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RESEARCH ARTICLE

Possibility of vertical transmission in Covid - 19 pregnancy - a hospital based prospective cohort study from Kerala, India

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ABSTRACT

Background: Knowledge regarding the possible risk of vertical transmission is very limited, but is crucial for guiding and counselling patient and also essential for formulating the principles of obstetric management. **Aim**: To estimate the incidence rate of vertical transmission of Corona virus disease 2019 (COVID - 19) in the third trimester. **Materials and methods**: A prospective cohort study was conducted among 50 consecutive admitted pregnant women who were infected with COVID - 19 in the 3rd trimester. To study the possibility of vertical transmission the collection of 3 biological samples were done namely 1) amniotic fluid, 2) cord blood and 3) nasopharyngeal swab samples from neonates collected after 24 hours of birth. All samples were processed for RNA isolation using QIAGEN QI Amp @ RNA minikit, according to manufactures instructions. The samples were subjected to RTPCR using SD Biosensor kit, detecting both E gene and RdRp genes. **Results:** Among the participated pregnant women (n=50), all were in their third trimester and 60 % were asymptomatic (B1 category) and 40% symptomatic (B2 category). 34% of the patients delivered after 10 days of testing COVID positive, 28% delivered between 3 to 10 days and 38% delivered in less than 72 hours. Of the total sample 34 % underwent vaginal delivery, 2% had instrumental delivery and 56% had caesarean section. Among the babies born, 66% were stable, with normal vitals and laboratory parameters. 12 % required NICU admission for monitoring. There was 1 term intrauterine death. The 3 biological samples collected for determining vertical transmission were amniotic fluid, cord blood and nasopharyngeal swab samples collected on the neonates after 24 hours of birth. All the collected biological samples tested negative for COVID-19 RNA. No maternal intensive care unit admission, maternal sepsis, or maternal mortality was observed. **Conclusion**: In our cohort study of pregnant women with COVID-19 infection during the third trimester of pregnancy we found that the risk of vertical transmission to the neonate is negligible.

Keywords: COVID-19, vertical transmission.

On March 11, 2020 WHO declared COVID-19 as an ongoing pandemic [1]. COVID-19 being a public health emergency of international significance, concerns have been raised about pregnant women and the fetus. Emphasis on of vertical transmission and variability in transmission has been discussed, but very limited literature is available on the same [2–7]. Vertical transmission can occur during the antepartum and intrapartum periods or during the postpartum period and most of the studies concluded that there is no evidence of vertical transmission [8-11].

Chances of intrauterine vertical transmission of COVID-19 in nine pregnant women with mild to moderate infection in the third trimester were the first among the studies. Amniotic fluid, cord blood and neonatal pharyngeal swab samples from six neonates were tested for SARS-CoV-2, using quantitative reverse transcriptase polymerase chain reaction (qRT-PCR). Each of these samples tested negative and it was concluded that intrauterine fetal infection did not occur during the third trimester of pregnancy [12]. There have been some studies which documented positive real time polymerase chain reaction (RT-PCR) in neonates soon after delivery, but these

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lacked essential clinical data and information regarding adequate isolation [13-16].

The receptor for SARS-CoV-2 in humans, angiotensin converting enzyme 2 (ACE2) and the interaction at the placental level is highly debated. Studies conducted by Dong et al in pregnant rats demonstrated transient ACE2 over expression and increased activity in the placenta, precisely in the syncytiotrophoblast, cytotrophoblast, endothelium, and vascular smooth muscle from both primary and secondary villi and reproductive organs [17, 18]. A study by Zeng et al contradicted these findings and found out that there is very low expression of ACE2 in the cells of early maternal fetal interface, which makes the placenta devoid of susceptible cells to the virus [19]. Damage caused in the placenta by the virus like vascular malperfusion and inflammation predisposes to vertical transmission by disrupting the placental barrier [20].

As more and more data are becoming available on the maternal fetal transmission of many emerging viral infections as the Zika virus, Ebola virus, Marburg virus etc, it is important that we undertake more studies to understand the obstetric management in pregnant women with COVID-19 infection. Also this is an important requirement from a public health point of view as well [21-24].

Materials and methods

A prospective cohort study was undertaken after getting institutional ethical clearance. It was conducted among 50 consecutive pregnant women who had been tested positive for COVID-19 in their 3rd trimester of pregnancy. To study the possibility of vertical transmission in COVID-19 in pregnancy the collection of 3 biological samples were done and tested for SARS-CoV-2 by use of qRT-PCR using a CDC recommended kit. Amniotic fluid was collected intrapartum and cord blood collected soon after delivery. Neonatal nasopharyngeal swab was obtained after 24 hours of delivery.

