Original Research Article

Biochemical Markers and Adverse Maternal Outcomes in COVID-19 Pregnant Women: A Prospective Study

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Abstract

Background-COVID-19 is a newly emerged virus that leads to severe consequences; hence a collaborative approach to COVID-19-positive pregnant women is required. Identifying clinical features of SARS-CoV-2 infection in pregnant women is important as early as possible to decrease it and lower mortality and morbidity associated with it. We have evaluated maternal parameters associated with COVID-19 pregnancy and their clinical outcomes. Obstetric outcomes were compared with the severity of the disease.

Material and methods- The study was a single-centred analysis of 71 pregnant women prospectively from April 2021-July 2021. All pregnant patients admitted to our hospital as COVID suspects were recruited. Data collected includes age, parity, gestational age, mode of delivery, comorbidity, haematological parameters, and complications during antenatal periods.

Results- Out of 71 cases, the majority, 59(83.1%) cases were symptomatic and 12(16.9%) cases were asymptomatic. According to SPO2 level out of 71 cases, 19(26.8%) cases had severe disease, 36(50.7%) had moderate, 10(14.1%) had mild disease and 6(8.5%) had normal. Maternal mortality was observed 29(40.8%). The mortality rate was higher among 14(48.3%) severe cases and 11(37.9) moderate cases. Serum ferritin was significantly associated with the maternal outcome severity.

Conclusion- Mortality was higher in patients with lower levels of spo2, accounting for 48.3%. In these pregnant women, we found a more elevated serum ferritin level, denoting a positive correlation of these biochemical markers with the severity of COVID-19, resulting in adverse maternal outcomes. As limited studies were found on the correlation between biochemical markers and the negative effects in COVID-19 pregnant females, this study can help advance the research further.

Keywords- COVID-19, Obstetric outcome, Serum ferritin

1. INTRODUCTION

Coronavirus disease 2019(COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a pandemic by the World Health Organization on March 11, 2020 [1]. In December 2019, a novel coronavirus (SARS-CoV-2) outbreak occurred in wuhan (Hubei province, China). On 30 January 2020, the World Health

Organization (WHO) declared the outbreak of COVID-19, a respiratory disease, as the sixth public health emergency of international concern [2,3]. Due to its highly transmissible nature, by 11 March 2020, WHO declared it a pandemic.

Coronaviruses, a genus of the Coronaviridae family, are enveloped viruses with a large plus-strand RNA genome [4]. The genomic RNA is 27-32 kb in size, capped, and polyadenylated. The coexistence of COVID-19 with pregnancy may lead to increased morbidity and mortality in pregnant women as well as in their newborns. Most of the pregnant women presented with the common cold or characteristically mimicked viral pneumonia, and these pregnant women reported for medical help too late, thus leading to higher morbidity and mortality. Analysis was done based on their blood parameters and radiologic findings to know more about their morbidity due to COVID-19. This hospital was designated a COVID-19 hospital on 14th April 2020-July 2021. Until now, there have been very few reports on clinical and haematological scenarios associated with pregnancy and COVID-19. By learning and knowing more about the manifestations of COVID-19 in pregnant females, proper management would be possible.

2. MATERIAL AND METHODS

This study was carried out in the Department of Obstetrics and Gynecology, R.D. Gardi Medical College and C.R.G.H Hospital, Surasa, Ujjain (M.P.). This hospital was a designated COVID centre and a higher referral centre for affected patients during the pandemic. During the pandemic, this hospital was a pooling centre for patients affected by the coronavirus. This is a prospective observational study conducted on all admitted pregnant women who are positive for COVID-19 and those who presented with COVID-19 symptoms. The study was started after obtaining ethical approval (**IEC Ref. No- 42/2021**) from the institutional ethic committee, R.D.Gardi Medical College, Ujjain, M.P. A total of 71 COVID-19-infected pregnant patients was recruited in the study, which includes symptomatic COVID-19-positive and negative pregnant women, Asymptomatic COVID-19-positive pregnant women.

