DR ORHAN SAHIN (Orcid ID : 0000-0002-7216-3816)

Article type : Original Paper

Corresponding author mail id: drorhansahin@gmail.com

Consideration factors with recovering COVID-19 short-term results and false negative Polymerase Chain Reaction test. A Prospective Cohort Study

Abstract

Aim:

To evaluate the clinical factors associated with false-negative RT-PCR result and to report the outcome of a cohort of pregnant women with COVID-19.

Methods:

This cohort study was conducted in a tertiary referral pandemic- hospital and included 56 pregnant women. A study including pregnant women with either a laboratory or clinical diagnosis for COVID-19 were included in the study. The primary outcome was clinical factors associated with false-negative RT-PCR results defined as a positive immunoglobulin M assessed by rapid testing in clinically diagnosed cases. Clinical outcomes of laboratory diagnosed cases were also reported.

Results

In total, 56 women with either RT-PCR or clinical COVID-19 diagnosis were included in the study. 43 women either had RT-PCR positivity or IgM positivity. The clinical outcome of these pregnancies were as follows: Mean maternal age 27.7, immunglobulin M positive cases 76.7%, RT-PCR positive cases 55.8%, maternal comorbidities 11.5%, complications in patients below 20 weeks 34.8%, complications in patients above 20 weeks 65.1%, elevated CRP 83.7%, lymphopenia 30.2%, time from hospital admission to final

follow-up days 37, stillbirth 8.3%. The proportion of women who tested positive for SARS-CoV-2 immunoglobulin M was 100% in the RT-PCR positive group and 56.5% in the clinical diagnosis group (*P*=0.002). The symptom onset to RT-PCR testing interval longer than a week (risk ratio: 2.72, 95% CI:1.14 – 5.40, *P*=0.003) and presence of dyspnea (risk ratio: 0.38, 95% CI:0.14-0.89, *P*=0.035) were associated with false-negative RT-PCR tests. The area under the curve of these parameters predicting false-negative RT-PCR was 0.73 (95% CI:0.57-0.89).

Conclusions

Symptomatic women with a negative RT-PCR should not be dismissed as potential COVID-19 cases, especially in the presence of prolonged symptom onset-test interval and in women without dyspnea.

KEYWORDS: COVİD-19, PCR, Pregnancy, Serology, Rapid test, SARS-CoV-2, Vertical.

Introduction

The coronavirus-19 infection (COVID-19) pandemic is reaching its peak with more than eighty million people infected worldwide. However, the number of pregnant women reported in the literature is disproportionally low [1]. Pregnant women are less likely to be admitted to the hospital compared to non-pregnant adults of similar age [2]. Whether this is due to higher rates of asymptomatic infection in pregnant women or a better ability of pregnant women to isolate themselves, i.e. fencing effect, is not clear. Although pregnant women do not appear to be at increased risk of COVID-19 related complications, the rate of iatrogenic preterm birth and caesarean section is increased [1]. Furthermore, vertical transmission of SARS-CoV-2 is yet to be established. However, the accumulating evidence suggests probable vertical transmission in a small percentage of cases[1]. There is still a need for data on pregnant women from different healthcare systems to elucidate clinical and social factors associated with short, as well as long-term, adverse outcomes. Most reports on pregnant women only include reverse transcriptase-polymerase chain reaction (RT-PCR) test positive cases[3]. Cases with a clinical diagnosis are often overlooked and rarely reported. The sensitivity of RT-PCR tests is affected by the sampling technique, storing, and transport of samples. However, clinical factors associated with false-negative RT-PCR testing in pregnant women are unknown. In this study we aimed to investigate the clinical factors associated with false-negative RT-PCR result and to report the outcome of a cohort of pregnant women with COVID-19.

