Original Article

COVID-19 in Pregnant Women: A Multicenter Case Series

Saima Chaudhary[1], Shehla M.Baqai[2], Shamsa Humayun[3], Viqar Ashraf[4], Hina Akhtar[5], Rabia Sajjad[6]

[1]Assistant Professor, Department of Obstetrics & Gynecology, Fatima Jinnah Medical University, Lahore [2]Head of Department, Department of Obstetrics & Gynecology, CMH Lahore Medical College, National University of Medical Sciences Lahore, [3]Head of Department, Department of Obstetrics & Gynecology, Fatima Jinnah Medical University, Lahore, [4]Assistant Professor, Department of Obstetrics & Gynecology CMH Lahore Medical College, National University of Medical Sciences Lahore, [5]Senior Registrar, Department of Obstetrics & Gynecology, Fatima Jinnah Medical University, Lahore, [6]Assistant Professor, Department of Obstetrics & Gynecology CMH Lahore Medical College, National University of Medical Sciences Lahore

Correspondence: *Dr Saima Chaudhary*
Assistant Professor, Department of Obstetrics & Gynecology, Fatima Jinnah Medical University, Lahore
drsaimach@gmail.com

Abstract

Objective: To report clinical features, obstetrical outcomes, and vertical transmission in pregnancies affected by COVID-19.

Methodology: It was a multicenter observational study conducted at two tertiary care hospitals of Lahore including Sir Ganga Ram hospital and Combined Military Hospital (CMH) Lahore, Pakistan.

The record of COVID-19 positive pregnant women treated for three months (April to June 2020) was collected. Data was collected using predesigned proforma including clinical features, obstetric outcome, and vertical transmission. Quantitative variables were expressed as mean ± standard deviation, while qualitative variables as the frequency with percentages. SPSS version 24 was used to analyze data.

Results: Seventy COVID-19 positive pregnant women were included in the case series. The mean age was 28.6+3.98 years and mean gestational age of 34± 8.004 weeks. Of these 57.1% were asymptomatic. Among symptomatic women, the commonest symptoms were fever and cough in 66.7%, followed by shortness of breath in 30%, and myalgia in 26.7%. Two women expired due to severe pneumonia. Two cases of miscarriage, while no case of intrauterine demise, spontaneous preterm labor, neonatal death, or vertical transmission was observed.

Conclusion: Pregnancy did not modify the course of the disease. The clinical characteristics of the disease were the same in pregnant and non -pregnant patients.

Keywords: COVID-19, feto-maternal outcome, lung infiltrates, pregnancy, vertical transmission.

Cite this article as: Chaudhary S, Baqai SM, Humayun S, Ashraf V, Akhtar H, Sajjad R.COVID-19 in pregnant women: A multicenter case series.J Soc Obstet Gynaecol Pak.2020; Vol 10(4):249-254.

Introduction

SARS CoV2 is a single stranded RNA virus, grouped among the corona viruses known to cause severe acute respiratory disease in human. High transmissibility and low pathogenicity are two characteristics which differentiate it from other members of the family (SARS-CoV and MERS-CoV).[1]Since first reported case of COVID-19 pneumonia in December 2019 from Wuhan, Hubei Province in China, in less than three months it was declared as public health emergency of international concern. WHO declared it as pandemic on 11th March 2020.[2,3,4] The respiratory system involvement with fever, cough, and shortness of breath is the most common presentation besides diarrhea, abdominal

Authorship Contribution: [1]Conception, Synthesis and planning of the research, [2,3] Data collection/Analysis, [4]Supervised the study, [5,6]Active participation in active methodology

Funding Source: none
Conflict of Interest: none

Received: Sept 12, 2020
Accepted: Mar 05, 2021

pain, fatigue, sore throat, muscle pain, and loss of smell and taste.[5] The incubation period ranges from 2 to 14 days with median 5 days.[6] Symptoms vary from mild to moderate or rapidly progressing to viral pneumonia and multi-organ failure. The severity of the disease is influenced by sex, age, ethnicity, and associated comorbidities.[7,8]

Owing to physiological adaptations in the cardiopulmonary and immune system, pregnant females show increased susceptibility to severe respiratory infections and intolerance to hypoxia.[9] The serious illness and reported high mortality (37% & 25%) among pregnant women in the 1918 influenza pandemic and 2003 SARS-CoV-1 outbreak, were of great concern for health authorities during current pandemic.[10,11] The available evidence has shown a milder course of disease in pregnancy as compared to structurally similar MERS-CoV and SARS CoV. The unexpected clinical outcome of COVID-19 during pregnancy surprised the clinicians and researchers. It is speculated that cytokines storm playing a pivotal role in the severe disease and mortality, is blunted during pregnancy due to physiological “silencing” of the Th1 pro-inflammatory response.[12] Published evidence to date seems to be reassuring that COVID-19 is not linked with adverse pregnancy outcome.[13] The available data on the feto-maternal effects of COVID-19 lack enough evidence to discern infrequent risks attributable to COVID-19 infection.[14,15] The aim of this multicenter study of 70 COVID-19 infected pregnant women was to observe the clinical presentation, pregnancy outcome, and vertical transmission of COVID-19.

