

COVID-19 and Pregnancy Outcome: An Experience in 'COVID-19 Management Designated' Tertiary Care Hospital, Rawalpindi, Pakistan

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Abstract

Background: The current COVID-19 pandemic has affected almost 17.3 million victims worldwide with mortality of almost 674K. Pregnancy is one of the most susceptible conditions for COVID-19 infection, but limited data is currently available about the clinical characteristics of pregnant women with the disease. **Objective;** to describe the clinical characteristics, co-morbidities, management, feto-maternal, and neonatal outcome in COVID-19 positive pregnant women.

Methodology: A descriptive case series study was conducted in Obs/Gynae dept of Benazir Bhutto Tertiary Care Hospital, Rawalpindi, including all asymptomatic/symptomatic COVID-19 positive pregnant women and clinical suspects (COVID-19 PCR negative women) delivered in our hospital from 01st April 2020 to 31st July 2020. Their medical records were reviewed for clinical characteristics, management, feto-maternal and neonatal outcomes. Continuous variables were expressed in Mean & Range and Categorical variables as number & Percentage.

Results: During the study period a total of 17 cases were reviewed. The mean maternal age was 28.94 yrs. Primigravida (07), Multipara (10). Mean gestational age was 37 wks (range; 30-41wks). Presenting symptomatology was varied. Asymptomatic; (29%), COVID-19 specific symptoms; fever & flu (12%), fever&cough (6%), shortness of breath(SOB) alone (6%), fever & SOB(6%) and pregnancy-related manifestations were labour pains (17%), eclampsia(6%), hydrocephalous fetus (6%) and hepatic encephalopathy(6%). The commonest co-morbidity was Hypertensive disorders of pregnancy (24%). Five women (29%) required ICU care. Lower segment caesarean sections(LSCS) (59%), vaginal delivery (41%). Eleven babies delivered with good Apgar score and birth weight. Two were early neonatal deaths (ENND) and 04 were received intra-uterine fetal deaths (IUDs). Fetal demise was associated with strong obstetric risk factors. Out of 13 live-born babies, RT-PCR Covid-19 testing was done in 10 (77%) cases and was negative. One mother was expired due to complications of hepatic encephalopathy, sepsis, and burst abdomen.

Conclusion; The clinical course of COVID-19 disease in pregnancy seems to be no different from non-pregnant women. Clinical manifestations are diverse and infection contracted in the third trimester of pregnancy is associated with good fetomaternal and neonatal outcomes.

Keywords; COVID-19, SARS-COV-2, Pandemic, Fetomaternal outcome, Neonatal outcome.

Introduction

The current Coronavirus infection 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-COV-2)¹ has been declared as a Pandemic by WHO on 11th March 2020.² The first reported case was in December 2019 in Wuhan city, Hubei province of China.³ Since then it has affected almost 17.3 million victims worldwide with mortality of almost 674K. In Pakistan, till now 278 K positive cases and 5.9K deaths have been reported.⁴

This highly contagious disease with the main predilection for pulmonary system spreads by respiratory droplets during coughing, sneezing and close physical contact.⁵⁻⁷ The most susceptible population is believed to be elderly people (>65yrs), people with chronic disease, or an immunocompromised condition.^{7,8} Being an immunocompromised state, pregnancy is believed to be an important risk factor for COVID-19 infection.^{9,10} Both pregnancy and COVID-19 infection share the same immune response characterized by a decrease in lymphocytes and an increase in certain pro-inflammatory cytokines.^{11,12} Furthermore, placental villi have angiotensin-converting enzyme-2 (ACE2) receptors through which coronavirus enters the host cells. These receptors can also facilitate the vertical transmission of infection.¹⁰

As infection is a rise in the general population so are the pregnant women too at more risk. Almost 15,735 pregnant women with laboratory-confirmed infection and 37 deaths have been reported in the United States alone.¹³ There is a paucity of knowledge regarding various aspects of this novel virus disease. Since the start of the pandemic, multiple studies are being carried out to understand its clinical manifestations and management not only in the general population but also in special conditions like pregnancy. Index study was plotted with the same aim to contribute to a globally gathered pool of obstetric knowledge and management plan in COVID-19 positive pregnant women. Our hospital is "Exclusive COVID-19 Management" declared hospital by the government of Punjab and our obstetric department has been

managing COVID-19 positive pregnant women since the start of this pandemic in the region. In this study, we are sharing our experience regarding the clinical presentation, management, fetomaternal and neonatal outcome of COVID-19 positive pregnant women. This will be a beneficial data for other tertiary maternity care hospitals which are managing pregnant women in this pandemic.