Maternal indices collected included age, gravity, parity, gestational age at delivery. Any co-morbidities were also noted; hypertension, diabetes, asthma, smoking. We noted clinical and laboratory characteristics of the study subjects such as fever, cough, shortness of breath and any gastrointestinal symptoms. Laboratory parameters like white blood cell count, lymphocyte count, platelet count, and chest X-ray results of both mother and newborn were documented. We categorised the patients as B1 and B2 and C as per the guidelines [25]. Mode of delivery and maternal complications due to COVID-19 infection which required supplemental oxygen therapy/ invasive mechanical ventilation, intensive care unit (ICU) admission were noted. We looked for maternal sepsis and maternal mortality. Birth weight, Apgar score, neonatal intensive care unit (NICU) admission, and NICU length of stay were noted in the case of neonates. We looked for neonatal complications including transient tachypnoea of the neonate (TTN), respiratory distress syndrome (RDS), invasive mechanical ventilation, sepsis and neonatal death.

RNA extraction of all the samples was done using QIAamp® Viral RNA extraction kit, according to manufacturer's instructions. The samples were subjected to RTPCR using SD Biosensor kit, detecting both E gene and RdRp genes.

For statistical analysis, the data were described as either continuous or categorical variables. The continuous variables were presented as mean with standard deviation, while the categorical variables were presented as frequency and percentages. The primary outcome studied was the incidence rate of vertical transmission of COVID-19 to the neonate when maternal infection occurred during the third trimester.

Results

We included 50 pregnant women in the third trimester of pregnancy, in our study; n=50. Among these 50% were between 18 and 25 years of age, 42% had their age between 26 and 35 years and 8 % were more than 35 years of age. Mean age was 25.76±4.42 (table 1).

Table 1: Age of the patients (n= 50)

Age	Percentage
<35	46 (92 %)
>35	4 (8%)

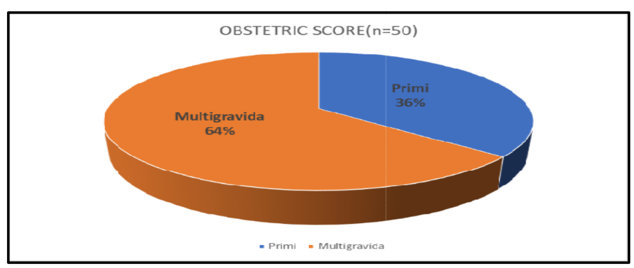

Figure 1: Obstetric score

Gestational diabetes was documented in 7 patients. Other significant findings noted were; 2 were hypertensive, 6 were hypothyroid, 1 had mitral valve prolapse and 1 was hyperthyroid on treatment. Prior history of COVID-19 infection was not given by any of them. None of the patients included in our study had received COVID-19 vaccine. Obstetric score of the study population is as shown in figure 1. As mentioned earlier, all pregnant women were in their third trimester; 84% were term pregnancy, 12% were late preterm and 2% were preterm (figure 2).

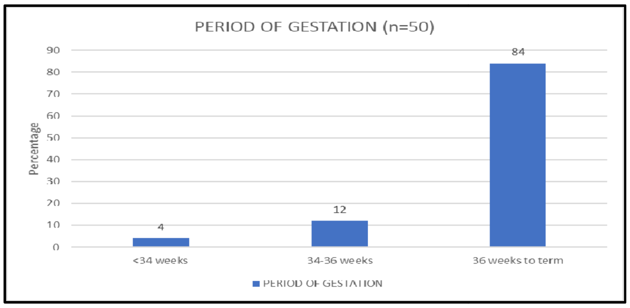

Figure 2: Period of gestation

Majority were asymptomatic (60%) and belonged to B1 category. Fever with cough (18%), fever (8%), breathlessness (2%), headache (2%), palpitations (2%), diarrhea (4%), myalgia (4%) were the common symptoms noted in B2 category (figure 3).

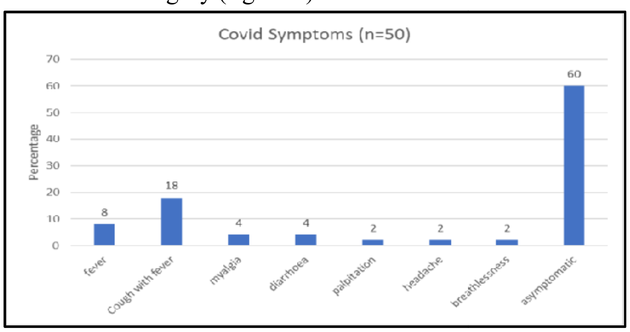

Figure 3: COVID - 19 symptoms

Among the selected patients, 34% delivered after 10 days of testing COVID-19 positive, 28% delivered between 3 to 10 days of testing COVID-19 positive and 38% delivered in less than 72 hours of testing COVID-19 positive (figure 4). Eleven (22%) patients had abnormal laboratory parameters. There were neither maternal intensive care admissions nor maternal deaths. The indications for caesarean sections were mainly obstetrical causes (table 2).

