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The rate of SARS-CoV-2 positivity in asymptomatic pregnant women admitted to hospital for delivery: Experience of a pandemic center in Turkey

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ABSTRACT

Objective: To investigate the rate of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positivity in asymptomatic pregnant women admitted to hospital for delivery in a Turkish pandemic center.

Study Design: This prospective cohort study was conducted in Ankara City Hospital between April, 15, 2020 and June, 5, 2020. A total of 206 asymptomatic pregnant women (103 low-risk pregnant women without any defined risk factor and 103 high-risk pregnant women) were screened for SARS-CoV-2 positivity upon admission to hospital for delivery. Detection of SARS-CoV2 in nasopharyngeal and oropharyngeal samples was performed by Real Time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) method targeting RdRp (RNA dependent RNA polymerase) gene. Two groups were compared in terms of demographic features, clinical characteristics and SARS-CoV-2 positivity.

Results: Three of the 206 pregnant women participating in the study had positive RT-PCR tests (1.4 %) and all positive cases were in the high-risk pregnancy group. Although, one case in the high-risk pregnancy group had developed symptoms highly suspicious for COVID-19, two repeated RT-PCR tests were negative. SARS-CoV-2 RT-PCR positivity rate was significantly higher in the high-risk pregnancy group (2.9 % vs 0%, p = 0.04).

Conclusion: Healthcare professionals should be cautious in the labor and delivery of high-risk pregnant women during the pandemic period and universal testing for COVID-19 may be considered in selected populations.

Introduction

Coronavirus disease 2019 (COVID-19) has radically influenced the world in a short period of time. Beyond the mortality and morbidity it caused, it left deep marks on social life and lifestyle [1]. As no efficent treatment nor vaccine is available at present, the most important management option is the prevention of disease transmission. For this reason governments have taken precautions like lockdown, social distancing, compulsory use of personal protective equipments and comprehensive regulations in healthcare policies [2]. Moreover, health authorities all over the world have prepared guidelines and management protocols to control the disease [3]. On the other hand, no consensus has been reached on the optimal COVID-19 screening policy, procedure specific precautions for healthcare workers and treatment modalities for infected patients.

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Obstetricians and midwifes are especially at high risk for COVID-19 transmission due to the nature of their specialities. Management of delivery necessitates close contact with pregnant women and exposure to various potential infectious particles. For this reason, delivery of COVID-19 positive patients should be performed in special isolated negative pressure rooms by appropriately equipped healthcare professionals [3–6]. Furthermore, infected patients may be asymptomatic on admission to the hospital and they may easily transmit disease during delivery [4,4,5,6]. Up to 13.5 % of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positivity rate was reported in asymtomatic pregnant women [7,8]. For this reason, obstetricians should be extremely cautious during the pandemic period.

Turkish Ministry of Health has pursued an effective and rational policy since the beginning of the pandemic. The pandemic process was successfully managed in line with the recommendations of the established scientific committee and the spread of the disease was brought under control in a short period of time [9]. However, no information is available on the rate of SARS-CoV-2 positivity for asymptomatic pregnant women in Turkey. Furthermore, to the best of our knowledge, none of the studies in the current literature has investigated the positivity rate in asymptomatic high-risk pregnancies. Thus, we believe studies on this issue are valuable to establish more comprehensive management protocols for pregnant women in our country. Additionally, the results of these studies will make a significant contribution to the current literature.

The aim of this study is to investigate the rate of SARS-CoV-2 positivity in asymptomatic pregnant women admitted to hospital for delivery in a Turkish pandemic center.

Materials and methods

This prospective cohort study was conducted in Ankara City Hospital between April, 15, 2020 and June, 5, 2020. A total of 206 asymptomatic pregnant women (103 low-risk pregnant women without any defined risk factor and 103 high-risk pregnant women) were screened for SARS-CoV-2 positivity upon admission to hospital for delivery. Informed consent was obtained from all participants and study protocol was approved by institutional ethics committee (E1−20-586).

