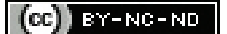Original Article

Impact of COVID-19 on the Risk of Development of Oligohydramnios in Pregnancy: A Retrospective Observational Study

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ABSTRACT

Introduction: The Coronavirus Disease-2019 pandemic is considered the most catastrophic disease of the last decades, with evolving knowledge and improved management over time. Pregnant women are known to be particularly vulnerable, and COVID-19 has been shown to damage the endothelium due to its proinflammatory nature.

Aim: To determine the occurrence of oligohydramnios in pregnant women who tested positive for COVID-19.

Materials and Methods: A retrospective observational study was conducted at the Department of Obstetrics and Gynaecology, Koru Health Groups, Ankara, Çankaya, Turkey from January 2023 to June 2023. The study included a total of 459 women who were followed during pregnancy and delivered in the same hospital between April 2020 and October 2022. The patients were divided into two groups: COVID-19 positive group (n=101) and negative group (n=358). Various parameters such as age, parity, gestational week at birth, Body Mass Index (BMI), 1^s and 5th-minute Appearance, Pulse, Grimace, Activity and Respiration (APGAR) scores, weight of the newborn, Amniotic Fluid Index (AFI), and the risk of developing oligohydramnios

were assessed between the positive and negative groups. Parametric variables were analysed using independent t-tests and non parametric ones using Mann-Whitney U tests. Chi-square test was used to compare categorical variables. A p-value of <0.05 was considered statistically significant.

Results: The mean age of the pregnant women was 29.2±4.4 years, ranging from 20 to 43 years. Oligohydramnios was detected in 95 women, with 64 of them testing positive for COVID-19. There were no statistically significant differences in terms of age, parity, gestational week of birth, weight at birth, and 1st and 5th-minute APGAR scores between the two groups. However, BMI was significantly higher in COVID-19 positive patients compared to negative ones (p=0.003). Oligohydramnios was found to be significantly higher in COVID-19-positive pregnant women (n=64) compared to negative ones (n=31) (p<0.0001).

Conclusion: The COVID-19 pandemic has caused an unprecedented level of global health problems. The virus's prothrombotic tendency leads to placental insufficiency, predisposing to oligohydramnios and intrauterine growth retardation.

Keywords: Coronavirus disease-2019, Pandemic, Placenta, Prothrombotic, Relative risk

INTRODUCTION

The COVID-19 pandemic has caused a distressing worldwide health problems. Three waves were witnessed in most countries [1]. Turkey reported its first case in March 2020 [2]. The authors knowledge about the disease has changed over time with the progression of the pandemic. Its clinical presentations, complications, and management have been affected by the severity of the disease and risk to the population. Obese, elderly people, some ethnic groups, and pregnant women have been defined as high-risk population groups [3]. Several studies have shown that COVID-19 infection in pregnant women was associated with impaired liver and renal functions [4,5], leading to higher rates of Intensive Care Unit (ICU) admission and mortality [6]. COVID-19 was shown to cause severe oligohydramnios and preterm births [3,7]; therefore, higher rates of caesarean section were reported [8,9]. Besides, vertical transmission of this virus was shown in some cases in the third trimester [10].

Unfavourable vascular effects of Severe Acite Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection that damage the endothelium were shown to be the results of exaggerated systemic inflammatory responses [11]. Dysregulation of placental Angiotensin-converting Enzyme 2 (ACE2) by SARS-CoV-2, which is highly expressed at the maternal-foetal interface, might be the possible reason for oligohydramnios and preeclampsia in pregnant women [12]. During pregnancy, ACE2 plays a crucial role in the regulation of arterial pressure and expresses itself in huge amounts in

placental tissue, including syncytiotrophoblast, cytotrophoblast, endothelium, and vascular smooth muscle of the villi [11]. COVID-19 infection in pregnancy can alter ACE2 expression by disrupting the renin-angiotensin system, thus resulting in vasoconstriction, oligohydramnios, and preeclampsia [11]. Knowledge of COVID-19 infection in pregnancy and newborns is crucial in defining research priorities and future public policies. With this background, the present study was conducted with the aim of evaluating the relationship between COVID-19 and oligohydramnios in pregnancy.