Methodology

It was a multicenter observational study conducted at two tertiary care hospitals of Lahore including Sir Ganga Ram Hospital and Combined Military Hospital (CMH) Lahore, Pakistan. After permission from the Institutional ethical review board. Three months data of COVID-19 positive pregnant females admitted in designated COVID-19 wards of the identified two hospitals was collated from April 2020 to June 2020.

Pregnant women presenting with or without any symptoms and positive COVID-19 RT-PCR report were enrolled in the study after informed consent. Written consent was replaced by informed verbal consent to avoid disease spread. Ensuring Confidentiality and anonymity, a predesigned proforma was used to record information including patient demographic details, clinical features of COVID-19 e.g. cough, fever, shortness of breath, loss of taste or smell, body aches, etc. Details of obstetrical history were also collected including parity, age, gestational age, obstetrical problems, previous mode of delivery, and risk factors like diabetes or hypertension.

Investigations including complete blood count, CRP(C-reactive protein), and chest X-ray/ CT chest were done as per requirement. Enrolled patients were followed during the hospital stay to record the duration of hospital stay, mode of delivery, indication of caesarean section, and obstetric complications like miscarriage, intrauterine death, fetal distress, preterm labor, and preterm rupture of membranes. The fetal outcome was observed including neonatal RT-PCR COVID-19, APGAR score at 1 and 5-minute, admission to neonatal intensive care, and need of resuscitation.

Statistical analysis: Data analysis was done by using SPSS (Statistical Package for Social Sciences) version 24. Categoric variables were expressed as mean ± standard deviation (SD) e.g. Parity, age, pregnancy duration, hospital stay, and a number of family members diagnosed with COVID-19 etc. Numerical variables were expressed as frequency e.g. symptoms, obstetrical complications, mode of delivery, neonatal RT-PCR COVID-19 etc.

Results

Seventy pregnant women tested COVID-19 RT PCR positive admitted in COVID-19 isolation wards of both tertiary care hospitals were enrolled in the study. The mean age of women was 28.6$\pm$3.98. The majority of women were multiparous. (Table) The gestational age ranged from 8^{+2} to 41weeks (mean± SD 34± 8.00). The majority presented after 37 weeks gestation (Table I). All of the women were housewives except 2.

At the time of admission 40/70 (57.1%) women were asymptomatic while the remaining 30 (42.9%) women were symptomatic. Fever and cough were observed to be the commonest symptoms, followed by shortness of breath and myalgia.

Table I: Demographic details and clinical outcome of COVID-19 positive pregnant females. (n=70)	
Clinical characteristics	**All women**
Age (years)	
Mean± SD	28.6 ±3.98
Range	19 – 38
Gestational age on admission (weeks)	
Mean± SD	34± 8.00
Range	8^{+2}– 41
<13+6	4 (5.7%)
14-27+6	9 (12.9%)
28-36+6	13 (18.6%)
>37	44 (62.8%)
Parity	
Primiparous	13 (18.6%)
Multiparous	57 (81.4%)
Working status	
Housewife	68 (97.1%)
Working	2 (2.9%)
Average duration of hospitalization	6 days
Clinical presentation	
Asymptomatic	40 (57.1%)
Symptomatic	30 (42.9%)
Symptoms	
Fever	20 (66.7%)
Cough	20(66.7%)
Body aches	8 (26.7%)
Shortness of breath	9 (30%)
Diarrhea	1 (3.3%)
Nausea/vomiting	1 (3.3%)
Sputum	0
Obstetric Complications	
Miscarriage	2 (2.9%)
Preterm labour	0
Premature rupture of membranes	0
Fetal distress	2 (2.9%)
Intrauterine death	0
Delivered during hospital stay	40 (57.1%)
Delivered after discharge	9 (12.9%)
Mode of Delivery	
Total delivered	49
Vaginal delivery	16(67.3%)
Cesarean section	33(32.7%)
Indication of cesarean section	
Previous scarred uterus	24(72.7%)
Fetal distress	5(15.15%)
Maternal wish	2(6.1%)
Placenta previa	1(3%)
Transverse lie	1(3%)
Neonatal outcome	
Apgar score 1 minute (mean)	7
Apgar score 5 minute (mean)	9
Severe asphyxia	0
Death	0
Neonate COVID-19 status	
COVID -19 negative	49
COVID-19 positive	0
Clinical outcome	
Discharged	68 (97.1%)
Died	2 (2.9%)

