CLINICAL COURSE OF SARS COV-2 INFECTION IN HOSPITALISED 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 observational study.

Place and Duration of Study: Obstetrics Unit of Pak Emirates Military Hospital (PEMH) and Combined Military Hospital (CMH) Rawalpindi, from May 2020 to Jun 2020.

Methodology: All patients reporting for childbirth were tested for SARS CoV-2 and those testing positive were included. Demographic and reproductive profile including age, parity, occupation, contact and travel history, period of gestation at diagnosis and mode of delivery where applicable noted. The primary outcome was Virus clearance time and categorization according to severity of disease into asymptomatic, mild, moderate, severe and critical. Comparison was done between presence of co-morbid conditions and symptoms to category of COVID-19. 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 08 (19.5%), moderate 04 (9.8%) and severe 01 (2.4%) category. There was significant association of COVID category with presence of symptoms (p-value <0.005) and comorbid (p-value <0.001). Mean virus clearance time was 8.2 ± 1.66 days. During hospital stay 34 (82.9%) delivered. All 34 (100%) of the delivered babies had no evidence of vertical transmission.

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

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

INTRODUCTION

We are living in unprecedented times. Practicing and performing healthcare in the era of SARS-CoV-2 pandemic is not only one of its own kind but extremely challenging as well. The emerging data from around the globe suggests that SARS-CoV-2 is less lethal than the Middle East Respiratory Syndrome Corona Virus (MERS-CoV) and Severe Acute Respiratory Syndrome Corona Virus (SARS-CoV) but it is far more contagious than these two. The limited data so far available from various sources worldwide do not indicate that pregnant women are more at risk of severe disease than the general population. However, there is critical requirement of further robust data on maternal and perinatal outcomes in women infected with SARS-CoV-2[1].

The immune system in pregnancy becomes less aggressive, so that it does not attack the genetically different fetus inside the mother. As a result, the pregnant women become susceptible to various infections, including the viral illnesses. In addition to that multiple physiological changes in pregnancy like edema of the respiratory tract, increase in respiratory secretions and oxygen requirements, elevated diaphragm and decreased functional residual capacity are the contributing factors towards the worse obstetric outcomes in pregnant women who had viral pneumonia so far reported in literature. The limited published data with COVID-19 in China suggests worst perinatal outcome in some of the pregnancies, which includes prematurity and perinatal deaths[2]. Though

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pregnant women are not currently recognized vulnerable population amid the coronavirus pandemic, more research is required to understand the effect of the novel coronavirus on the mother and unborn baby[3]. There is much focus on emergency departments and Intensive Care Units, but very little on labor, delivery and pregnancy. Low and middle income countries are at crossroads in addressing their otherwise fragile maternal health system and managing the pandemic. Although concerns have been raised about women at 36 weeks and beyond who have been exposed to SARS-CoV-2, and its impact on the mother and the neonate but its effect on fetal exposure during first and second trimesters of pregnancy is an area of further research[4].

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

METHODOLOGY

This study was conducted at obstetrics unit of Pak Emirates Military Hospital (PEMH) and Combined Military Hospital (CMH) Rawalpindi, from April 2020 to June 2020. Patients were included by consecutive non probability sampling technique after informed consent and institutional review board approval (A/28/EC1117). Patients' confidentiality was ensured. Coding was not done as there were no open ended questions. All pregnant women reporting for childbirth were tested for SARS CoV-2 using RT-PCR kits. Data was collected from the patients testing positive. Demographic and reproductive profile including, age, occupation, travel history, parity, period of gestation at diagnosis mode of delivery and comorbids was noted. The primary outcome was categorization according to severity of disease into asymptomatic, mild, moderate, severe and critical. COVID-19 related outcome included virus clearance time which was taken from first positive report to negative report, length of hospital stay, respiratory compromise and maternal death. Women were excluded if they had presumed COVID-19 infection but laboratory testing was negative. Asymptomatic were the patients who were nasopharyngeal swab RT-PCR positive for SARS CoV-2 but exhibiting no symptoms. Mild disease was presence of fever, cough, flu like symptoms, malaise, myalgia, headache and gastrointestinal symptoms without any hemodynamic compromise, laboratory or radiological findings. Moderate disease was oxygen saturation ≤94% or mild infiltrates on chest x-ray or persistent high-grade fever for 3 days or above. Severe disease was diagnosed by shortness of breath, blood oxygen saturation ≤93% on room air, lung infiltrates >50% on chest imaging with moderate to severe pneumonia without meeting the criteria for critical disease. Critical disease was defined by respiratory failure, septics hock, or multiple organ dysfunction with the laboratory evidence of COVID-19 infection. Secondary outcome were symptoms of fever, cough, myalgia, flu like symptoms, shortness of breath and gastrointestinal symptoms. Vital signs at admission noted 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 abdominal shield was done in all pregnant women and chest CT scans were done where indicated by the clinical condition. Patients were admitted in designated COVID facility (PEMH Rawalpindi). Although no support person was allowed in the ward, daily communication by healthcare staff and updating about the patient's condition was ensured. Daily fetomaternal monitoring was done by symptoms, vital signs, oxygen saturation and electronic fetal heart rate monitoring twice daily. Consultant visited the patients twice a day. Nasopharyngeal swab was repeated on seventh day of admission.