Materials and Methods

The present cohort study was conducted on pregnant women treated for COVID-19 in Professor Cemil Tascioglu City Hospital, Istanbul between 28th March 2020 and 20th May 2020. The study was approved by the Institutional Review Board and Ethics Committee (177-19.05.2020) and written informed consents were obtained before the study participation. Pregnant women with either a laboratory or clinical diagnosis for COVID-19 were included in the study. Laboratory diagnosis was made with RT-PCR test (*DirectDetect SARS-CoV-2 Detection Kit; Coyote Bioscience, Beijing, China*) method targeting the

ORF1ab and N gene according to the manufacturer's instructions. The clinical diagnosis was made when pregnant women experienced multiple cardinal symptoms of COVID-19 (fever, cough and dyspnea) with either radiology findings of pneumonia or a household member with proven COVID-19 infection as per local protocol. Cases with a positive contact history but no clinical symptoms or covid-19-like complaints in the last 2 months were excluded from the study. The information of all patients, including demographic data, clinical characteristics, prenatal course, laboratory results, and outcomes, were collected prospectively. RT-PCR tests were performed on nasopharyngeal and throat swab samples on pregnant women and born neonates during study period. Swabs were taken by trained healthcare personal equipped with adequate personal protective equipment. Sterile synthetic fiber swabs with plastic shafts were used to collect nasopharyngeal and throat samples from patients. After collection, fresh samples stored immediately at 2-8 C° in cool-pack handbag and were transferred to the laboratory within 2-4 hours in a viral transport medium in keeping with the cold chain transportation regulations . The results were available to physicians within 24 hours. All pregnant women with a COVID-19 diagnosis were admitted for either isolation or supportive treatment as per national guidelines[4]. Drug treatment for COVID-19 included either hydroxychloroquine or lopinavir/ritonavir to all pregnant women admitted following national COVID-19 management guidelines[4]. Oseltamivir was added for patients presenting during the flu season. Favipiravir was used in women with features of severe COVID-19. Low molecule weight heparin thromboprophylaxis was started in patients with prolonged hospitalization (i.e. >5days) or risk factors for deep vein thrombosis. Nasal oxygen support was started in patients with oxygen saturation below 96%. Women with persistently low oxygen saturation below 93%, prolonged tachypnea (respiratory rate >30 per minute), partial oxygen pressure less than 60mmHg, or partial oxygen pressure/inspired oxygen ratio less than 300 were admitted to the intensive care unit. Women completing their respective treatment regimens and remaining symptom-free more than 48 hours were discharged. All patients were called for a follow-examination at least one week following the hospital admission. Presenting patients were offered rapid antibody tests for COVID-19 (*Weimi Diagnostic, Guangzhou Weimi Bio-Tech, Guangzhou, China*). Patients were assessed for the presence of symptoms, fetal heart rate, and any pregnancy complications. The primary outcome was clinical factors associated with false-negative PCR results defined as a positive immunoglobulin M assessed by rapid testing in clinically diagnosed cases. Secondary outcomes were short term pregnancy outcomes of convalescent pregnant women with COVID-19.

Statistical analysis

Continuous variables are represented as mean and standard deviation or median and interquartile range depending on the distribution assumption of that variable. Normality was tested with Shapiro-Wilk test and parametric representation was used for variables with a normal distribution. Categorical variables were represented as number and percentage of the total. Group comparisons were made with either t-test or Wilcoxon-rank sum test depending on distribution assumptions. Chi-squared test or Fisher's test were used for categorical variables. Log-binomial generalized linear models were used to test factors associated with false-negative RT-PCR tests. The accuracy of the final model was tested with the receiver operating characteristics curve. P values below 0.05 are considered statistically significant. All analyses were performed using R for Statistical Computing Software (Version 4.0.2)

Results

In total, 56 women with either RT-PCR or clinical COVID-19 diagnosis were included in the study (shown in Fig. 1) The baseline characteristics of RT-PCR positive and clinical diagnosis groups are presented in Table 1. There were no significant differences between RT-PCR positive and clinical diagnosis groups regarding maternal age (*P* =0.771), body-mass index (*P* =0.116), smoking status (*P* =0.617), parity (*P* =0.100), presenting symptoms (*P* >0.05 for all), gestational age at presentation (*P* =0.999), body temperature (*P* =0.841). The proportion of women with COVID-19 positive family members was higher in RT-PCR positive group compared to clinical diagnosis (50.0 vs. 18.7%, *P* =0.013). The symptom onset to RT-PCR test interval was longer in the clinical diagnosis group compared to RT-PCR (median: 3.0 vs. 2.0 days, *P* =0.044). At the time of follow-up, 16 women out of 24 in RT-PCR positive group and 29 women out of 32 in the clinical diagnosis group presented for assessment and immunoglobulin testing. The proportion of women who tested positive for SARS-CoV-2 immunoglobulin M was 100% in the RT-PCR positive group and 65.5% in the clinical diagnosis group (*P* =0.002).

