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Clinical Course of SARS CoV-2 Infection in Hospitalized Pregnant Patients

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ABSTRACT

Objective: To determine the clinical course and outcome of hospitalized pregnant patients with laboratory-confirmed SARS-CoV-2 (COVID-19) infection

Study Design: Prospective longitudinal study

Place and Duration of Study: Obstetrics Units of Pak Emirates Military Hospital and Combined Military Hospital, Rawalpindi Pakistan, from May to Jun 2020.

Methodology: All patients reporting for childbirth were tested for SARS-CoV-2, and those testing positive were included. The primary outcome was virus clearance time and categorization according to the severity of the disease into asymptomatic, mild, moderate, severe and critical. Furthermore, a comparison was made between the presence of comorbid conditions and symptoms in the category of COVID-19. In addition, neonatal sample evaluation for SARS-CoV-2 was done.

Results: Out of the 881 women giving birth, 41(4.6%) tested positive for SARS Cov-2. Majority were asymptomatic 28(68.3%) followed by mild 8(19.5%), moderate 4(9.8%) and severe 1(2.4%) category. There was a significant association of the COVID categories with symptoms (p-value<0.005) and comorbid condition (p-value<0.001). The mean virus clearance time was 8.20±1.66 days. During hospital stay 34(82.9%) delivered. All 34(100%) delivered babies had no evidence of vertical transmission.

Conclusion: Pregnant women with COVID-19 infection have a nearly similar clinical course to non-COVID women in this study. There is also no evidence of vertical transmission to the neonate.

Keywords: Clinical course, COVID-19, Neonatal, Pregnancy.

How to Cite This Article: *Ansari A, Siraj A, Khan S, Jalil R, Choudary A, Khalil H. Clinical Course of SARS CoV-2 Infection in Hospitalized Pregnant Patients. Pak Armed Forces Med J 2022; 72(6): 1858-1862. DOI: https://doi.org/10.51253/pafmj.v72i6.4512*

INTRODUCTION

Practising and performing healthcare in the era of the SARS-CoV-2 pandemic is not only one of its kind but extremely challenging.[1] The emerging data from around the globe suggests that SARS-CoV-2 is less lethal than the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV).[2] However, it is far more contagious than these two. Furthermore, the limited data from various sources worldwide do not indicate that pregnant women are more at risk of severe disease than the general population. However, there is a critical requirement for further robust data on maternal and perinatal outcomes in women infected with SARS-CoV-19.[3,4]

There is anxiety among pregnant women, and our limited ability to answer their queries is somehow affecting the healthcare of women. Therefore, the lack of direction about the impact of SARS-CoV-2 on pregnancy became the driving force behind the effort to compile the data on the clinical course of pregnant patients with SARS-CoV-2 who reported to our military tertiary care centre for evaluation and further management.

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Received: 15 Jun 2020; revision received: 21 Jul 2020; accepted: 23 Jul 2020

METHODOLOGY

This prospective longitudinal study was conducted at the Obstetrics units of Pak Emirates Military Hospital and Combined Military Hospital, Rawalpindi Pakistan from April to June 2020. Patients were included by consecutive nonprobability sampling technique after informed consent and Institutional Review Board approval (A/28/EC1117).

Inclusion Criteria: All patients reporting for childbirth were tested for SARS-CoV-2, and those testing positive were included in the study.

Exclusion Criteria: Pregnant women were excluded if they had presumed COVID-19 infection, but laboratory testing was negative.

All pregnant women reporting for childbirth were tested for SARS-CoV-2 using RT-PCR kits. The primary outcome was categorization according to the

severity of the disease into asymptomatic, mild, moderate, severe and critical. COVID-19-related outcomes included virus clearance time taken from the first positive report to the negative report, length of hospital stay, respiratory compromise and maternal death.

