# Thrombotic Pathology in Placenta of COVID Positive Pregnancy

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## ABSTRACT

Covid positive pregnant women were increasingly getting delivery in the health institution. Most of them were asymptomatic and had positive report after their obstetric event was over because of emergency nature of care. Lack of autopsy is the lacunae in determining tissue pathology. One case of sudden intrauterine fetal death in Covid positive patient had induced delivery in the hospital and the placental histopathology examination showed widespread villous infarction, decidual arteriopathy with thrombosis and chorioamnionitis.

Keywords: Covid positive; fetal death; placenta; thrombosis

### INTRODUCTION

COVID-19 in pregnancy is a challenge to deal with two lives at a time and both are vulnerable for both treatment and research. Despite of potentially severe form of disease the maternal and perinatal outcomes are far better than anticipated. Transmission would be accelerated during labor because of its nature of transmission, thus the mode of delivery would be skewed to caesarean section if diagnosed early. Isolating mother and neonate would be more costly logistically especially in non-covid center.<sup>1,2</sup> While seeking placental changes in stillborn fetus of COVID-19 positive mother, the inflammatory and thrombotic placental pathology have been revealed in this case report.

#### **CASE REPORT**

There were 20 (2%) COVID-19 positive deliveries (9 vaginal deliveries and 11 Caesarean Sections) out of 1022 in three months from September to November 2020. Eight out of 11 Caesarean Sections were for obstetric indications and three chose it electively. Few of them were observed in hospital isolation ward and others in home isolation with their choice. One case was intrauterine preterm fetal death and 19 term pregnancy had normal neonatal outcome. All of them were asymptomatic and the maternity service was provided with recommended precaution (PPE).

A 33 years old  $G_4P_{1+2}$  at 33 weeks 4 days of pregnancy suddenly stopped perceiving fetal movement without any inciting event. She was on regular prenatal check-

up visits starting from 16 weeks of pregnancy. Obstetric ultrasound revealed intrauterine fetal death (IUFD), amniotic fluid index (AFI) of 8.5 cm and grade two placental maturity. Blood sugar, complete blood count, haemoglobin, coagulation profile (BT, CT, INR, PT) and prenatal routine serology (HIV, VDRL, HBsAg, HCV) were all normal. All patients during that time period used to have test for SARS COV-2 who were undergoing any surgical intervention and delivery; she was tested for it; and came to be positive in RT-PCR. Then she was planned for medical induction with prostaglandins and delivered a stillborn fetus of 2.0 Kg at 33 weeks 6 days of pregnancy.

There was no any gross anomaly to the stillborn. Amniotic fluid and placenta were not planned for genetic testing but placenta was kept for histopathological examination with prior verbal consent for the academic purpose. Histopathology revealed widespread villous infarction, decidual arteriopathy with thrombosis and chorioamnionitis on Hematoxylin and Eosin staining. Grossly the placenta revealed thrombosis and hemorrhage predominantly on maternal surface extending up to the fetal surface of placenta. microscopic details were: large areas of central as well as peripheral villous infarctions; villous edema and chorangiosis in the viable villi; significant perivillous fibrin deposition; multiple foci of thrombus in the small and medium sized vessels and intervillous areas; foci of lymphocytic villitis and intervillous hemosiderin deposits; decidual arteriopathy in the form of mural hypertrophy and fibrinoid necrosis of the vessels; multiple foci of dense acute inflammatory

Correspondence: Dr Gehanath Baral, Nobel Medical College, Kathmandu University, Biratnagar, Nepal. Email: gehanath@gmail.com, Phone: +9779841228829. cell infiltrate; and unremarkable umbilical cord sections (Figure 1).



Figure 1. Thrombosis in vessel lumen (A and B), acute inflammatory infiltrate (C).

Patient was discharged same day from the hospital with no other immediate peripartum complications. Postpartum follow up was uneventful. Written informed consent received from her to publish her report with concealed identity.

