Original Article

A Histomorphological Study of Placentas of Covid 19 Affected Patients at a State Covid Hospital

Aparna C[1], Srilakshmi A[2], Geetha Sree A[3], Nagaraja Bhargavi C[3], Khadeeja T[3], Baleswari G[4]

Authors' affiliations: [1]Professor, Dept. of Pathology; [2]Associate Professor, Dept. of Obstetrics & Gynecology; [3]Post Graduate; [4]Professor and Head, Dept. of Pathology, Kurnool Medical College, Kurnool
Correspondence: Dr. Nagaraja Bhargavi C, Email: nagarajabhargavi93@gmail.com, Mobile No.:8500179768

ABSTRACT

Background: Covid 19 pandemic has caused a significant death toll across the world, its effects on placental morphology are of great concern to the obstetricians and pregnant women because it effects the health of the fetus.

Objective: To study the histomorphological features of placentas and correlate with clinical features and other related studies.

Methods: A total of 151 placentas were studied from July 1st to October 15th. It is a descriptive, Cross-sectional study.

Results: Out of 151 placentas retroplacental hematomas are seen in 46 cases, central infarction in 21 cases, peripheral villus infarction in 23 cases, fetal vessel mural fibrin in one case, chorangiosis in 24 cases, inter villus fibrin in 98 cases, membranes with hemorrhage in 77, intervillus hemorrhages in 73 cases, ghost villi in 38 cases, calcifications in 53 cases.

Conclusion: Although a few cases showed features of vascular malperfusion, there is no effect on the fetus.

Key words: inter villous fibrin, inter villous hemorrhages, ghost villi, chorangiosis.

INTRODUCTION

Placenta is a unique organ that possesses dual blood circulation and is vital for the survival and health of the fetus. The pathologic conditions associated with pathologic maternal blood flow are known under the terminology Maternal Vascular Mal perfusion(MVM) according to Amsterdam consensus.[1] The various gross and microscopic features are placental infarction, retroplacental hematoma, increased syncytial knots, delayed villus maturation etc. There has been a great debate whether antenatal patients are more vulnerable to Covid19 or not and if it can cross the placenta, and its influence on the fetus. Histo pathological study of placenta can reveal significant information regarding the health of both mother and fetus. So far effects of various viruses like CMV, SARS, MERS, Varicella, herpes, Zika on antenatal cases have been studied and proved to cause various congenital anomalies, miscarriages etc.[2] there had been a few studies on covid 19 affected placentas with controversial results. In the present study an attempt has been made to study the histopathological changes caused by covid19 on placentas so that this information may help in the future management of obstetric cases.

METHODS

This study is approved by the Institutional Ethics Committee. We have received 151 placentas. After weighing the placentas, a thorough gross examination is done. Length of the umbilical cord, diameter and hypercoiling/knots or edema are noted. Sections submitted included two from membrane rolls, two from umbilical cord ;one from cut end, one from insertion, two from the center of the placenta, two from the periphery of the placenta, extra sections from grossly visible lesions. All the sections are subjected to routine processing and staining.

Out of 151 cases 53 are normal vaginal deliveries, 96 are cesarian sections. Only four cases showed fetal anomalies and one fetal death due to septic encephalitis. Seven cases are preterm deliveries but no fatal anomalies are found. Six patients presented with preclampsia and one case with gestational diabetes mellitus. APGAR score is 8-10 for all live births. All the neonates tested for Covid at the time of discharge are negative.

RESULTS

All the morphological changes of the placenta were depicted in the table 1. Findings of the present study are; all the placental weights were within the 10th percentile of normal range. One umbilical cord one showed velamentous insertion(fig1), One umbilical cord showed only two vessels.(fig 2) Majority showed central insertion; 139, 11 cases showed marginal insertion,. There is one case of twin pregnancy with monoamniotic dichorionic placenta. Retroplacental hematomas are seen in 46 cases (30.4%). Central villus infarction is seen in 21 cases (13.9%), peripheral villus infarction in 23(15.2%) fetal vessel mural fibrin is seen in one case(0.66%), chorangiosis is seen in 24 cases(15.4%).(Table I) . acute maternal inflammation in one case, fetal inflammation in five cases, chronic villitis –low grade in one case, Increased perivillus fibrin (fig) found in 98 cases (64.9%) membranes with hemorrhage in 77 cases(fig) (49.6%), calcifications in 53 cases(fig)(34.4%), intervillus hemorrhages in 73 cases (fig)(47%), ghost villi in 38 cases (22.5%), accelerated villus maturation assessed by the presence of syncytial knots in > 33% of vill , is found in one case.

