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Research Paper

A spectrum of pathological changes induced by SARS-COV-2: An observational study in a cohort of pregnant women from Mizoram, India

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ABSTRACT

Background: Maternal infection by SARS-CoV-2 may lead to adverse pregnancy outcomes and causes pathological changes in the placenta. However, consensus regarding characteristic pathological features is lacking. Researchof the placental histopathology in a cohort of women from Mizoram, India, was conducted to relate the SARS-CoV-2 infection's effectswith pregnancy and its outcome.

Materials and methods: The characteristics of 72 pregnant women diagnosed positive for SARS-CoV-2 who eventually delivered at Zoram Medical College Hospital, Mizoram, neonates' well-being, and histopathological features of placentas were studied.

Results: Of 72 women in this study, 59 (81.9%) gave birth at full term. Among these births, 5 were normal vaginal deliveries, while the remaining 67 (93.1%) were delivered via cesarean section. The reasons for cesarean delivery were either related to SARS-CoV-2 infection (n = 49), existing obstetric problems (n = 15) or fetal-distress (n = 5). All deliveries resulted in live births of COVID-negative babies, with 80.6% (n = 58) of the newborns having a birth weight of over 2.5 kg. APGAR scores ranged from 4 to 6 in 61 (84.7%) of the babies, and 10 neonates required resuscitation, of which 8 were managed in the neonatal intensive care unit (NICU). The placental histopathology showed increased fibrin thrombi in 8 cases (11.1%), while 20 cases (28%) showed focal infarction, microcalcification levels were elevated in 16 cases (22.2%), and a small percentage of cases (1.4%) exhibited small fibrotic villi and inter-villus agglutination. Placental chorioangiosis was detected in 28 (38.9%) of the cases, while avascular villi were seen in 6 cases. Meconium-stained liquor was observed in a single case. Intervillous hemorrhage was found in 42 cases, whileintervillous inflammation and increased syncytial knots were present in 14 and 5 cases, respectively. The placenta pathology of 10 neonates who required resuscitation/NICU admission was not significantly different from that of the 62 neonates who did not require it. However, a higher proportion of placenta from the asymptomatic group showed no abnormality compared to the symptomatic group (p = 0.046).

Conclusion: SARS-CoV-2 infection causes a range of morphological changes and lesions in the placenta, including chorangiosis, villositis, chorioamnionitis, fetal vascular malperfusion/thrombosis, fibrin-deposition, increased syncytial-knotting, increased microcalcification, increased villous agglutination, focal infarct, intervillous-hemorrhage as well as inflammation. Placental histopathological findings from this study can provide additional information to the existing literature on the subject.

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1. Introduction

The clinical features of SARS-COV-2/COVID-19 are varied, ranging from asymptomatic state to acute respiratory distress syndrome and multi organ dysfunction. The symptoms are usually fever, cough, sore throat, breathlessness, fatigue, malaise among others. The disease is mild in most people; in some (usually the elderly and those with comorbidities), it may progress to pneumonia, acute respiratory distress syndrome (ARDS) and multi organ dysfunction. Many people are asymptomatic[1]. Data from various studies suggested that besides causing obvious respiratory illnesses, the virus also manifests its clinical effect on extrapulmonary multisystem organs. The infection induces pharyngitis, myalgias, cytokine storm, thrombotic events, acute respiratory distress syndrome, endothelial damage, pneumonia, and diarrhea, among others[2,3]. Placentas are particularly vulnerable to the SARS-CoV-2 virus as it binds to the angiotensin-converting enzyme 2 (ACE-2), a functional receptor present in abundance on the cell surface of the placenta, particularly the syncytiotrophoblast layer. Pregnant women undergo significant immunological and hormonal changes that increase their-vulnerability to viral infections, such as SARS-CoV-2[4,5].

