Section: OBG

Original Research Article

UNVEILING HISTOPATHOLOGICAL ALTERATIONS IN PLACENTAS OF PREGNANT WOMEN AFFECTED BY COVID-19: A COMPREHENSIVE ANALYSIS

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Abstract

Background: The effects of COVID-19 on expectant mothers and newborns remain mainly unknown and of critical interest. Placenta is an immunoprivilaged organ, which creates the maternal-fetal interface between the mother and the fetus. It is the possible target for pathological insults due to a poor maternal environment, such as hypoxia, inflammatory activation, and an increase in thrombotic events **brought** on by COVID-19 infection. This can have a negative impact on the prognosis of pregnancy. The placental tissue can provide valuable information about the health of the mother and the fetus through histopathological analysis. **Materials and Methods:** In this study, 60 serologically proven COVID- positive women in labour as the study group, 60 non-covid pregnant women in labour as the control group were enrolled. All the participants were followed till delivery, and the placentas were subjected to histopathological evaluation. **Result:** Maternal vascular mal-perfusion was the most observed placental pathology in the study group. Among maternal vascular mal-perfusion following observations were noted in the study group compared to control group - Intervillous fibrin was the commonest finding -98%(P >0.559), followed by Perivillous fibrin 93.3%(P>0.001), villous infarction 36.6%(P>0.001), Villous agglutination and Intervillous thrombus. Among the decidual arteriopathy, fibrinoid necrosis was the commonest followed by mural hypertrophy of membrane arterioles, atherosis.The following fetal vascular malperfusion features were noted in study group compared to control group : avascular villi - 36.6% (P>0.001) followed by lymphocytic villitis-93.3%(P>0.001), calcification-25%(P>0.001), fetal vessel chorangiosis -45%, (P>0.001), edema of the villi- 98% (P>0.001) **Conclusion:** The study concludes that SARS-CoV-2 infection in pregnant women lead to placental dysfunction, by causing micro vasculopathy leading to intrauterine hypoxia, and may effect fetal outcome. This understanding of pathogenesis helps us in formulating management plans for SARS COV-19 affected pregnancies.

INTRODUCTION

Within a few months of its first known occurrence, the coronavirus disease 2019 (COVD-19) caused by SARS coronavirus 2 (SARS-CoV-2) has become an worldwide pandemic.[1] The epicenter of COVID-19 is reported to be China, in the city of Wuhan, Hubei.[2] Coronavirus are single stranded encapsulated RNA viruses which causes upper respiratory tract infection.[3] In mammals, the placenta plays the vital role of transmitting oxygen and nutrients to the growing embryo and takes away the waste products, in addition to being a protective barrier against toxic materials.[4] Pregnancy is an immunocompromised state, making it more vulnerable to viral respiratory infections. The placenta, which creates the maternal-fetal interface, is known to harbor a number of viral infections and has an impaired immune response. The placenta is a possible target for the pathological insult that could result in unfavourable pregnancy outcomes because of unfavourable maternal settings such hypoxia, inflammation activation, and increased thrombotic

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events brought on by COVID-19 infection.[5] The placental tissue's histopathologic study can reveal important details about the mother's and fetus's health. Covid-19 infecion has been associated with Hypercogulability with development of ischemic changes including gangrene of fingers and toes, with evidence of d-dimer elevation. The increased systemic thrombotic events and microvascular injury syndrome seen in COVID-19 infection can affect the placenta leading to turbulent and slow blood flow, progressive rise in fibrin degradation products, decreased fibrinolysis and increased hypoxic-ischemic injury. This suggests that maternal covid 19 infection is associated with propensity for thrombosis in the fetal circulation.[6] This in turn have significant clinical implications for the mother and the infant.

The effect of COVID-19 on expectant mothers and newborns is the major area of interest. This study tries to find out the changes that occur histopathological in the placenta of covid19 affected and unaffected pregnancies as it may affect maternal and fetal outcomes. With this context in mind, a study was devised to compare the histopathological alterations in the placentas of Covid-19 positive and negative pregnancies.

MATERIALS AND METHODS

The prospective cohort study was conducted in the Department of Obstetrics and Gynecology of Shri B M Patil Medical College Hospital and Research Centre (BLDE), Vijayapura, Karnataka, over a period of 4 months from (June 2021 to September 2021). BLDE Institution register board certificate has been taken. Inclusion criteria were pregnant women with gestational age between 28-40 weeks with serologically COVID-19 positive in labour, and Exclusion criteria were pregnant ladies with any medical or obstetrical complications other than COVID-19.

