

Pregnancy Outcome in First and Second Trimester Covid Infection

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ABSTRACT

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Background: Covid 19 is entering its third year now. Most studies have concentrated on third trimester. We have attempted to study outcome in pregnancies afflicted with covid in first and second trimester.

AIM: To study outcome of pregnancies with covid in first and second trimester

Methods: We reviewed pregnancy outcome retrospectively in 153 pregnant women with covid in first and second trimester admitted in our institution between March 2020 - January 2022.

Results: 39.86% were between 26-30 years, 32.02% between 20-25 years. 49.01% were < 14 weeks of gestation, 40.52% > 14 and < 26 weeks of gestation, 10.45% were 26 - 28 weeks. Intrauterine growth restriction [IUGR] was seen in 13.07% patients, gestational diabetes mellitus [GDM] in 7.8%, hypertensive disorders of pregnancy [PIH] in 4.5% patients. 7.1% patients developed foetal distress. There were 42 miscarriages (27.45%), 42 normal deliveries (27.45%), 11 preterm deliveries [PTL (7.1%), 54 caesarean sections [CS]{30 emergency}. Asymptomatic patients had 80.95% of total abortions. Those with fever and upper respiratory tract infection (URT) and severe acute respiratory illness [SARI] contributed 36.66% each of total emergency CS. 36.66% of total cases of PTL were contributed by SARI while 36.36% were in asymptomatic group. In asymptomatic patients 57.62 % had miscarriages,13.55% required emergency caesarean and 6.7% PTL.

In group with fever and URTI, 12% abortions, 22.91% emergency CS 6% PTL. There was one miscarriage in group with fever and diarrhoea. Those < 14 weeks, 38.66% miscarriages, contributing to 69.04% of total abortions. 10.66% emergency caesarean [two< 34 weeks]. 5.3% PTL [one < 34 weeks]. In patients > 14 -< 26 weeks, 20.96% miscarriages, 8% PTL (one< 34 weeks), 19.35% emergency CS [two< 32 weeks]; one maternal, 2 intrauterine and one neonatal death. In patients 26-28 weeks, 62.5% required emergency caesarean [three< 32 weeks]. There was one maternal death, 2 patients PTL <34 weeks.

The maternal and neonatal death occurred in patients with SARI.

Conclusion: Our study shows increased abortions in early trimester irrespective of severity. The emergency caesarean and PTL rates increased in late second trimester and severe disease.

Keywords: Abortion, CS, COVID 19, PTL IUGR, PIH, GDM

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INTRODUCTION

Covid 19 caused by SARS COV 2 virus pandemic has held the world hostage since the wake of 2020. Numerous studies have examined the effects of covid in late-trimester pregnancies. In our study we have followed the course of pregnancy in the first and second trimesters, observing rates of miscarriages, PTL and CS.

Our institute, a tertiary referral centre, has catered to 1500 covid positive pregnant women till date since the

beginning of covid in 2020. 170 belonged to the first and second trimesters, 17 of whom were lost to follow up. The hospital records of the remaining 153 women were studied for their outcome.

AIM

To study outcome of pregnancies affected with covid in first and second trimester [miscarriage, PTL, emergency CS] with period of gestation and severity of disease.

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METHODS

A retrospective analysis of case records of covid positive pregnant patients admitted to our institution between March 2020 - January 2022 was done. 170 patients with period of gestation \leq 28 weeks were included. Their records till the end of pregnancy were analysed. The data was analysed using Microsoft Excel. The institutional ethical committee approval was taken for the study.

RESULTS

Among 153 patients, 39.86% were between 26-30 years, 32.02% between 20-25 years, 25.49% between 31-45 years and 2.6% < 19 years. 49.01% < 14 weeks of gestation, 40.52% were > 14 and <26 weeks gestation (Table 1).

38.56% had no complications. IUGR and abnormal Doppler were seen in 13.07% of patients. GDM seen in 7.8% of patients, PIH in 4.5% of patients. 7.1% of patients developed foetal distress (abnormal nonstress test/ cardiotocogram (CTG) (Figure 1).

There were 42 miscarriages (27.45%), 42 normal deliveries (27.45%), 11 PTL (7.1%), 54 CS [30 emergency] (Figure 2). Abnormal CTG, severe IUGR and abnormal Doppler [reversed umbilical artery flow] were the most common indications for emergency CS.