As the SARS-CoV2 antibody test gold reference, RT-PCR's apparent sensitivity, specificity, positive likelihood ratio and negative likelihood ratio are 45.71% (95% CI: 28.8 to 63.3%), 50.0% (95% CI: 27.2 to 72.8%), 0.91% (95% CI: 0.52 to 1.61%) and 1.09% (95% CI: 0.64 to 1.85%), respectively. (Table 3) . In the univariable log-binomial regression, symptom onset to RT-PCR testing interval longer than a week (risk ratio: 2.72, 95% CI: 1.14 – 5.40, *P* =0.003) and presence of dyspnea (risk ratio: 0.38, 95% CI: 0.14-0.89, *P* =0.035) were associated with false-negative RT-PCR tests (Table 4). The area under the curve of a model incorporating time interval from symptom onset to testing longer than one week (odds ratio: 9.02,

95% CI: 1.04-203.2) and lack of dyspnea (odds ratio: 4.43, 95% CI: 1.05-21.5) was 0.73 (95% CI: 0.57-0.89) (shown in Fig. 2). Symptom onset to testing interval and presence of dyspnea were moderately predictive of false-negative RT-PCR result.

The treatment details and clinical outcomes of 43 women with laboratory confirmation (RT-PCR or immunoglobulin testing) of COVID-19 are presented in Table 2. The most common laboratory abnormalities were elevated C-reactive protein (83.7 %) and lymphopenia (30.2%). Three women had early pregnancy complications which included one early pregnancy loss, one threatened miscarriage, and one pregnancy termination on maternal request. Three women developed severe preeclampsia. One woman with twin pregnancy was delivered at 25 weeks' gestation due to critical COVID-19 and fetal distress. One of the babies was stillborn and the other died two days later in the neonatal intensive care unit. There were four preterm deliveries and only one of them was spontaneous preterm delivery.

The median gestational age at admission was 27.0 weeks (IQR: 16.0 to 32.0) and the duration of hospitalization was 7 days (5.0-10.0). Twelve women were treated with nasal oxygen and 2 women required mechanical ventilation; one of them was due to deterioration after hospital discharge. Two women were treated in the intensive care unit. There were no maternal deaths and no neonatal RT-PCR positive cases.

Discussion

Summary of key study findings

A longer symptom onset to RT-PCR testing interval and lack of dyspnea were associated with false-negative RT-PCR results. Short-term follow-up of convalescent women showed good obstetric outcomes with an increased iatrogenic preterm delivery rate. RT-PCR negative women with symptoms of

COVID-19 positive and contact history or radiology findings should not be overlooked. Women with a clinical diagnosis of COVID-19 should be followed up as RT-PCR positive COVID-19 until proven otherwise in view of the possibility of a false negative swab PCR, especially in case with prolonged symptom onset-test interval and in cases without dyspnea as presenting symptom.

Strength and limitations

The strengths of our study include follow-up of these pregnant women and serology testing of clinically diagnosed cases. However some limitations apply to our findings. First, we could not validate the rapid immunoglobulin test kits used in this study. To date, both the '' European Center for Disease Prevention and Control '' (ECDC) and the '' World Health Organization '' (WHO) have used reverse transcription polymerase chain reaction (RT-PCR) testing in respiratory samples as the gold standard in the diagnosis of Covid-19. However, RT-PCR has several practical limitations. In our study, we found all RT-PCR positive patients tested positive for immunoglobulin M, which suggests the sensitivity of this kit is acceptable. Furthermore, the reported specificity of point of care tests was very high [5]. Second, some patients were lost to follow-up. Eleven (19.6%) of the patients did not return when the antibody test was called. Reasons for not being followed were determined as possible curfews or fear of getting sick again from hospitals when asked by phone. This may introduce bias into our results as patients without any complaints or complications are less likely to show up for a follow-up visit. Third, we used a very broad definition of clinical COVID-19 as opposed to more commonly used criteria, which mandates radiology findings. Pregnant women usually do not prefer computed tomography and chest x-ray due to fetal exposure concerns, limiting the utility of radiology for clinical COVID-19 diagnosis. However, household exposure and multiple COVID-19 symptoms are also strong indicators of COVID-19 [6].

