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Research Article

Fetomaternal Outcome in Pregnancy with COVID-19

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Abstract

Aims and Objectives: This study was to done to find the feto-maternal outcome when universal screening for COVID -19 was done in pregnancy. The effects of COVID-19 on placental histology and any evidence of vertical transplacental transmission were also investigated.

Materials and Methods: A total of 850 pregnant women were screened from April 2020-July 2020 Eighty nine mothers were found positive for covid-19 with RTPCR. All pregnancies with covid 19 positive screen were admitted. 30 women were referred to labour room for intrapartum care and their feto maternal outcome was studied.

Results: Covid -19 pregnancy is associated with miscarriages, preterm labour and intrauterine deaths. Placental lesions commonly observed are perivillous fibinous exudates, microthrombi and microinfracts. All newborns were covid negative tested by RT-PCR and hence transplacental transfer is not recorded in this preliminary report.

Conclusion: The placenta acts as a barrier against transmission of COVID -19, though placental affection with microthrombi, infarcts and perivillous fibrosis were evident in almost all placenta in Pregnancy with Covid -19.

Keywords: Covid-19; Pregnancy; Fetus; Newborn; Placenta

Introduction

There is an increase in number of pregnancies with Covid-19 cases in the past 5 months [1]. Covid 19 in pregnancy specifically is a difficult scenario. Pregnancy is a state of elevated diaphragm and reduced tidal volume, this leads to exacerbated hypoxia and drop in pulse oxygen levels as compared to non pregnant women. In addition, the nasal mucosa and alveolar lining is congested as a result of increased peripheral vascularity in pregnancy. Furthermore, there are fewer treatment options of covid 19 with pregnancy and the teratogenic potential of antiviral drugs remains unidentified. The teratogenic influence of covid-19 on pregnancy is also unknown.

Due to the upregulation of Angiotensin-converting enzyme (ACE)-2 and the SARS-CoV-2 receptor during pregnancy, there is an increased the risk of covid -19 infection [2-4]. SARS-CoV-2 and SARS-CoV-1 enter the host cell by binding their S proteins to ACE receptors located on the surface of the host cells [5,6]. ACE2, a dimer, functions as a carboxyl to lyse the single residues of ANG I to generate the single residues of ANG 1-9 and ANG II which is broken down as ANG 1-7. ANG 1-7 has vasodilatory function which can oppose the contractile effects of ANG II. ACE2 further plays a pivotal role in post-infection regulation activities like immune response, cytokine secretion, and viral genome replication [7-9].

Pregnancy with Covid also poses a difficult ICU scenario as pregnancy in itself a hypercoagulable state and covid increases the D-Dimers secondary to microthrombi. The pregnant hypoxic lady is also difficult to intubate. Steriods used to treat covid patients if used in pregnancy can lead to congenital anomalies like cardiac defects and cleft lip and cleft palate [10].

An overzealous use of anticoagulants like heparin and aspirin may also lead to retroplacental haemorrhage and clots collecting in the choriodecidual space can shear out the placenta leading to premature placental separation and in third trimester result in abruptio placenta [11]. The fetomaternal interphase is specifically affected by the hypercoagulability in microcirculation at choriodecidual interphase. In addition these microinfarcts in the primary and secondary and tertiary fetal stem villi are responsible for decreased feto-maternal gas exchange across the placental blood barrier. This results in fetal asphyxia and accumulation of toxic metabolites in fetal circulation.

The fetus mounts a protective sympathetic response and there is a compensatory increase in erythropoiesis and vascular redistribution in fetus to vital organs evidenced by fetal Doppler studies in Covid pregnancies in third trimester. The cardiovascular changes, the increase in metabolic rate and oxygen consumption, the decrease in functional residual capacity, and ventilation perfusion mis match, lead to the occurrence of hypoxic respiratory failure in these patients [12]. Hence this study was done to identify the common clinical presentations of Covid in pregnancy correlate it with the fetomaternal outcome in Covid pregnancies.

Materials and Methods

In this prospective study all antenatal women attending the outpatient department of Saveetha Medical College were offered a voluntary COVID screening and fetomaternal outcome was recorded in all women with singleton pregnancies. This study was approved by the ethical and research board. Written consent was obtained in all cases. A first trimester scan was done to measure CRL (Crown Rump Length) to date the pregnancy in all cases.