MATERIALS AND METHODS

A retrospective observational study was conducted at the Department of Obstetrics and Gynaecology, Koru Health Groups, Ankara, Çankaya, Turkey from January 2023 to June 2023. The study protocol was approved by the Ethics Committee of Yüksek htisas University with the decision number 2022-14-03. Informed consent was obtained from every participant.

Inclusion and Exclusion criteria: A total of 459 women who were followed during pregnancy and delivered in the same hospital between April 2020 and October 2022 were included in the present. Patients with chronic diseases, especially hypertensive disorders and diabetes, were excluded from the study.

Study Procedure

The patients were divided into two groups: COVID-19 positive group (n=101) and negative group (n=358). The severity of COVID-19 was

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categorised as per the clinical management protocol for COVID-19 in adults [13]. Patients with uncomplicated upper respiratory tract infection, which manifested with mild symptoms such as fever, cough, and sore throat, were defined as the mild group. In the present study, 87 of the COVID-19 positive pregnant women were classified in the mild group. Patients with pneumonia and no signs of severe disease were categorised as the moderate group, while those with severe pneumonia were placed in the severe group. Among COVID-19 positive pregnant women, eight had moderate disease, and six had severe disease. The infection was diagnosed using Reverse Transcription-polymerase Chain Reaction (RT-PCR) or Rapid Antigen Test (RAT). Nasopharyngeal swabs were obtained from all neonates within 24 hours of delivery and tested for COVID-19 infection using the RT-PCR test.

Retrospective data collection was performed using the medical records of these pregnant women. Age, parity, gestational week at birth, BMI, first and fifth-minute APGAR scores, newborn weight, AFI, and risk of developing oligohydramnios were compared between the COVID-19 positive and negative groups. Oligohydramnios was defined as amniotic fluid volume <5% for gestational age. It was diagnosed when the AFI was <5 cm or the maximal deepest pocket was <2 cm in ultrasound [14].

STATISTICAL ANALYSIS

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 22.0 (SPSS Inc. Chicago, IL). The Kolmogorov-Smirnov test was conducted to assess normal distribution. The homogeneity of variance was determined by the Levene test. Parametric variables were analysed using the independent t-test, and non parametric variables were analysed using the Mann-Whitney U test. The Chi-square test was used to compare categorical variables. The level of statistical significance for descriptive statistics was set at $p < 0.05$.

RESULTS

The mean age of pregnant women was 29.2±4.4 years, ranging from 20 to 43 years. The mean gestational period at birth was 38.1±9.8 (weeks+days), with a range of 216 days to 291 days [Table/Fig-1]. The rate of preterm delivery was 14 (13.8%) among COVID-19 positive patients and 44 (12.3%) among negative cases. Two babies tested positive within 24 hours of delivery.

In the present study, 369 (80.4%) of women had a caesarean section, while 90 (19.6%) had a vaginal delivery. Failed induction was the most common indication for the caesarean section (n=191), followed by a previous caesarean operation (n=128), foetal distress (n=24), unwilling labour trial (n=19), and malpresentation (n=7).