There were two cases of maternal mortality. First lady G4P3 (previous 3 cesarean sections) presented with severe pneumonic symptoms including cough, fever (100ºF) and dyspnea for 3 days. Her blood pressure was 150/80mm with tachycardia. Due to critical condition of the patient CT chest could not be done, whereas bilateral lung infiltrates were found on X-ray chest. Although oxygen saturation was already low (76%) on admission, a further sudden drop on 2nd day of admission steered to intubation and mechanical ventilation. Two days after admission she expired after cardiac arrest. The second lady 26 years old $P1^{+1}$ presented 2 days after caesarean section due to failed induction at some private hospital. She was short of breath with a history of fever and jaundice for 3 days. On admission, she had fever (101ºF), tachycardia, jaundice, hypotension (90/60mm of Hg), and oxygen saturation of 60%. Her medical record showed bilateral infiltrates on X-ray chest, raised CRP, thrombocytopenia, and markedly deranged LFTs (bilirubin=6.9, ALT=4940, AST=5693). Renal function tests were normal. Report of viral markers was still awaited. Her initial management was initiated, and investigations sent. A half-hour after admission she collapsed, resuscitation was done but she could not be revived. Her baby was healthy at home.

Out of 70 COVID-19 positive women 49 delivered during the study period, 2/70 (2.9%) had a miscarriage, 18/70 pregnancies continued owing to be in the first, second or early third trimester. During hospital stay 40 women delivered while the remaining 9 delivered later after discharge from hospital. The mode of delivery was vaginal in 16/49 (67.3%) and cesarean section in 33/49 (32.7%) women. The cesarean section were performed purely based on obstetric indications: 24/33 (72.7%) were done on account of the previously scarred uterus, 5/33 (15.15%) due to fetal distress, 2/33 (6.1%) on account of the patient's request, 1/33 (3%) due to transverse lie and 1/33 (3%) due to placenta previa. Two cases of miscarriage were observed, which had evacuation and curettage by MVA. Preterm labor was not observed in any case. Intrapartum or postpartum period was uneventful in all women without any complication. After clinical recovery and two negative PCR reports, all patients were discharged (table I).

There was no case of intrauterine fetal demise. The neonates delivered during hospital stay were tested for COVID-19 by taking nasopharyngeal swab at 12 hours and 24 hours after birth and all reported negative. No

case of neonatal asphyxia or death was observed. All newborns had satisfactory 1 and 5- min APGAR score.

Lab reports showed leukocytosis in 20 (28.6%) patients (Table II). In the remaining cases leucocyte count was normal. Lymphopenia, lymphocytosis and raised CRP were also observed in few patients. The majority of patients had normal X ray chest (Table II).

Table II: Laboratory and radiological findings of COVID -19 positive pregnant females at admission.

Total leucocyte count (× 10^3/uL)	
Mean ± SD	9.52±3.52
Normal	50 (71.4%)
Decreased	0
Increased	20 (28.6%)
Neutrophils (Normal range 40-60%)	
Mean± SD	51.7± 21.68
Normal	22 (31.4%)
Decreased	18 (25.7%)
Increased	30 (42.9%)
Lymphocytes (normal range 20-40%)	
Mean± SD	35.7±20.45
Normal	41 (58.6%)
Decreased	11 (15.7%)
Increased	18 (25.7%)
Chest X Ray	
B/L peripheral opacities	12 (17.1%)
Negative findings	58 (82.9%)
CRP	
Raised	12 (17.1%)
Normal	58 (82.9%)

Discussion

SARS COV-2 a rapidly transmissible disease led to the biggest pandemic of the century named COVID-19. We reported a case series of 70 COVID-19 positive pregnancies to add to literature for better understanding of clinical characteristics and its implications in pregnancy. In our case series' most COVID-19 Positive pregnant women had mild disease. It was observed that the incidence of obstetric complications did not increase in COVID-19, moreover pregnancy was also not found to modify the disease course.

Similarities observed between COVID-19 and other corona virus infections in past like SARS-COV2 and MERS-COV 2 enhanced obstetrician's concern about the feto-maternal outcome in COVID-19.[2,9,14,16,17] Limited evidence is available regarding COVID-19, showing disease course during pregnancy and feto-maternal outcome in South Asian population in the perspective of the recent emergence of corona virus. Our case series from two major tertiary care hospitals dealing COVID-19 pregnant women adds the data of 70 COVID-19 positive patients to the already available evidence.

