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Has the COVID-19 delayed the diagnosis of fetal anomalies and reduced in the follow-up of high-risk pregnancies?

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Abstract

Objective: COVID-19 has deeply affected our lives in terms of social, economic, education, and health issues. Pregnant women have had concerns about routine antenatal care visits and decreased follow-up numbers due to concern of COVID-19 transmission. We aimed to evaluate whether there is a delay in the diagnosis of fetal anomaly during the COVID-19 pandemic period and whether patients diagnosed with fetal anomaly attend antenatal care regularly or not, and to investigate the factors that prevent them from regular follow-up.

Methods: Pregnant women diagnosed with fetal anomaly during pandemic period (March 1, 2020 to September 1, 2020) and diagnosed with fetal anomaly before pandemic period (September 1, 2019 to February 28, 2020) were compared with a questionnaire in terms of antenatal follow-up frequency and gestational age of fetal anomaly diagnosis.

Results: In the during pandemic period group, regular pregnancy follow-up was decreased from 87% to 51% because of maternal anxiety, fear of virus transmission in hospital and the anxiety of passing it on to baby. Attending a detailed ultrasound scan for detecting fetal anomaly at 18–22 weeks was significantly lower in the during pandemic group. In the pandemic period, the most commonly diagnosed fetal anomalies were central and peripheral nervous system, and cardiovascular and gastrointestinal system anomalies similar to the before pandemic period group. The mean frequency of follow-ups in the third trimester in the before pandemic period group and during pandemic period group was 6.02 (±2.36) times and 4.02 (±1.97) times, respectively, and it was a considerable and statistically significant decrease. In addition, the mean week of fetal anomaly diagnosis was 23±6 weeks in during pandemic group, while it was 22±5 weeks in before pandemic group, and there was no statistically significant difference.

Conclusion: Antenatal follow-up of the patients has been decreased significantly during the pandemic period, although it does not seem to cause delay in the diagnosis of fetal anomaly. In experienced perinatal centers, if the concerns of patients are relieved and they are examined under suitable conditions for the pandemic, there will be no delay in diagnosis of fetal anomalies.

Keywords: Fetal anomaly, antenatal care, COVID-19, prenatal screening.

Introduction

COVID-19 was declared as a pandemic by the World Health Organization and since that time, it has deeply affected our lives in social, economic, health, and education issues.[1] The public was instructed to stay at home and reduce hospital admissions for non-emergency situations by authorities. In Turkey, lockdowns were imposed, the number of outpatient clinic visits and examination hours was reduced, the number of attendants for inpatients was limited, and elective surgeries were postponed.

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Pregnant women had to consider both their own health and the health of the fetus during the pandemic, and the uncertainty about how the disease would affect the course of pregnancy also created a source of stress and anxiety.[2,3] Therefore, they have had concerns about routine antenatal care visits and decreased follow-up numbers due to concern of COVID-19 transmission.[4] This situation can be at least as harmful as the COVID-19 disease itself.

During the pandemic, many obstetric associations have suggested and limited antenatal care visits with first trimester scan at 11–13th weeks, detailed ultrasound screening at 20–22nd weeks, laboratory tests and vaccines at 28th week, group B streptococcus and HIV screening at 36th week and other visits via telehealth systems.[5,6] In our country, it has reduced the number of antenatal care by following these recommendations. However, it was not possible to limit the number of follow-ups of pregnant women who were followed up by high-risk pregnancy units. Delayed diagnosis and interventions at pregnancies with fetal chromosomal or structural anomalies can lead to negative consequences on both mother and fetus health.[7]

There are a limited number of studies on obstetric follow-up and fetal anomaly diagnosis and treatment in the literature.[8–10] In none of these studies, the week of fetal anomaly diagnosis, and factors affecting the frequency of antenatal follow-ups of pregnancies with fetal anomalies in the pandemic period were mentioned. We aimed to evaluate whether there is a delay in the diagnosis of a fetal anomaly during the COVID-19 pandemic period, and whether patients diagnosed with fetal anomaly attend antenatal care regularly or not, and to investigate the factors that prevent them from regular follow-up.