Parameters	Total	COVID-19 (+)	COVID-19 (-)	p-value
N	459	101 (22%)	358 (78%)	
Age (years)	Mean: 29.2	Mean: 29	Mean: 29.2	0.671^t
	Median: 29	Median: 28	Median: 29	
	SD±:4.4	SD±: 4.6	SD±: 4.3	
	Range: 20-43	Range: 21-41	Range: 20-43	
Parity	Mean: 1.4	Mean: 1.3	Mean: 1.4	0.144^m
	Median: 1	Median: 1	Median: 1	
	SD±: 0.6	S.D.±: 0.5	S.D.±: 0.6	
	Range: 1-5	Range: 1-3	Range: 1-5	
Gestational week at birth (week+day)	Mean: 38+1	Mean: 38+1	Mean: 38+2	0.584^t
	Median: 38+3	Median: 38+3	Median: 38+4	
	SD±: 9.8*	SD±: 10.1*	SD±: 9.7*	
	Range: 216-291*	Range: 216-281*	Range: 225-291*	
Body Mass Index (BMI)	Mean: 25.5	Mean: 26.1	Mean: 25.3	0.003^t
	Median: 25	Median: 26	Median: 25	
	SD±: 2.4	SD±: 2.5	SD±: 2.4	
	Range: 20-33	Range: 22-33	Range: 20-33	
APGAR 1st minute	Mean: 8.7	Mean: 8.7	Mean: 8.7	0.896^t
	Median: 9	Median: 9	Median: 9	
	SD±: 0.7	SD±: 0.6	SD±: 0.7	
	Range: 5-10	Range: 7-10	Range: 5-9	
APGAR 5th minute	Mean: 9.7	Mean: 9.7	Mean: 9.7	0.714^t
	Median: 10	Median: 10	Median: 10	
	SD±: 0.6	SD±: 0.5	SD±: 0.6	
	Range: 6-10	Range: 8-10	Range: 6-10	
Weight of newborn (gr)	Mean: 3177.5	Mean: 3109.2	Mean: 3196.8	0.094^t
	Median: 3220	Median: 3200	Median: 3230	
	SD±: 464	SD±: 504.2	SD±: 450.8	
	Range: 1300-4480	Range: 1300-4270	Range: 1350-4480	
Amniotic Fluid Index (AFI) (cm)	Mean: 6.3	Mean: 4.5	Mean: 6.8	0.001^t
	Median: 6	Median: 4	Median: 7	
	SD±: 2.3	SD±: 2.1	SD±: 2.1	
	Range: 1-16	Range: 1-13	Range: 2-16	
Oligohydramnios	95 (20.7%)	64 (63.4%)	31 (8.6%)	0.001^c

[Table/Fig-1]: Comparison of demographic and clinical datas of COVID-19 positive and negative patients.
*Number of days t t-test^m Mann-Whitney U test^c Chi-square test

The BMI was significantly higher in COVID-19 positive patients compared to the negative ones (p=0.003). The AFI was significantly lower in COVID-19-positive pregnancies compared to negative pregnancies (p<0.0001). Oligohydramnios was significantly higher in COVID-19 positive pregnant women compared to negative ones (p<0.0001) [Table/Fig-1]. The Relative Risk (RR) was found to be 7.32, indicating that the likelihood of developing oligohydramnios was 7.32 times higher in COVID-19-positive pregnant women than in the negative group. Among patients in the COVID-19 positive group, the gestational weeks of the patients in the oligohydramnios positive subgroup were significantly lower compared to the patients in the oligohydramnios negative subgroup (p=0.006) [Table/Fig-2]. In the COVID-19 negative group, the birth weights of the babies in the subgroup of oligohydramnios positive were significantly lower than the babies in the oligohydramnios negative subgroup (p=0.002) [Table/Fig-2].

a total of 447 deaths in their study, and most of the cases (60.3%) were detected in the third trimester of pregnancy. Organ dysfunction was reported in 90.4% of women during admission, and preterm delivery occurred before oligohydramnios developed. Therefore, the incidence of it remained low in their study. Soto-Torres E et al., also claimed that there were no significant differences in the volume of amniotic fluid between COVID-19-positive and negative pregnant women [20]. This is likely to be related to the small number of COVID-19-positive pregnant women (n=106) and negative pregnant women (n=103) in their study population; hence, the difference in the number of women that developed oligohydramnios did not reach a statistical significance. Singh V et al., found that preterm delivery, low birth weight, and neonatal admissions were higher in the COVID-19-positive group; however, the incidence of neonatal and intrauterine death was low [21]. No neonatal deaths due to COVID-19 infection were seen in the present study.