The mean gestational age in our study was lower than reported by others.[9,14,16,17] The mean age of our population was younger with the majority of multiparous woman as compared to other reported series.[9,17,18]

Disease severity during pregnancy was observed to be same as in non-pregnant. The commonest presentation was fever and cough in addition to myalgia, difficulty in breathing, sputum, headache and diarrhea.[2,19] Our study revealed that one third of the infected women did not show any symptoms. R other studies among the symptomatic women, the commonest were fever and cough.[9,15-20] In our series two patients got admitted with severe pneumonia and expired. In comparison, Chen's case series revealed the majority of women 112/118 (95%) being symptomatic.[18] Chen et al reported fever and cough as most observed symptoms like many other researchers.[9,15,16,17] The data in our case series was collected during the early stage of pandemic. To restrict disease transmission official guidelines were followed to hospitalize all COVID-19 positive pregnant patients irrespective of disease severity. This policy may explain the higher number of mild cases in our series. Younger age, different ethnicity and immune status in our population might be responsible for the observed difference in disease severity. This hypothesis still needs to be proven by more research in the field.

We observed two miscarriages in our case series, but no case of intrauterine death, preterm rupture of membranes, spontaneous preterm labor was reported in accordance with research by Yan et al.[9] In contrast to our results iatrogenic preterm delivery for maternal resuscitation have been reported in few studies in severe cases of COVID-19 but no case of spontaneous preterm labor.[14,15,16,20,21] In our series, among 70 women 49 were delivered, mostly by caesarean. Other researchers have also reported caesarean as preferred mode of birth in COVID-19 patients.[9,15,16,18,20] Mothers and obstetricians both have expressed fear about the vertical transmission of infection. A study reported four cases of vertical transmission.[22] In our case series no case of vertical transmission was reported. In concordance with our findings, other researchers also did not report any case of vertical transmission. Similarly, following our study neonatal death, asphyxia, or intrauterine death was also not found to be associated with COVID-19 by most of the studies.[14,16,-

[23] Many researchers tested cord blood, amniotic fluid and placenta to detect COVID-19 transmission, but the limitation of our study was lack of this kind of testing due to shortage of testing kits and financial constraints.

Most of our patients had normal C-reactive protein (82.9%) whereas Yan reported raised levels in 44% cases.[9] The plausible explanation could be the asymptomatic or mild disease in most women in our study.

Lymphopenia in COVID-19 patients is perceived as a predictor of disease prognosis and an indicator of disease severity.[24] In severe disease lymphopenia is proposed to be due to direct lymphocyte infection, lymphatic tissue destruction, inflammation causing lymphocyte apoptosis, and suppression of lymphocytes by metabolic disorders such as lactic acidosis.[25] We found lymphopenia in11 (15.7%) and leucopenia in none of the cases. Yan et al reported lymphopenia in 44% of 116 patients.[2,19] Yan et al reported lung Infiltrates on CT chest in 96% of cases.[9] In our study lung infiltrates were detected in 12 (17.1%) cases on X-ray chest. The mild nature of disease and use of X-ray instead of CT chest in our case series could be the reason for this observation.[25]

Acknowledgments

We acknowledge the effort of our residents Dr. Sadaf, Dr Raima, Dr. Somia, and Sister incharge Miss Rubina Butt who helped in obtaining the verbal consent and proforma filling.

Conclusion

In conclusion, Pregnancy did not modify the course of the disease. The pregnant and non -pregnant patients had same clinical characteristics. COVID-19 infection has not shown higher occurrence of spontaneous preterm labor, intrauterine death, miscarriage or vertical transmission. This will be a valuable addition in already generated evidence regarding pregnancy outcomes in the COVID-19 pandemic.