Detection of SARS-CoV2 in nasopharyngeal and oropharyngeal samples was performed by Real Time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) method targeting RdRp (RNA dependent RNA polymerase) gene. Sterile Dacron or rayon swabs with flexible plastic shafts were used to collect nasopharyngeal samples from patients. After collection, swabs were placed into 2 mL of sterile Viral Transport Medium (VTM; various manufacturers). Samples were transported to Molecular Virology Laboratory within 12 h after collection and tested immediately after admission. RNA extraction from nasopharyngeal samples was performed by using Biospeedy Viral Nucleic Acid Isolation Kit (Bioeksen, Istanbul, Turkey) according to the manufacturer's instructions; swab samples in VTM were vortexed for 15 s and then 100 μL sample was transferred to a 1,5 mL microcentrifuge tube containing 100 μL viral nucleic acid extraction buffer supplied by the manufacturer. After vortexing once again, the tube was ready for PCR reaction. Real-time reverse-transcription PCR was performed by using Bio-Speedy COVID-19 RT-qPCR Detection Kit (Bioeksen, Istanbul, Turkey). A 20 μL reaction contained 5 μL of RNA, 5 μL of Oligo Mix (RdRp gene for SARS-CoV-2 detection, Rnase P gene for internal control), 10 μL of 2 × Primer Script Mix containing Taq Polymerase, each deoxyribo triphosphates (dNTP), reverse transcriptase and ribonuclease inhibitor. Thermal cycling was performed at 45 °C for 10 min for reverse transcription, followed by 95 °C for 3 min and then 45 cycles of 95 °C for 5 s, 55 °C for 35 s. in Rotor-Gene Q device (Qiagen, Hilden, Germany). Cycle threshold (Ct) values of less than 40 were defined as positive.

Maternal age, gravidity, parity, number of previous miscarriages, body mass index (BMI) (kg/m2), gestational age at birth, birth weight, 1st-5th minute Apgar scores, route of delivery (spontaneous vaginal deliver yor cesarean section) and SARS-CoV-2 positivity rates were compared between the healthy and high-risk pregnant women. Thereafter, clinical characteristics of patients with SARS-CoV-2 were evaluated in detail.

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS.22, IBM SPSS Statistics for Windows, Version 22.0 Armonk, NY: IBM Corp.). Visual (histograms, probability plots) and analytical methods (Kolmogrov-Smirnov test) were used in order to determine normality of distribution. As the data were not normally distributed, medians and interquartile range values were used for descriptive analysis. Additionally, the Mann-Whitney *U* test was conducted to compare the median values and the chi-square test was used to compare categorical variables among the groups. A two-tailed P value < 0.05 was regarded as statistically significant.

Results

Ankara City Hospital is a new tertiary reference center in the capital of Turkey which was established in June 2019. Its Department of Obstetrics and Gynecology is one of the main maternity centers in our country with approximately 1100 deliveries per month. Moreover, it has been serving as one of the main national pandemic centers since the beginning of COVID-19 outbreak. Since March, 27, 2020, a total of 25,817 SARS-CoV-2 RT PCR tests had been performed and 3042 (11.7 %) were found to be positive.

Three of the 206 pregnant women participating in the study had positive RT-PCR tests (1.4 %) and all positive cases were in the high-risk pregnancy group. Although, one case in the high-risk pregnancy group had developed symptoms highly suspicious for COVID-19, two repeated RT-PCR tests were negative.

The distribution of risk factors among the high-risk pregnancy group was shown in Table 1. Preterm delivery, hypertensive disorders of pregnancy, diabetes mellitus and fetal growth restriction were the leading defined risk factors in the high-risk pregnancy group.

Comparision of high-risk and low-risk pregnancy groups in terms of demographic features and clinical characteristics was shown in Table 2. Significantly lower BMI, gestational age at birth,

Table 1
Distribution of risk factors among the high-risk pregnancy group.

Risk factor	n, %
Gestational diabetes mellitus	10 (9.7 %)
Pregestational diabetes mellitus	3 (2.9 %)
Gestational hypertension	5 (4.8 %)
Preeclampsia	8 (7.8 %)
Epilepsy	5 (4.8 %)
Thrombophilia	4 (3.8 %)
Fetal growth restriction	11 (10.7 %)
Preterm delivery	15 (14.5 %)
Preterm premature rupture of the membranes	6 (5.8 %)
Twin pregnancy	8 (7.7 %)
Oligohydramnios	4 (3.8 %)
Polyhydramnios	4 (3.8 %)
Placenta previa	4 (3.8 %)
Fetal anomaly	5 (4.8 %)
Asthma	3 (2.9 %)
Maternal heart disease	6 (5.8 %)
Maternal thrombocytopenia	1 (0.9 %)
Maternal Arnold Chiari Malformation	1 (0.9 %)

Table 2
Comparision of high-risk and low-risk pregnancy groups in terms of demographic features and clinical characteristics.