Table 2: Modes of delivery

Vaginal delivery	17(34%)
Instrumental delivery	5(10%)
Caesarean section	28(56%)

NICU admission was required for 6 babies; 4 were admitted for being preterm and 2 required admission for mild respiratory distress (table 3). From 3 patients, we were unable to collect amniotic fluid as one had severe oligohydramnios and the other 2 had prelabour rupture of membranes. The cord blood of all the newborns was collected at the time of delivery (except from the fetus that died intrauterine). The neonatal throat swab was collected from all the neonates after 24 hours of delivery. We did RTPCR with the collected biological samples and all the tested samples were negative for COVID-19 (figure 5).

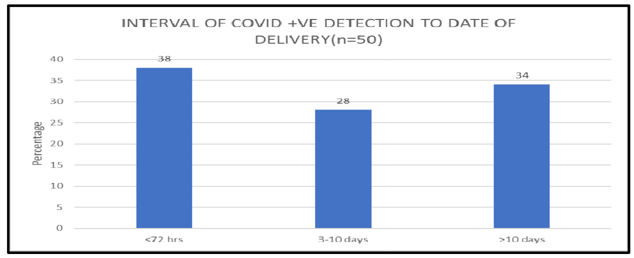

Figure 4: Interval of Covid positive detection to date of delivery

Table 3: Conditions of the baby

Condition of the baby	
Mothers side	43(86%)
NICU admission	6(12%)
IUD	1(2%)

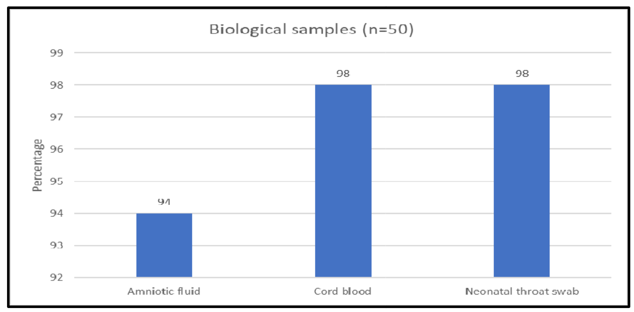

Figure 5: Biological samples

Discussion

We studied the chances of vertical transmission of COVID-19 using the biological samples collected from infected pregnant women and their neonates. Mean age of the patients was 25.76±4.42 years. Pregnant women infected in their third trimester were included in the study. Among the study subjects, 60 % were asymptomatic and 40 % had mild symptoms. Our results showed that SARS-CoV-2 RNA was negative in all the biological samples taken for examination. In the study conducted we could not pick up any cases of vertical transmission of COVID-19 among the pregnant women with mild symptoms or no symptoms. Our findings are in accordance with what was observed in SARS, which has a similar sequence to SARS-CoV-2 [26, 27].

A shorter interval between maternal symptoms and delivery is an important factor which decides vertical transmission [28]. In our study among the maximum interval between testing COVID-19 positive and delivery was 10 days, still there was no evidence of vertical transmission. The mode of delivery also did not seem to play a role in transmitting infection to the fetus.

The major strengths of this study are a) it is a prospective study, b) the study samples included a systematic collection of 3 biological samples and c) follow-up of neonates was done for the COVID-19 symptoms. Most of the studies done on COVID-19 vertical transmission included symptomatic pregnant women. So there is a fairly high chance that patients with asymptomatic infections were underrepresented. But our selection criteria made sure that even asymptomatic pregnant women with COVID-19 infection were also included.

The limitation of our study is that it did not include patients with severe symptoms and also our samples did not include COVID-19 infections during the first or second trimester. There is a chance that we could have missed some cases of vertical transmission, owing to the smaller sample size taken.

Conclusion

There was no evidence of vertical transmission in our study group. All the study subjects were in their third trimester; majority were asymptomatic and others were with mild symptoms. Our data provides additional evidence to support that vertical transmission of COVID-19 is negligible and this can be used for patient management and will be a point of reassurance when counselling patients.

Conflict of interest: None. **Disclaimer:** Nil.

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