Another limitation is the possibility that patients with antibody positivity may have had the disease before, and may not actually have covid-19 disease during the study period with symptoms similar to covid-19, and the possibility of antibody positivity caused by previous covid-19 attacks. We tried to reduce this potential bias by excluding patients with covid-19-like complaints in the last 2 months. However, it was not possible to exclude asymptomatic cases. Furthermore, a more strict clinical diagnosis criteria would likely increase the seroconvalescence rate in the clinical diagnosis group. Finally, our numbers were too small to compare clinical features and outcomes of women with clinical diagnosis and RT-PCR diagnosed COVID-19 and document the actual sensitivity and specificity of the tests.

Clinical and research implications

False-negative RT-PCR test is a common problem for COVID-19 diagnosis. Although there are known technical factors associated with false-negative RT-PCR, the clinical factors associated with it in pregnant women are yet to be determined [7-10]. False-negative rate in adults are reported to be around

5% but these studies use repeat RT-PCR testing rather than checking seroconvalescence [11]. In non-pregnant adults SARS-CoV-2 viral loads dramatically decrease a week from symptom onset [12]. A prolonged time interval from symptom onset to RT-PCR test and may be associated with lower viral loads in respiratory specimens of pregnant women, which may result in a false RT-PCR result. To the best of our knowledge, the lack of dyspnea is a novel finding of our study, which was not mentioned in the literature. Dyspnea is a common feature of severe COVID-19 and may correlate with higher viral loads and fewer false-negative results. Clinicians should be aware of these factors as not to miss potential cases. Radiology imaging is advised for RT-PCR negative patients with COVID-19 symptoms but most pregnant women are reluctant to undergo computed tomography (CT) or chest X-rays due to concerns regarding radiation exposure. Although lung ultrasound is a safe alternative to high-energy imaging studies, it is not widely available and requires expertise [13]. Therefore, it is important to investigate the clinical factors associated with false-negative RT-PCR results for clinicians to recognize women at risk.

Interpretation of study findings and comparison with published literature

Short-term pregnancy outcomes were in line with the published literature suggesting a mild course of the disease and few pregnancy complications. A recent publication suggested an increased rate of preeclampsia in women with COVID-19. We had three cases of severe preeclampsia out of 30 women beyond 20 weeks' gestation (10%), a rate which is higher than the incidence of severe preeclampsia (<1%) [14]. However, neither our study design nor the sample size is adequate to detect a potentially increased rate of preeclampsia in women with COVID-19. According to the case series by Sahin *et al*, only 29% pregnant women with positive symptoms were RT-PCR positive for SARS-CoV-2. This finding is lower than the rate of %42.8 in our study and likely due to the varying prevalence of COVID-19 in these two regions. On the other hand, the study did not analyze or follow-up suspicious cases with a negative [15]. Our study suggests some of these women seroconvert during the follow-up and should not be dismissed entirely. In a retrospective study that included 52 patients diagnosed with Covid-19, Alay *et al*. revealed the results of 25 patients who were negative for Covid-19 RT-PCR but had CT scanning positive. However, they did not show the short and long-term results of patients with positive symptomps who were both RT-PCR negative and CT scanning negative [16]. Although, in our study in the RT-PCR negative patient group who did not recieve CT due radiation concerns, the positivity of the antibody was 65.5%. From this point of view, another approach should be considered for patients who have not had CT and are negative for RT-PCR but with suspicious symptoms.

Several studies that have emerged suggest the possibility of in utero COVID-19 transmission by measuring the fetal IgM blood level, possibly as a fetal immune response secondary to the infection. In our study, RT-PCR was negative in all (0/12) newborns of the patients who gave birth during the follow-up

period. Taking into account all the available evidence, there are very few reported cases to conclude whether SARS-CoV-2 has an intrauterine vertical transmission. Therefore, it is not possible to state any exact conclusions at this point [17]. Short-term follow-up of convalescent mothers with COVID-19 shows good obstetric outcomes apart from an increased rate of iatrogenic preterm birth. In our study, we found a preterm delivery rate of 8.8% in covid-19 pregnant women (4/45) (laboratory and clinical diagnosis). A more recent review reveals preterm rates of about 25% in covid-19 pregnant women [17]. This rate is higher than the rate in our study. The reason for this difference may be that the average week of gestation in our study was compatible with the second trimester. Longitudinal studies and clinical analysis are needed to assess the clinical course of RT-PCR negative cases. We believe that our results offer a positive contribution and a different perspective to currently available data for the diagnosis and treatment of pregnant women with positive and negative RT-PCR test results.