Fig 1 ; Gross picture of placenta showing velamentous insertion of the umbilical cord.

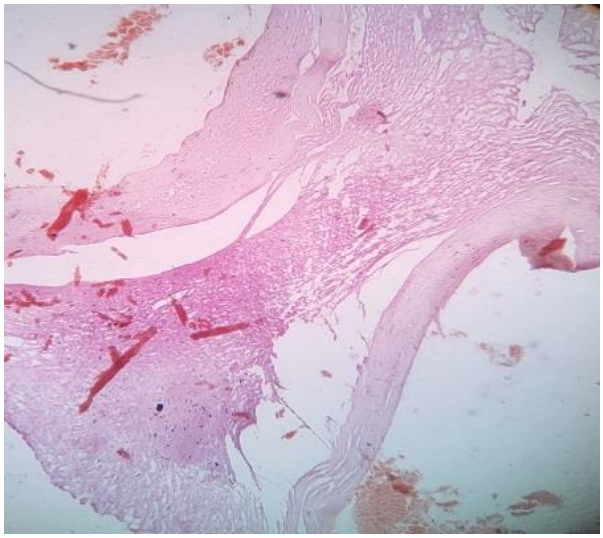

Fig2; 4x10 x H&E Umbiical cord showing two vessels.

DISCUSSION

Placenta through its unimpeded flow of oxygenated blood, supplies oxygen and nutrients to the fetus, thus pathologic conditions affecting maternal vasculature and circulation can produce significant adverse effects on the fetus. The physiologic and immunologic changes that occur as a normal component of pregnancy can have systemic effects that increase the risk for complications from respiratory infections. Changes in the maternal cardiovascular and respiratory systems, including increased heart rate, stroke volume, oxygen consumption, and decreased lung capacity, as well as the development of immunologic adaptations that allow a mother to tolerate an antigenically distinctive foetus, increase the risk for pregnant women to develop severe respiratory disease.[3] Viruses such as cytomegalovirus, herpes simplex, Rubella, HIV ,Zika, influenza have been shown to cross the placental barrier and may be associated with foetal malformations. The histological changes observed in CMV infection are lympho plasmacytic villitis, enlarged villi, intravillous hemosiderin deposition.

Table 1: Depicting the incidence of histomorphological changes

Features	Cases	%
Umbilical cord		
Two vessels.	1	0.6
velamentous insertion	1	0.6
Maternal vascular malperfusion;		
Central villus infarction	21	13.9
Peripheral villous infarction	23	15.2
Accelerated villous maturation or delayed villus maturation	1	0.6
Mural hypertrophy of membrane arterioles	0	
Absence of spiral arteriole remodelling	0	
Retro placental hematoma	46	30.4
Fetal vascular malperfusion;		
Clustered avascular villi	0	
Fetal vessel mural fibrin	1	0.6
Hyper coiled umbilical cord	0	
Chorangiosis	24	15.5
Acute inflammatory pathology -		
Maternal inflammatory pathology stage 2	1	0.6
Fetal inflammatory pathology stage 2	5	3.3
Chronic inflammatory pathology-		
Chronic villitis low grade	1	0.6
Chronic decidualitis with plasma cells or lymphohistiocytic villitis	0	
Accreta or villus edema	0	
Increased inter villous fibrin	98	64.9
Intervillous hemorrhages	73	47.0
Increased circulating nucleated RBC	0	
Membranes with hemorrhage	77	49.6
Calcifications	53	34.4
Ghost villi	39	22.5

Intervillositis is seen with Zika and Dengue infections. SARS,MERS during pregnancy can cause increased miscarriages, IUDs, preterm deliveries.[4] where as Ng etal have proved vertical transmission of SARS in Hongkong.[5] The course of Covid 19 has been intriguing since its first appearence in Wuhan, China. It is associated with hyper coagulability, raised D-dimers, vasculopathy, DIC, affecting several organs mainly lung causing ARDS. So, in the present study an attempt has been made to unravel the pathological changes in the Covid 19 affected placentas, so that this information may help in the future management of obstetric cases. As this is a national health problem , it may help in formulating guidelines in the management of Covid 19 effected pregnancies.