The research was included in 28 Covid-19 with pregnancies as the study group. Pregnant women were recruited between 1 April 2020 and 31 July 2020 after getting written informed consent from participants in local language. Multiple Pregnancies and pregnancies with congenital anomalies were excluded. Detailed maternal factors like age, gestational age, parity, pre-pregnancy body mass index, previous low birth weight, haemoglobin levels, chronic hypertension, gestational diabetes and previous preeclampsia were recorded subsequently. Covid-19 symptoms like fever, running nose, headache, ansomia and breathlessness were recorded. Temperatures, Pulse rate, Blood pressure, oxygen saturation were measured at the time of admission. All women were admitted in separate Labor room meant exclusively for Covid Care. Post partum care was given in the same ward till postpartum day 5. All newborns were tested for Covid-19.

Placental problems like infarcts, retroplacental calcifications, small placenta, and premature separation were also reported. Placenta from 28 normotensive, nonproteinuric pregnant women with standard pulsatility index (< 1.55) of uterine artery was studied as a control group. On the day of delivery, the placenta was weighed and 12 full thickness blocks of placenta were made from center and periphery. The blocks were incubated in 4% buffered formalin for 12 hours and sections were taken at 5 microns spacing. Placental specimens were scored for staining in trophoblast, stromal cells, vessel walls and Hofbauer cells.

Results

Covid -19 pregnancy is associated with miscarriages, preterm labor and intrauterine deaths. Placental lesions commonly observed are perivillous fibinous exudates, microthrombi and micro infracts. All newborns were Covid negative and hence transplacental transfer is not recorded in this preliminary report.

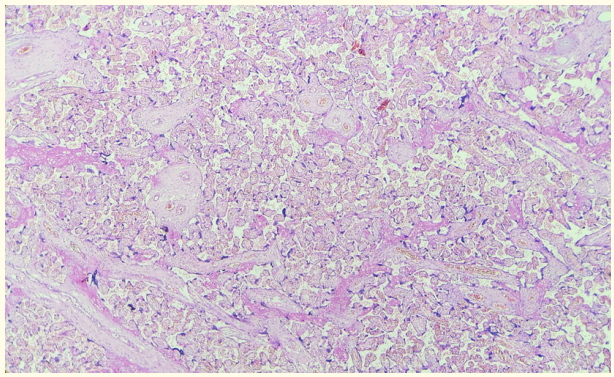

Figure 1: Placental histology showing microthrombi and microinfarcts (100X).

S. No	Age	Gestational age	Medical Co-morbidities	Associated Obstetrical Problems	Procedure done/outcome	Baby weight/sex	Apgar score (after 1 min, after 5 min)	Histology
1	23y	G2 A1 with 22 weeks intrauterine death	Hypothyroidism	Previous abortion at I trimester	MTP with Misoprostol 400 micrograms p/v 4hrly	Nil	Nil	Placental microthrombi
2	33Y	G2 P1 L1 With 38 Weeks	Nil	Cephalopelvic disproportion	LSCS With ST	2.690kg/boy	8/10,9/10	Chorioangiosis
3	27y	Primi with term gestation	Nil	Failed Induction	LSCS With ST	2.630kg/girl	8/10,9/10	Focal Perivillous fibrinous exudates
4	32y	G2 P1 L1 With 38 Weeks	Nil	Previous LSCS with Cephalopelvic disproportion	LSCS With ST	2.5kg, boy	8/10,9/10	Chorioangiosis
5	32y	Primi with term gestation	Nil	Cephalopelvic disproportion, moulding	LSCS With ST	2.560kg/girl	8/10,9/10	Chorioangiosis
6	23y	Primi with 12 weeks	Nil	Nil	Suction and evacuation	Nil	Nil	Placental microthrombi and empty fetal villi
7	30y	G3 P1 L1 A1 with term gestation	nil	Previous LSCS with Cephalopelvic disproportion	Emergency LSCS	3.220kg, boy	8/10,9/10	Hyalinization and focal fibrosis
8	27y	Primi with 40 weeks	Nil	Oligohydramnios, post dated pregnancy	Emergency LSCS	3.150kg, girl	8/10,9/10	Increased syncytial giant cells
9		G4 P1 L1 A2 38weeks +1 day	Nil	Previous 2 miscarriages in first trimester	Normal vaginal delivery with episiotomy	3.00 kg , boy	8/10,9/10	Chronic inflammation increased neutrophils infiltrates
10	21y	Primi with 40 weeks	Nil	Cephalopelvic disproportion	Emergency LSCS	3.1 kg, girl	8/10,9/10	Chorioangiosis
11	28y	G2 P1 L1 With term gestation	Bilateral pedal edema	Nil	Normal vaginal delivery with episiotomy	2.95 kg, boy	8/10,9/10	Focal perivillous fibrinous exudates
12	28y	Primi with term gestation	Nil	Severe oligohydramnios, IUGR, fetal distress	Emergency LSCS	2.49 kg, boy	8/10,9/10	Microthrombi, focal fibrosis and hyalinization
13	32y	G3 P2 L2 with 36 weeks	Nil	Previous LSCS	LSCS With ST	2.930kg, girl	8/10,9/10	Focal fibrosis and neutriphilic infiltration
14	32y	Primi with 38 weeks	Nil	Minor Cephalopelvic disproportion, history of cord around the neck	Emergency LSCS	1.66kg, girl	8/10,9/10	Microthrombi and infracts