When assessed with symptoms, asymptomatic patients contributed to 80.95% of total abortions. Those with fever and URTI as well as SARI contributed 36.66% each of total emergency CS. 36.66% of total PTL contributed by sari while 36.36% were in asymptomatic group (Figure 3).

When each group was separately analysed it was found that asymptomatic patients 57.62 % had miscarriages, 13.55% had emergency caesarean while 6.7% had PTL. In group with fever and URTI, 12% abortions, 22.91% emergency CS and 6% PTL (Figure 4).

Table 1. Period of gestation [weeks]

| Period of gestation | Number of patients | Percentage |
|---------------------|--------------------|------------|
| < 14 WEEKS | 75 | 49.01 |
| >14 AND <26 WEEKS | 62 | 40.52 |
| 26-28 WEEKS | 16 | 10.45 |

There was one miscarriage in the group with fever and diarrhoea.

When analysed alongside period of gestation it was found that at < 14 weeks- 38.66% had miscarriages, contributing to 69.04% of total abortions. 10.66% underwent emergency caesarean with two < 34 weeks of gestation. 5.3% delivered prematurely [one < 34 weeks] (Figure 5).

In patients > 14 and < 26 weeks, 20.96% miscarriages, 8% PTL (one < 34 weeks), and 19.35% emergency CS [two < 32 weeks]. There was one maternal, 2 intrauterine and 1 neonatal death.

In patients between 26-28 weeks, 62.5% required emergency caesarean [three <32 weeks]. There was one maternal death. 2 patients PTL <34 weeks [severe oligohydramnios].

Maternal and neonatal death occurred in patients with SARI

DISCUSSION

Although vaccines have provided an effective shield, disease outcomes is unpredictable. Studies show no differences in symptoms between pregnant and non-