Variables	High-risk pregnancy group (n = 103)	Low-risk pregnant women without any defined risk factor (n = 103)	p value
Maternal age (years)(median, IQR)[a]	29 (7)	27 (6)	0.23
Gravidity (median, IQR)[a]	2 (2)	2 (1)	0.07
Parity (median, IQR)[a]	1 (2)	1 (1)	0.51
Previous miscarriage (median, IQR)[a]	1 (1)	1 (1)	0.10
BMI (kg/m [2]) (median, IQR)[a]	28.28 (7.04)	29.74 (6.15)	**0.02**
Gestational age at birth (weeks) (median, IQR)[a]	37 (4)	39 (2)	**<0.001**
Birth weight (g) (median, IQR)[a]	2800 (990)	3380 (720)	**<0.001**
Apgar 1st minute (median, IQR)[a]	7 (2)	8 (1)	**<0.001**
Apgar 5th minute (median, IQR)[a]	8 (1)	9 (1)	**<0.001**
Route of delivery			**<0.001**
Spontaneous vaginal birth (n, %)[b]	32 (31.1 %)	73 (70.9 %)	
CS (n, %)[b]	71 (68.9 %)	30 (29.1 %)	
SARS-CoV-2 RT-PCR positivity (n, %)[b]	3 (2.9 %)	0 (0%)	**0.04**

BMI: Body mass index, CS: Cesarean section, IQR: Inter quartile range, RT-PCR: Real time polymerase chain reaction.
[a] Statistical analysis was performed by Mann-Whitney *U* test.
[b] Statistical analysis was performed by chi-square test.

birth weight, 1st-5th Apgar score values and significantly higher cesarean section rates were found in the high-risk pregnancy group (p values were 0.02 for BMI and <0.001 for the remaining). Moreover, SARS-CoV-2 RT-PCR positivity rate was significantly higher in the high-risk pregnancy group (2.9 % vs 0%, p = 0.04).

Defined risk factors in the 3 SARS-CoV-2 RT-PCR cases were maternal Chiari malformation, preterm delivery and preeclampsia, respectively. First case was a 24 year old primigravid woman with Chiari malformation. Her BMI was 38.36 kg/m [2] and a 4010 g boy was delivered by cesarean section under general anesthesia at 38 weeks of gestation. Computerized tomography (CT) revealed bilateral ground-glass specific opacities in her lungs. However, her clinic was mild and no medication was necessitated. Two repeated RT-PCR tests with 24 h apart were negative and she was discharged from hospital in 2 days. Second case was a 24 year old multiparous woman with a history of preterm delivery. She was admitted to hospital with preterm premature rupture of the membranes and preterm labor. Due to the history of previous cesarean operations and persistance of contractions, a 1630 g boy was delivered by cesarean section under regional anesthesia at 31 weeks of gestation. Her clinic was mild and there was no finding in her CT. She was discharged from hospital after 2 days without any medication. Third case was a 19 year old primiparous women with asthma. She lost one of her twins in the first trimester and followed up at perinatology clinic during her pregnancy. Her BMI was 35.75 kg/m [2]. A 3410 g girl was delivered by cesarean section at 37th weeks of gestation due to mild preeclampsia under regional anesthesia. Again, her clinic was mild, no finding was present in CT and no medication was administered. She was discharged from hospital after two consecutive negative RT-PCR tests. All cases with SARS-CoV-2 positivity were followed up regularly during the antenatal period at the perinatology clinic of our institution.

The case with suspicious clinic but negative RT-PCR test was a 31 year old primigravid woman with fetal growth restriction and maternal thrombocytopenia. She was referred to our clinic from another hospital and she had a history for irregular antenatal follow up. She was diagnosed as Immune thrombocytopenic purpura (ITP). Preterm labor occurred during her hospitalization and a 1800 g boy was delivered by cesarean section under general anesthesia after necessary transfusions. She became symptomatic after delivery. A fever of 37.7 °C was measured and she felt difficulty in breathing. Chest CT revealed bilateral ground-glass opacities and septal thickening. According to the recommendations of the infectious diseases, hydroxychloroquine (2 × 400 mg p.o at first day and 2 × 200 mg/day p.o for 5 days) and azithromycin (500 mg p.o at first day and 250 mg/day p.o for 5 days) were administered immediately. However, two repeated RT-PCR tests were negative and the diagnosis of COVID-19 was excluded. The neonates of the mentioned 4 cases were tested for SARS-CoV-2 and all of them were found to be negative. Furthermore, all of the healthcare staff who took part in the labor and delivery of these 4 patients were evaluated by special filiation teams for COVID-19. Fortunately, none of them were found to be positivie for SARS-CoV-2.