15	23y	Primi with 39 weeks +6 days	Nil	Cephalopelvic disproportion	Emergency LSCS	3.070kg, boy	8/10,9/10	Chronic neutrophilic exudates
15	28y	Primi with 40 weeks	Nil	Cephalopelvic disproportion	Emergency LSCS	2.970kg, boy	8/10,9/10	Chronic neutrophilic exudates
16	25y	Primi with 14 weeks with intrauterine death	Hyperemesis	nil	MTP with Misoprostol 400micrograms p/v 4hrly	3.65 kg, boy	8/10,9/10	Perivillous hyalinization
17	31y	Primi with 17 weeks +6 days	Abdominal pain for evaluation	nil	MTP with Misoprostol 400micrograms p/v 4hrly	Nil	Nil	Microinfracts
18	38y	G3 P1 L1 A1 37weeks +4days	Nil	Previous LSCS, Cephalopelvic disproportion	Emergency LSCS with sterilisation	2.794 kg, girl	8/10,9/10	Perivillous fibrosis
19	24y	G4 A3 37 weeks +2days	Nil	Bad obstetric history	Emergency LSCS	3.364 kg, girl	8/10,9/10	Perivillous fibrosis microthrombi neutriphilic cell infiltrates
20	24y	G2 P1 L1 37 weeks + 5 days	Nil	Previous LSCS	Emergency LSCS with sterilisation	2.210 kg, boy	8/10,9/10	Perivillous fibrosis
21	26y	G4 P2 L2 D2	Nil	Previous LSCS, Premature rupture of membranes, transverse lie	Emergency LSCS with sterilisation	2.75 kg, boy	8/10,9/10	Perivillous fibrosis
22	32y	Primi with term gestation	Nil	Cephalopelvic disproportion	LSCS	2.020 kg, girl	8/10,9/10	Microthrombi and empty fetal villi
23	26y	G3 P2 L2 with term gestation	Nil	Nil	Normal vaginal delivery	2.84 kg, girl	8/10,9/10	Microinfracts
24	22y	Primi with term gestationn	Nil	Cephalopelvic disproportion	LSCS	2.09 kg, girl	8/10,9/10	Chorioangiosis
25	25	G2P1L1 at term	Nil	Nil	Normal Delivery with episiotomy	2.605 kg, girl	8/10,9/10	Microthrombi
26	28	G2P1L1 at 38+3	Nil	Cephalopelvic disproportion	Elective repeat LSCS	3.040kg, boy	8/10,9/10	Perivillous Fibrosis
27	27	G2 P1 L1 AT 38 weeks	Nil	Previous LSCS, intrauterine fetal growth restriction	Emergency LSCS	2.630kg, girl	8/10,9/10	Microinfarcts and perivillous fibrosis
28	28	G2 P1 L1 at 34 weeks	HELLP syndrome, thrombocytopenia	Previous LSCS	Emergency LSCS	1.8kg, boy	8/10,9/10	Microinfarcts and autoamputation of tertiary fetal stem villi

Table 1: Clinical details and histology findings in COVID-19 with pregnancy.

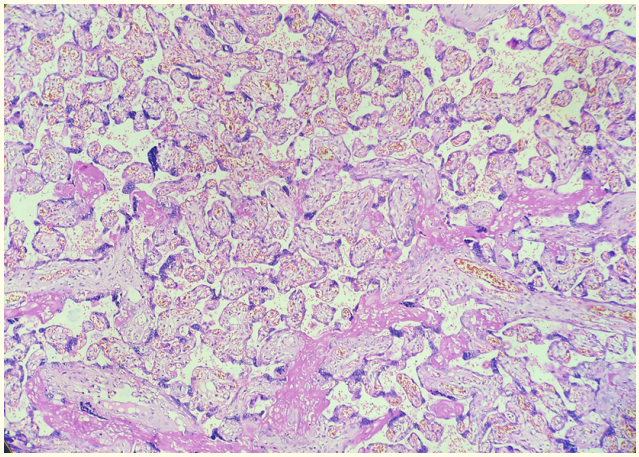

Figure 2: Placenta histology showing perivillous fibrosis (100X).