References

1. Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W, Lou Y, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. International journal of infectious diseases. 2020;92:214-7.
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, et al. Clinical features of patients infected with novel coronavirus in Wuhan, China. Lancet 2020; 395: 497-506.
3. Tait R. Czechs get to work making masks after government decree. The Guardian. At https://www. theguardian. com/world/2020/jun/30/czechs-get-towork-making-masks-aftergovernment-decree-coronavirus.(accessed June 2020)
4. Director-General's opening remarks at the media briefing on COVID-19', (Press release), Available at: https://www.who.int/dg/speeches/detail/who-director-general-sopening-remarks-at-the-mediabriefing-on-covid-19-11-march-2020
5. Centers for Disease Control and Prevention (CDC) (2020), 'Symptoms of Coronavirus, Available https://www.cdc.gov/coronavirus/ 2019 ncov/symptoms testing /symptoms.html
6. Velavan TP, Meyer CG. The COVID-19 epidemic. Tropical medicine & international health. 2020 Mar;25(3):278.
7. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, et al. 'The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health— The latest 2019 novel coronavirus outbreak in Wuhan, China'. International Journal of Infectious Diseases.2020; 91:264–266.
8. Perez-Saez FJ, Lauer SA, Kaiser L, Regard S, Delaporte E, Guessous I, et al. Serology-informed estimates of SARS-CoV-2 infection fatality risk in Geneva, Switzerland. Lancet Infect Dis.2020; doi:10.1016/S1473-3099(20)30584-3
9. Yan J, Guo J, Fan C, Juan J, Yu X, Li J, Feng L, et al. Coronavirus disease 2019 in pregnant women: a report based on 116 cases. American journal of obstetrics and gynecology. 2020 Jul 1;223(1):111-e1.
10. Gottfredsson M. The Spanish flu in Iceland 1918. Lessons in medicine 549 and history. Laeknabladid. 2008; 94:737-745.
11. Schwartz DA, Graham AL. Potential maternal and infant outcomes from Coronavirus 2019-nCoV (SARS-CoV-2) infecting pregnant women: Lessons from SARS, MERS, and other human coronavirus infections. Viruses. 555 2020; 12:194.
12. Ghi T, di Pasquo E, Mekinian A, Calza L, Frusca T. Sars-CoV-2 in pregnancy: Why is it better than expected?. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2020 Sep 1;252:476-8.
13. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. 2020.
14. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, Li J, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. The lancet. 2020 Mar 7;395(10226):809-15.
15. Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations, and outcome of SARS-CoV-2 infection during pregnancy. J Infect 2020, doi: https://.org/10.1016/j.jinf.2020.02.028.
16. Mullins E, Evans D, Viner R.M, Brien P.O, Morris E. Coronavirus in pregnancy and delivery: rapid review. Ultrasound ObstetGynecol 2020; 55: 586–592.
17. Qiancheng X, Jian S, Lingling P, Lei H, Xiaogan J, Weihua L. sixth batch of Anhui medical team aiding Wuhan for COVID-19. Coronavirus disease. 2019:376-83.
18. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, et al. Clinical Characteristics of Pregnant Women with Covid-19 in Wuhan, China. N Engl J Med. 2020;382(25):e100. doi:10.1056/NEJMc2009226
19. Matar R, Alrahmani L, Monzer N, Debiane LG, Berbari E, Fares J, et al. Clinical Presentation and Outcomes of Pregnant Women with Coronavirus Disease 2019: A Systematic Review and Meta-analysis. *Clinical Infectious Diseases*.2020. ciaa828 https://doi.org/10.1093/cid/ciaa828
20. Khalil A, Kalafat E, Benlioglu C, O'Brien P, Morris E, Draycott T. SARS-CoV-2 infection in pregnancy: A systematic review and meta-

analysis of clinical features and pregnancy outcomes. EClinicalMedicine 25 (2020). https://doi.org/10.1016/j.eclinm.2020.100446

21. Abdollahpour S &Khadivzadeh T. Improving the quality of care in pregnancy and childbirth with coronavirus (COVID-19): a systematic review. The Journal of Maternal-Fetal & Neonatal Medicine 2020. DOI: 10.1080/14767058.2020.1759540
22. Ashraf MA, Keshavarz P, Hosseinpour P, Erfani A, Roshanshad A, Pourdast A, Nowrouzi-Sohrabi P , et al. Coronavirus Disease 2019 (COVID-19): A Systematic Review of Pregnancy and the Possibility of Vertical Transmission. J ReprodInfertil. 2020;21(3):157-168.
23. Sun M, Xu G, Yang Y, Tao Y, Pian-Smith M, Madhavan V, Xie Z, et al. Evidence of mother-to-newborn infection with COVID-19. Br J Anaesth. 2020. doi: 10.1016/j.bja.2020.04.066
24. Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, Wang Q, Miao H. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. Signal transduction and targeted therapy. 2020 Mar 27;5(1):1-3.. DOI: 10.1038/s41392-020-0148-4.
25. Huang G, Kovalic AJ, Graber CJ. Prognostic Value of Leukocytosis and Lymphopenia for Coronavirus Disease Severity [published online ahead of print, 2020 May 8]. Emerg Infect Dis. 2020;26(8):10.3201/eid2608.201160. doi:10.3201/eid2608.201160