In the prospective observational study, after obtaining written and informed consent, a detailed history of all study patients, including their demographic data, age, education, occupation, income, and socioeconomic status, were taken. Information regarding their parity, gestational age, presentation, the onset of labour, and the number of fetuses were recorded. These antenatal women were monitored properly from the date of admission till discharge. Pregnant women presenting at the hospital with COVID-19-infected symptoms were tested. COVID-19 confirmation was done by testing the nasopharyngeal and oropharyngeal swabs by the reverse transcription-polymerase chain reaction (RT-PCR) method. Study cases of antenatal women were thoroughly examined with an initial assessment, including their general condition, assessing their breathing difficulty, gasping, cough, pallor, pedal oedema, icterus, and cyanosis. Vital signs like temperature, pulse, blood pressure, heart rate, respiratory rate, and oxygen saturation were recorded. Her systemic examination and obstetric examination were done. Preliminary investigations like the Covid antigen test and RT-PCR were done. Laboratory investigations, including routine ANC profile, Ultrasound and add-on investigations like LFT, RFT, Serum electrolyte, C-reactive protein, D-dimer, LDH, serum Ferritin, and coagulation profile, were done. Chest X-rays with abdominal lead shields and CT-scan were performed in case of acute respiratory symptoms or oxygen saturation < 95% on room air. In the case of mild symptoms without comorbidities, a detailed assessment was done, and treatment was suggested as per the

severity of the disease. The mild infection required home isolation and management, including adequate hydration, the use of antipyretics, and the use of pulse oximetry to monitor saturation. Specific instructions were given for routine pregnancy visits, laboratory tests, and screening ultrasounds were postponed until the end of the isolation period (4 weeks after the appearance of symptoms) or following negative RT-PCR tests after two weeks from the presence of symptoms. Moderate and severe cases required hospital admission under vital signs monitoring (blood pressure, heart rate, respiratory rate, and oxygen saturation) under a high-dependency isolation unit. Admitted patients were treated to keep Spo2 >94% via nasal cannula or venturi mask (up to 40% Fio2), followed by continuous positive pressure masks, maintaining hydration and avoiding fluid overload. If needed, paracetamol was given up to 4 g/day. Monitoring of fetal heart rate (CTG if >28 weeks) was done, and a decision for the mode of delivery was made. Management, without a doubt, was done in ICU by a multidisciplinary team of critically ill pregnant women. Some patients required emergency cesarean section, while some required continuous monitoring of FHS, the progress of labour, and delivered vaginally along with simultaneous monitoring of Spo2, fever, dyspnea, and other parameters. Discharge of the antenatal patient was done on medications, and was advised for frequent follow-up visits. Discharge of postnatal patients and their neonates were planned once both of them were stable, tested negative, and stayed without any symptoms for four weeks after the beginning of symptoms or after the PCR test was negative. Assessment of pregnancy risks, fetal growth, and well-being was recommended throughout pregnancy. Due to concern about fetal growth, serial ultrasounds in the third trimester (28, 32, 37 weeks) were advised. For neonates, rooming-in and breastfeeding were advised as appropriate preventive measures.

RESULTS

Out of 71 cases, majority 59(83.1%) cases were symptomatic and 12(16.9%) cases were asymptomatic.

Table1-Distribution of the severity of disease of the cases

SPO2 level	N(%)
Mild (90 - 95 %)	10(14.1)
Moderate (80 - 90 %)	19(26.8)
Severe (< 80 %)	36(50.7)
Total	71(100)

The severity of COVID-19 disease in pregnant women is a critical determinant of maternal outcomes. In this study, we evaluated the distribution of disease severity in 71 COVID-19-infected pregnant women. According to the SPO2 level, which is an essential indicator of respiratory function, 36 cases (50.7%) were classified as moderate, 19 cases (26.8%) as severe, and 10 cases (14.1%) as mild. These findings highlight the potential severity of

COVID-19 infection in pregnant women and the importance of monitoring respiratory function.

Table2- Maternal mortality in total cases

Maternal Mortality	N(%)
Yes	29(40.8)
No	42(59.2)

Out of 71 cases, maternal mortality was observed in 29(40.8%).

Table3- Association between disease severity and maternal mortality

Severity of disease (SPO2 level)	Maternal Mortality	
	Yes	No
	N(%)	N(%)
Mild (90 - 95 %)	3(10.3)	7(16.7)
Moderate (80 – 90 %)	11(37.9)	8(19.0)
Severe (< 80 %)	14(48.3)	22(52.4)

Table 2 shows that out of 71 cases, maternal mortality was observed in 29 (40.8%) cases. In Table 3, a significant association was observed between the severity of the disease and maternal mortality, with the mortality rate being higher in severe cases. Specifically, 14 (48.3%) severe cases experienced maternal mortality, as compared to 11 (37.9%) moderate cases and 3 (10.3%) mild cases.

Table 4- Comparison of Mean Serum Ferritin according to maternal mortality

Maternal Mortality		N	Mean	SD	p
Serum Ferritin	Yes	29	248.62	162.64	0.047
	No	42	169.80	161.13	

Table 4 compares the mean serum ferritin levels between cases with and without maternal mortality. The results showed a statistically significant difference between the two groups, with cases experiencing maternal mortality having a higher mean serum ferritin level (248.62 ng/mL) as compared to cases without maternal mortality (169.80 ng/mL) (p=0.047). This suggests that there may be a positive correlation between serum ferritin levels and the severity of COVID-19 infection in pregnant women, leading to adverse maternal outcomes.

