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Original Research Article

A Study to Evaluate Transmission Potential of Covid 19 Infection from Mother to Neonate

Bharti Parihar[1], Jaya Patel[2], Deepti Chaurasia[3]

[1]Professor, Department of Obstetrics & Gynaecology, GMC Bhopal, MP, India

[2]Assistant Professor, Department of Obstetrics & Gynaecology, GMC Bhopal, MP, India

[3]Professor & Head Department of Microbiology, GMC Bhopal, MP, India

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Corresponding author: Dr Jaya Patel

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Abstract

Objective To see the potential of transmission of COVID 19 in amniotic fluid,breast milk & neonatal nasal swab from mother to neonate by comparing two modes of delivery.

Methods After taking written informed consent amniotic fluid samples from patients with COVID-19 infection was obtained via direct syringe aspiration during labour and neonatal throat swab samples was collected immediately after delivery & breast milk samples from mother were be collected within 3 hours of delivery. The presence of SARS-CoV-2 in these clinical samples were processed at the Virology Lab of Gandhi medical College Bhopal for evaluating the vertical transmission.

Results 58 patients were included in the study. Most of the patients were asymptomatic. Regarding delivery 46 patients underwent emergency LSCS, 2 had PTVD, 1 VBAC and 9 patients have Normal Vaginal Delivery. All samples of Breast milk and nasopharengeal swab of neonate were negative for COVID RTPCR. 2 samples of Amniotic fluid were found positive for COVID RTPCR.COVID 19 infection was observed in 2 out of 46 neonates delivered via LSCS and none following normal vaginal delivery.

Conclusion None of the neonate tested negative for COVID-19 after birth, so we suggest that vertical transmission is unlikely.But more study is need with the large sample size for future study.

Keywords: COVID-19, RTPCR, breast milk, Amniotic fluid, nasopharengeal swab

Introduction:

Severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) infection or novel coronavirus infection is a new emerging viral infection that leads to coronavirus disease was first reported in Wuhan, Hubei Province, China, in December, 2019, followed by an outbreak across Hubei Province and other parts of the country. [1,2]

The disease has since quickly spread worldwide, and has been declared a public

health emergency of international concern (PHEIC) by the World Health Organization (WHO) .As of June 05, 2020, WHO confirmed 6,535,354 cases of (SARS-COV-2) infections worldwide, and nearly 400,000 deaths were declared.In addition, airborne transmission of the virus from human to human is confirmed. In gynecology, the effect of COVID-19 during pregnancy needs further studies. As noted by Rasmussen et al the data regarding maternal outcomes with COVID-19 infections during pregnancy are limited. [3-6]

Pregnant women develop a special immunological adaptation, which is necessary for maintaining tolerance of the fetal semiallograft (Weetman, 2010). This state of transient suppressed immunity is modulated by suppressing T cell activity, and hence predisposes pregnant women to viral infections (Longman and Johnson, 2007; Pazos et al., 2012).In addition, the physiological changes occurring in the respiratory and circulatory systems might worsen clinical outcomes when infected with a virus during pregnancy (Rasmussen et al., 2020). [7]

The clinical characteristics and vertical transmission potential of COVID-19 pneumonia in pregnant women is unknown.Viral pneumonia is one of the leading causes of pregnancy deaths worldwide Multiple reports have been published recently on characteristics of patients with COVID-19 in the general population, but there is little information on pregnancy-related presenting symptoms and outcomes. However, to date, there are limited studies pertaining to the outcomes of COVID-19 during pregnancy, differences in clinical course, and the potential risks to the unborn child. Moreover, currently there has been no evidence of intrauterine vertical transmission of SARS-CoV-2 infection in pregnant women with COVID-19. The potential of vertical mother-to-child transmission of COVID-19 infection is also still unclear. We therefore analyzed current literature to identify any evidence of vertical transmission. Intra-uterine vertical transmission was defined as positive identification of SARS-CoV-2 in placenta, amniotic fluid, cord blood or neonatal pharyngeal/ throat swabs through reverse transcriptase polymerase chain reaction (RT-PCR) taken immediately after birth. [8-15]

The aim of the study is to see the rate of transmission of COVID 19 from mother to neonate and to assess the relative potential of transmission in amniotic fluid, breast milk & neonatal nasal swab and comparison of rate of transmission in normal vaginal delivery & caessarean section and also to evaluate the clinical characteristics of COVID-19 positive mother.