Material and Methods

Study Design, Setting and Material

This single centered, descriptive case series study was carried out in the Obstetrics & Gynaecology department of "exclusive COVID-19 management designated" Benazir Bhutto Tertiary Care Hospital, an Allied teaching hospital of Rawalpindi Medical University, Pakistan. After approval of the institutional ethical committee, we reviewed the medical records of all symptomatic/asymptomatic confirmed Reverse transcriptase-polymerase chain reaction (RT-PCR) COVID-19 positive pregnant women and strong clinical suspects with RT-PCR COVID-19 negative status and managed in our obstetrics department from 1st April' 2020 to 31st July' 2020. There was no exclusion criterion. Whether women were our booked/Non-booked or referred from other health facilities, medical charts of all were reviewed.

Method/Procedure; After admission, the SARS-COV-2 status of all affected women was reconfirmed by a hospital designated experienced healthcare personnel, who took nasopharyngeal swabs for real-time RT-PCR using WHO guidelines. There was a designated labour room, operation theatre, and ward for managing pre-natal and post-natal mothers. Though per departmental policy, there was a low threshold for caesarean delivery for COVID-19 positive women those who presented in an active phase of labour or multigravida with good bishop score were encouraged to deliver vaginally. At birth, babies were promptly attended by a paediatrician and then transferred to a neonatal isolation room for further needful management, and COVID-19 testing after 24hrs was done as per the policy of paediatric department.

Mothers were discharged once they were afebrile/stable and had two consecutive negative RT-PCR tests 24 hrs apart after approval of a multidisciplinary team comprising of an obstetrician, anaesthetist, and medical specialist/pulmonologist. Maternal and neonatal status at the time of discharge was recorded on medical charts. Completed charts were saved and later on reviewed for the study descriptive outcome variables like; demographic profile, clinical presentation, co-morbidities, maternal obstetric complications, management plan (mode of delivery), feto-maternal and neonatal outcome during a hospital stay. Neonatal outcome was measured in terms of mortality and morbidity like; compromised birth Apgar score, baby weight, admission to NICU, COVID-19 vertical transmission. All data were recorded on a specially designed proforma.

Statistical Analysis: Data was entered on SPSS version 22. Continuous variables were expressed in Mean & Range while Categorical variables as Number & Percentage.

Results

During the study period total of seventeen (n=17) medical charts were reviewed. Fourteen (n=14) pregnant women were confirmed COVID-19 positive on repeat RT-PCR testing while 03 were COVID-19 negative, but being strong clinical suspects they were managed as COVID-19 positive and included in the study. The first case was admitted on 18th April 2020 and the last one on 10th July 2020.

One woman was our booked case, 07 were booked, and referred cases from other public/private hospitals while 09 were non-booked. All women were Rhesus positive. Mean maternal age was 28.94 yrs (Range; 18-39 yrs). Primigravida was 07, Multipara was 10. Mean gestational age at presentation was 37 wks (range; 30-41wks) 06 (35%) preterm (<37 wks), 09 (53%) at 37-40 wks and 02 (12%) at 41 wks. Presenting symptomatology was varied (Figure 1). Asymptomatic women had their COVID-19 test done because of some affected close contact. The commonest co-morbidity was Hypertensive disorders of pregnancy (Figure 2). Five patients (29%) required ICU admission, two needing high flow oxygen, and one with hepatic encephalopathy required ventilatory support as well. Ten women (59%) delivered by LSCS under regional spinal anaesthesia while 2 had general anaesthesia. Uneventful spontaneous vaginal deliveries were 07 (41%) including one vaginal birth after caesarean

(VBAC) and one case of induction of labour in a multiparous post-dated woman. Indications for LSCS are shown in Table 1.

