and presented at Table 2. The average birth weight was 1597 ± 1038 (500-4700) grams. Fetal birth weight was lower in stillbirths during the pandemic period (1649 ± 1056 vs 1469 ± 999). Sixty percent of the deliveries ($n = 71$) were performed by vaginally. Similar rates were observed between groups in terms of delivery mode (52.94% vs 63.85%). Fetal sex was 52.1% male ($n = 61$). Male sex was observed twice as common in stillbirths during the pandemic period (32.35% vs 60.24%). In other words, male sex was dominant in pre-pandemic period and female sex was more common during the pandemic period. There were no significant differences in other study outcomes (birth weight, mode of delivery, smoking consumption) except stillbirth ratio (Table 2).

Table 2: Comparison of the perinatal outcomes

	Pre-pandemic period	Pandemic period	P value
Stillbirth ratio	83/10419 (0.80)	34/1361 (2.50)	<0.001*
Birth weight	1649+1056	1469+999	0.3
Fetal sex (male ratio)	50/83 (60.24%)	11/34 (32.35%)	0.005*
Mode of deliver (vajinal ratio)	53/83 (63.85%)	18/34 (52.94%)	0.3

* statistically significant

DISCUSSION

The rapid progression of the outbreak and the uncertainties about the virus led to fear and panic all over the world. But in the light of the current data, we have almost sufficient information about the transmission of the virus. The virus is generally transmitted by droplet spread ¹⁰. The virus is generally causing respiratory infections. Many patients suffer from fever, cough and dyspnea ¹¹. But also it is known that, asymptomatic and symptomatic patients are similar in terms of viral load, which play a role in the spread of the virus ¹².

On the other hand, the debate about the vertical transmission of the Covid-19 infection is still ongoing. It is now known that Covid-19 infection leads to acute respiratory distress syndrome, respiratory failure, requirement for mechanical ventilation, and systemic complications including multi organ dysfunction syndrome⁹. Although no vertical transmission of the Covid-19 virus has yet been reported, in some case studies, it was stated that perinatal outcomes due to these complications may be adversely affected. Perinatal complications including preterm labor, premature rupture of membranes, intra uterine growth restriction, low birth weight, fetal distress, stillbirth and neonatal death were observed more frequently in pregnant women infected with covid-19¹³⁻¹⁵. In our study, the unusually high number of stillbirths during the pandemic period supports the relationship of covid-19 infection with perinatal complications

Some studies that raise suspicion regarding the vertical transmission of the virus have also been published^{15,16}. However, most of the case reports were early neonatal infections diagnosed within two days of delivery. As the postnatal neonatal test was delayed in most cases, it could not be clearly shown whether the infection was passed on to the newborn before or after birth. In an interesting study, specific antibodies and increased cytokine levels were detected in the newborn in the second postnatal hour, but even in this case, the presence of virus in the nasal swab of the newborn could not be confirmed^{16,17}.

The study represents an increase in the stillbirth ratio during the pandemic period. Although vertical transmission has not been proven, this increase may be a direct effect of Covid-19 infection. Besides, the increase in stillbirths may also be related to inadequate antenatal visits due to fear of contracting infection or the willingness not to increase the health service burden. Because it is known that inadequate antenatal visit and ultrasound scanning increase the risk of stillbirth. In addition, insufficient pregnancy follow-up also delays the diagnosis of emerging diseases that have the potential to complicate pregnancy. Although it was found to be not significant in our study, diseases such as maternal diabetes and hypertension may cause stillbirth due to inadequate antenatal visit.

In our study, we found that women who had stillbirths during the pandemic period were women with higher parity. This is probably due to the fact that women with higher parity are less likely to go to the hospital for antenatal visit because of their experience with pregnancy. Although there was no difference between diseases such as diabetes and hypertension in our study, we think that less physician control of women with high parity increased the rate of stillbirth during the pandemic period.

In our study, we also found that fetal sex was significantly more female in stillbirths during the pandemic period. Further studies are needed to reveal the relationship between Covid-19 infection and fetal sex in stillbirths.

The effect of increasing conditions due to the pandemic (such as inactivity, depression, domestic violence, loss of financial income) on stillbirths should be investigated with further studies.

Conclusion

No doubt, in obstetrical practice stillbirth is one of the most destructive consequences for pregnant women. In our study, it was observed that the stillbirth rates increased in the pandemic period. Although vertical transmission of Covid-19 has not been reported, the adverse perinatal outcomes have been provided in many studies. It should be noted that Covid-19 infection is generally asymptomatic. Considering increased stillbirth rates and asymptomatic process of the infection, we think that pregnant women with adverse perinatal outcomes maybe routinely tested for Covid-19 especially during the outbreak. Additionally, we think that the routine implementation of

the Covid-19 test will reveal the possible relationship between stillbirths and the infection more clearly.

Conflict of interest

The authors declare that they have no conflict of interest.

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