Materials and methods

Study Centre Single-centre study, conducted in the Department of Obstetrics and Gynaecology SZH, Gandhi Medical College Bhopal

Study Design Prospective Observational study

Duration of the Study This was a for a period of six months after clearance from Institutional Ethical Committee.

Inclusion Criteria All pregnant women who are positive for COVID 19 infection in labour were included in the study, covid-19 positive patient admitted within 3 hours of delivery .

Exclusion Criteria

- Clinical feature suggestive of covid-19 infection but whose laboratory results for RT-PCR come as covid-19 Negative
- Non-consent
- covid 19 positive patient admitted after 3 hours of delivery

Methodology Amniotic fluid samples from patients with COVID-19 pneumonia were obtained via direct syringe aspiration at the time of delivery. Neonatal throat swab samples were collected immediately after delivery in the Labour-room/Operation Theatre. Additionally, breastmilk samples from patients with COVID-19 pneumonia were collected within 3 hrs of delivery. Evidence of vertical transmission was evaluated by testing for the presence of SARS-CoV-2 in these clinical samples. All samples were processed at the Virology Lab of Gandhi medical College Bhopal.

Consent: Written consent was obtained from the relatives of patients after explaining them the nature and purpose of the study. They were assured that confidentiality would be strictly maintained. The option to withdraw from the study was always open.

Observation Chart

Table 1: Demographic Profile

1. AGE	**18-20 YRS**	**21-30 YRS**	**31-40 YRS**	**>40 YRS**	**TOTAL**
	4	44	9	1	58
2. GRAVIDA	**PRIMIGRAVIDA**	**MULTIPARA**	**TOTAL**		
	21	37	58		
3. GESTATIONAL AGE	**<37 weeks**	**37-40 weeks**	**>40 weeks**		**TOTAL**
	12	39	07		58
4. SYMPTOMA-TOLOGY	**FEVER**	**COUGH**	**ASYMPTOMATIC**		**TOTAL**
	3	2	53		58

Table 2: Associated Obstetric Complications

S.NO	COMPLICATIONS	NO.OF PATIENT
1	Severe Preeclampsia	4
2	Gestational HTN	2
3	Chronic HTN	1
4	GDM	2
5	Hypothyroidism	1
6	LRTI	2
7	Anaemia A. Moderate anaemia B. Severe anaemia	 1 1
8	Transverse Lie	4
9	Severe IUGR	4
10	Oligohydramnios	1
11	Twin pregnancy	2
12	Rubella IgG positive	1
13	IUFD	2
	TOTAL	28

Table 3: Mode Of Delivery

LSCS	PTVD	VBAC	FTND	TOTAL
46	2	1	9	58

Table 4: Indication of Lscs

S.NO	INDICATION	NO OF PATIENT
1	Fetal Distress	24
2	Transverse lie	4
3	Cephalopelvic Disproportion	4
4	Scar Tenderness	6
5	Previous 2 LSCS in labour	2
6	Non-progress of Labour	3
7	Severe oligohydramnios	1
8	Contracted pelvis	1
9	Not giving consent for VBAC	1
	TOTAL	46

Table 5: Relative Potential of Transmission in Amniotic Fluid, Breast Milk & Neonatal Nasal Swab

SAMPLE	AMNIOTIC FLUID	BREAST MILK	NEONATAL SWAB
Positive for Covid-19	2	0	0
Negative for Covid-19	56	58	58

Table 6: Comparison of Transmission in Neonates Delivered Via Normal Vaginal Route And Cesarean Section

SAMPLE	LSCS	NVD
Positive for Covid-19	2	0
Negative for Covid-19	44	12
P value	0.96	

Results

There were 58 patients included in the study. All were in third trimester on admission, the earliest presenting at 29 weeks 3 days and all had a known source to COVID 19.Most of the patients were asymptomatic & found positive during routine screening in antenatal clinics. Out of 58 only 3 patients had complaint of fever and 2 had cough on admission. All patients were given oxygen support and empirical antibiotic treatment. 37 patients were multigravida & 21 were Primigravida. Mean age of the females was 26.7±4.5 years. Out of 58 women 39 patients was full term pregnancy (POG 37-40 weeks). 28 patients had baseline comorbidities (Table no 2). Regarding delivery 46 patients underwent emergency LSCS, 2 had PTVD, 1 VBAC and 9 patients have Normal Vaginal Delivery. (Table no 3).Most common indication of emergency LSCS was Fetal distress that was found in 24 patents. All samples of Breast milk and nasopharengeal swab of neonate were negative for COVID RTPCR. 2 samples of Amniotic fluid were found positive for COVID RTPCR. Almost all the patients had uneventful intrapartum & post-partum period, only 2 had intrauterine fetal demise, rest of the babies were discharged from the hospital in satisfactory condition along with their mothers. COVID 19 infection was observed in 2 out of 46 neonates delivered via LSCS and none following normal vaginal delivery, but the observed association of transmission with mode of

delivery was statistically insignificant ($p>0.05$).