Methods

In this questionnaire-based study, 100 pregnant women diagnosed with fetal anomaly during the pandemic period (DPP) (March 1, 2020 to September 1, 2020) and 100 pregnant women diagnosed with fetal anomaly before the pandemic period (BPP) (September 1, 2019 to February 28, 2020) were included. The study was approved by Turkish Ministry of Health (T18_44_28) and Ankara City Hospital's Ethics Committee (E1-20-1145). The questionnaires were applied to the first group diagnosed with a fetal anomaly during the pandemic period at the high-risk pregnancy outpatient clinic. The second group diagnosed with fetal anomaly before the pandemic period was asked questions by phone.

Our questionnaire consisted of 3 parts. In the first part of the questionnaire, questions were asked to the patients in order to determine their demographic characteristics, in the second part their clinical characteristics, and in the third part their compliance with pregnancy follow-up.

Statistical analyses were performed by Statistical Package for the Social Sciences version 25.0 (IBM Corp., Armonk, NY, USA). Visual (histograms, probability plots) and analytical methods (Shapiro-Wilk test) were used in order to determine normality of distribution. Since our data were not in normal distribution, we presented medians and interquartile range values for descriptive analysis. We used Mann-Whitney U test to compare two groups for non-normally distributed parameters. Pearson's chi-square test was performed to compare categorical variables among the groups. Additionally, Fisher's exact test was used for nominal variables between groups when necessary. We used percentages to express categorical variables. Correlation analysis was performed by Pearson's test. A p-value <0.05 was regarded statistically significant. The sample size was calculated by G-Power; for an alpha of 0.05 with 90% power gave an effect size of 0.3, requiring a minimum of 91 subjects per group.

Results

Descriptive characteristics of the patients were given in **Table 1**. Descriptive characteristics were not significantly different between the two groups. There was no difference between before and during the pandemic periods in terms of folic acid, vitamin D, multivitamin and antianemic intake as recommended by the government's health system (**Table 2**).

In the DPP group, regular pregnancy follow-up was 87% before pandemic which was decreased to 51% during the pandemic period. In DPP group, 43 of 49 patients who did not come to follow-up regularly stated COVID-19 as the reason for not coming to follow-up, and the remaining 6 patients stated the reasons as difficulty in transportation to the hospital, familial problems, and lack of knowledge about the follow-up (**Table 2**).

Table 1. Comparison of descriptive characteristics of pregnant women diagnosed with fetal anomaly during pandemic period (Group 1) and pregnant women diagnosed with fetal anomaly before pandemic period (Group 2).

Variables	Group 1 (Pandemic period) (n=100)	Group 2 (Before pandemic period) (n=100)	p-value
Maternal age, years (median, IQR)	27 (9)	28 (9)	0.55
Gravida, n (median, IQR)	2 (2)	2 (2)	0.08
Parity, n (median, IQR)	1 (1)	1 (1)	0.08
Gestational age at fetal anomaly diagnosis, weeks (median, IQR)	22 (8)	22 (4)	0.63
Maternal education status, n (%)			
Primary school	37 (37%)	46 (46%)	0.130
High school	48 (48%)	34 (34%)	
University graduates	15 (15%)	20 (20%)	
Maternal occupational status, n (%)			
Employed	84 (84%)	82 (82%)	0.48
Unemployed	16 (16%)	18 (18%)	
Maternal socioeconomic status, n (%)			
Low	37 (37%)	44 (44%)	0.59
Moderate	40 (40%)	35 (35%)	
High	23 (23%)	21 (21%)	
Spouse education status, n (%)			
Primary school	42 (42%)	40 (40%)	0.79
High school	38 (38%)	36 (36%)	
University graduates	20 (20%)	24 (24%)	
Spouse occupational status, n (%)			
Employed	93 (93%)	87 (87%)	0.84
Unemployed	7 (7%)	13 (13%)	
Spouse socioeconomic status, n (%)			
Low	37 (37%)	44 (44%)	0.59
Moderate	40 (40%)	35 (35%)	
High	23 (23%)	21 (21%)	
History of disabled child, n (%)	4 (4%)	12 (12%)	0.06
If there was any disabled child, whether it was diagnosed during pregnancy, n (%)			
Yes	3 (75%)	9 (75%)	1.00
No	1 (25%)	3 (25%)	
Consanguineous marriage, n (%)	15 (15%)	18 (18%)	0.56
Smoking, n (%)	10 (10%)	6 (6%)	0.29
Maternal comorbid disease, n (%)	18 (18%)	26 (26%)	0.17
Drug use due to maternal disease, n (%)	15 (15%)	20 (20%)	0.35

IQR: interquartile range. p<0.05 was considered statistically significant.