## DISCUSSION

Vertical transmission of SARS COV-2, intrauterine fetal death and neonatal death are all found to be low at around 1% in a systematic review.<sup>3,4</sup> Transmission can be proven by testing amniotic fluid, placental biopsy and neonatal nasopharyngeal swab test depending on the clinical protocol in place.<sup>5</sup> Efforts tend to be focused on deployment process during pandemic period compromising additional tests and respective research studies in most of the institutions.<sup>1</sup> Vertical or peripartum transmission of SARS COV-2 has not been definitely proven yet and neonatal outcome of most of the deliveries are reassuring with no placental histology changes in live born.<sup>6-9</sup>

Placentae of five fetal deaths in between 21-38 weeks of gestation had acute chorioamnionitis on placental histology, massive deposition of fibrin, mixed intervillitis/villitis, and intense neutrophil and lymphocyte infiltration.<sup>10</sup> Similar thrombotic pathology was detected in this study. But such inflammatory response doesn't definitely label the COVID infection except for the thrombotic events.<sup>11,12</sup>

Venous thromboembolism was found in 25% (20/81) and there was a significant increase in D-dimer in severe

degree of COVID infection.<sup>13</sup> This test was not performed at the this site besides supportive and clinical treatment.

The polarized expression (strongest at the membrane adjacent to the cytotrophoblast and villous stroma) of ACE2 away from the maternal blood and pronounced paucity of TMPRSS2 expression in trophoblast indicate further research on relatively normal fetal outcome in COVID positive mother.<sup>11</sup> The widespread coagulation and exaggerated inflammatory response appear to be the its pathogenesis.<sup>10</sup>

## CONCLUSIONS

Perinatal death is very low and overall neonatal outcome doesn't differ from uninfected population. SARS Cov2 PCR testing of amniotic fluid or fetal swab or placental swab along with inflammatory and thrombotic placental pathology would indicate the vertical transmission.

## REFERENCES

- CDC. Deployment Processes: COVID-19 Considerations. Updated June 23, 2020. <u>https://www.cdc.gov/</u> coronavirus/2019-ncov/global-covid-19/deploymentprocesses-covid-19-considerations.html
- Savitsky LM, Albright CM. Preventing COVID-19 transmission on labor and delivery: A decision analysis. Am J Perinatol. 2020;37(10):1031.[PubMed]
- Zaigham, M, Andersson, O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. Acta Obstet Gynecol Scand. 2020;99:823-9. [Article]
- Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy. J Infect. 2020 Mar 4.[PubMed]
- WHO. COVID-19 Clinical management: living guidance. Published 25 January 2021. <u>https://www.who.int/</u> publications/i/item/WHO-2019-nCoV-clinical-2021-1
- Parazzini F, Bortolus R, Mauri PA, Favilli A, Gerli S, Ferrazzi E. Delivery in pregnant women infected with SARS-CoV-2: A fast review. Int J Gynecol Obstet. 2020;150(1):41-6.[Article]
- Chen S, Huang B, Luo DJ, Li X, Yang F, Zhao Y, et al. Pregnancy with new coronavirus infection: clinical characteristics and placental pathological analysis of three cases. Zhonghua Bing Li Xue. 2020;49(5):418-23.[Article]
- Liu D, Li L, Wu X, Zheng D, Wang J, Yang L, et al. Pregnancy and perinatal outcomes of women with coronavirus disease (COVID-19) pneumonia: A preliminary analysis. AJR Am J Roentgenol. 2020;215(1):127-132.[Article]

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- Di Mascio D, Khalil A, Saccone G, Rizzo G, Buca D, Liberati M, et al. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. Am J Obstet Gynecol MFM. 2020;2(2):100107.[Article]
- Richtmann R, Torloni MR, Otani ARO, Levi JE, Tobara MC, Silva CA, et al. Fetal deaths in pregnancies with SARS-CoV-2 infection in Brazil: A case series. Case Rep Womens Health. 2020; 27:e00243. ISSN 2214-9112.[Article]
- Hecht JL, Quade B, Deshpande V, Kenudson MM, Ting DT, Desai N, et al. SARS-CoV-2 can infect the placenta and is not associated with specific placental histopathology: a series of 19 placentas from COVID-19-positive mothers. Mod Pathol. 2020;**33**, 2092–2103.[Article]

- Shanes ED, Mithal LB, Otero S, Azad HA, Miller ES, Goldstein JA. Placental Pathology in COVID-19. Am J Clin Pathol. 2020;154(1):23-32. [Article]
- Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. J Thromb Haemost. 2020;18(6):1421-4. [Article]