These findings highlight the importance of monitoring serum ferritin levels in COVID-19-infected pregnant women, as it may help predict the severity of the disease and subsequent maternal outcomes. (Table 4)

Table 5- COVID-19 comparison according to the severity

Spo2 level	Mild	Moderate	Severe	ICU admission
Awale et al (2021)	44.6%	15.4%	15%	83.3%
M.kasraeian et al (2020)	78%	62%	40%	33%
Zlatkin et al (2020-2021)	27.38%	2.38%	3.60%	3.60%
Shree et al. (2020-2021)	94.3%	84.6%	3.8%	1.9%
The present study (2020-2021)	14.1%	26.8%	50.7%	28.8%

Table 6- Association between maternal mortality and comorbidities

	Maternal Mortality	
	Yes	No
	N(%)	N(%)
Pre-eclampsia	7(16.7)	2(10.0)
GDM	2(10.0)	2(4.8)
Hypothyroidism	2(10.0)	6(14.3)
Anaemia	7(36.8)	6(14.3)

Table 5 compares COVID-19 severity levels reported in various studies, including the current study. The percentage of patients with mild, moderate, and severe disease and ICU admissions varied across the studies. In the present study, 14.1% of the cases had mild disease, 26.8% had moderate, and 50.7% had severe disease. Table 6 presents the association between maternal mortality and comorbidities. Pre-eclampsia and anaemia were significantly associated with maternal mortality, with 7 (16.7%) cases and 7 (36.8%) cases, respectively.

However, the association between maternal mortality and GDM or hypothyroidism was not statistically significant. These findings suggest that pre-existing conditions may increase the risk of adverse outcomes in COVID-19-positive pregnant women.

Table 7- Neonatal outcome

Neonatal outcome	N(%)
APGAR score <7 at 5 min	14(22.6)
Low birth weight	6(9.7)
Prematurity	2(3.2)
Neonatal sepsis	3(4.8)
NICU admission	10(16.1)

Table 7 provides information on the neonatal outcomes in our study. Out of 62 live births, 14 (22.6%) neonates had an APGAR score of less than seven at 5 minutes after birth, indicating a need for medical intervention. Six (9.7%) neonates had a low birth weight, and two (3.2%) were born prematurely. Three (4.8%) neonates were diagnosed with neonatal sepsis, and ten (16.1%) required admission to the neonatal intensive care unit (NICU) for further management.

3. DISCUSSION

The present study was conducted on 71 pregnant women who were admitted at the time of COVID-19 in our hospital. In the present study, there were 59 (83.1%) symptomatic cases and 12 (16.9%) asymptomatic cases. In symptomatic cases- fever was seen in 54(76.1%) cases, dyspnea was seen in 61(85.9%) cases, the cough was seen in 54(76.1%) cases, cold was seen in 21(29.6%) cases, sore throat was seen in 14(19.7%) cases, diarrhea was seen in 15(21.1%) cases, pneumonia was seen in 54(76.1%) cases and chest X-ray changes was seen in 54(76.1%) cases. The mean values of Serum Ferritin were significantly increased according to the severity of the disease. Limited studies were done on maternal outcomes based on serum ferritin levels. Thus early analysis of ferritin levels in patients with COVID-19 might effectively define the severity of the disease [5]

Pregnant women having co-morbidities such as gestational diabetes, hypertension or pre-eclampsia, anaemia, and other miscellaneous comorbidities; maternal age > 35 years old was considered a risk factor. Pregnant women infected with COVID-19 and the presence of co-morbidities in these women result in the worst maternal outcome and maternal morbidity.

Fetal and neonatal mortality and morbidity outcomes included stillbirth, perinatal death, early and late neonatal death, and admission to the NICU. Pregnancies with a severe form of COVID-19 were more likely to present with adverse maternal and neonatal outcomes such as preterm delivery, low neonatal birth weight, neonatal infection, and/or admission to the NICU.

4. CONCLUSION

COVID-19 is one of the major causes of maternal mortality and long-term maternal morbidity. This study will aid in planning the strategies to handle the epidemic of COVID-19 infection in pregnancy. This data is extremely important to develop rational management strategies for protecting pregnant women against possible adverse effects of COVID-19. The present study revealed that the severity of COVID-19 infection and abnormal biochemical markers have a substantial correlation. Serum ferritin was found to be the bad prognostic marker. Therefore, ferritin holds a crucial role as a simple complementary tool for guiding clinical decisions and treatment [5].

5. REFERENCES

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