When the two groups were compared, attending first trimester scan, second trimester scan and oral glucose tolerance test was not significantly different (p>0.05). However, attending a detailed ultrasound scan for detecting fetal anomaly at 18–22 weeks of gestation was significantly lower in the pandemic group (p=0.01) (**Table 3**). Comparing the two groups, the mean frequency of follow-ups in the third trimester in the BPP and DPP were 6.02 (±2.36) times and 4.02 (±1.97) times, respectively, and a considerable and statistically significant decrease was found in the frequency of follow-up in the DPP (p<0.001).

Table 2. Comparison of clinical characteristics of pregnant women diagnosed with fetal anomaly during pandemic period (Group 1) and pregnant women diagnosed with fetal anomaly before pandemic period (Group 2).

Variables	Group 1 (Pandemic period) (n=100)	Group 2 (Before pandemic period) (n=100)	p-value
Folic acid use, n (%)	72 (72%)	75 (75%)	0.63
Vitamin D intake, n (%)	52 (52%)	54 (54%)	0.77
Multivitamin supplementation, n (%)	64 (64%)	63 (63%)	0.88
Anti-anemic intake, n (%)	60 (60%)	64 (64%)	0.56
Regular pregnancy follow-up in previous pregnancies, n (%)	54 (54%)	63 (63%)	0.86
Pregnancy follow-up regularly before pandemic, n (%)	87 (87%)	90 (90%)	0.50
Pregnancy follow-up regularly during pandemic, n (%)	51 (51%)	-	
Reasons for not regularly attending follow-up during pandemic, n (%)	49 (49%)		
COVID-19	43 (43%)	-	
Other reasons	6 (6%)		
Healthcare institution, n (%)			
State hospital	70 (70%)	77 (77%)	
Private hospital	12 (12%)	12 (12%)	0.31
University hospital	18 (18%)	11 (11%)	

Statistical analysis was performed by chi-square test. p<0.05 was considered statistically significant.

Table 3. Comparison of compliance for antenatal follow-up of pregnant women diagnosed with fetal anomaly during pandemic period (Group 1) and pregnant women diagnosed with fetal anomaly before pandemic period (Group 2).

Variables	Group 1 (Pandemic period) (n=100)	Group 2 (Before pandemic period) (n=100)	p-value
First trimester scan, n (%)			
Attended	65 (65%)	74 (74%)	0.16
Reasons for not attending first trimester scan, n (%)	35 (35%)	26 (26%)	
COVID-19	19 (54%)	0	**0.002**
Patient's own decision	16 (46%)	26 (100%)	
Second trimester scan, n (%)			
Attended	51 (51%)	60 (60%)	0.20
Reasons for not attending second trimester scan, n (%)	49 (49%)	40 (40%)	
COVID-19	24 (48%)	0	**0.001**
Patient's own decision	14 (29%)	25 (62%)	
Presence of other screening test	11 (22%)	15 (38%)	
Detailed ultrasound scan at 18–22 weeks, n (%)			
Attended	80 (80%)	92 (92%)	**0.01**
Reasons for not attending detailed ultrasound scan, n (%)	20 (20%)	8 (8%)	
COVID-19	15 (75%)	0	**0.02**
Patient's own decision	5 (25%)	8 (100%)	
Invasive diagnostic procedures (chorionic villus sampling / amniocentesis /cordocentesis)	16 (16%)	17 (17%)	0.092
Oral glucose tolerance test, n (%)			
Attended	42 (42%)	42 (42%)	1.00
Reasons for not attending oral glucose tolerance test, n (%)	58 (58%)	58 (58%)	
COVID-19	17 (29%)	0	**0.001**
Patient's own decision	41 (71%)	58 (100%)	
Mean frequency of follow-ups in the third trimester	4.02 (±1.97)	6.02 (±2.36)	**<0.001**

Distribution of the fetal anomalies was shown in **Table 4**. In the pandemic period, the most commonly diagnosed fetal anomalies were central and peripheral nervous system, and cardiovascular and gastrointestinal system anomalies similar to the before pandemic period group. In the DPP and BPP groups, the mean

Table 4. Comparison of fetal anomalies between pregnant women diagnosed with fetal anomaly during pandemic period (Group 1) and pregnant women diagnosed with fetal anomaly before pandemic period (Group 2).