Furthermore, a hostile maternal environment, characterized by factors such as inflammation, hypoxia, and increased risk of blood clots resulting from a SARS-CoV-2 infection, can also make the placenta highly susceptible to pathological damage. This can ultimately result in negative outcomes for the pregnancy.[6,7] Nonetheless, placental infections have not always been associated with maternal infections, and even evidence of viral infection in the placenta does not warrant intrauterine vertical transmission to the fetus. Noteworthy, despite the placentas testing positive for SARS-CoV-2, very few neonates were found to be infected. By and large, the defensive mechanism of the placenta against viral infection, restricting infection of newborn infants, remains unsolved. However, reports have marked the implications of maternal SARS-CoV-2 infections in adverse pregnancy outcomes[8].

Several studies have examined the impact of SARS-CoV-2 infection during pregnancy on placental histopathology, revealing that a significant number of placentas showed signs of placental hypoperfusion and inflammation. However, consensus regarding characteristic pathological features is yet lacking. This may partly be due to the fact that there are limited studies reporting changes in placental histomorphology and ultrastructure of women infected with SARS-CoV-2. Furthermore, the severity of the infection and the resulting mortality rates have been found to vary among different ethnic groups.[9,10]

Thus, we aim to investigate the relationship between SARS-CoV-2 infection and placental histopathological changes in a cohort of ethnic Mizo women from Mizoram, India. We will also analyze the impact of the infection on pregnancy and fetal outcomes.

2. Material and method

This randomized study was carried out at the hospital attached to Zoram Medical College, Mizoram, anortheastern state of India. The state of Mizoram selected this multi-facility hospital as a dedicated hospital where suspected SARS-CoV-2 cases from all over the state were referred to during the SARS-CoV-2 pandemic.

2.1. Study participants

The study participants included pregnant Mizo women referred to the Zoram Medical College Hospital (ZMCH) and subsequently delivered at the hospital between April and June 2021. All the cases/subjects were COVID-positive pregnant patients who went into delivery during the study period in Zoram Medical College, Mizoram and were collected by purposive sampling. After being admitted, the study recruited patients only after obtaining the patients' or their spouses' consent. Thereverse transcription-polymerase chain reaction (RT-PCR) test confirmed their SARS-CoV-2-positive status at the time of admission. The characteristics of these women were followed till delivery, and fetal outcome and neonate's wellness were also noted. After acquiring informed consent from all participants, approval for the study was obtained from the ZMCH Ethics Committee.

2.2. Study of placental morphology

As a precaution, all placentas were stored at 4 °C for 48 h to reduce infectivity, if any. They were suitably numbered, and 10% buffered formalin was used for fixation. Sections were extracted from each placenta to evaluate the maternal and fetal surfaces, umbilical cord, full-thickness membranes, and all apparent macroscopic lesions. The sections were processed following a standard protocol and later stained with eosin and hematoxylin. The Amsterdam Consensus Criteria was used to interpret the histopathological findings[11]. After examining the histological lesions, a histopathologist classified them as either due to maternal vascular under perfusion or fetal vascular under perfusion.

2.3. Study of neonates

As per the hospital protocol, all neonates born at the hospital during the period were tested for SARS-CoV-2 infection after 48 h of birth using PCR of nasopharyngeal swabs.

2.4. Statistical analysis

A spreadsheet computer program (Microsoft Excel 2010) was used to enter and compile the recorded data, which was then exported to the data editor page of IBM SPSS version 22.0 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics were calculated. Bivariate associationswere determined through Fisher's exact and Chi-square tests. The p-value wasset at ≤ 0.05 for all tests.

3. Results

The study participants comprised 72 pregnant women (mean age 28.92 ± 6.48 years) who were suspected SARS-CoV-2 positive. They were referred from peripheral health centers/hospitals, with a majority of them belonging to the age group 20-30 years(Table 1). RT-PCR tests conducted during admissions to ZMCH ensured all the study participants were diagnosed as SARS-CoV-2-positive. Except for one, all were married and healthy. Among these women, 28 (38.6%) were primigravida, and 37 (51.4%) had 1-3 children. Despite being SARS-CoV-2 positive, the majority (n = 59; 81.9%) of them delivered at term; however, only 5 had a normal vaginal delivery. Because of SARS-CoV-2-related issues, 49 had a cesarean delivery, whereas pre-existing obstetric complications required the administration of cesarean sections in 15 patients. Fetal distress was observed in 5 cases, and hence cesarean sectioning was carried out in these cases as well. All deliveries resulted in births of singleton live babies (male = 44, female = 28), with 80.6% (n = 58) with more than 2.5 kg birth weight and 61 having APGAR scores ranging between 4 and 6. Most neonates did well, and only 10 required resuscitations, of which 8 were later admitted to the neonatal intensive care unit (NICU).