Asymptomatic were the patients who were nasopharyngeal swabs RT-PCR positive for SARS CoV2 but exhibiting no symptoms. The mild disease was the presence of fever, cough, flu-like symptoms, malaise, myalgia, headache and gastrointestinal symptoms without any hemodynamic compromise, laboratory or radiological findings. The moderate disease was oxygen saturation ≤94% or mild infiltrates on chest x-ray or Persistent high-grade fever for three days or above. Severe disease was diagnosed by shortness of breath, blood oxygen saturation ≤93% on room air, and lung infiltrates >50% on chest imaging with moderate to severe pneumonia without meeting the criteria for the critical disease.[5] The critical disease was defined by respiratory failure, septic shock, or multiple organ dysfunction with laboratory evidence of COVID-19 infection.[6] The secondary outcome was symptoms of fever, cough, myalgia, flu-like symptoms, shortness of breath and gastrointestinal symptoms. Vital signs at admission were Blood pressure, pulse, temperature and respiratory rate. Oxygen saturation at admission and deterioration, if applicable, was noted. Laboratory findings other than routine blood tests and urinalysis included C-reactive protein, liver function tests, renal function tests, D-dimers, fibrinogen levels, lactate dehydrogenase (LDH) and serum ferritin. Chest X-Ray with the abdominal shield was done in all pregnant women, and the clinical condition indicated chest CT scans. Patients were admitted to the designated COVID facility. Although no support person was allowed in the ward daily communication by healthcare staff and updates about the patient's condition were ensured. Daily fetomaternal monitoring was done by symptoms, vital signs, oxygen saturation and electronic fetal heart rate monitoring twice daily. The consultant visited the patients twice a day. The nasopharyngeal swab was repeated on the seventh day of admission. The criteria for discharge were two consecutive negative samples done 24 hours apart. Delivery or cesarean section was conducted in a designated theatre taking care of all the infection prevention protocols. Standard monitoring was done during labour with minimum required staff in personal protective gear. Patients wore face masks during hospital stays and labour. During the postnatal period, they were monitored according to their disease categorization and comorbidities inward, high dependency unit or intensive care. The moderate and higher category was nursed in intensive care. Neonatal outcome was noted, including Apgar score, fetal weight, neonatal sample evaluation for SARS CoV-2 and perinatal mortality. Neonates were kept in dedicated neonatal intensive care, and SARS-CoV-2 was evaluated in neonatal samples after 24 hours of birth. Breastfeeding was not allowed till the patients remained CoVid positive. The asymptomatic patients who became negative during admission and did not require delivery were discharged and referred to non-COVID hospitals for further management or delivery. They were given 24 hours access to telemedicine for follow-up and discussion about the development of any new symptoms.

Statistical Package for Social Sciences (SPSS) version 21.0 was used for the data analysis. Quantitative variables were summarized as mean±SD and qualitative variables were summarized as frequency and percentages. The comparison was made between the presence of comorbid conditions and symptoms to the category of COVID 19 by applying the chi-square test, and the *p*-value of ≤0.05 was considered statistically significant.

RESULTS

One thousand one hundred seventy patients were hospitalized during the study period for obstetric indications. Out of these, 881(75.2%), women gave birth, and 41(4.6%) tested positive for SARS Cov-2. Demographic and reproductive data was shown in Table-I. The majority 37(90.2%) at the time of diagnosis, were in the third trimester of pregnancy. Pre-existing comorbid conditions were present in 17(41.4%) of patients. Majority of the patients were asymptomatic 28(68.3%) followed by mild 8(19.5%), moderate 4(9.8%) and severe 1(2.4%). All the symptoms and presence of comorbid conditions were compared with the categories of COVID-19, and there was a significant association of the COVID categories with the presence of symptoms (*p*-value <0.005) and comorbid condition (*p*-value <0.001) (Table-II).