Comment

Healthcare professionals have been fighting with devotion in the frontline since the beginning of the COVID-19 pandemic. For this reason, they are at great risk for disease transmission. This risk may reach much higher levels especially in branches like obstetrics [3–6]. In order to protect physicians, nurses and midwifes from infection during delivery, many organisations all over the world have prepared guidelines, flowcharts and management protocols [3–6]. Appropritate screening for patients at risk for COVID-19, strict use of personal protective equipment and delivery of suspected / positive cases in isolated negative pressure rooms seem to be the key points in prevention [3–6]. However, there are rising concerns of the physicians about the management of asymptomatic patients without any defined risk factors for COVID-19 transmission. It has been known that asymptomatic patients with SARS-CoV-2 positivity can easily transmit disease to other people [7,8]. Thus, researchers are trying to answer two questions: '' Should we approach each patient as COVID-19 positive or should we screen every pregnant patient admitted to the hospital?''. Furthermore, there are studies in the literature indicating the association between COVID-19 and various obstetric complications like preterm delivery, fetal distress and preterm prelabor rupture of the membranes [10–12]. These findings bring to mind the following questions: ''Are high-risk pregnancies at greater risk for SARS-CoV-2 positivity or COVID-19 itself causes more frequent pregnancy complications?''. On the other hand, our knowledge is still limited on these subjects and more data is necessary in order to conclude more precise results. Therefore, studies investigating the answers for mentioned questions are valuable. To the best of our knowledge this is the first study from Turkey on SARS-CoV-2 positivity rate in asymptomatic pregnant women and first study in the literature comparing high-risk and healthy pregnancies at this point.

Sutton et al. reported that 29 of the 211 (13.7 %) asymptomatic pregnant women admitted to hospital for delivery were positive for COVID-19 and they underlined the benefit of universal testing [7]. Breslin et al. identified that 14 out of 43 (32.6 %) COVID-19 pregnant women were asymptomatic on admission to hospital and

2 (14.3 %) of them developed critical disease requiring intensive care unit admission [13]. Another study by Khalil et al. tested 129 pregnant women on admission to hospital and 9 (7%) patients were found to be positive. Positive cases were asymptomatic except one patient (88.9 %) [14]. London et al. reported that 22 of 75 (29.3 %) asymptomatic pregnant women were positive at admission to hospital and none of them had preterm delivery or need of respiratory support [8]. LaCourse et al. found positive or inconclusive result in 2 of 170 patients (1.2 %) with on-site rapid testing [15]. Doria et al. reported 12 (11.7 %) positive cases among 103 tested pregnant women upon admission to hospital and 11 (91.6 %) of these 12 positive patients were asymptomatic [16]. The positivity rate in present study was much more lower than the previous literature and detected cases were all in the high-risk pregnancy group. These findings were important in two aspects: first of all most possibly due to the strict triage system of our institution and early identification of asymptomatic cases by national filiation teams resulted in lower percentage of positive cases in universal testing in this study. Secondly, presence of positive cases in the high-risk pregnancy group indicated that there might be an association with COVID-19 and maternal/fetal risk factors. These patients might be more susceptible to disease or disease itself might cause pregnancy complications. On the other hand, mentioned patients had risk factors like obesity and chronic systemic diseases. This might be an another important factor behind the higher rate of virus positivity. Moreover, number of antenatal visits in the low-risk pregnant patients were decreased during the pandemic. On the other hand, the high-risk pregnant group had to go to the controls at close intervals and made more contact with the hospital setting. This factor might also be related to the high positivity rate observed in this group.

Identification of asymptomatic cases in this study provided application of efficient management protocols in a timely manner and prevention of disease transmission to healthcare professionals, other patients and the newborns. Thus, universal screening might be a reasonable strategy in the presence of adequate facilities. However, health policies should balance the benefits of universal screening with cost-effective issues and each country should establish its own unique algorythm.

The strenghts of this study were prospective design, large number of cases and comparison of high-risk pregnancy group with low-risk pregnancy group. However, lack of long term follow up was the limitation.

In conclusion, healthcare professionals should be cautious in the labor and delivery of high-risk pregnant women during the pandemic period and universal testing for COVID-19 may be considered in selected populations.

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Declaration of Competing Interest

The authors state that they have no conflict of interest in this study.

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