Most women presented with the typical symptoms of SARS-CoV-2, with the most routine symptoms being fever and cough **(Table 2)**. Hemoglobin levels and total leucocytecounts were normal in most women at the time of admission to the ZMCH. In less than 10% of women, liver function tests and kidney function tests were deranged. Contrast Enhanced Computerized Tomography of the chest was warranted in 9 women and only 6 of these showed moderate to severe changes.

Out of the 72 participants, 45 had clear SARS-CoV-2 symptoms, whereas the remaining 27 were asymptomatic. We compared the placental pathology between symptomatic and asymptomatic participants **(Table 3)**. The frequencies of occurrence of placental pathologies amongst participants without and with SARS-CoV-2 symptoms did not

Table 1
Characteristics of mothers admitted to the hospital and their neonatesn (%).

Mothers	
Maternal age (years)	
<20	6 (8.3)
20–30	34 (47.2)
31–40	29 (40.3)
>40	3 (4.2)
Marital status	
Unmarried	1 (1.4)
Married	71 (98.6)
Parity	
Primigravida	28 (38.9)
Multigravida (1–3 children)	37 (51.4)
Grand multigravida (≥4 children)	7 (9.7)
Gestation period at delivery	
Term	59 (81.9)
Pre-term	13 (18.1)
Abortion/Hysterectomy	0
Mode of delivery	
Normal vaginal	5 (6.9)
Cesarean	67 (93.1)
Indication of Cesarean delivery	
COVID related	49 (73.1)
Obstetric complication	15 (22.4)
Fetal distress	3 (4.5)
Neonate	
Fetaloutcome	
Live Born	72 (100.0)
Still Born/Abortion	0
Birth weight	
<1 kg	1 (1.4)
1–1.5 kg	1 (1.4)
1.6–2.5 kg	12 (16.7)
>2.5 kg	58 (80.6)
APGAR Score (done at 5 min)	
0–3	11 (15.3)
4–6	61 (84.7)
>7	0
Resuscitation	
Not needed	62 (86.1)
Needed	10 (13.9)
ICU admission	8 (out of the above 10)

Table 2
Symptoms and results of clinical parameters of mothers.

Variables			Subjects (%)
Symptoms	Fever		35 (48.0)
	Cough		35 (48.6)
	Myalgia		9 (12.5)
	Sore Throat		8 (11.1)
	Ansonia		12 (16.7)
	Breath Shortening		13 (18.1)
	Other		8 (11.1)
Biochemical Parameters	Hemoglobulin	Normal	50 (69.4)
		Mild	15 (20.8)
		Low	4 (5.6)
		Severe	3 (4.2)
	Total Leucocyte	Normal	59 (81.9)
	Count	Increased	12 (16.7)
		Decreased	1 (1.4)
	Liver Function	Normal	67 (93.1)
	Test	Deranged	5 (6.9)
	Kidney Function	Normal	67 (93.1)
	Test	Deranged	5 (6.9)
	Coagulation profile	Normal	72 (100.0)
Biophysical Parameter	Contrast Enhanced	Not done	63 (87.5)
	Computerized	Normal	1 (1.4)
	Tomography of chest	Mild	2 (2.8)
		Moderate	5 (6.9)
		Severe	1 (1.4)

differ. However, in the asymptomatic group, a significantly higher proportion of placentas showed no abnormality than in the symptomatic group ($p = 0.046$).

Table 3
Comparative assessment of placental pathology with COVID status of mothern (%).