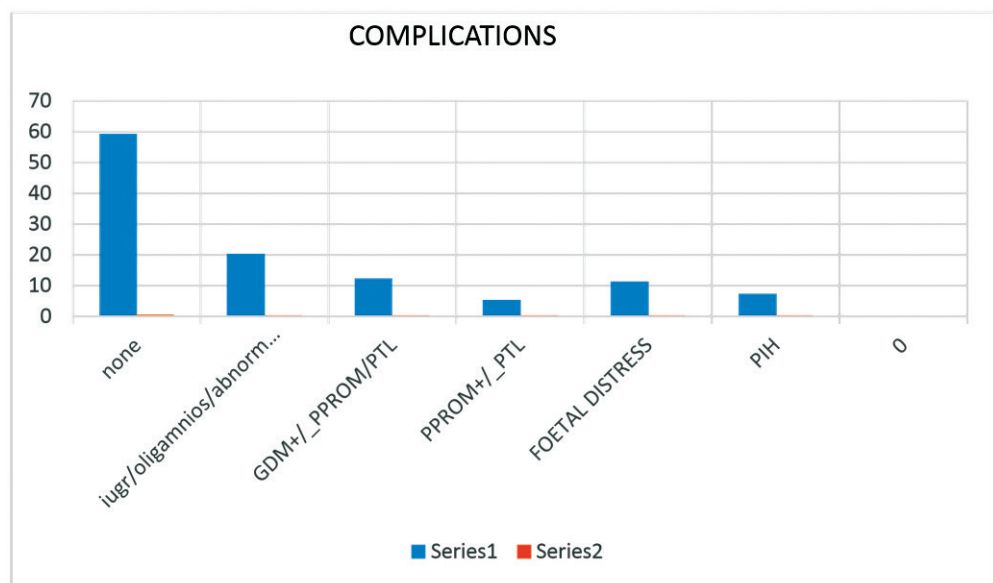


Figure 1. Complications

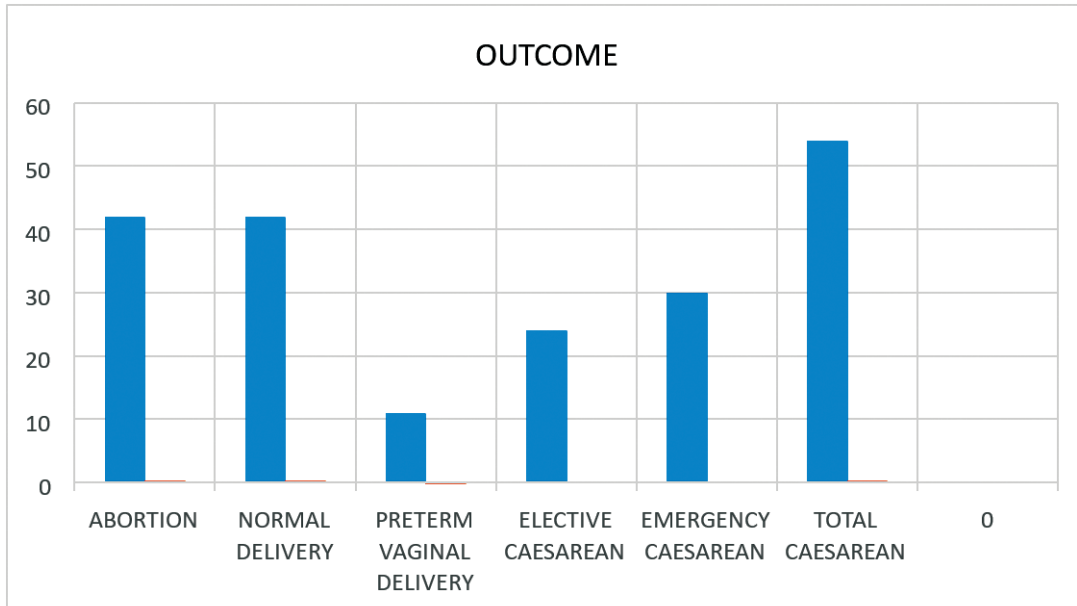


Figure 2. Outcome

pregnant women with COVID-19. However pregnant women were more likely to develop severe symptoms requiring intensive care.^{1,2} Some studies showed increased incidence of preterm labour, premature rupture of membranes, maternal/ foetal distress and caesarean rates in COVID pregnancies.³

A systematic review by jasmine abu-Amara et al⁴ demonstrated villitis and perivillous fibrin deposition with elevated levels of proinflammatory markers tumour necrosis factor (TNF- α) and interleukin (IL)-6 associated with endothelial activation and apoptosis of the trophoblastic cells. This was again reiterated by a study by Wu et al.⁵

The findings of our study correlate with these, with abortion rates varying between 12-50 % in the different groups studied. Incidentally, 80% of miscarriages were seen in asymptomatic patients, indicating placental changes in the absence of maternal symptoms.

Sacinti et al. (2021)⁷ compared the incidence of miscarriage in 13 week period and found that miscarriages increased by 25% during the SARS-CoV-2 pandemic [overall rate 11.8%].

The rate of PTL in healthy pregnant women worldwide is approximately 11%. A study by Yu n et al⁸ showed increased PTL in Covid pregnancies. Higher rates of