Maternal Pre-partum complications were encountered in 5 (29%) cases; Sepsis-02 (12%), Scar dehiscence-01 (6%), Aspiration pneumonia-01 (6%), Hepatitis E Hepatic Encephalopathy-01 (6%). Post-partum complications were seen in 6 (35%) cases; Low O₂ saturation-02 (12%), Burst Abdomen-02 (12%), Sepsis-01 (6%) and Typhoid fever- 01 (6%)

The majority of babies (n=11) delivered alive with a good one minute Apgar score of 7-8. Liquor was clear and adequate in 10 cases and oligohydramnios in only one case. The other 6 cases had 3rd-degree meconium, out of which 2 expired in 1st week of life (ENND) and 4 were received IUDs (Fig.03). Obstetric risk factors associated with fetal demise are shown in Table 2.

Majority of babies (71%) had birth weight of 2.5-3.5 kg, 24% of <2.5kg and 5% were >3.5kg. Breastfeeding was not established in any case during a hospital stay. Out of 13 live-born babies, RT-PCR Covid-19 testing was done in 10 (77%) and was negative, 02 babies had ENND, one was taken home and could not be tested. One mother was expired due to complications of hepatic encephalopathy, sepsis, and burst abdomen. Two mothers left against medical advice (LAMA), while the other 14 (82%) were discharged as per discharge criteria in stable condition.

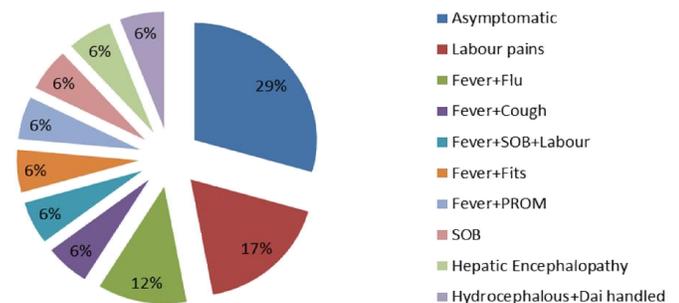


Figure 1: Symptomatology

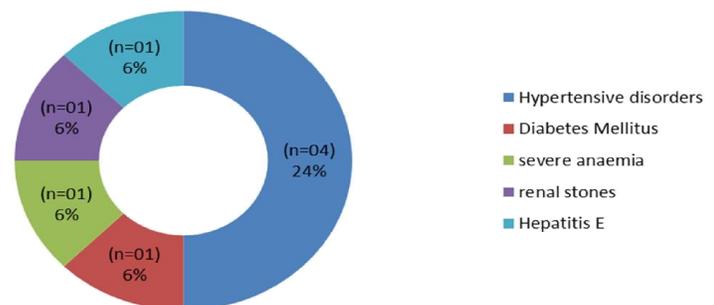


Figure 2: CO-Morbidities

Table 1: Indications for Caesarean Delivery

| Sr. # | Indication | Number/10 (%) |
|-------|-------------------------|---------------|
| 01. | Previous 01 LSCS | 01 (10) |
| 02. | Previous 02 LSCS | 02 (20) |
| 03. | Previous 03 LSCS | 01 (10) |
| 04. | Chorio-amnionitis | 02 (20) |
| 05. | Precious Pregnancy & DM | 01 (10) |
| 06. | CPD | 01 (10) |
| 07. | Fetal Distress | 01 (10) |
| 08. | Eclampsia | 01 (10) |

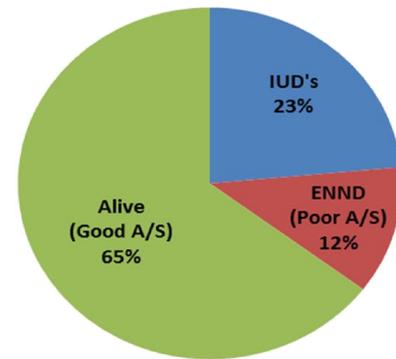


Figure 3: Fetal Outcome

Table 2: Risk Factors for Fetal demise

| Sr. # | Gest. Age (wks) | Obstetric complication | Liquor | Fetal outcome |
|-------|-----------------|--|----------|---------------|
| 01 | 31 | Eclampsia | Meconium | IUD |
| 02 | 34 | Uterine Scar dehiscence | Meconium | IUD |
| 03 | 30 | Hepatitis E Encephalopathy | Meconium | IUD |
| 04 | 36 | Chorio-amnionitis | Meconium | IUD |
| 05 | 39 | Chorio-amnionitis | Meconium | ENND |
| 06 | 37 | Fever & Flu (non-obstetric complication) | Meconium | ENND |