Conclusion

Women without dyspnea and RT-PCR tests performed one week after the onset of symptoms are more likely to have false-negative results. Clinicians should be aware of this factor to avoid cases with severe suspicious symptoms, negative RT-PCR results, and those who do not wish to have a lung tomography scan. Studies involving more patients are needed to clarify the subject.

Declarations

Ethics approval and consent to participate

Subjects have given their written informed consent, and the study protocol as a number (177-19.05.2020) was approved by the local departmental ethics committee of Prof.Dr.Cemil Tascioglu City Hospital

Availability of data and materials

Raw data of the study are available upon request to the corresponding author.

Conflict of Interest Statement

No author has any potential conflict of interest.

Funding Sources

There was no funding source for this research.

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Table 1. Maternal, pregnancy characteristics of women with an initial RT-PCR positive and clinical diagnosis of COVID-19

	RT-PCR diagnosis (n=24)	Clinical diagnosis (n=32)	P value
Maternal age in years, median (IQR)	27.0 (25.7-29.2)	27.5 (23.7-33.0)	0.771
BMI in kg/m2, mean (SD)	27.9 (2.42)	26.8 (2.72)	0.116
Obesity (BMI >30kg/m2)	5 (20.8)	3 (9.3)	0.225
Multiparous, n (%)	21 (87.5)	22 (68.7)	0.100
Smoker, n (%)	2 (8.3)	4 (12.5)	0.617
Symptoms (subjective complaints), n (%)			
- Cough	10 (41.7)	9 (28.1)	0.289
- Fever or chills	10 (41.7)	10 (31.2)	0.420
- Dyspnea, shortness of breath	12 (50.0)	15 (46.8)	0.816
- Fatigue	11 (45.8)	14 (43.7)	0.876
- Diarrhoea	2 (8.3)	1 (3.1)	0.391
- Loss of taste or smell	0 (0.0)	2 (6.2)	0.603
- Family member with positive RT-PCR for COVID-19	12 (50.0)	6 (18.7)	0.013
Body temperature in Celsius, median (IQR)	36.8 (36.5-37.1)	36.8 (36.5-37.1)	0.841
- Normal, n (%)	21 (87.5)	29 (90.6)	0.816
- Sub febrile, n (%)	2 (8.3)	1 (3.1)	
- Fever, n (%)	1 (4.2)	2 (6.3)	
Heart rate in beats per minute, median (IQR)	80.0 (77.5-84.5)	79.0 (74.0-88.0)	0.720
Tachycardia (>100 bpm), n (%)	2 (8.3)	4 (12.5)	0.617
Gestational age at admission, n (%)			
- <14 weeks	5 (20.8)	6 (18.7)	0.999
- 14-28 weeks	7 (29.2)	10 (31.2)	
- >28 weeks	12 (50.0)	16 (50.0)	
Symptom to first PCR test in days, median	2.0 (0.0-4.5)	3.0(2.0-6.0)	0.044

(IQR)			
Follow-up with antibody test after discharge, n (%)			
- Immunoglobulin M positive	16/16 (100.0)	29/19 (65.5)	0.002
- No follow-up	8 (33.3)	3 (9.3)	

Note: Quantitative variables are shown as mean (standard deviation). Qualitative variables are shown as absolute number (percentage). RT-PCR: reverse transcriptase polymerase chain reaction, IQR: interquartile range, BMI: body-mass index, SD: Standart Deviation,

Table 2. Treatments and clinical outcomes of laboratory confirmed COVID-19 in pregnancy

	SARS-CoV-2 RT-PCR positive or RT-PCR negative and Ig M positive (n=43)
Maternal age in years, mean (SD)	27.7 (4.95)
- <20	2 (4.6)
- 20-35	39 (90.6)
- 35-40	2 (4.6)
Maternal comorbidities, n (%)	
- Systemic lupus	1 (2.3)
- Diabetes	2 (4.6)
- Arrythmia	1 (2.3)
- Epilepsy	1 (2.3)
BMI in kg/m2, mean (SD)	27.9 (2.5)
Obesity (BMI >30kg/m2), n (%)	8 (18.6)
Gestational age at admission, n (%)	
- <14 weeks	9 (20.9)
- 14-28 weeks	19 (44.1)
- >28 weeks	15 (34.8)
RT-PCR positive, n (%)	24 (55.8)
Immunoglobulin M positive, n (%)	33 (76.7)
Gestational age at admission, median (IQR)	27.0 (16.0-32.0)
Duration of hospitalization, median (IQR)	7.0 (5.0-10.0)
Readmission, n (%)	1 (2.3)
Respiratory support, n (%)	
- Nasal oxygen	12 (27.9)