The women who were positive serologically for COVID-19 either by IgM or IgG or both were enrolled in Study Group / Group A. The women who are negative for Covid-19 were enrolled into the Control group/ Group B. All the participants were followed till delivery and the placentas were weighed and sent to the department of pathology in 10% formalin along with all the details of the patients. After routine fixation, histopathological examination was done, and representative tissue sections were given for microscopic evaluation. About 3–4-micron thickness sections were taken and subjected to Hematoxylin and Eosin staining and observed under microscope for the pathological changes by the single observer to avoid observer bias.

The information's collected was entered into the excel sheet and analyzed for statistical significance between variables. Institutional Ethics Committee clearance and informed consent from pregnant women were taken before the start of the study.

RESULTS

A total of 120 Placentas were collected in the study. About 60 belong to the study group and 60 to the control group-(Figure-1). The mother's age ranged between 18-32 years (Average 25 years) at birth. Here 66% of patients delivered at term and 33% at preterm (33 weeks to 36.6 weeks). Out of 60 cases, 20 (33.3%) were small for gestational age. One placenta was large for gestational age (750g), as shown in [Table 1].

Maternal vascular mal perfusion was the most observed placental pathology in the study group. Among maternal vascular mal perfusion following observations were noted in the study group compared to control group - Intervillous fibrin was the commonest finding among both the groups - SG-98%; CG-96.6%; (P >0.559), followed by Perivillous fibrin- SG:93.3, CG:66.6% (P>0.001)-[Figure 2], villous infarction – SG:36.6%, CG:26.9% (P>0.001)-[Figure 3], Villous agglutination-CG: 45%, SG:1.2% (P>0.001), Intervillous thrombus- SG:25%, SG-0 (P>0.002). Among the decidual arteriopathy, fibrinoid necrosis – SG: 96%, CG: 16.6% (P>0.001), Mural hypertrophy of membrane arterioles- SG-60%, CG-0 (P>0.001)- [Figure 4], Atherosis -SG: 30%, CG-0 (P>0.002). [Table 2].

The following fetal vascular malperfusion features were noted in study group compared to control group [Table 3]: avascular villi - SG-36.6%, CG-23.3%; (P>0.001), lymphocytic villitis-SG-93.3%, CG-0(P>0.001), calcification-SG-25%, CG-0 (P>0.001), fetal vessel chorangiosis SG-45%, CG-0 (P>0.001)-[Figure 5], edema of the villi-SG- 98%; CG-0 (P>0.001)- [Table 3].

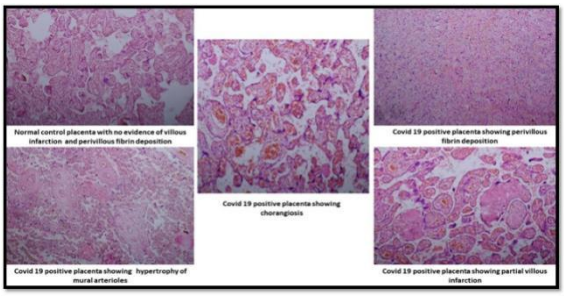

Figure 1: Histopathological changes of placenta

Table 1: Demonstrates the Demographic and clinical characteristics of COVID-19-infected mothers included in the study

Variables	Study Group	Control Group
Maternal age (years)	25.18(Median)	26.4(Median)
Gestational age[weeks]		
30-33 +6	02	03
34-36 +6	14	09

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37-41 +6	44	48
Preterm delivery	16	12
Mode of delivery		
LSCS	34	38
FTVD	26	22
Placental Size		
Small for gestational age	20	00
Large for gestational age	01	00
SARS CoV-2 test		
IgG Positive	15	04
IgM Positive	07	00
IgG and IgM positive	05	00
Birth weight		
LBW	21	5

Table 2: Demonstrates maternal surface abnormal placental histopathology (Group 1 n=60) and Normal placental findings (n=60).

MATERNAL SURFACE	Study Group		Control Group		CHI	P VALUE
a villous infarction	22	36.6%	0	0	26.939	.001*
b Villous agglutination	27	45%	02	1.2%	28.420	.002*
c Intervillous fibrin	59	98%	58	96.6%	.342	.559
d Perivillous fibrin	56	93.3%	40	66.6%	13.333	.001*
e intervillous Thrombus	15	25%	00	00	17.143	.002*
f1 Atherosis	18	30%	00	00	21.176	.002*
f2 Chorangiosis	28	46%	00	00	36.522	.001*
f3 Fibrinoid necrosis	58	96%	10	16.6%	78.190	.001*
f4 Mural hypertrophy of the membrane arterioles	36	60%	00	00	51.429	.001*
g Inflammatory cells	09	15%	00	00	9.730	.002*
h Calcification	35	58%	00	00	49.412	.001*