Significant findings in the present study are; Retroplacental hematomas are seen in 46 cases (30.4%). Majority showed central insertion i.e 139 cases, 11 showed marginal insertion, one case showed velamentous insertion.(fig 1). One umbilical cord showed two vessels only (fig 2).Central villus infarction is seen in 21 cases (13.9%), peripheral villus infarction in 23 cases (15.2%) . Fetal vessel mural fibrin is seen in one case, chorangiosis; criteria adopted are more than ten vessels in one villus , more than ten villi is seen in 24 cases(15.4%). (fig 3) As it is a viral infection we have expected inflammation but to our surprise , acute inflammation was found in one case and chronic villitis- low grade in one case.maternal inflammatory response was graded as

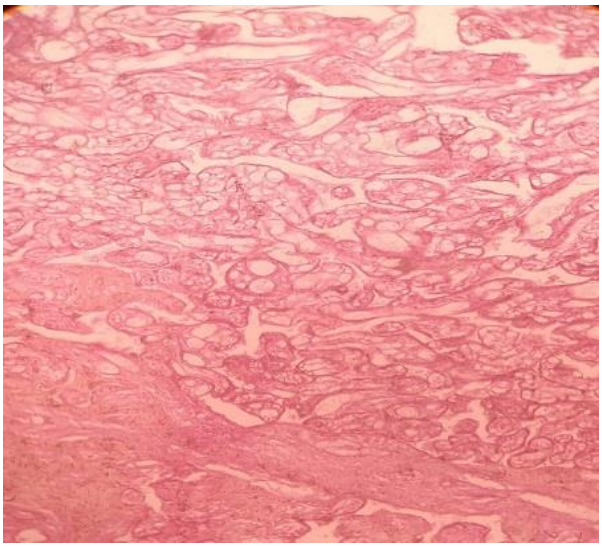

Fig3 40x10x showing chorangiosis .

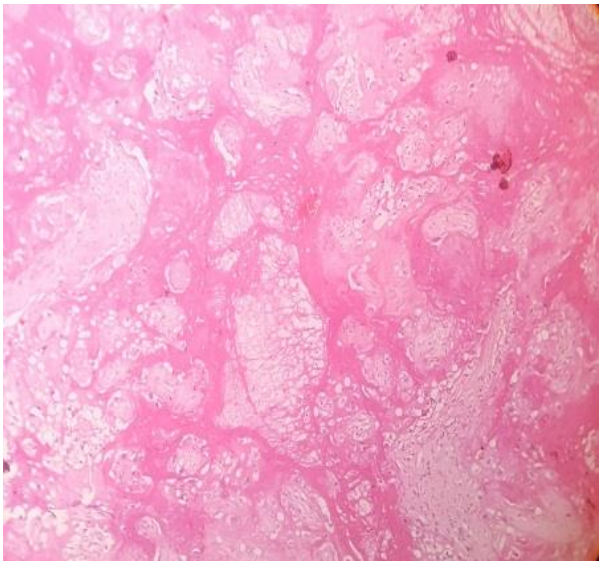

Fig4; 40x10xx H&E showing intervillous fibrin.