Placental Pathology	COVID -19 status		*P* value
	Symptomatic	Asymptomatic	
	n = 45	n = 27	
Increase fibrin thrombi	3 (6.7)	5 (18.5)	0.413
Focal infarct	16 (35.6)	4 (14.8)	0.064
Increase microcalcification	12 (26.7)	4 (14.8)	0.38
Small fibrotic villi	1 (2.2)	0	1
Inter villus agglutination	1 (2.2)	0	1
Placental chorangiosis	20 (44.4)	8 (29.6)	0.175
Others	1 (2.2)	1 (3.7)	
No histopathological abnormalities	4 (8.9)	8 (29.6)	0.046
Meconium stain	1 (2.2)	0	0.435
Avascular villi	5 (11.1)	1 (3.7)	0.399
Intervillous hemorrhage	29 (64.4)	13 (48.1)	0.711
Intervillous inflammation	12 (26.7)	2 (7.4)	0.65
Syncytial knotting increased	3 (6.7)	2 (7.4)	1

In placental vascular pathology, increased fibrin thrombi generation is known to be associated with obstetrical syndromes. In our study, we observed increased fibrin thrombi in only 8 out of 72 cases. The focal infarction was seen in 20 cases (28.0%), which is considered to be normal, as a minor infraction is observed in 25% of normal pregnancies and rarely affects pregnancy. Increased microcalcification was observed in 22% of the cases, whereas smallfibrotic villi and Inter villus agglutination were seen in 1.4% of the cases. These observations indicate that placental pathology was minimally affected despite infection by SARS-CoV-2. Placental chorioangiosis was detected in a relatively high number of cases (n = 28; 38.9%) though there was no obvious cause of maternal hypoxia. Histopathological abnormality was absent in 12 cases. Meconium-stained liquor was reported in only a single case reflecting thatfetal distress was almost negligible in babies born in the study. Avascular villi generally indicate thrombosis of fetal vessels, and in the current study, it was present only in 6 cases. Intervillous hemorrhage was observed in 42 cases. Fourteen cases were presented with Intervillous inflammation. In this study, maternal vascular mal-perfusion, for example, increased syncytial knots were surprisingly seen in 5 cases only. Fig. 1(A-E) Shows the pathological changes in placenta of SARS-CoV-2 positive pregnant women in Mizoram.

In this study, 10 out of 62 born neonates required resuscitation, and 8 required admission to the NICU. The placenta pathology of these 10 did not differ from the 62 neonates that did not require resuscitation(**Table 4**). In the case of these 10 neonates, delivery was pre-term.

4. Discussion

This is the first study carried out on an ethnic group from Mizoram, a northeast state of India, relating placenta pathology with the outcome of pregnancies in a cohort of pregnant Mizo women diagnosed as SARS-CoV-2-positive. Invaluable information for enhancing disease pathogenesis concepts and identifying underlying causes of adverse pregnancy outcomes can be extracted from placental examinations. Of the 72 pregnant women who were referred to ZMCH, nearly 40% were asymptomatic. This is in agreement with two systematic reviews and meta-analyses by Ma et al., 2021 (asymptomatic = 40.5%) and Villar *et at*, 2021 (asymptomatic = 44%) showed that around 2/5th of the individuals confirmed positive for SARS-CoV-2 were asymptomatic[12,13]. Asymptomatic infections play a significant role in spreading SARS-CoV-2 within the community with the gradual return of public life. However, the exact reason for an individual to be asymptotic is unknown; a combination of genetic factors, age, the virus' virulence, and the subject's susceptibility may be involved.[14]

The relationship between SARS-CoV-2 and its afflictions on the developing fetus during pregnancy is yet not fully established. These