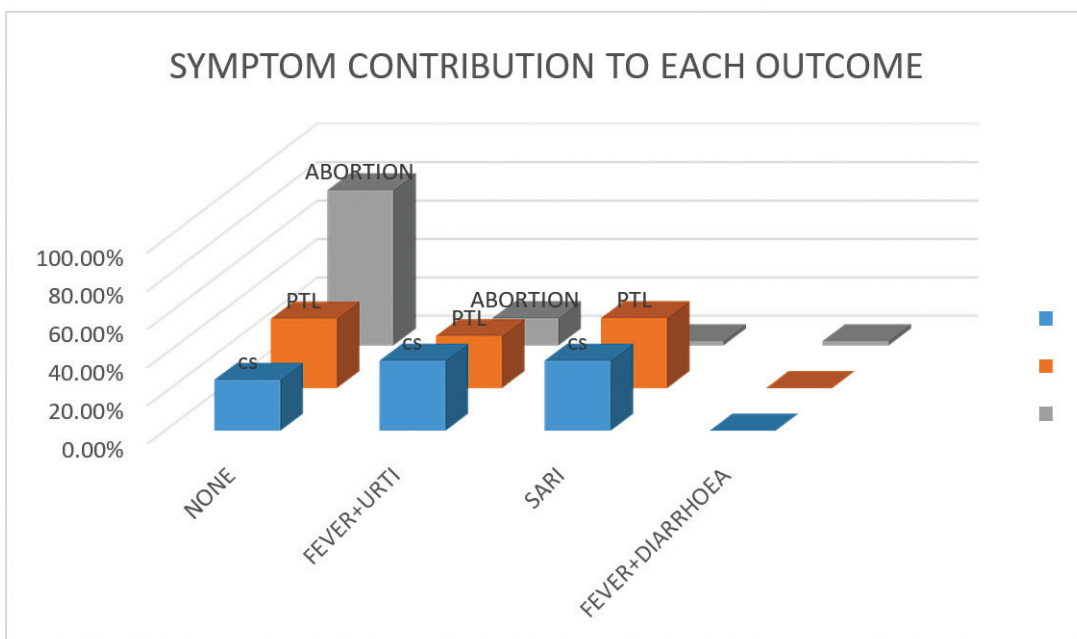


Figure 3. Symptom Contribution to Each Outcome

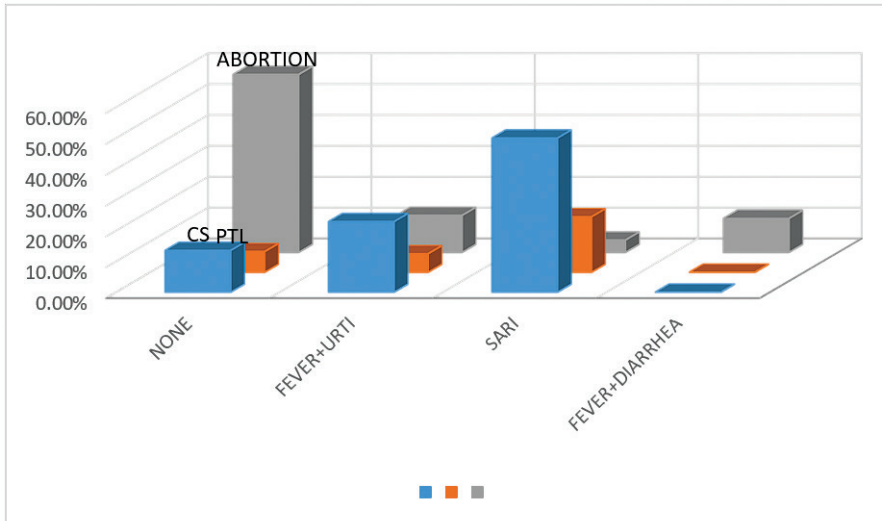


Figure 4. Outcomes in each symptom group

PTL and CS were seen in the study by Khalil et al.⁶ The rates of PTL varied between 5.3% to 38.65 in our study groups.

In our study, the caesarean rates varied from 13% in asymptomatic patients to 22.91% in patients with fever and URTI. The CS rates were as high as 62.5% in patients afflicted in the late second trimester. In our study there were 54 CS [30 emergency]; abnormal Cardiotocogram [CTG], severe IUGR and abnormal Doppler especially reversed umbilical artery flow being the most common indication for emergency CS.

In covid 19 pregnancies hypoxemia and immunopatho-

genesis (interferon release, natural killer (NK) cell activation, T cell activation, cytokine expression) were found to occur. These were associated with foetal demise/PTL, preeclampsia, IUGR, respiratory distress and immune system defects.⁹

Endotheliitis mimicking microvascular dysfunction of preeclampsia was seen in covid 19 patients leading to a pro-coagulopathic state.¹⁰⁻¹² Complement activation, seen in both preeclampsia¹³ and COVID-19¹⁴ was found to cause severe thrombotic vascular injury and progressive

vascular damage.

A study by Yun Liu et al¹⁵ showed an increased incidence of gestational diabetes mellitus [GDM] and PIH in COVID pregnancies resulting in PTL and low birth weight. Increased levels of inflammatory markers may increase the risk of developing T2 diabetes mellitus.¹⁶⁻¹⁸ Since GDM and T2 Diabetes mellitus have similar aetiologies, there is a likelihood that exposure to stressors like Covid during pregnancy could lead to chronic inflammation and increased risk of GDM.