Fetal anomalies	Group 1 (Pandemic period) (n=100)	Group 2 (Before pandemic period) (n=100)
Central and peripheral nervous system anomalies	**37**	**39**
Holoprosencephaly	2	1
Anencephaly		2
Arachnoid cyst		1
Corpus callosum agenesis	1	4
Dandy-Walker malformation	2	1
Diastematomyelia		1
Rhombencephalosynapsis	1	
Encephalocele	5	1
Open spina bifida	10	11
Vermian agenesis	2	1
Microcephaly	1	2
Hydrocephaly	5	7
Mega cisterna magna	1	1
Intracranial cyst	2	1
Ventriculomegaly	2	5
Intracranial hemorrhage	3	
Congenital heart disease	**26**	**29**
Aortic coarctation	1	
Atrial septal defect	1	2
Ventricular septal defect (VSD)	5	3
Atrioventricular septal defect	2	1
Transposition of the great arteries (TGA)	2	2
TGA + pulmonary stenosis	1	1
TGA + VSD	1	2
Double outlet right ventricle	1	3
Aortic arch anomalies	2	1
Ebstein anomaly		1
Fallot tetralogy	3	3
Tricuspid atresia	1	
Tricuspid insufficiency		1
Hypoplastic right heart	1	3
Hypoplastic left heart	3	5
Situs inversus	2	
Arrhythmia		1

Fetal anomalies	Group 1 (Pandemic period) (n=100)	Group 2 (Before pandemic period) (n=100)
Anomalies of the gastrointestinal tract and abdominal wall	**15**	**11**
Diaphragmatic hernia	3	3
Duodenal atresia	2	1
Duplication cyst	2	1
Gastroschisis	1	1
Omphalocele	2	2
Esophageal atresia	1	
Ileal atresia	1	1
Jejunal atresia	1	
Intestinal obstruction	1	1
Megacolon		1
Meconium peritonitis	1	
Anomalies of the urinary tract and external genitalia	**10**	**9**
Multicystic dysplastic kidney	5	4
Duplex collecting system	1	1
Ovarian cyst	1	1
Hydroureteronephrosis	2	1
Polycystic kidney		1
Renal agenesis	1	1
Skeletal dysplasias	**5**	**3**
Achondrogenesis		1
Lower limb hypoplasia	1	
Hemivertebra	1	
Kyphoscoliosis	1	
Rhizomelia	1	
Skeletal dysplasia of unspecified type	1	2
Thoracic anomalies	**5**	**2**
Congenital pulmonary airway malformation	2	1
Hydrothorax	1	
Pulmonary sequestration	2	1
Chromosomal and nonchromosomal syndromes	**2**	**7**
47,XXX		1
DiGeorge syndrome		1
Trisomy 21	1	2
Trisomy 18	1	2
Trisomy 12		1

weeks of fetal anomaly diagnosis were 23±6 and 22±5, respectively, and there was no statistically significant difference between the two groups (p=0.636).

A weak positive correlation was found between spouse education status, folic acid intake and frequency of follow-up in the third trimester after pandemic (r=0.179 and p=0.01 for spouse education status, and r=0.147 and p=0.03 for folic acid intake). There was a weak negative correlation for gravida, and a strong positive correlation for fetal anomaly history in previous pregnancies was found with regular pregnancy follow-up after pandemic (r=-0.220 and p=0.02 for gravida, and r=1.000 and p<0.001 for fetal anomaly diagnosed in previous pregnancies).

Discussion

The present study revealed there was a decrease in pregnancy follow-up because of maternal anxiety, fear of virus transmission in hospital, and the anxiety of passing it on to the baby. Besides, this study demonstrated that the reduction in prenatal visits did not cause a delay in the diagnosis of fetal anomaly.