Statistical analysis:

The collected data was summarized by using frequency, percentage, mean & S.D. To compare the qualitative outcome measures Chi-square test or Fisher's exact test was used. To compare the quantitative outcome measures Independent t test was used. If data was not following normal distribution, Mann Whitney U test was used. SPSS version 22 software was used to analyse the collected data. p value of <0.05 was considered to be statistically significant.

Discussion

Viral pneumonia is one of the leading causes of pregnancy deaths worldwide World Health Organisation (WHO) has reported that there is no apparent difference in the risk of developing clinical symptoms between non-pregnant and pregnant women of reproductive age .Pregnant women undergo physiological changes, which lead to altered immune systems Studies had reported that pregnant women were at a higher risk of infection with H1N1 influenza and SARS-CoV, and were also associated with poorer clinical outcomes in comparison with reproductive-aged non-pregnant women [18-20]

However, in our study, we found no association between pregnancy and poor clinical outcomes (including severity of disease). Similar results were also reported in study done by Chen et al & Xu Qiancheng et al.Patients most commonly present with mild symptoms of the infection including fever, cough, fatigue, and shortness of breath; however, some may be asymptomatic According to our study, pregnant women with COVID-19 pneumonia showed a similar pattern of clinical characteristics to non-pregnant adult patients, as recently reported. [2,7,8,30]

In this study out of 58 pregnant women 46 underwent caesarean section,9 had Full term vaginal delivery,2 had Preterm vaginal delivery & 1 patient had VBAC.Premature birth were not related to COVID-19 pneumonia. Most common indication for caesarean section was Fetal distress , Scar tenderness , cephalopelvic disproportion & transverse lie. None of the 58 patients & newborn babies developed severe pneumonia or died only 2 babies were IUFD at the time of admission. In the study done by Chen H showed that all nine pregnant women underwent a caesarean section. The indications for a caesarean included a history of caesarean sections, severe pre-eclampsia and fetal distress. Four of the nine patients had preterm labour. One neonate had a mild illness. None of the neonates needed special paediatric treatment. [2] In the study of Lei et al & Fen et al all patients were undervent caesarean section but Xiong et al studied one patient that undervent vaginal delivery. [13,25,31]

In our study all patients were in the third trimester on admission.28 patients had comorbidities including hypertension , GDM, hypothyroidism ,LRTI & anaemia.In the study of Arentz M et al nine patients included in the analysis. All patients were in the third trimester ,and all had a known source of exposure to COVID-19.None of the patients had baseline comorbidities, but one patient had gestational hypertension and another developed pre-eclampsia. [32]

In the current COVID-19 outbreak, pregnant women seemingly have had fewer maternal and neonatal adverse events than were reported for SARS and MERS (Qiao, 2020), but whether pregnant women have a comparable clinical course and outcome with non-pregnant women is still unclear. [33] In our study 2 samples of Amniotic fluid found positive in COVID RT-PCR test. None of the samples of Breast milk & Nasopharyngeal swab of neonate was tested

positive for SARS-CoV-2. In the studies done by Lei et al , Chen et al., Fan et a., Xiong et al tested amniotic fluid & neonatal naso-pharyngeal swabs, Breast milk and all were tested negative for SARS-CoV-. A recent review assessed 38 pregnant women and their newborns in China, and no evidence for vertical transmission was identified. In the first study investigating the possibility of intrauterine vertical transmission of covid 19 in 9 pregnant women with mild to moderate manifestation of laboratory confirmed covid 19 in third trimester , matched amniotic fluid , cord blood and neonatal pharyngeal swab samples from 6 neonates were tested for SARS-Co V-2, using quantitative reverse transcriptase polymerase chain reaction (qRT-PCR). All samples tested negative ,suggesting that intrauterine fetal infection did not occur during the third trimester of pregnancy. [30-35]]