Discussion

In this case series study, we described the clinical characteristics, feto-maternal, and neonatal outcome in seventeen COVID-19 positive pregnant women. Overall results were reassuring. Pregnant women are more prone to respiratory infections due to immunosuppression.¹² Studies are being carried out worldwide to explore the mutual effects of pregnancy and SARS-COV2 infection. Available data is scanty and controversial at this time. Very first study reporting the effect of COVID-19 infection on the feto-maternal and neonatal outcome from China in March 2020,⁵ concludes that COVID-19 contracted in advanced pregnancy have a good outcome. Multiple studies suggest that Clinical manifestation of COVID-19 in pregnancy is not different from non-pregnant adults,¹⁴⁻¹⁷ yet according to few studies pregnancy can complicate the clinical course of COVID-19 disease.^{5,14,18} The presenting symptomatology is diverse. An infected person can be asymptomatic at one end of the spectrum, going through mild common symptoms of fever, cough, sore throat, myalgias, fatigue¹⁹⁻²⁰ can culminate into severe complications of respiratory distress syndrome, cardiac injury, end-organ failure or even death at the other end.^{14,17} A recent report by the Center for Disease Control and Prevention (CDC)²¹ states that fever, muscle aches, chills, headache, and diarrhea are less reported among COVID-19 pregnant women than non-pregnant. In our study course of the disease was mainly mild and almost half of women were either asymptomatic (had COVID-19 test due to a close contact exposure) or they presented in labour with no COVID-19 specific symptoms. The main COVID-19 specific symptoms were fever and flu in 12% of women. Less common

were cough, myalgia, and shortness of breath. The commonest co-morbidity was a hypertensive disorder of pregnancy seen in 04 cases. The effect of COVID-19 infection upon pregnancy outcome is also conflicting. Deleterious effects reported by few studies^{5,17,22} are miscarriage, fetal distress, fetal growth retardation, preterm labour, respiratory distress, thrombocytopenia, abnormal liver function, or even foeto-maternal mortality yet another study²⁰ gives no evidence of fetus distress. Our study reported no case of miscarriage, preterm labour or severe respiratory distress.

Pro-inflammatory status of 1st and 3rd trimester and anti-inflammatory status of 2nd trimester of pregnancy is a fact.^{23,24} In our study all women were affected in the third trimester with overall satisfactory outcomes. Few other studies also reported good foeto-maternal and neonatal outcomes in late pregnancy infection.^{5,17} The one COVID-19 positive mother expired in our study had complications of hepatitis E-hepatic encephalopathy, postoperative sepsis, and burst abdomen.

Mode of delivery is subjected to individual departmental policy owing to uncertainty about the risk of intrapartum mother-to-baby transmission by vaginal delivery. For the same concern and to minimize the exposure time of health personnel involved in women care we opted for a low threshold for caesarean delivery for COVID-19 positive women but those women who presented in the active phase and good progress of labour were encouraged to deliver vaginally. No caesarean delivery was done solely due to COVID-19 infection and there were strong obstetric indications for the LSCS. In a few studies, all affected mothers had an elective caesarean delivery.^{5,17} Another study reported that vaginal secretions are negative for this virus and vaginal delivery is a safe option.²⁵ In our study women who delivered vaginally, their course of labour was not altered by the COVID-19 disease. There was one VBAC and even one induction of labour in a multiparous woman at 41 wks who successfully accomplished vaginal delivery. General anesthesia should be avoided and Spinal anesthesia is the choice for COVID-19 positive cases.²⁶ We conducted all LSCS under spinal anaesthesia except two cases; one of eclampsia and another woman was in hepatic encephalopathy. The same two women required ICU admission, the other 3 women were admitted in ICU for oxygen demand and in just an anticipating of deterioration of their symptoms and had an uneventful recovery. Recently CDC reports²¹ that