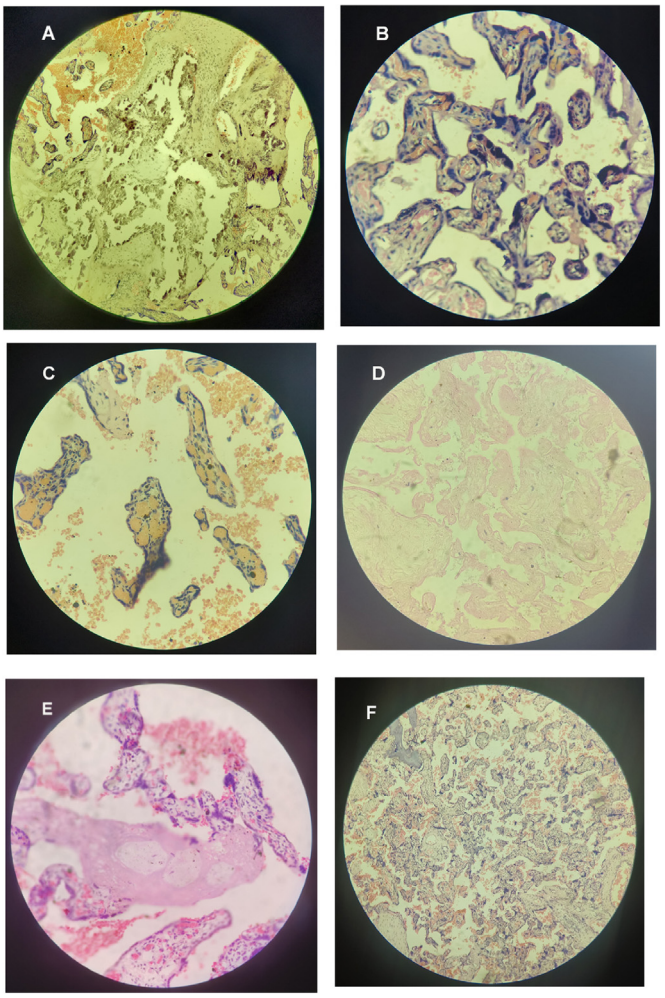

Fig. 1. Pathological changes in placenta of SARS-CoV-2 positive pregnant women in Mizoram. A. Chorionic villi with area of calcification (× 100); B. Term placenta with chorangiosis (× 400); C. Villous stromal hemorrhage (× 100); D. Groups of villi with ischemic necrosis (× 100); E. Groups of villi surrounding an avascular villi (× 400); F. Increased syncytial knots (× 100).

complications may include stillbirth, pre-term birth, or prolonged complications for the newborn. Adverse pregnancy and neonatal outcomes of a study conducted on 827 pregnant women vaccinated with the SARS-CoV-2 mRNA vaccine were comparable to those reported in similar studies conducted before the pandemic[15]. Moreover, it is postulated that the SARS-CoV-2 infection triggers a "cytokine storm," amplifying the mother's immune system through an uninhibited inflammatory cytokine release and causing increased incidences of pre-term labor, fetal growth restriction, placental damage, and abortion[16,17]. In our study, 18% of women delivered pre-term. Two studies from northern states of India reported pre-term deliveries in 52%[18] and 15.5%[19] of women diagnosed as SARS-CoV-2-positive. In 2021, Son et al., working on a US-based extensive population data, could not determine any association between adverse pregnancy outcomesand SARS-CoV-2 infection of the mother, including pre-term birth or Cesarean birth, or postpartum hemorrhage[20]. In contrast, Jering *et al.*observed a clear link between SARS-COV-2 deliveries and most of the above-mentioned outcomes[21]. Metz et al. commented that both of these studies have no mention of the risk severity of SARS-CoV-2 in their studies[18,22].

In this study, 93.1% of women had Cesarean deliveries either due to SARS-CoV-2-related issues or pre-existing obstetrics complications, or fetal distress. In Indian studies, it ranges from 64.7% to 77% against the national average of 21.5% reported by the National Family Health Survey[13,18]. Data from a group of 68 infected women who delivered from December 2019 to March 2020 in China also showed a cesarean section rate of 93%, confirming the increased caesarean section rate among infected pregnant women who delivered in the first wave of SARS-CoV-2 pandemic[23]. Notably, most studies do not present evidence of a SARS-CoV-2 infection in neonatal throat swabs, amniotic fluid, umbilical cord, or breast milk samples. This is linked to the fact that an immunological barrier is present in the human placenta to block the entry of pathogens and maintain fetal cell immune tolerance. The innate immune system has been proposed to be crucial in protecting fetuses and neonates against SARS-CoV-2 infection[24]. The various immune cells of the innate immune system present in the maternofetal interface, including decidual macrophages, natural killer cells, and CD4 T cells, all act as barriers to transmission[25]. Also, the outermost chorionic villilayer comprising syncytiotrophoblast cells and in direct contact with the maternal blood, lack intercellular gap junctions and thus effectively prevents pathogen entry from the bloodstream.