Utilizing similar methodology, Lei et al. demonstrated no evidence of vertical transmission in 4 pregnant women with covid 19 infection in the third trimester , and vaginal secretion samples also tested negative for SARS-Co V-2 RNA. In the study by Chen et al, paired placental tissues from 3 pregnant females with confirmed covid 19 in the third trimester and neonatal pharyngeal swab samples were used to evaluate the potential risk of intrauterine vertical transmission and all samples tested negative for SARS-Co V-2RNA. Notably, a neonate born to a pregnant woman with covid 19 tested positive for SARS-CoV-2 RNA in the pharyngeal swab sample obtained 36 hours after birth , but it was subsequently confirmed that qRT-PCR testing of the placental and cord blood sample was negative for SARS-CoV-2/ suggesting that intrauterine vertical transmission might not have occured. Thus, based on existing data, there is currently no evidence of intrauterine infection caused by vertical transmission in women with COVID 19 in later third trimester. [13,25,26,33]

Most recently , two studies explored the possibility of vertical transmission of SARS-Co V-2 in a combined total of seven affected pregnancies ,by testing for SARS-Co V-2 specific antibodies (IgG & IgM) in neonatal serum samples using recently developed automated chemiluminescence immunoassays. Based on the detection of anti-SARS-Co V-2 IgM antibodies in blood samples obtained following birth from three neonates , the two studies concluded that SARS-Co V-2 could be transmitted in utero. However , in all three neonates , pharyngeal swab samples were negative for SARS-Co V-2RNA and testing of cord blood and placental samples was not performed thus there was no direct evidence of infection .Of note , the sensitivity and specificity of the immunoassay used in the two studies have not been evaluated extensively.(Furthermore ,it is well known that IgM assay are more prone to false-positive results. [36-38]

In a cohort study by Zeng et al , three of 33 (9%) infants were diagnosed with neonatal early -onset infection with SARS-Co V-2 based on positive qRT-PCR result in two consecutive nasopharyngeal and anal swab samples obtained on day 2 and day 4 of age. Though strict infection control and prevention measures were implemented during delivery, the possibility of postpartum neonatal infection can not be completely excluded because of the delay in testing. All 3 infants tested negative for SARS-Co-V-2 RNA on day 6 (n=20 or 7 (n=1) of age.Whether neonatal SARS-Co V-2 infection has the same virological profile as that of adult infection requires further investigation.According to the Royal College of Obstetricians and Gynaecologists (RCOG), vertical transmission from the woman to her baby may be possible, as suggested by new evidence . A few

emerging studies have reported the probability of in utero COVID-19 transmission by measuring the foetal IgM blood level.High quality research is needed to elucidate whether SARS-CoV-2 ican be transmitted in utero from mother to the fetus. [17,39]

First , we propose that cohort studies evaluating risk of fetal adverse outcome , including structural malformation , miscarriage and fetal growth restriction , in pregnant females with COVID-19 contracted during the first or second trimester are essential in investigating whether vertical transmission of SARS-CoV-2 can occur. Second, collection of appropriately matched biological samples immediately after delivery,using aseptic technique, from pregnant women with COVID-19 is important to help determine whether SARA CoV-2 can be transmitted vertically. [35-40]

Conclusion

There is currently no concrete evidence of intrauterine vertical transmission of SARS CoV-2, but further high quality research is needed. Virological and serological evidence is valuable to clarify this issue, however, the study design should be used, and longitudinal follow up of infants for 6-18 months after birth is essential to draw reliable conclusions when serological results are used.

Declarations:

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Availability of data and material: Department of Obstetrics and Gynaecology SZH, Gandhi Medical College Bhopal

Code availability: Not applicable

Consent to participate: Consent taken

Ethical Consideration: There are no ethical conflicts related to this study.

Consent for publication: Consent taken

Contribution by different authors

First author Dr Bharti Parihar Professor Department of Obstetrics & Gynaecology, GMC Bhopal ,MP, India Concept and Guidance

Second and Corresponding author Dr Jaya Patel Assistant Professor Department of Obstetrics & Gynaecology, GMC Bhopal, MP, India E-mail sunshinejaya@gmail.com Data collection and statistical analysis

Third author Dr Deepti Chaurasia Professor & Head Department of Microbiology, GMC Bhopal,MP,India References and Discussion

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