Only one patient required intubation due to respiratory compromise, but she had mixed valve lesions with severe pulmonary hypertension, and three (7.3%) became oxygen dependent but recovered with treatment. There was no maternal mortality or obstetric morbidity. The mean virus clearance time was 8.2±1.66 days, with three days minimum and 14 maximum days for the test to become negative. Of the admitted

COVID patients, 34(82.9%) delivered during the hospital stay and the rest were discharged home after testing negative for COVID. Of the delivered babies, 30 (73.2%) were born alive and healthy, whereas 03(7.3%) had meconium-stained liquor and 1(2.4%) intrauterine death at term. Neonatal outcome was 33(80.5%) term, 1(2.4%) preterm and 7(17.0%) remained undelivered. The mean APGAR score was 9.00±1.10, mean fetal birth weight was 2.99±0.30kg. They were kept in dedicated neonatal intensive care, and SARS-CoV-2 was evaluated in neonatal samples. All 34(100%) of the delivered babies tested negative for the virus; hence no evidence of vertical transmission.

Table-I: Demographic and Reproductive Characteristics (n=41)

Characteristics	n(%)
Age Mean ± SD	29.24±4.50 years
Residence	
Local	29(70.7%)
Outstation	12(29.3%)
Occupation	
Housewife	36(87.8%)
Health care staff	5(12.2%)
Travel history	
Intercity	14(34.1%)
International	00
Nil	27(65.8%)
History of contact	
Family	13(31.7%)
Workplace	4(9.75%)
No contact	24(58.5%)
Parity	
Primigravida(PG)	9(21.95%)
Multipara (P1-P4)	31(75.7%)
Grandmultipara (≥5)	1(2.45%)
Gestation at admission	
POG(mean)	36.46±5.70
Outcome of pregnancy	
Cesarean section	19(46.3%)
Vaginal delivery	14(33.11%)
Twin delivery	1(2.4%)
Miscarriage	0
Continued pregnancy	7(17.1%)
Comorbids	
Anemia	8(19.5%)
Hypertension	3(7.3%)
Diabetes mellitus	0
Pulmonary disease(asthma)	1(2.4%)
Cholestasis	2(4.9%)
Heart disease	1(2.4%)
Hypothyroidism	2(4.9%)
None	24(58.5%)

Table-II: Association of COVID -19 Categories with Comorbid and Symptoms (n=41)

Co-morbids	COVID-19 category				*p*-value
	Asympto-matic (n=28)	Mild (n=8)	Moderate (n=4)	Severe (n=1)	
Anemia	6(75%)	1(12.5%)	1(12.5%)	0	<0.001
Asthma	0	0	1(100%)	0	
Cholestasis	2(100%)	0	0	0	
HeartDisease	0	0	0	1(100%)	
Hypertension	3(100%)	0	0	0	
Hypothyroidism	0	2(100%)	0	0	
None	17(71%)	5(21%)	2(8%)	0	
Fever	0	7(63.6%)	4(36.4%)	0	<0.001
Cough	0	8(61.5%)	4(30.8%)	1(7.7%)	<0.001
Flu	0	8(66.7%)	4(33.3%)	0	<0.001
Myalgia	3(20%)	8(53.3%)	4(26.7%)	0	<0.001
Dyspnea	0	4(57.1%)	2(28.6%)	1(14.3%)	<0.001
GIT Symptoms	0	3(100%)	0	0	0.004

DISCUSSION

In this study, we aimed to determine the clinical course and outcome of hospitalized pregnant patients with laboratory-confirmed SARS-CoV-2 (COVID- 19) infection. The demographic profile of our study population showed that the mean age of the patients was 29.2±4.5 years, the majority were at 36.4±5 weeks gestational age, and 75% were multipara (P1-4). This result agrees with two studies in which the majority were 25-35yrs and 26-40 yrs.[6,7] In another study compared COVID-19 and normal patients, there was no difference between parity (1-4) or age 20-40yrs and gestation period at delivery which was 38 weeks.[8] In a similar study done in the USA on pregnant COVID-19 patients, gestational age at onset of symptoms was 29wks±6, and at admission 30±6.[9] Family members of all our patients were tested, and 31.7% were found to be COVID-positive. In a study done in Iran by Hantoushzadeh *et al.* family contacts of pregnant COVID positive were traced, and 100% were found positive. Out of all these, only the patients were critical and died, and all others recovered.[10] Mean duration of hospital stay was 9.1± days. Whereas in the USA cohort study by Pierce-Williams *et al.* mean duration of admission was 10.5 for critical and six days for severe disease.[9]