	COVID-19 positive (n=101)			COVID-19 negative (n=358)		
	Oligohydramnios (+)	Oligohydramnios (-)	p-value	Oligohydramnios (+)	Oligohydramnios (-)	p-value
Age (mean) (Years)	29.2	28.8	0.351[t]	29.55	29.22	0.342[t]
Parity (mean)	1.26	1.46	0.128[m]	1.39	1.43	0.357[m]
Gestational week at birth (mean)	37+6	38+4	0.006[t]	37+6	38.+2	0.069[t]
Body Mass Index (mean)	26.03	26.27	0.320[t]	25.48	25.29	0.332[t]
1st minute APGAR (mean)	8.67	8.7	0.404[t]	8.68	8.69	0.446[t]
5th minute APGAR (mean)	9.69	9.76	0.266[t]	9.7	9.7	0.482[t]
Weight of newborn (gr) (mean)	3029	3247	0.017[t]	2981	3217	0.002[t]

[Table/Fig-2]: Comparison of demographic and clinical data of patients with and without oligohydramnios.
[t]T-test
[m]Mann-Whitney U test

DISCUSSION

The COVID-19 pandemic has caused an unprecedented level of health problems globally. It has been shown that SARS-CoV-2 infection creates a proinflammatory state that leads to systemic endothelial dysfunction and preeclampsia [11,12]. We hypothesise that the prothrombotic tendency of the virus causes placental insufficiency, which predisposes to oligohydramnios and intrauterine growth retardation. Oligohydramnios can also be associated with an excessive host inflammatory response to COVID-19 and poor foetal vascular perfusion of the placenta [15]. The association between oligohydramnios and COVID-19 is not yet clear enough; however, clinicians should pay attention to foetal well-being when oligohydramnios is detected in pregnant women with COVID-19.

Aliji N and Aliu F, in their case report, reported a sudden severe decrease in amniotic fluid in a pregnant woman one week after the symptoms of COVID-19 infection. They reported that the pregnant woman was at 34 weeks gestation and an urgent caesarean section was performed. Therefore, they claimed that COVID-19 infection was the reason for the development of oligohydramnios in their case and they suggested more frequent follow-up [7].

Kasuga Y et al., reported a patient who developed temporary anhydramnios at 25 weeks gestation. They reported that she had conceived by in-vitro fertilisation and embryo transfer and was infected with COVID-19 at 23 weeks gestation. Although they reported that the amniotic fluid had increased spontaneously, they pointed out that clinicians should pay attention to oligohydramnios in pregnant women with COVID-19 [16].

Khoiwal K et al., revealed that oligohydramnios was significantly more frequent in COVID-19 positive pregnant women than COVID-19 negative ones (p=0.048). Furthermore, preterm birth and caesarean rates were found to be higher in the COVID-19 positive group in their study [17]. In another study, oligohydramnios was found in 31.3% of pregnant women with COVID-19 [18].

Maza-Arnedo F et al., reported the incidence of oligohydramnios as 3%, which was much lower than our results [19]. They identified

Several studies have reported a high rate of caesarean sections during the pandemic [8,9,22] due to various factors, especially the demand for caesarean section in isolated areas. In the present study, the patients mostly had a caesarean section for obstetric indications. Singh V et al., revealed that severe oligohydramnios was significantly more common in COVID-19 positive patients [1]. In their study, they revealed that oligohydramnios was one of the reasons for the caesarean section. They reported that four women in the first wave and seven women in the second wave of the pandemic had severe oligohydramnios [1].

Many other reviews have revealed high rates of preterm deliveries among pregnant women with COVID-19 [10,23,24], but in the present study, the rate of preterm delivery among COVID-19-positive patients was found to be almost the same as among negative ones. It was proven that vertical transmission of SARS-CoV-2 is possible [10]. Hosier H et al., showed that this virus affected the syncytiotrophoblast cells at the maternal-foetal interface of the placenta [25]. In the present, two asymptomatic babies were found to be positive for COVID-19 and were discharged with their mothers.

Limitation(s)

The present study data was provided from a single centre, which is a limitation of the present study. The risks of the development of oligohydramnios as per the severity of the COVID-19 infection were not separately calculated. Furthermore, long-term follow-up is required to show the delayed effects of the disease.

CONCLUSION(S)

The COVID-19 infection causes oligohydramnios. This information about COVID-19 infection in pregnancy helps in modifying the management protocols for better outcomes. In our study, it was also emphasised that the gestational week at birth significantly decreased in the oligohydramnios positive subgroup of COVID-19-positive pregnant women. Since the course of this infection is difficult to predict, larger studies are needed to understand the effects of the disease on both maternal and foetal morbidity.

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