The criteria for discharge were two consecutive negative samples done 24 hours apart. Delivery or cesarean section was conducted in designated theatre taking care of all the infection prevention protocol. Standard monitoring was done during labor with minimum required staff in personal protective gear. Patients wore face masks during hospital stay and labor. During postnatal period they were monitored according to their disease categorization and comorbidities in ward, high dependency unit or intensive care. 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 presence of SARS-CoV-2 was evaluated in neonatal samples after 24 hours of births. Breast feeding 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 hospital (CMH Rawalpindi) for further management or delivery. They were given 24 hours access to telemedicine for follow-up and discussion about development of any new symptoms. Patients data was collected and analyzed using SPSS 21 and descriptive statistics were presented as frequencies and percentages. Comparison was done by chi square test between presence of comorbid conditions and symptoms to category of COVID-19 and the *p*-value of ≤0.05 was considered statistically significant.

RESULTS

A total of 1170 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 is shown in table-I. Majority 37 (90.2%) at the time of diagnosis were in third trimester of pregnancy followed by 04 (9.7%) second trimester and none in first trimester. Preexisting comorbid conditions were present in 17 (41.4%) of patients. Patients were placed into different categories based on their signs, symptoms, laboratory and radiological investigations. Majority of the patients were asymptomatic 28 (68.3%) followed by mild 08 (19.5%), moderate 04 (9.8%) and severe 01 (2.4%). Signs noted at admission showed mean temperature 98.96 ± 0.68 °F, respiratory rate 18.24 ± 3.1 /min, pulse 87.61 ± 8.7 bpm, systolic blood pressure 117.8 ± 14.4 mmHg, diastolic blood pressure 76.22 ± 8.8 mmHg and oxygen saturation 97.2 ± 2.01%. The symptoms in order of frequency were myalgia 15 (36.6%), cough 13 (31.7%), flu 12 (29.3%) fever 11 (26.8%), shortness

Table-I: Demographic and reproductive data.

Variables	n (%)
Age (Mean ± SD)	29.24 ± 4.5 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	-
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	
Period of Gestation (mean)	36.46 ± 5.7
Outcome of Pregnancy	
Cesarean section	19 (46.3%)
Vaginal delivery	14 (33.11%)
Twin delivery	1 (2.4%)
Miscarriage	-
Continued pregnancy	7 (17.1%)
Comorbids	
Anemia	8 (19.5%)
Hypertension	3 (7.3%)
Diabetes mellitus	-
Pulmonary disease(asthma)	1 (2.4%)
Cholestasis	2 (4.9%)
Heart disease	1 (2.4%)
Hypothyroidism	2 (4.9%)
None	24 (58.5%)

of breath 7 (17.1%) and gastrointestinal symptoms 03 (7.3%). All the symptoms and presence of comorbid conditions were compared to category of COVID-19 and there was significant association of COVID category with presence of symptoms (p<0.005) and comorbid (p<0.0001) table-II.

Table-II: Association of COVID-19 category with comorbid and symptoms.

Co-Morbid	COVID-19 Category				*p*-value
	Asymptomatic	Mild	Moderate	Severe	
Anemia	6	1	1	0	
Asthma	0	0	1	0	
Cholestasis	2	0	0	0	
Heart Disease	0	0	0	1	<0.0001
Hypertension	3	0	0	0	
Hypothyroidism	0	2	0	0	
None	17	5	2	0	
Fever	0	7	4	0	<0.0001
Cough	0	8	4	1	<0.0001
Flu	0	8	4	0	<0.0001
Myalgia	3	8	4	0	<0.0001
Dyspnea	0	4	2	1	<0.0001
GIT Symptoms	0	3	0	0	0.004

COVID-19 related maternal outcome is shown in figure. Only one patient required intubation due to respiratory compromise but she had mixed valve lesions with severe pulmonary hypertension and 03 (7.3%) became oxygen dependent but recovered with treatment. There was no maternal mortality or obstetric morbidity. Mean virus clearance time was 8.2 ± 1.66 days with 3 days minimum and 14 maximum days for test becoming negative. Of the admitted COVID patients 34 (82.9%) delivered during hospital stay and 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, 01 (2.4%) preterm and 07 (17.0%) remained undelivered. Mean APGAR score was 9 ± 1.1, mean fetal birth weight was 2.99 ± 0.3 kg. They were kept in dedicated neonatal intensive care and presence of 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.

