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## Effect of COVID-19 pandemic process on prenatal diagnostic procedures

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### ABSTRACT

**Objective:** To evaluate the accessibility of pregnant women to prenatal screening and diagnostic tests during the COVID-19 pandemic process and analyze the effect of the pandemic process on acceptance-rejection rates of fetal diagnostic procedures for high risk pregnancies.

**Materials and methods:** As part of this cross-sectional study, during the pandemic, between the dates of 11 March 2020–30 June 2020 at Karadeniz Technical University Faculty of Medicine Perinatology Clinic, fetal structural anomaly detected by ultrasonography or with increased risk in screening test in the first and second trimester of high risk pregnancies, who were therefore recommended a prenatal diagnosis test, were defined as the control group and retrospectively compared with high risk pregnancies of the same periods (11 March 2019–30 June 2019) in the previous year.

**Results:** A total of 267 cases were evaluated within the scope of the study. The rate of pregnant women undergoing the first and second trimester screening tests was 83% in the control group and 56% for pregnant women in the study group. When the total number of prenatal diagnostic procedures and the year each of the procedures performed are compared, a statistically significant difference was found between the study and control groups ( $p = .041$  and  $p < .001$ , respectively). When evaluating the rates of performed prenatal diagnostic procedures during the first patient visit in comparison to years, a statistically significant difference was observed in the A/S group and in the total number of cases ( $p = .023$ ,  $p < .001$ , respectively). Similarly, the rate of performed prenatal diagnostic procedure during the first patient visit and the patient's city of residence was similarly statistically significant from year to year ( $p < .05$ ).

**Conclusions:** The decrease in number of prenatal diagnosis and screening tests during the COVID-19 pandemic draws attention. Prenatal care services are a serious issue that cannot be overcome by any deficiencies in both maternal and fetal care.

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### KEYWORDS

COVID-19; high-risk pregnancy; invasive procedure; pregnancy; prenatal diagnosis



## Introduction

A new type of coronavirus, first detected in Wuhan, China in December 2019, was reported as the cause for cases of pneumonia [1]. In February 2020, the World Health Organization defined the Coronavirus disease 2019 as COVID-19 [2]. The virus that causes COVID-19 is a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. Later, COVID-19 quickly spread to many countries and as of 11 March 2020 causing the death of more than 4,000 people, the World Health Organization officially declared the disease as a pandemic [3]. The first case in Turkey was reported on 11 March 2020, and since has been one of the most affected countries in the world with

201,098 cases and 5150 deaths from this disease (<https://covid19.saglik.gov.tr/>, 1 Temmuz 2020).

COVID-19 has a poorly defined clinical course for vulnerable populations, especially including pregnant women [4]. Fetal complications of COVID-19 include abortion (2%), intrauterine growth restriction (10%) and preterm labor (39%) [1,5]. Given the previous outbreaks, the clinical consequences of COVID-19 on pregnant women are not clear, but their negative psychological consequences are almost certain [6,7]. The psychological consequences of the outbreak can have even greater effects.

Fetal structural malformations and chromosomal anomalies are abnormalities that affect the continuation of pregnancy by leading to fetal mortality and

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morbidity [8]. Both the advances in ultrasound technology and the increase in first and second trimester screening tests have enabled the earlier prenatal diagnosis of chromosomal anomalies and fetal malformations and determination of the management techniques [9]. Diagnostic procedures of chromosomal anomalies are chorionic villus biopsy (CVS), amniocentesis (A/S) and cordocentesis. Although the risk of complications from the procedures is low, families can experience anxiety on this matter and some can choose not to perform fetal diagnostic procedures for this reason.

Pregnant women were also affected by the restrictions applied to prevent the spread of COVID-19. In this process, it was noticed that the number of pregnant women who applied to the outpatient clinic had decreased and there was increasing concern among the pregnant women who continued their routine antenatal follow-up.

For this reason, in our study, we aimed to reveal the accessibility of pregnant women who applied to our clinic to prenatal screening and diagnostic tests and to evaluate the effect of the pandemic process on acceptance-rejection rates of fetal diagnostic procedures in high risk pregnancies.

## Materials and methods

As part of this cross-sectional study, during the pandemic between the dates of 11 March 2020 and 30 June 2020 at Karadeniz Technical University Faculty of Medicine Perinatology Clinic, fetal structural anomaly detected by ultrasonography or with increased risk in screening test in the first and second trimester of high risk pregnancies, who were therefore recommended prenatal diagnosis test, were defined as the control group and retrospectively compared with high-risk pregnancies of the same periods (11 March 2019–30 June 2019) in the previous year. All pregnant women in the study group were asymptomatic and no diagnostic tests were performed for the COVID-19 disease since they did not meet the criteria set by the national health department for testing.

For the 267 cases evaluated in this study, the maternal age, gravida/parity, the results of the first- and second-trimester screening tests, the gestational week at the time of diagnosis, the gestational week at the time of the procedure, the city of residence, and the acceptance-rejection rates for chorionic villus biopsy (CVS), amniocentesis (A/S) and cordocentesis were recorded through the hospital automation system. All CVS procedures were performed trans-

abdominally. The CVS procedure was performed between 10 and 14 weeks of gestation, amniocentesis between 15 and 23 weeks and cordocentesis was performed at  $\geq 24$  weeks.

