

## Effect of SARS-COV-2 on pregnancy outcome in Covid positive mothers

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### Abstract:

**Background:** Pregnancy represents a unique immune condition that is modulated, but not suppressed. However, it is unknown how COVID-19 infection behaves in key populations such as pregnant women. The impact of SARS- CoV- 2 infection in pregnant women and their neonates is an area of research interest. To date, there is limited knowledge about outcome of pregnancy with COVID-19 positive mothers and any correlation with  $\Delta$ Ct values.

**Material and Methods:** This was a Cross-sectional study from April 2020 to December 2020 where nasopharyngeal swabs from suspected COVID-19 pregnant women were tested for the presence of SARS CoV-2 RNA using RT-PCR. The  $\Delta$ Ct value of RT-PCR assay of all positive mothers were followed and outcomes such as gestational age at the time of delivery, mode of delivery, maternal mortality, abortion, IUFDs, neonatal morbidity and mortality were noted. Correlation of the outcome with the  $\Delta$ Ct values were also done.

**Results:** The present study included a total of 10477 mothers delivered in a tertiary care hospital. Out of these, 152 (1.45%) mothers and 10 (0.09%) neonates were tested positive for COVID-19 by RT-PCR. Asymptomatic pregnant women were noted to be 111(73.02%). All the pregnancy outcomes were noted. Among all 152 cases,138(90.78%) were delivered full term,7(4.60%) spontaneous abortion and 5(3.28%) intrauterine fetal death (IUFD). The caesarean section was done in 38(27.53%) cases for obstetric indication. Two (1.31%) maternal deaths were attributed by cytokine storm (one due to uremic encephalopathy and another due to acute kidney injury with HELLP syndrome). All 10 positive neonates were admitted in NICU and discharged successfully. Pregnancy outcomes were also compared with respective  $\Delta$ Ct values. Fisher's exact test showed no statistical significance between  $\Delta$ Ct values and pregnancy outcome.

**Conclusion:** SARS-Co-V-2 infection did not affect maternal and perinatal outcome. Vaginal delivery did not increase the risk of mother to child transmission of infection. Also, there is no correlation between  $\Delta$ Ct values and pregnancy outcome in COVID 19 positive mothers.

**Key words:** SARS CoV-2, COVID-19, RT-PCR, pregnancy outcome .

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### I. Introduction

The novel coronavirus is responsible for the coronavirus disease 2019 (COVID- 19) pandemic and thereby moving an unprecedented public health emergency all around the world <sup>1</sup>. In December 2019, a novel coronavirus (SARS-CoV-2) outbreak occurred in Wuhan (Hubei province, China). Since the first case of pneumonia was described, SARS- CoV-2 infection (coronavirus disease 2019 [COVID-19]) rapidly spread worldwide, being declared a pandemic infection on March 11 by the World Health Organization (WHO) <sup>2</sup>.

The effect of SARS- CoV- 2 infection in pregnant women admitted for delivery and their neonates is an area of research interest. Consequences of infection with SARS-CoV-2 for pregnancies are uncertain, with no evidence so far of severe outcomes for mothers and infants; however, the possibility should be considered. The recent experience with Zika virus suggests that when a new pathogen emerges, the health-care community should be prepared for the worst-case scenario. Therefore, recommendations for management of pregnant women at risk of SARS-CoV-2 infection are urgently needed <sup>3</sup>. Reports from the beginning of the COVID- 19 pandemic have characterized pregnant women as a vulnerable group in comparison to the general population for developing severe SARS- CoV- 2 infection with adverse maternal- perinatal outcomes as well <sup>4</sup>.

It is, however, unknown how COVID-19 infection behaves in key populations more commonly susceptible to viral diseases, such as pregnant women <sup>5</sup>, as well as whether there is the possibility of vertical transmission or premature birth.

The changes in the immune system of pregnant women make them more susceptible to infectious processes, in addition to the manifestations of the infection, with the risk of adverse maternal and neonatal complications, premature birth, spontaneous abortion, application of endotracheal intubation, restriction of

intrauterine growth, hospitalization in an intensive care unit, renal failure, intravascular coagulopathy, and transmission to the fetus or newborn <sup>6</sup>.