In our study group incidence of preeclampsia was found to be 7.8% and 4.5% of the patients developed

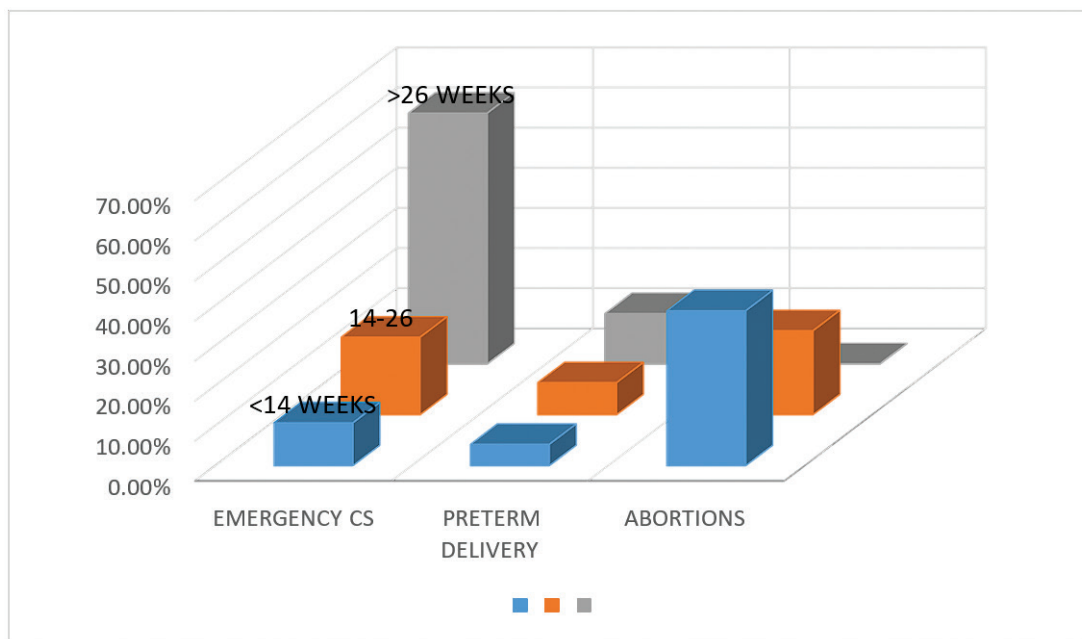


Figure 5. Outcome with gestational age

GDM. However these rates were not found to be statistically significant compared to general population.

Zhu et al. reported 10 neonatal deaths, with 6 cases of respiratory distress.¹⁹ in our study group, there were 2 maternal deaths one at 14 weeks, another at 26 weeks of gestation. Both had SARI.

There were 2 intrauterine and one neonatal death, both extremely premature, with severe associated maternal symptoms.²⁰

SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) as its functional receptor for infecting human cells.²¹ Pulmonary infection by COVID leads to pulmonary oedema, hyaline membrane formation and pulmonary interstitial thickening²² associated with respiratory distress. Maternal respiratory failure with hypoxemia decreases placental blood and oxygen transport causing foetal distress, miscarriage, premature delivery, need for operative intervention. These changes may be responsible for maternal/foetal morbidity and mortality in affected patients in our group as well since mortalities occurred in patients with severe symptoms.

Studies have demonstrated increased activation of immune cells and interferon production, causing immune damage in COVID-19. Placental morphological changes due to exposure to human chorionic explants to IFN-I in the second trimester were found to increase the risk of foetal demise and IUGR.^{23,24,26}

In the placenta, Natural Killer [NK] cells with trophoblast cells facilitate uterine vascular remodelling causing increased placental blood.^{27,28} Activation and decrease in the number of NK cells in peripheral blood leads to failure of NK cell accumulation in decidua impeding uterine vessel reconstruction.²⁵

All these complex mechanisms postulated to happen following COVID-19 infection need extensive studies for validation. However, they open up wide vistas for future studies which could help us in the future in combating similar viruses as well.

SUMMARY

Our study found an increased incidence of miscarriages, preterm deliveries and emergency caesarean sections in COVID-19 pregnancies. This correlates with the available literature. Miscarriages were seen even in patients without symptoms. Hence outcome of early pregnancies may be disproportionate to the severity of the disease.

Covid 19 not only threatens the mother and neonate in the intrapartum period but also jeopardises the long-term development of neonates. Although COVID cases are declining, it is re-emerging in new forms. These studies could fortify our therapeutic arsenal in the fight against all viruses including Covid 19 and its variants. We hope that the data provided through our humble attempt will help form a base for further molecular and allied studies against Covid 19.

END NOTE

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