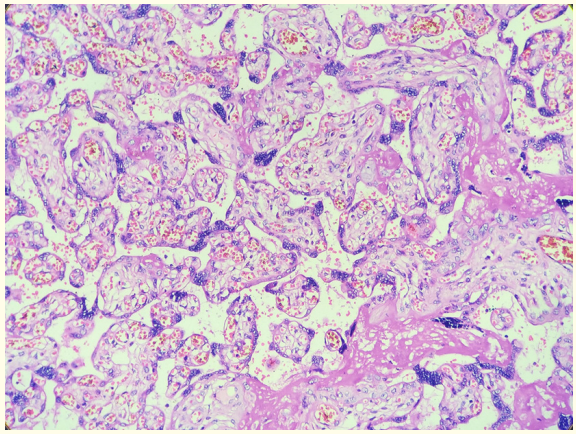

Figure 4: Placenta histology showing chorioangiosis (400x).

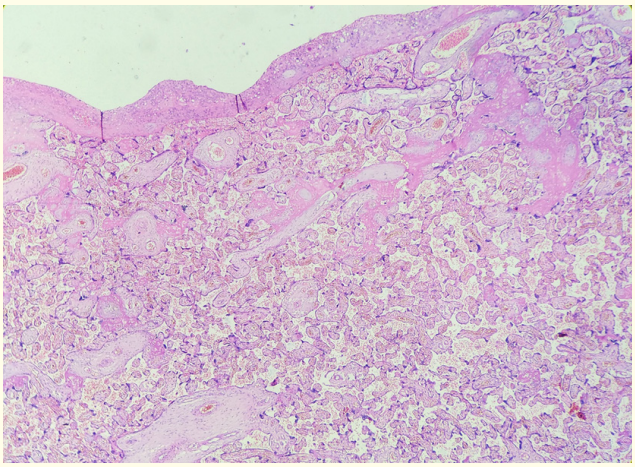

Figure 3: Placenta Histology showing neutrophilic infiltration (100x).

Discussion

This is a preliminary study of effects of COVID-19 on human pregnancy and placenta. Animal studies with mouse corona virus has been demonstrated to cause placental lesions and result in intrauterine fetal hypoxia. Most human studies done recently for transplacental transfer have not shown to affect the fetus. Recently, there was a case report where the newborn was found positive for Covid-19 IgM antibodies and high IL-6 levels. In our study of 28 patients we did not find newborn transfer. Some possible explanations could be that ACE-2 receptors are down regulated in fetus and newborn and the presence of different colonies of viruses and bacteria in mucosa of lungs and the airway limiting the growth of the SARS virus by direct competition and interaction.

The presence of maternal antibodies and the various changes that their immune system undergoes after environmental exposure can explain why newborns are relatively safe from the virus. We have demonstrated placental vascular malperfusion in our case. This could be a part of systemic vasculitis and microthrombi deposition as happens in all organs affected with COVID vasculopathy. This is an antiviral immune response and placenta too exhibits villitis of unknown etiology in COVID-19 infected mothers. In our series of 28 patients other causes of placental vasculitis like preeclampsia and gestational diabetes were ruled out as exclusion criteria. Thus, these placental changes of focal microthrombi and villitis and infarcts can be attributed to COVID -19. These changes were also seen in miscarriages, intrauterine deaths and preterm placenta of COVID-19 pregnant women. Further studies are required to study the pathophysiology of Intrauterine fetal demise and miscarriages in COVID -19 with pregnancy.

Conclusion

Placental affection in COVID-19 IS a part of systemic vasculitis of COVID-19 pathophysiology. The microthrombi and microinfarcts can lead to fetal malperfusion. The systemic Cytokine response can lead to Fetal inflammatory response syndrome (characterized by IL-6 > 11 pg/ml) even if there is no direct transfer of virus transplacentally. This immense sympathetic stimulation leads to secretion of neurotoxins as a part of inflammatory cascade and induce fetal mononuclear production of TNF alpha, IL-6 and IL-1. This may be a cause for miscarriages and fetal deaths in COVID -19. Further studies on newborn inflammatory markers are required to confirm our preliminary findings.

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