- Mechanical ventilation	2 (4.6)
Intensive care unit admission, n(%)	2 (4.6)
Medical treatments received (any), n(%)	42 (97.6)
- Oseltamivir	7 (16.2)
- Hydroxychloroquine	16 (37.2)
- Lopinavir/Ritonavir	34 (79.0)
- Favipiravir	2 (4.6)
LMWH use, n(%)	28 (65.1)
Laboratory findings, n(%)	
- Elevated CRP *[N:(mg/L) (< 5)]* or procalcitonin *[N:(µg/L) (<0.12)]*	36/43 (83.7)
- Lymphopenia (absolute count<1.1) (10^3/uL)	13/43 (% 30.2)
- Neutrophil/lymphocyte ratio	3.7 (2.5-5.5)
- Elevated transaminases *[N: AST; (U/L) (< 35),* - *N: ALT ;(U/L) (0-50)]* (ALT or AST >40)	6 /43 (% 13.9)
- Elevated creatinine (>1mg/dL) *[N: (mg/dL) (0.51-0.95)]*	1/43 (2.3)
Time from hospital admission to final follow-up in days, median (IQR)	37.0 (18.0-43.0)
Maternal death, n(%)	0 (0.0)
Complications in patients below 20 weeks , n(%)	15/43 (34.8)
- Threatened abortion	2/15 (13.3)
- Early pregnancy loss	1/15 (6.6)
- Pregnancy termination (maternal request)	1/15 (6.6)
Complications above in patients above 20 weeks, n(%)	28/43 (65.1)
- Severe preeclampsia	3/28 (10.7)

- Cholestasis	1/28 (3.5)
- Spontaneous preterm delivery (<37 weeks)	1/11 (9.0)
- Iatrogenic preterm delivery (<37 weeks)	3/11 (27.2)
Delivered	11/28 (39.2)
-Stillbirth	1/12 (8.3)
-Neonatal death	1/ 12 (8.3)
Neonatal PCR positivity	0/12

Note: Quantitative variables are shown as mean (standard deviation). Qualitative variables are shown as absolute number (percentage), N: Normal Range Value

Table 3. Diagnostic accuracy of PCR testing in pregnant women with serology data (n=43 ,antikor positive cases)

Predictive accuracy parameter	***Value (95% Confidence Interval)**

Sensitivity	45.71 (28.83-63.35)
Specificity	50.0 (27.20-72.8)
Positive Likelihood Ratio	0.91 (0.52-1.61)
Negative Likelihood Ratio	1.09 (0.64-1.85)

*All values represent percentages

Table 4. Factors associated with false negative RT-PCR

	Risk ratio (95% CI)	**P value[a]**
Maternal age >35 years	0.92 (0.06-2.83)	0.925
Obesity	1.5 (0.44-3.38)	0.395
Smoker	0.88 (0.35-4.57)	0.833
Gestational age at assessment, third trimester	1.08 (0.43-2.53)	0.861
Fever	1.11 (0.41-2.57)	0.812
Dyspnea	0.38 (0.14-0.89)	0.035
Cough	0.80 (0.29-1.88)	0.619
Family member with confirmed COVID-19	1.25 (0.47-2.87)	0.609
Symptom to first RT-PCR test ≥ 1 week	2.72 (1.14-5.40)	**0.003**

CI: confidence interval, RT-PCR: reverse transcriptase polymerase chain reaction

[a]log-binomial generalized linear regression

FIGURE 1: Study Flow Chart

FIGURE 2: The receiver operating characteristics curve for predicting false negative PCR result on admission. Increasing time interval from symptom onset to testing (OR 9.02, 95% CI: 1.04-203.2) and lack of dyspnoea (OR 4.43, 95% CI: 1.05-21.5) were associated with false negative PCR result in the multivariable model. The area under the curve of the model was 0.73 (95% CI 0.57-0.89).

Supplementary Files

This supplementary file regarding Strobe-chekclist associated with this manuscript.