Being a novel disease, the clinical course was unknown initially, engendering various theories predicting the outcome. A consistent correlation was however found between high viral load of SARS-CoV-2 and poor prognosis <sup>7</sup>. The Cycle threshold ( $\Delta Ct$ ) values of the PCR reaction correlate inversely with the viral load; low Ct values indicate high viral loads and vice versa <sup>8</sup>.

The present study was undertaken with an objective of studying effect of SARS-CoV-2 on pregnancy outcome and its correlation with the  $\Delta Ct$  Value of RT-PCR.

## II. Materials And Methods

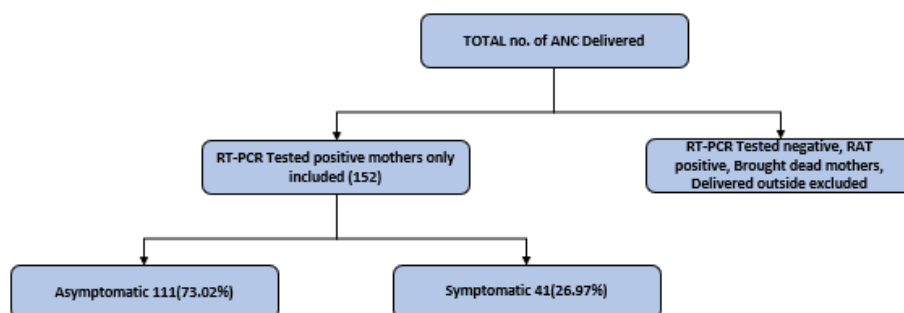
The present study is a Cross-sectional study where all RT-PCR positive pregnant women delivered in a tertiary care hospital were included. RT-PCR tested negative, COVID-19 positive mothers tested with RAT (Rapid Antigen Test), delivered outside and brought dead cases were excluded. These women were tested for the presence of SARS COV-2 RNA using Reverse Transcriptase Polymerase Chain Reaction (RT-PCR), in a period of nine months, from 1<sup>st</sup> April 2020 to 31<sup>st</sup> December 2020. The nasopharyngeal samples collected from such patients were transported in cold chain and triple-layer packaging to the Viral Research and Diagnostic Laboratory, Department of Microbiology with minimal delay. Ribonucleic Acid (RNA) Extraction was carried out by both the manual and automated technique with extraction control. The extracted RNA was subjected to RT-PCR, with the amplification of extraction control determining the validity of the reaction. Various kits approved for use by the (ICMR) Indian Council of Medical Research were used for RT-PCR according to the current government guidelines. The targets for amplification were E-gene or S-gene as a screening assay, and RdRp gene, ORF1b gene, or N-gene as a confirmatory assay, according to the kit used. The Cycle Threshold for positivity was determined as per the kit literatures. The  $\Delta Ct$  values of RT-PCR assay of all positive mothers were correlated with the outcomes.

Pregnancy outcome was noted in the form of gestational age at the time of delivery, mode of delivery, maternal mortality, abortion, IUFDs, neonatal morbidity and mortality. The data obtained were compiled using Microsoft Excel. Statistical test of significance, Fishers exact test was used to analyse the data.

## III. Results

The present study included a total of 10477 mothers delivered in Tertiary care hospital. Out of which, 152 (1.45%) mothers tested positive by RT-PCR, 111(73.02%) of pregnant women were asymptomatic and 41(26.97%) were symptomatic at the time of admission. Amongst 152 mothers tested positive by RT-PCR, 150 (98.68%) were discharged and 2(1.31%) died. The  $\Delta Ct$  values for the same were also evaluated. The babies born to these positive mothers were also screened by RT-PCR. Around 10 (0.09%) neonates were tested positive. All were full term normal weight asymptomatic neonates on breast feed. The babies were admitted in NICU for observation and eventually discharged.