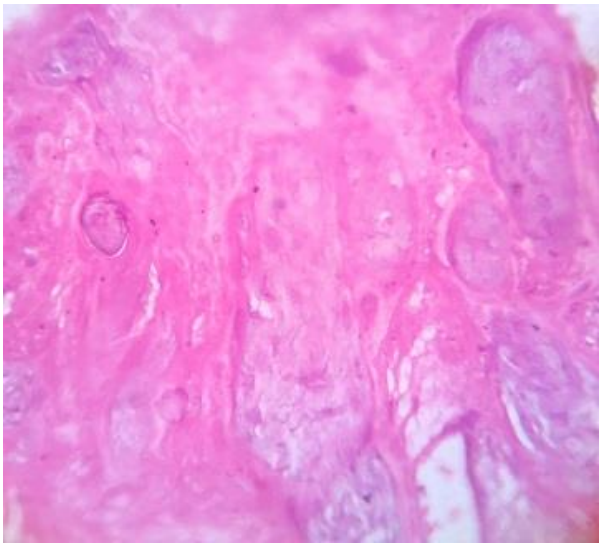

Fig5; 40x10x ,H&E showing ghost villi.

grade 1:, mild to moderate.[6] Increased inter villus fibrin(fig4) found in 98 cases (64.9%) membranes with hemorrhage in 77 cases (49.6%), calcifications in 53 cases(34.4%), intervillus hemorrhages in 73 cases(47%), ghost villi in 39cases (22.5%), (fig5)collapsed or increased intervillus space are not found.. But in all these cases there is no fetal hypoxia clinically. APGAR score is 8-10 at one minute and 9-10 at 5 minutes. Accelerated villus maturation ; assessed by the presence of syncytial knots in > 33% of vill which is found in one case. Delayed villus maturation , absence of spiral arteriolar remodeling, mural hypertrophy are not found. Calcifications are indication of aging of the placenta, can be seen in normal term placentas also, But chorangiosis and intervillus fibrin, increased syncytial knots are indications of fetal hypoxia.

David A Schwartz has studied 38 pregnant women whose placentas were negative for SARS Covid2 and also did not result in any effects on the fetus.[7] In Marian Knight etal 's cohort study in U.K.including 427 pregnant women of which most had good outcome and transmission of SARS COVID 2 was uncommon.[3] Fabio Facchetti etal have demonstrated vertical transmission by detecting SARS-COV-2 RNA in fetal tissues and the neonate developed pneumonia soon after birth..[8]

Thomas Menter etal studied five placentas and concluded that prominent lympho histiocytic villitis seen in Covid19 should not be attributed to Covid 19 infection of the placenta. According to him chorangiosis is a sign of fetal vascular malperfusion, intervillus fibrin is a sign of maternal vascular malperfusion. In Elisheva etal study, 16 placentas were examined , findings were increased features of maternal vascular malperfusion, intervillous thrombi and chorangiosis which is correlating with the present study. But finally they have concluded that there are no pathognomonic features and increase antenatal surveillance is not warranted.[9] Huijun Chen studied nine cases , in which there is no evidence for intrauterine infection caused by vertical transmission in women who develop COVID-19 pneumonia in late pregnancy, The clinical characteristics of COVID-19 pneumonia in pregnant women were similar to those reported for non-pregnant adult patients who developed COVID-19 pneumonia.[10]

However, in another study demonstration of IgM antibodies to Covid-19 in a single neonate, who also had elevated cytokines suggests that vertical transmission is possible, even though uncommon.[11] Rebecca and Debra have studied 20 placentas , of which ten of them have shown features of vascular mal perfusion, suggesting that maternal Covid-19 infection might be associated with propensity for thrombosis in the foetal circulation.[12] In a systematic review, conducted by Danielle etal ;women affected by COVID-19 disease had higher rates of preterm birth, and preeclampsia, while the babies had a 2.4% rate of stillbirth, a 2.4% rate of neonatal death, and higher rate of admission to the NICU. [13] This is in contrast with the present study.

In the present study though we could not subject placenta to in situ hybridization for the detection of virus particles, all the neonates tested negative. Hithero there are controversial studies regarding the vertical transmission of Covid19. But the perinatal outcome is good in all the studies.

CONCLUSION

Though a few maternal vascular mal perfusion changes are seen in the placentas, Covid 19 did not effect the perinatal outcome. This may be due to the infection in late trimester. If the study had included normal case controls, it would have been more prudent and statistically significant.

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