Collectively, the structural barrier, innate immune system, and interactions of the invading fetal extravillous trophoblasts and the decidual immune cells play a significant role in the protective mechanisms of the placenta against SARS-CoV-2 viral invasion[25]. However, a multinational cohort study observed that the cesarean delivery mode/in SARS-CoV-2-positive mothers was associated with increased risk for neonatal test positivity (RR, 2.15; 95% CI, 1.18–3.91)[26]. Chorionic villi contain fetal blood vessels (BVs) and continuously form branching villi throughout gestation. Exchange between maternal blood and the fetal compartment occurs across the villus surface via syncytiotrophoblasts (STBs) a multinucleate syncytium for exchange of key substances and a physical barrier to the entry of pathogens. Maternal viremia and infection of cells in the basal decidua therefore expose STBs to virions in blood and released locally into the intervillous blood. In addition, infection in the parietal decidua could spread to the chorionic membrane adjacent to the amniotic membrane[27].

All deliveries resulted in the birth of singleton live babies. In two studies from India, >97% of cases resulted in the birth of live babies[19,26]. In this study,80.6% had more than 2.5 kg birth weight, and most of the neonates showed APGAR (at 5 min), with scores ranging between 4 and 6. Based on 246 articles, Chao M*et al.* concluded that the status of maternal SARS-CoV-2 positivity is related to an APGAR score of less than 7 in neonates[25]. However, in this study, most neonates did well, and only 10 required resuscitations, of which 8 (11.1%) were later admitted to the NICU, which is comparable to other studies from India[19,26,28].

Fever and cough were the most typical symptoms in patients enrolled in our study. This is consistent with other studies[8,26,29]. Hemoglobin (Hb) level and Total leucocyte count (TLC) were normal in most women in our study. However, in a retrospective cohort study, Hb levels were shown to be significantly lower and TLC significantly higher in pregnant women diagnosed as SARS-CoV-2-positive than in pregnant women who tested negative for SARS-CoV-2[30].

Pregnancy-specific disorders are the primary cause of abnormal results in liver function tests during pregnancy. The prevalence of liver injury in pregnant women diagnosed as SARS-CoV-2-positive was reported to be high[31,32]. In contrast, we found liver function tests deranged in only 6.9% (n = 5) of the study population (the placental pathology associated with the deranged liver is given in Supplementary Table 1.)

The coronavirus potentially damages kidney tissues by infecting kidney cells with receptors enabling the virus to attach, invade, and make copies of itself. According to an update released on corona in May 2022 by Dr. Seprati CJ, Director of the Nephrology Fellowship Training Program, John Hopkins Medicine stated that besides the virusinvading kidney cells and causing damage directly, virus-induced hypoxia, cytokine storm, and blood clots might damage the kidney as well[33]. He further added many studies indicate that >30% of patients hospitalized with SARS-CoV-2 infection develop kidney injury, and >50% of patients in the intensive care unit with kidney injury require dialysis. Thankfully,

Table 4
Comparison of placental pathology in cases where neonates required admission to NICU with neonates who did not require NICU admission.

Placental pathology	None-NICU		NICU		*P* Value
	N = 62		N = 10		
	n	%	n	%	
Increased fibrin thrombi	8	12.9	0	0	–
Focal infarct	19	30.6	1	10.0	0.278
Increasedmicrocalcification	14	22.6	2	20.0	0.883
Small fibrotic villi	0	0	1	10.0	–
Inter villus agglutination	0	0	1	10.0	–
Placental chorangiosis	23	37.1	5	50.0	0.617
Others	1	1.61	1	10.0	0.156
No histopathological abnormalities	11	17.7	1	10.0	0.597
Meconium stain	1	1.6	0	0	–
Avascular villi	4	6.5	2	20.0	0.204
Intervillous hemorrhage	36	58.1	6	60.0	0.950
Intervillous inflammation	11	17.7	3	30.0	0.471
Syncytial knotting increased	3	4.8	2	20.0	0.120

in the study, only 2.7% of women had deranged kidney function tests (the placental pathology associated with a deranged kidney is given in Supplementary Table 1).