COVID-19 infected women are more prone to hospitalization, ICU admission, and needing mechanical ventilation than non-pregnant women, but their risk for death remains the same. A Sweden study also found that pregnant women with COVID-19 are five times more likely to be admitted in ICU and four times more prone to receive mechanical ventilation than non-pregnant women.²⁷

Regarding neonatal outcomes, the majority of our babies were delivered with good Apgar score and birth weight. Two babies of febrile mothers were delivered with 3rd-degree meconium and expired within 24 hrs while 4 were received IUDs. As shown in the results cause of fetal demise in such cases seems to be associated with some strong Obstetric risk factor. There is currently no report of vertical transmission of COVID-19 infection, and the barrier role of the placenta against viral and bacterial infections is a fact.²⁴ However, increased expression of ACE2 receptors over the placenta renders not only mothers more susceptible to COVID-19 but may also facilitate vertical transmission.^{10,28} Multiple studies give no evidence of vertical transmission.^{20,29,30} and in studies with women affected in the 3rd trimester, all babies born were negative for SARS-COV-2.^{5,17,31} Same was the result in our study. All 10 babies who made to life and were tested later on were COVID-19 negative. All these studies are small sampled and done in advanced pregnancy, evoking uncertainty about how this infection will affect the fetus in the first or second trimester.

Breastfeeding by COVID-19 positive mothers is also not spared of controversy. In the early months of the pandemic, researchers suggested keeping neonates of suspected or confirmed COVID-19 diseased mothers isolated for at least two weeks after birth and not be breastfed.^{31,32} Another study reported that breast milk from affected mothers is free of SARS-COV2.¹⁷ Instead of such controversy our paediatric team refrained mothers from breastfeeding during active disease and babies were kept isolated. However, at times mothers were also given the option of expressed breast milk for a neonate or to even establish breastfeeding with adequate precautionary measures (handwashing, use of face masks) but mothers and family were too reluctant to establish breastfeeding due to anxiety of disease. The latest recommendation by CDC³³ and WHO³⁴ is now for breastfeeding, as available data is insufficient to conclude vertical transmission of COVID-19 through breastfeeding. Moreover, infants are at low risk for this infection which is typically mild or asymptomatic for them, while the consequences of

no breastfeeding and 'mother-child bonding' are significant. As benefits of breastfeeding outweigh the risks associated with COVID infection, breastfeeding should be initiated and continued with adherence to infection control measures by the mother, who in coordination with her family must also be involved in this decision making.

Strengths of the Study

Our study is perhaps the first one in the region reporting upon fetomaternal and neonatal outcome in pregnant women with COVID-19 infection. This case series reports upon 17 COVID-19 positive pregnant women and we could not find another research study in the literature (excluding review articles) reporting upon this many numbers of cases. The study results are genuine reflecting the selfless and dedicated health services by our obstetric department during this highly contagious pandemic and we hope our results will contribute to already gather a pool of information and will provide a framework to be adopted by other tertiary maternity hospitals managing pregnant women in this pandemic.

Limitations of the Study

Nevertheless, the study had few limitations. Firstly, as we reviewed medical charts so we could not get a long term to follow up on mother and baby. Secondly, it was a single centre study and sample size, as well as generalization of results, could have been improved by the multicenter study. Third, reviewed literature was mainly international and from developed countries, no local original study could be retrieved to relate to our results. Fourth, all studied cases were in the third trimester, and the effect of COVID-19 infection in the first and second trimester could not be assessed.

Conclusion

Pregnancy represents a special vulnerable condition for any infectious disease. The clinical course of COVID-19 disease in pregnancy seems to be no different from non-pregnant women. Clinical manifestations are diverse and infection contracted in advanced pregnancy is associated with good fetomaternal and neonatal outcomes. The vertical transmission of COVID-19 infection seems to be less

likely and the decision for a mode of delivery should not be altered by this disease. Breastfeeding should be established with adequate infection control prevention measures. Obstetricians and maternity services providers must have updated knowledge according to evolving WHO guidelines for better maternal and neonatal care and the self-protection. To overcome the controversies several aspects of COVID-19 disease in pregnancy need to be explored with large sample-sized multicenter studies.

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