FİGURE 1: Study Flow Chart

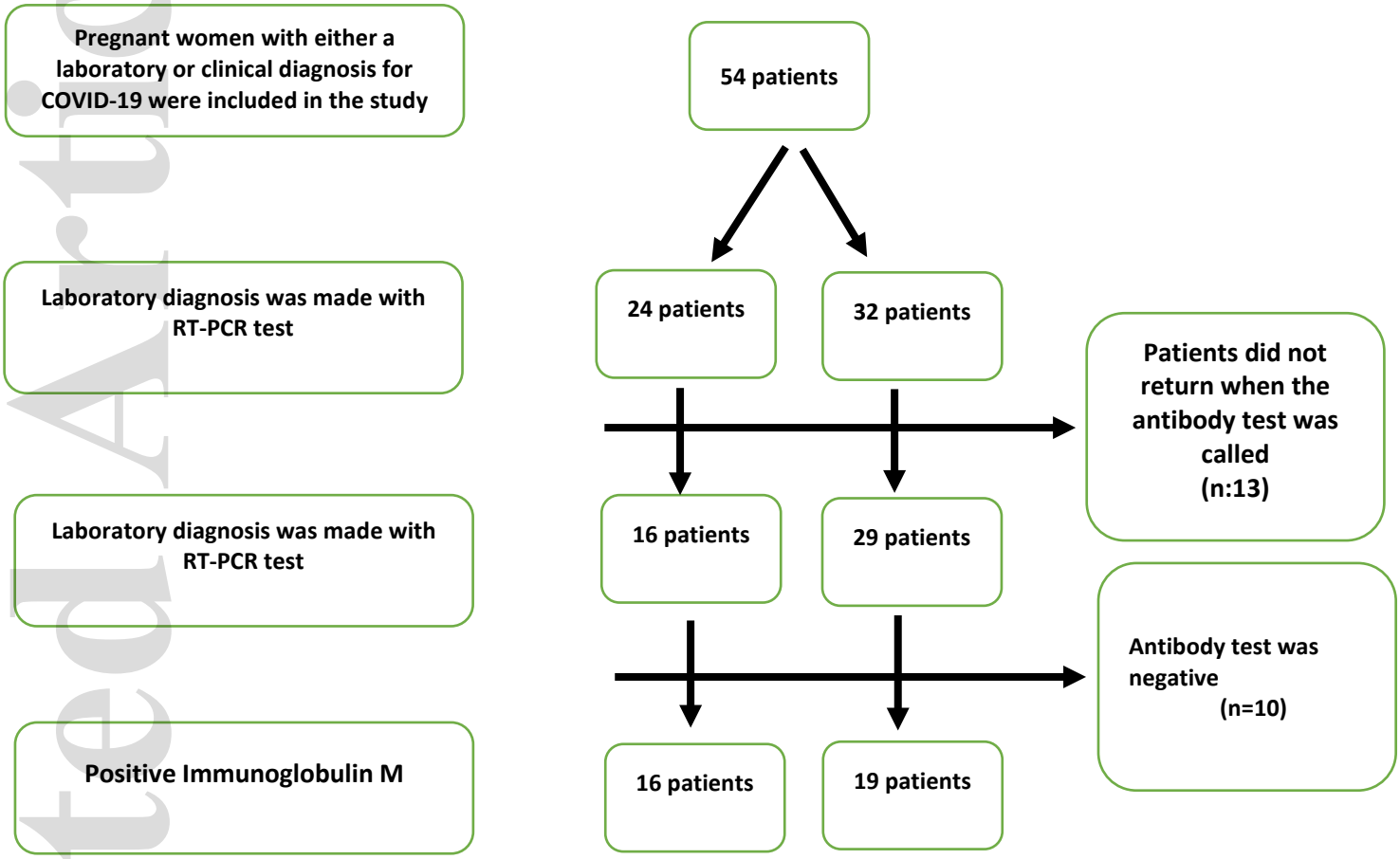

FİGURE 2: The receiver operating characteristics curve for predicting false negative PCR result on admission. Increasing time interval from symptom onset to testing (OR 9.02, 95% CI: 1.04-203.2) and lack of dyspnoea (OR 4.43, 95% CI: 1.05-21.5) were associated with false negative PCR result in the multivariable model. The area under the curve of the model was 0.73 (95% CI 0.57-0.89).