In the pre-pandemic period, the frequencies of regular antenatal follow-up of the two groups were found to be similar. While pregnant women in the DPP group regularly attended pregnancy follow-ups before the pandemic, the frequency of regular antenatal follow-ups was decreased in the post-pandemic period. This result strongly supported our concern that pregnant women have not received adequate antenatal care at the time of the pandemic. Peahl et al. found a 31.6% decrease in the antenatal visit frequency between the pre-pandemic period and the post-pandemic period similar to our result.[11] In a study, it was determined that the number of admissions to cardiology outpatient clinics for all reasons decreased during the pandemic period.[12] In a recent study about pediatric cancers, 3 children with hematologic cancer who were late in admission to the hospital because of COVID-19 and came in a life-threatening situation were presented.[13] Snapiri et al. presented seven children with delay on diagnosis of complicated appendicitis because of parental concern, telemedicine use and insufficient evaluation.[14] The decrease in the number of hospital admissions and delayed diagnosis seems to have affected not only pregnant women but also other patient groups due to pandemic.

The mean week of fetal anomaly diagnosis was 23 weeks in the post-pandemic group, while it was 22 weeks in the before pandemic group, and there was no statistically significant difference contrary to assumption. Our hospital is a tertiary center with a high capacity that receives referrals from all over the region. We did not reduce the number of outpatient clinics or patients even during the peak of the pandemic. In our opinion, there was no delay in the diagnosis of fetal anomalies for these reasons.

There was no difference between before and during the pandemic periods in the use of folic acid, vitamin D, multivitamin and antianemic. The reason for this was probably that the use of these drugs is supported within the government health policy and patients can get these drugs without prescriptions from health centers and family physicians without going to the hospital.

Although the rates of first trimester scan, second trimester scan and oral glucose tolerance test were similar in the pre- and post-pandemic groups, it was observed that the detailed ultrasonography rate decreased in a statistically significant way in the post-pandemic group. The reason for the decrease may be social distance is the least and time is the longest in the detailed ultrasonography among the antenatal screening test.

In our study, while the rate of the invasive procedures was 17% in the group diagnosed with fetal anomaly before the pandemic, the rate was 16% in those diagnosed during the pandemic period, and we did not observe any significant decrease. The reason for this may be that most of our patients are referred from other centers and our perinatology clinic is the highly experienced last step center. In addition, we informed the patients in detail that fetal diagnostic procedures are time-sensitive and delaying them may worsen outcome for pregnant woman and fetus. In a review conducted by Deprest et al., it was stated that the risk of spontaneous vertical transmission of the coronavirus in the invasive diagnostic procedures is minimal and unproven. They concluded that the risk of vertical transmission should not prevent minimally invasive procedures such as chorionic villus sampling or amniocentesis.[8]

In the DPP group, there was a significant decrease in antenatal follow-ups in the third trimester. After the diagnosis of fetal anomaly, most of the patients disrupted their follow-ups in the third trimester during the pandemic period. In addition to this, while there was no correlation with maternal educational status, a positive correlation was found between the education status of the spouse and the frequency of follow-up in the third trimester. In our society, due to the cultural factors, paternity factors are very important for issues of perinatal care.

A negative correlation was found between the patient's gravida and the frequency of follow-up during the pandemic period. As the patient's gravida decreases, her concerns about the baby may be weighed down to her concerns about the COVID-19. There was a positive correlation between follow-up during the pandemic period and fetal anomaly history in previous pregnancies. In many studies, anxiety and stress levels were found to be very high in mothers with disabled children.[15,16] In addition to maternal anxiety, patients who had a disabled child was diagnosed with fetal anomaly during antenatal follow-up in their previous pregnancy may have increased trust in the antenatal care and screening tests.

Conclusion

In conclusion, antenatal follow-up frequency of the patients has been decreased significantly during the pandemic period, although it does not seem to cause delay in the diagnosis of fetal anomaly. In experienced perinatal centers, if the concerns of the patients are relieved and they are examined under suitable conditions for the pandemic, there will be no delay in the diagnosis of fetal anomalies. Our study is valuable since there are very few studies in the literature about how prenatal follow-ups are being affected during the pandemic period and there is no study on the follow-up of pregnant women diagnosed with a fetal anomaly.

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