In Wuhan China, where this virus originated, studies found the comparable clinical course of COVID-19 amongst pregnant and non-pregnant women regarding the severity of disease, virus clearance time and duration of hospital admission.[11] Majority of our patients were asymptomatic 68% followed by mild 19.5%, moderate 9.8% and severe 2.4%. The results of

our study are similar to another done in NewYork by Breslin *et al*. in which the majority had mild disease 85%, severe disease 10% and critical 5%.[12] In another study done in China on 118 patients, 92% had mild disease followed by 7% severe and 1% critical.[13] In 12 USA institutions over a six-week duration similar to our study period, there were 64 pregnant women, 69% severe and 31% in critical category.[9] In our study, it is notable that a maximum number of patients were asymptomatic, which is quite alarming as these patients were infecting others unknowingly, indicating widespread community spread. This agrees with two USA studies in which 32.6% were asymptomatic, and 29 of 33 positive patients were asymptomatic.[14,15] Preoperative or pre-admission PCR testing in our patients revealed COVID-19 infection in asymptomatic patients but 4(9.7%)later on developed symptoms like breathing difficulty and fever.

The most common presenting symptoms were fever and cough in studies done in China, whereas in our study commonest symptom was myalgia 36%, cough 31% and flu 29%.[16,17] Only 41.1 %of the women had comorbidities, of which the leading was anaemia. Comorbidities like hypertension, diabetes, and respiratory illnesses make the women more vulnerable to the effects of COVID-19.[18] In another systematic review reporting on 41 delivered patients preterm delivery rate was 41%, and perinatal deaths were 07%.[19] In another published series of 43 patients from New York, labour was induced in 50%,44% delivered by cesarean section, and preterm delivery was 5% compared to 2.4% preterm deliveries in our study.[20] Our study found that most pregnant patients were young and in good health, and there were no obstetric complications. The mode of delivery was the cesarean section in 55% of patients, whereas rates reported from other studies were almost 91%,100%, and 94%.[8,9,20]

A previous study reported , only 3 of the 33 infants had evidence of mild neonatal infection and a favourable outcome.[8] In another cohort of 18 patients born to COVID-positive mothers from the USA tested negative.[12] This agrees with our study results in which none of the newborns tested positive. A limited number of studies report no evidence of the secretion of the virus in breast milk.

LIMITATIONS OF STUDY

Limitation of the study was a small study cohort. Considering that COVID-19 is a novel virus, it will give confidence in managing these patients and help update our protocols and guidelines depending upon the clinical course taken by our patients.

CONCLUSION

In this study, pregnant women with COVID-19 infection have a nearly comparable clinical course to non-COVID women. The aim of care for these women is categorized according to disease severity and individualized management plan to provide optimum care according to available evidence. Although there is no evidence of vertical transmission to the neonate, care measures should be taken to prevent infection transmission to healthcare workers, other patients and neonates.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

AA & AS: Study design, drafting the manuscript, approval of the final version to be published.