Genetic counseling was given to each family who underwent karyotyping for prenatal diagnosis. Written and verbal information was given about the technique and possible complications of karyotyping, and informed consent was obtained.

The necessary ethics committee permission was obtained under terms of 2020/212 mandate of the Karadeniz Technical University Faculty of Medicine Ethics Committee. All procedures were carried out in accordance with the ethical standards of the institutional and/or national research committee and the principles set out in the Helsinki Declaration.

## Statistical analyses

SPSS Version 24 (IBM Corp., SPSS Statistics for Windows, Version 24.0. Armonk, NY.) was used in the study to record and calculate statistical data. The compatibility of numerical variables to normal distribution was tested with the Kolmogorov–Smirnov test. Categorical variables were determined using frequency and percentage, numerical variables using mean and standard deviation or median and minimum-maximum values. The relationship between two categorical variables was investigated with chi square test. The independent variables were compared with the Mann-Whitney U test. The study was conducted in a 95% confidence interval.  $p < .05$  value was considered statistically significant.

## Results

The average age of the 267 cases evaluated within the scope of the study was  $30.3 \pm 3.9$  (20–41). Of these cases, 53.9% agreed to undergo invasive procedures. 70% of the patients had undergone had at least one of the first and second trimester screening tests (83% of the pregnant women in the control group, 56% of the pregnant women in the study group). 49.4% of the cases who underwent prenatal diagnostic procedure were living in the city where the procedure was performed. Demographic data and invasive features of the cases are shown in [Table 1](#).

A prenatal diagnostic test was recommended to 138 pregnant women in the control group, and while 50 pregnant women refused to undergo the procedure (36.2%), 88 pregnant women (63.8%) accepted. In the study group, out of a total number of 129

**Table 1.** Demographic data of the cases evaluated within the scope of the study.

	<i>n</i> = 267
Patient age	30.3 ± 3.9 (20–41)
Gravida	2 (1–6)
Parite	1 (0–4)
Number of patients undergoing a procedure	144 (% 53.9)
Number of patients undergoing screening test	187 (% 70)
Patient's residence	
Same city as the clinic	132 (% 49.4)
Different city from the clinic	135 (% 50.6)
Gestational week at which the procedure is recommended	18.7 ± 3.8 (11–28)
Gestational week during the procedure	18.9 ± 3.9 (11–29)
Recommended invasive procedure type	
CVS	46 (% 17.2)
AS	199 (% 74.5)
Cordocentesis	22 (% 8.3)

**Table 2.** Comparative analysis of prenatal invasive procedures by years.

	2019	2020	<i>p</i> *
CVS	19	14	.000
AS	67	36	.000
Cordocentesis	2	6	.000
Total	88	56	.041

\**p* < .05.

pregnant women who were recommended prenatal diagnostic test, 73 of these pregnant women refused the procedure (56.6%) and 56 patients accepted (43.4%). This situation is statistically significant, both in terms of the total number of procedures and invasive interventions when compared with each other (*p*: .041 and *p* < .001, respectively). The number of each invasive procedure by years and their comparative analysis by years are as shown in Table 2.

When comparing the rates of performing prenatal diagnostic procedure at the first patient visit by years, while a statistically significant difference was observed in the A/S group and in total cases (*p* = .023, *p* < .001, respectively), no significant difference was found in the CVS and cordocentesis groups, but patients in the study group undergoing CVS and cordocentesis procedures increased in the first visit. The rate of performing prenatal diagnostic procedure in the first visit in relation to the patient's residence was also similarly statistically different from year to year (*p* < .05). Comparisons of the type of procedure, the rate of the procedure performed in the first patient visit and the city of residence of the patient are shown in Table 3.

## Discussion

The main data we obtained in this study are (I) during the COVID-19 pandemic period, while the number of invasive procedures that were performed during the earlier weeks of pregnancy like CVS and A/S decreased, the number of cordocentesis performed in the later

weeks of pregnancy increased, (II) while the total number of invasive procedures decreased during the pandemic period, when the total cases that accepted the procedure were evaluated, the rate of acceptance and performance of the procedure increased at the time of the first visit, (III) when the city of residence of the patients were compared, it was seen that the patients who were referred from different cities had higher rates of having the procedure at the first visit.

Pregnant women, like the rest of the society, have been affected by many restrictions applied to prevent the spread of COVID-19 [10]. Many societies have proposed new prenatal care instead of traditional protocols to prevent infection and spread of the disease during the COVID-19 outbreak for pregnant women [11,12]. Due to the applied curfew restrictions, changes in the provision of health services and the risk of pregnant women being infected, the reduced number of admissions to hospitals led to disruptions in routine prenatal care programs.