Table 3: Demonstrates Fetal Surface abnormal placental histopathology (Group 1 n=60) and Normal placental findings (Group 2 n=60)

Fetal surface	Study Group		Control Group		CHI	P VALUE
i Avascular villi	43	36.6%	14	23.3%	28.104	.002*
j Chorangiosis	27	45%	00	00	38.839	.001*
K Edema of the Villi	16	98%	00	00	18.462	.001*
l Lymphocytic villitis	19	93.3%	00	00	22.574	.001*
m Calcification	32	25%	00	00	43.636	.002*
o Necrosed villi	28	30%	14	23.3%	7.179	.001*

Table 4: Comparison of present findings with other studies

Placental changes	Our study	Joshi B, et al.	Elisheva D et al.	Rebecca N Baergen et al.
Maternal Surface				
Maternal Vascular malperfusion	55%	27.93%	80%	NA
a villous infarction	36.6%	NA	20%	NA
b Villous agglutination	45%	NA	20%	NA
c Intervillous fibrin	98%	22.9%	NA	NA
f1 Atherosis	30%	NA	20%	NA
f3 Fibrinoid necrosis	96%	NA	20%	NA
f4 Mural hypertrophy of the membrane arterioles	60%	NA	33%	NA
g Inflammatory cells	15%	6.7%	NA	NA
h Calcification	58%	NA	NA	NA
Fetal Surface				
Fetal vascular malperfusion	45%	NA	NA	45%
l Lymphocytic villitis	93.3%	NA	NA	40%

DISCUSSION

The current study findings indicate that in Acute COVID-19, significant lymphohistiocytic villitis and villi oedema may occur and may be caused by SARS-CoV-2 infection of the placenta. Maternal malperfusion features like Villous infarction, Villous agglutination, Intervillous Fibrin, Perivillous fibrin, Intervillous thrombus and Fetal vascular malperfusion features like Fetal vessel chorangiosis, Calcification, Clustered avascular villi, Necrosed villi, small thrombi in blood vessels are the pathological findings which might have relation to an alternative coagulative state induced by SARS-CoV-2.

The Covid -19 pandemic affected the world, leading to large amounts of mortality and morbidity. The exact mechanism of pathogenesis in pregnancy needed to be elucidated. Several studies were conducted during the pandemic on pregnant women with covid to identify the pathogenesis few of them are as follows.

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Joshi B, Et al, conducted a study on 173 covid-19 pregnant women with gestational age >20 weeks, with placental histopathological reporting women at a tertiary center in North India found placental abnormalities, including maternal vascular malperfusion, villous fibrin deposits, fetal vasculopathy, and acute inflammation.[5]

Elisheva D et al. compared the placentas from pregnant women with COVID-19 who delivered between March 2020 and May 2020 to historical controls and found that placentas of patients with coronavirus 2 (SARS-CoV-2) showed one of the features of maternal vascular malperfusion, specifically abnormal or injured maternal vessels and intervillous thrombi. They have seen central and peripheral villous infarction, villous agglutination, accelerated villous maturation, decidual arteriopathy, atherosis and fibrinoid necrosis of maternal arteries, and mural enlargement of membrane arterioles.[2]

Hameda Abd Al-Mahdi Ghazi et al.: In their review article based on the published articles during the period between December 2019 and April 2022, they documented histopathological changes in the placenta of pregnant women with SARS-CoV-2infection such as chorangiosis, thrombus formation in the subchorionic spaces and the intervillous space, villous agglutination, Trophoblast necrosis, Focal avascular villi, decidual arteriopathy, accelerated villous maturation, fibrinoid necrosis, retro placental hematoma and edematous hematoma.[4]

Rebecca N Baergen et al. examined the placentas of 20 covid positive patients and assessed the lesions using Amsterdam criteria. Fetal vascular malperfusion was the most prevalent lesion they discovered. Most instances had intramural fibrin deposition in one or two foci, two cases had just foci of villous stromal vascular karyorrhexis, and a few had intramural non-occlusive thrombi and chronic villitis.[6]

CONCLUSION

The study concludes that SARS-CoV-2 infection in pregnant women lead to placental dysfunction, by causing micro vasculopathy leading to intrauterine hypoxia, and may effect fetal outcome. This understanding of pathogenesis helps us in formulating management plans for SARS COV-19 affected pregnancies.

In this study effort was made to rule out confounding factors like Diabetes mellitus and pregnancy induced hypertension for the placenta changes with detailed history. But all relevant investigations were not done.

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