**FIGURE 1:** Flow chart indicating the SARS- CoV- 2 symptoms among RT- PCR positive 152 pregnant women admitted for delivery



**Table 1:** Maternal outcome (Mode of Delivery) in correlation with  $\Delta Ct$  value

Mode of Delivery	Vaginal delivery (100)	LSCS (caesarean section (38)
$\Delta Ct$ value <25	40	10
$\Delta Ct$ value $\geq$ 25	60	28
n	100	38
P value	0.076	0.11

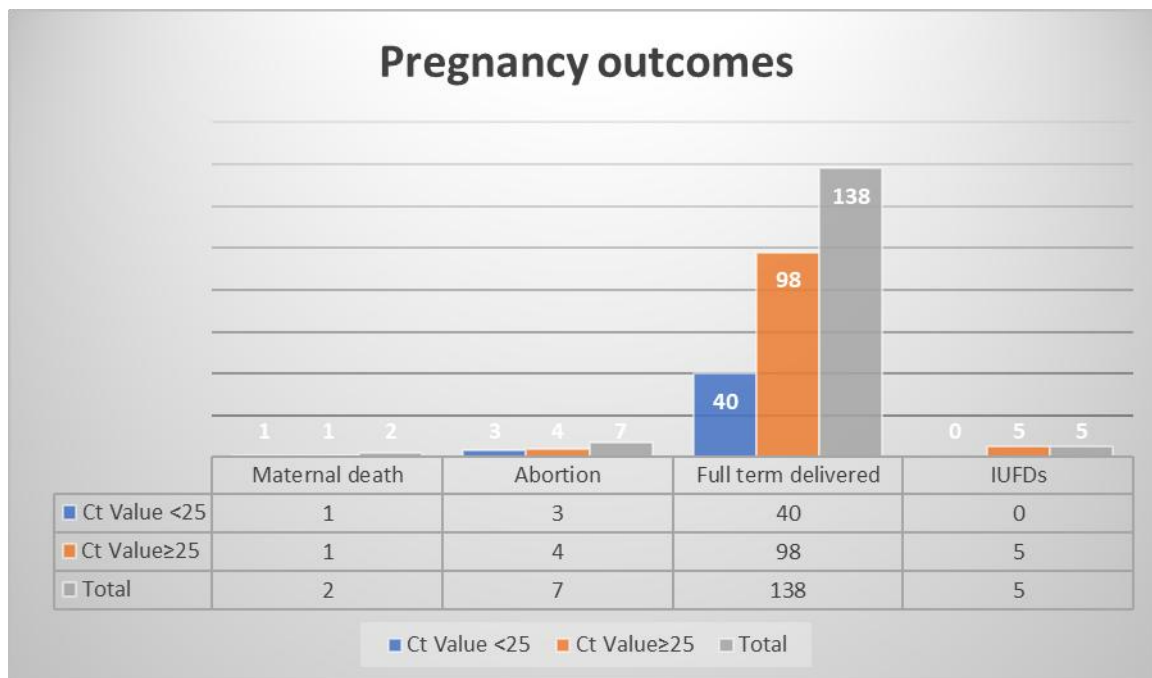
A total of 138 cases were delivered full term. Amongst these 100(72.46%) were delivered vaginally. Out of these 40 had  $\Delta Ct$  values  $<25$  and 60 had  $\Delta Ct$  value  $\geq 25$ . The rest of 38(27.53%) pregnant women were delivered by caesarean section with 10 showing  $\Delta Ct$  value  $<25$  and 28 having  $\Delta Ct$  value  $\geq 25$ . As  $p>0.05$  the correlation of  $\Delta Ct$  value on mode of delivery was statistically not significant. [Table 1]

**Table 2:** Correlation of  $\Delta Ct$  value with maternal outcome

Pregnancy Outcome	Maternal death	Abortion	IUFDs	Full Term Delivered
$\Delta Ct$ value $<25$	1	3	0	40
$\Delta Ct$ value $\geq 25$	1	4	5	98
<b>Total=152</b>	2	7	5	138
<b>P value</b>	0.49	0.327	0.176	0.62

Pregnancy outcome was compared with respective  $\Delta Ct$  values. A  $\Delta Ct$  value of  $<25$  was taken low for simplicity corresponding to high viral load<sup>7</sup> and  $\Delta Ct$  value  $\geq 25$  was taken high corresponding to low viral load. On comparing the  $\Delta Ct$  values with the pregnancy outcome, from total 152 deliveries maternal mortality was 2(1.31%) with 1(50%) showing  $\Delta Ct$  value  $<25$  and 1(50%) showing  $\Delta Ct$  value  $\geq 25$ . From these 7 (4.6%) were cases of abortion. The  $\Delta Ct$  value was  $<25$  in 3 (42.85%) cases and  $\geq 25$  in 4 (57.14%) cases. Five (3.28%) cases were IUFD. All of these had  $\Delta Ct$  values of  $\geq 25$ . A total of 138 cases were delivered full term. A  $\Delta Ct$  value of  $<25$  was observed in 40(28.98%) and  $\geq 25$  in 98(71.01%).