A systematic review of 151 autopsies in SARS-CoV-2-positive cases revealed that 85 (56.3%) cases had the presence of microthrombi in the lungs[34]. The endotheliotropicbehavior of SARS-CoV-2 via the ACE2 receptor on endothelial cells makes it prone to cause vascular endothelial dysfunction, leading to a complement-induced coagulopathy state in SARS-COV-2 infected patients and henceforth susceptible to microthrombi formation[35]. In the current study, contrast-enhanced computerized tomography of the chest demonstrated the presence of abnormal pathology in 6 out of 9 (66.7%) cases, with 4 of them havingmoderate to severe pathologies. Compared to controls, anomalous or injured maternal vessels and intervillous thrombi are significantly higher in the placentas of SARS-CoV-2- afflicted women.

Increased microcalcifications and fibrin thrombi were observed in the placentas of SARS-CoV-2-positive pregnant women, reflecting either an underlying hypercoagulable state induced by SARS-CoV-2 infection or major injury to syncytia-trophoblast[36]. In consistency with these findings, in our study, we observed an increased prevalence of microthrombi (11.1%), microcalcifications (22.2%), and syncytial knotting (6.9%).

We observed focal infarctions in 28% of cases. Infractions in the placenta are, in general, seen in about 25% of all uncomplicated pregnancies and do not affect the pregnancy. However, more serious infarctions due to severe SARS-CoV-2 infection and preeclampsia can directly cause fetal distress and are associated with developmental delays and cerebral palsy[37,38]. A notably high frequency (38.9%) of Chorangiosiswas observed in our study, as reported previously by Shane et al.[39]. Chorangiosis is characterized by decreased maternal oxygen saturation and is common in women inhabiting high altitudes like Mizoram. In contrast to findings by Smithgall et al., which described that villous agglutination was statistically more common in SARS-CoV-2 cases, we observed villous agglutination in only a single case[40]. In normal pregnancy, villous agglutination occurs in about 2% of cases[39]. Further, we observed placentas of deliveries beyond 37 weeks of gestations showed maximum pathological abnormalities compared to earlier weeks of gestation (Details are given in Supplementary Table 2).

No significant differences between the symptomatic and asymptomatic groups were observed in placenta pathologies. About 17.9% ~33.3% of infected patients were estimated tostay asymptomatic[41,42]. Similarly, the placental pathology of neonates requiring admission to NICU did not differ from the neonates not requiring NICU admission.

5. Limitations

The lack of comparison with a control group comprising SARS-CoV-2 negative individuals in the experimental setting is the most significant limitation of our study. To compensate for this, we have compared and discussed our results in light of the findings of other similar studies. The greatest strength of the study is all the women belong to the same ethnic group, and thus, variations in the results due to ethnicity are controlled.

6. Conclusions

In summary, this current work investigated pathological changes in SARS-CoV-2-positive pregnant women's placentas that might correlate with maternal and fetal outcomes. Our analysis indicated that SARS-CoV-2 infection leads to manifestations of morphological changes and lesions in the placenta. These lesions includedchorangiosis, villositis, chorioamnionitis, fetal vascular malperfusion/thrombosis, massive fibrin deposition, increased syncytial knotting, increased microcalcification, increased villous agglutination, focal infarct, intervillous hemorrhage as well as inflammation. However, this study is inconclusive, and the small sampling size and single geographical location limit its scope. This study should, therefore, be considered a learning point for elucidating SARS-CoV-2 pathophysiology.

Competing interests

The authors declare that they have no competing interests.

Ethical approval and consent

After acquiring informed consent from all participants, approval for the study was obtained from the ZMCH Ethics Committee.

Consent for publication

All authors read and approved the final version of the manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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None.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gocm.2023.05.001.

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