DISCUSSION

COVID-19 has become the biggest public health challenge faced by mankind in decades. Not only is it an unusual situation for individuals, communities and countries but also for health care providers. The management strategies are evolving and modifying everyday according to the available evidence. Pregnancy being a special situation raises management issues regarding

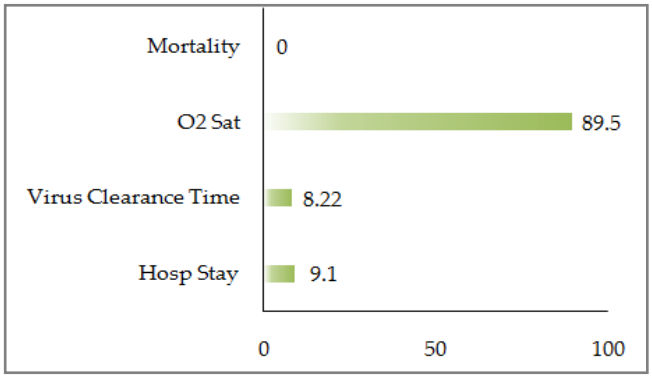

Figure: COVID-19 related maternal outcome.

delivery of optimum care to pregnant woman who are affected with COVID-19. There is also fear and uncertainty amongst the health care staff about a situation in which working as well as being admitted in a highly infectious environment requires protection and well developed protocols[5]. An effort to collect as much data as

possible will lead towards evidence based practices which was the main aim of this study. In our study demographic profile of the patients showed that mean age was 29.2 ± 4.5 years, majority were at 36.4 ± 5 weeks gestational age and 75% were multipara (P1-4). This agrees with two studies in which majority were 25-35 years and 26-40 years[6,7]. In another small study comparing COVID-19 and normal patients there was no difference between parity (1-4) or age 20-40 years and period of gestation at delivery which was 38 weeks[8]. In a similar study done in USA on pregnant COVID-19 patients gestational age at onset of symptoms was 29 weeks ± 6, and at admission 30 ± 69. 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. Where as in the USA cohort study by Williams *et al* mean duration of admission was 10.5 days for critical and 6 days for severe disease[9].

In Wuhan China where this virus originated studies found comparable clinical course of COVID-19 amongst pregnant and non-pregnant women regarding 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 New York by Breslin *et al*, in which majority had mild disease in 85%, severe disease in 10% and critical in 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 six week duration which is similar to our study period, there were 64 pregnant woman 69% severe and 31% in critical category[9]. In our study it is notable that maximum number of patients were asymptomatic which is quite alarming as these patients were infecting others unknowingly indicating wide community spread. This is in agreement with two USA studies in which 32.6% were asymptomatic and in another 29 of 33 positive patients were asymptomatic[12,14]. Preoperative or pre admission PCR testing in our patients revealed COVID-19 infection in asymptomatic patients but 04 (9.7%)later on developed symptoms like breathing difficulty and fever. This is in agreement to a study in New York in which 10 out of 14 asymptomatic patients developed fever during hospitalization. WHO joint mission investigated pregnant women in China between 16-24 Feb and found that there were 147 pregnant women, 64 confirmed, 82 suspected and one asymptomatic with COVID-19. Out of these only 08% had severe and 01% critical disease. They concluded that pregnant women are not at a higher risk of developing severe disease[15]. Our study also demonstrates this fact which is in contrast to a retrospective case series done in Iran over a 30 day period which collected data from seven centers level 3 hospitals. Nine cases with severe disease were reported of which sevendied. None of the patients had preexisting co-morbidities. The most plausible cause was delay in reporting to hospital[10].

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 anemia. Comorbidities like hypertension, diabetes, respiratory illnesses make the women more vulnerable to effects of COVID-19[18,19]. 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 labor was induced in 50%, 44% delivered by cesarean section and preterm delivery was 5% compared to 2.4% preterm deliveries in our study. Majority of pregnant patients were young and in good health, in our study and there were no obstetric complications. Mode of delivery was cesarean section in 55% of patients whereas rates reported from other studies were almost 91%, 100%, 94%[8,9,19].

Although the evidence is still fluid and evolving but definitive evidence of vertical transmission is lacking. Previous epidemics of Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome resulted in high maternal and perinatal morbidity and mortality. For SARS out of 12 pregnant patients reported three died with a case fatality ratio of 25% whereas 11 reported pregnant MERS patients had adverse clinical outcome in 91% of cases[20]. Our study reported no maternal death. Neonatal outcome showed no vertical transmission, average birth weight 2.9 kg, preterm 2.4% and 2.4% perinatal mortality. Compared to other viral illnesses fetal complications in COVID-19 patients seem less[9]. A systematic review of articles reported on 108 pregnant patients with one fetal and one neonatal death only[2]. Although further research is required as the data is limited regarding the long term effects of COVID-19 on baby, small studies comparing COVID-19 and normal patients showed no difference in baby's outcome and birth weight (3.1kg)[8]. Inspite of the potential benefits of breast milk and recommendations of WHO and CDC favoring breast feeding, infants born amongst our study cohort were not breast fed while they were positive according to a locally agreed protocol. In a study reported in JAMA only 3 of the 33 infants had evidence of mild neonatal infection and a favorable outcome[8]. In another cohort of 18 patients born to COVID-19 positive mothers from USA all 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 secretion of virus in breast milk[21-23]. Limitation of the study is small study cohort but considering that COVID-19 is a novel virus it will give confidence in managing these patients and help in updating our own protocols and guidelines depending upon the clinical course taken by our patients.

CONCLUSION

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

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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