SK & RJ: Conception, data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

AC & HK: Data interpretation, critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Dong L, Tian J, He S, Zhu C, Wang J, Liu C, et al. Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn. JAMA 2020; 323(18): 1846-1848. doi: 10.1001/jama.2020.4621.
2. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. Acta Obstet Gynecol Scand 2020; 99(7): 823-829. doi: 10.1111/aogs.13867.
3. Buekens P, Alger J, Bréart G, Cafferata ML, Harville E, Tomasso G. A call for action for COVID-19 surveillance and research during pregnancy. Lancet Glob Health 2020; 8(7): e877-e878. doi: 10.1016/S2214-109X(20)30206-0.
4. Chen Y, Peng H, Wang L, Zhao Y, Zeng L, Gao H, et al. Infants Born to Mothers With a New Coronavirus (COVID-19). Front Pediatr 2020; 8(1): 104. doi: 10.3389/fped.2020.00104.
5. Urooj U, Ansari A, Siraj A, Khan S, Tariq H. Expectations, Fears and Perceptions of doctors during Covid-19 Pandemic. Pak J Med Sci 2020; 36(COVID19-S4): COVID19-S37-S42. doi: doi:10.12669/pjms.36.COVID19-S4.2643.
6. Cheng B, Jiang T, Zhang L, Hu R, Tian J, Jiang Y, et al. Clinical Characteristics of Pregnant Women With Coronavirus Disease 2019 in Wuhan, China. Open Forum Infect Dis 2020;7(8): ofaa294. doi: 10.1093/ofid/ofaa294.
7. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020; 382(8): 727-733. doi:10.1056/NEJMoa2001017.
8. Zeng L, Xia S, Yuan W, Yan K, Xiao F, Shao J, et al. Neonatal Early-Onset Infection With SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China. JAMA Pediatr 2020; 174(7): 722-725. doi: 10.1001/jamapediatrics.2020.0878.

9. Pierce-Williams RAM, Burd J, Felder L, Khoury R, Bernstein PS, Avila K, et al. Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. Am J Obstet Gynecol MFM 2020; 2(3): 100134. doi: 10.1016/j.ajogmf.2020.100134.
10. Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, Seferovic MD, Aski SK, Arian SE, et al. Maternal death due to COVID-19. Am J Obstet Gynecol 2020; 223(1): 109.e1-109.e16. doi: 10.101111116/j.ajog.2020.04.030.
11. Qiancheng X, Jian S, Lingling P, Lei H, Xiaogan J, Weihua L, et al; sixth batch of Anhui medical team aiding Wuhan for COVID-19. Coronavirus disease 2019 in pregnancy. Int J Infect Dis 2020; 95: 376-383. doi: 10.1016/j.ijid.2020.04.065.
12. Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K, et al. Coronavirus disease 2019 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals. Am J Obstet Gynecol MFM 2020; 2(2): 100118.
13. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet 2020; 395(10226): 809-815. doi: 10.1016/S0140-6736(20)30360-3. Erratum in: Lancet. 2020; 395 (10229): 1038-1040.
14. Sutton D, Fuchs K, D'Alton M, Goffman D. Universal Screening for SARS-CoV-2 in Women Admitted for Delivery. N Engl J Med 2020; 382(22): 2163-2164. doi: 10.1056/NEJMc2009316.
15. Lamouroux A, Attie-Bitach T, Martinovic J, Leruez-Ville M, Ville Y. Evidence for and against vertical transmission for severe acute respiratory syndrome coronavirus 2. Am J Obstet Gynecol 2020; 223(1): 91.e1-91.e4. doi: 10.1016/j.ajog.2020.04.039.
16. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020; 323(13): 1239-1242. doi: 10.1001/jama.2020.2648.
17. Ng OT, Marimuthu K, Chia PY, Koh V, Chiew CJ, De Wang L, et al. SARS-CoV-2 Infection among Travelers Returning from Wuhan, China. N Engl J Med 2020; 382(15): 1476-1478. doi: 10.1056/NEJMc2003100.
18. World Health Organization. Novel coronavirus (2019-nCoV): situation report. [Internet] available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200201-sitrep-12-ncov.pdf?sfvrsn=273c5_2). (Accessed on June 12, 2020)
19. Smith LH, Dollinger CY, VanderWeele TJ, Wyszynski DF, Hernández-Díaz S. Timing and severity of COVID-19 during pregnancy and risk of preterm birth in the International Registry of Coronavirus Exposure in Pregnancy. BMC Pregnancy Childbirth 2022; 22(1): 775. doi: 10.1186/s12884-022-05101-3.
20. Schwartz DA, Graham AL. Potential Maternal and Infant Outcomes from (Wuhan) Coronavirus 2019-nCoV Infecting Pregnant Women: Lessons from SARS, MERS, and Other Human Coronavirus Infections. Viruses 2020; 12(2): 194. doi: 10.3390/v1202014564694.