Fisher’s exact test was applied to see the association of  $\Delta Ct$  values on pregnancy outcome. In case of maternal death  $p=0.49$ , in abortion  $p=0.327$ , in IUFDs  $p=0.176$  and in full term delivered  $p=0.620$ . As  $p>0.05$  the correlation of  $\Delta Ct$  value on pregnancy outcome was statistically not significant. [Table 2]



#### IV. Discussion

The present study included a total of 10477 pregnant women delivered in a tertiary care hospital. All pregnant women were tested for SARS- CoV- 2 using RT- PCR. Amongst these, 152 mothers tested positive by RT-PCR. Out of these, 150 (98.68%) were discharged and 2(1.31%) died by cytokine storm [one due to uremic encephalopathy and another due to acute kidney injury with HELLP (Hemolysis, Elevated liver enzymes, low platelet count) syndrome]. The  $\Delta Ct$  values for the same were also evaluated. The babies born to these positive mother’s were also screened by RT-PCR. Around 10 (0.09%) neonates were tested positive. All were full term normal weight asymptomatic neonates on breast feed. The babies were admitted in NICU for observation and eventually discharged.

In our study, 111(73.02%) of total pregnant women who were tested positive by using RT-PCR were asymptomatic at the time of admission. Similar findings of asymptomatic pregnant women were found in the study carried out by Maru et al.<sup>9</sup> (72%) and Vintzileos et al.<sup>10</sup> (77%). In another study done by Gupta et al.<sup>1</sup> 90.6% of pregnant women were asymptomatic at the time of admission.

The present study showed a prevalence of 1.45% for SARS- CoV- 2. The findings were similar in a study carried out in Jammu Kashmir by Gupta<sup>1</sup> et al where the prevalence was 3.4%. However, the prevalence of SARS- CoV- 2 infection in a large diverse cohort of pregnant women was found to be 0.43% in Southern California.<sup>11</sup>

In the present study, 100(72.46%) cases infected with SARS -Co-V-2 had successful vaginal delivery and 38(27.53%) required caesarean section. In all the cases caesarean section was done for an obstetric indication. All the pregnancy outcomes were noted. Among these, there were 2 (1.31%) maternal deaths ,7 (4.6%) spontaneous abortions, 5 (3.28%) IUFDs and no neonatal deaths.

In a study conducted by Chen L et al<sup>12</sup> from China, 93% underwent a caesarean section. There were 3 spontaneous abortions, no maternal and neonatal deaths. In a study of corona virus disease in pregnant women at tertiary care hospital by Gadappa et al<sup>13</sup>, 11(29.72 %) required caesarean section. There was only one maternal death,3 abortions, 3 IUFDs and one neonatal death. The study by Gupta et al<sup>1</sup> showed, 21 (19.4%) cases underwent elective cesarean delivery. There were 2 (1.9%) neonatal deaths and 1(0.9%) maternal death.

A positive linear correlation between number of pre-existing co-morbid conditions in a COVID—19 positive patient and the outcome was found by Iravane et al. In another study by Shah S et al<sup>8</sup> there was no correlation between  $\Delta$ Ct values and severity of disease or mortality in patients with COVID 19 disease in general population. The present study showed negative correlation of  $\Delta$ Ct values on various pregnancy outcomes confirmed by Fisher's exact test. The test was not statistically significant ( $p>0.05$ ).

## V. Conclusion

SARS-Co-V2 infection did not affect maternal and perinatal outcome. Vaginal delivery did not increase the risk of mother to child transmission of infection.

Out of the various maternal and neonatal outcome analysed in our study there was no statistical significance between the  $\Delta$ Ct values of COVID positive mothers and their outcomes.

Though the result show that the outcome of pregnancy is not affected by  $\Delta$ Ct values, relentless monitoring is required for pregnant women who reports positive for COVID-19. Especially in developing countries like India, where there is difficulty in attending regular perinatal care. If we correlate the risk for babies there is no confirmation of vertical transmission though we cannot neglect this possibility.

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