All of humanity is fighting against the first and most powerful threat of the twenty-first century, that is the COVID-19 outbreak. Another inevitable consequence of such an event is the psychological impact on vulnerable populations like pregnant women. Studies in the literature have shown that the COVID-19 pandemic process negatively affects the psychological behavior of pregnant women and creates a predisposition to depression and anxiety [13]. Mirzadeh and Khedmat [14] drew attention to different aspects of pregnancy during the COVID-19 outbreak, underlining the need for psychological support for pregnant women during this crisis.

Prenatal diagnostic procedures serve to reveal the diagnosis of chromosomal anomalies and genetic diseases in the intrauterine period. However, these procedures have various complications such as chorioamniotic separation, amniotic fluid leakage, fetomaternal bleeding, fetal injury, fetal loss and vertical transmission [15,16]. Most parents want to be sure

**Table 3.** Comparative analysis of the rates of invasive procedures at the first patient visit and the effect of the patient's city of residence at the time of procedure.

	2019	2020	<i>p</i>
Procedure type and rate of application in the first visit			
CVS	13 / 19 (%68.4)	12 / 14 (% 85.7)	.234
A/S	42 / 67 (%62.7)	30 / 36 (%83.3)	.023*
Cordocentesis	1 / 2 (% 50)	5 / 6 (%83.3)	.464
Patient residence and the rate of diagnostic procedures during the first visit			
Same city as the clinic	20 / 44 (% 45.5)	18 / 26 (% 69.2)	.007*
Different city from the clinic	36 / 44 (% 81.9)	29 / 30 (% 96.7)	.008*
Total	56 / 88 (% 63.6)	47 / 56 (% 83.9)	.000*

\**p* < .05.

that their unborn babies are healthy. Inevitably, any invasive diagnostic procedure aimed at providing this type of assurance will cause anxiety in parents, both in terms of the risk of procedure-related complications and results of the performed test.

The risk of vertical transmission associated with invasive prenatal diagnostic procedures has been described in some case reports for infections such as hepatitis virus, cytomegalovirus, toxoplasmosis, and HIV [17,18]. Vertical transition was not detected in invasive procedures performed after the application of highly active antiretroviral therapy (HAART) in pregnant women who had HIV [19,20]. There are no strong data on the vertical transition of SARS-CoV2 from mother to fetus [5]. Studies reported so far have shown that newborns born from mothers infected with COVID-19 do not have a vertical transition [21,22]. This is supported by evidence showing that there is no virus load in the amniotic fluid and cord blood [23–25]. But symptomatic cases in the neonatal period have also been described. In one case, SARS-CoV-2 was positive in the nasopharyngeal swab of the newborn, suggesting that the fetus may have been exposed to the virus in the inutero period [26]. When looking at the data in the literature, the scope and clinical importance of the vertical transition remain uncertain. In a 2020 review published by Deprest et al., it was stated that performing an invasive procedure in a SARS-CoV2 positive woman in terms of fetal intervention would potentially increase the risk of vertical transmission, as was observed in HIV-positive women before the administration of antiviral treatments, and therefore emphasized that the transition should be avoided, especially due to the risk of intra-amniotic bleeding and feto-maternal barrier deterioration [27]. However, if the infection is positive during pregnancy, the intervention should be postponed until the disease becomes asymptomatic. In light of these recommendations, the conclusion from this review is that vertical transmission concerns do not prevent clinically minimally invasive procedures such as A/S or fetoscopy [27].

In line with all this information, the increased risk of the fetus for a chromosomal or genetic disease, the risk of complications of the proposed invasive procedure itself and the psychological effects of the pandemic process on pregnancy make the situation difficult for pregnant women. In our study, compared to the control group, we found that the rate of pregnant women undergoing screening tests decreased significantly during the pandemic period. We also found a decrease in the number of invasive diagnostic procedures such as CVS and A/S in the study group. We have seen that the number of cordocentesis performed during this period increased. We think that the reason for the increase in the performance of cordocentesis is related to the detection of abnormal fetal findings in the later period as a result of unperformed or delayed screening tests or ultrasound examinations due to the pandemic. The rates of procedures performed during the first patient visit were significantly higher for the study compared to the control group. We think that this is due to patients avoiding repeated applications to the hospital in order to minimize the risk of infection during the pandemic. At the same time, the rates of procedures performed during the first visit of patients who were referred from outside the city were higher than those patients who were residing in the same city as our clinic. We think that transportation restrictions and increased risk of transmission of the infection are involved in the decision-making process of patients applying from outside of the city during the pandemic process.

The strength of this study evaluates the effect of COVID-19 pandemic on prenatal diagnostic procedures. There is very limited information in this field in the literature. The fact that it is retrospective and the number of cases is limited are the limitations of the research. However, this study may be considered a pilot study of prospective studies to be conducted with a more extensive patient population in the future.

As a result, there is a notable decrease in the number of prenatal diagnosis and screening tests during the COVID-19 pandemic. However, thorough prenatal

care services hold grave importance for both maternal and fetal health. Current literature data on prenatal care and especially for the vertical transition will be very valuable during this period. It is important for pregnant women to receive the most accurate prenatal care and information about their fetuses in order to eliminate their growing concerns. We are curiously waiting for new data that will contribute to prenatal care in these difficult times.

### Disclosure statement

No potential conflict of interest was reported by the author(s).

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