

Impact of Covid - 19 infection and its severity during pregnancy in 2021 - a retrospective observational study

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ABSTRACT

Objectives: 1. Categorisation of disease severity in pregnant covid patients, 2. Evaluation of disease progression and severity in different trimesters of pregnancy and 3. Correlation of severity with laboratory parameters, treatment protocol and pregnancy outcome at our tertiary care centre. **Methods:** This retrospective observational study was carried out at a tertiary care hospital from 1st January 2021 to 30th June 2021. 122 covid 19 positive pregnant females were analysed for categorisation and comparison of severity, management protocol and disease outcome. **Results:** 46 out of 122 antenatal patients (37.70%) needed oxygen support and 22% were severely affected. Most commonly reported clinical symptoms were fever (63.3%), cough (71.4%) and dyspnoea (34.4%). CRP was found to be significantly affected with disease severity ($p < 0.00001$). Patients in second trimester were observed to require remdesivir more frequently than others because they were observed to be more severely affected. Patients who were admitted after one week of symptom onset were more severely affected than the patients who were admitted within 5 days of symptom onset. Majority [47 (74.6%) of the 63 patients] who terminated pregnancy underwent cesarean section. Of the 14 patients that died, 11 patients had symptoms for more than 10 days. **Conclusion:** Pregnancy had a severe impact on the course of covid-19 infection. Covid infection led to more adverse pregnancy outcomes than those who were not affected by covid-19 in view of maternal respiratory distress that led to increase maternal mortality.

Keywords: Covid – 19, antenatal, pregnancy outcome.

In December 2019, in Wuhan city, Hubei province, China emerged unexplained clusters of pneumonia cases, which were extensively researched thereafter. Scientists isolated the responsible virus whose genetic sequence was 70% similar to that of human severe acute respiratory distress syndrome coronavirus (SARS-CoV). WHO named the novel coronavirus 2019-nCoV which causes corona virus disease 2019 (COVID-19). WHO declared it as a pandemic on 11th of March 2020. The first case in India was reported on 31st January 2020^{1,2}.

Pregnancy is a physiological state that predisposes women to viral respiratory infections due to the rise in progesterone levels which stimulate the brain's respiratory

centre and creating a functional state of hyperventilation. Also, the expanding gravid uterus raises the diaphragm and decreases lung volumes thus causing subsequent respiratory discomfort which adds on to the already known respiratory afflictions of COVID-19 on lung functions. Pregnant women are thus presumed to be more vulnerable to COVID-19 infection than the general population. With the emergence of this ongoing pandemic, there was justified concern that this disease might have similar effects on pregnant women as influenza or other corona virus infections as in past pandemics of SARS CoV 2003 and MERS CoV 2012^{3,4}.

Fortunately, Indian data from the first wave of the COVID-19 pandemic showed that the symptoms in pregnant

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women were comparable with those of the general population despite an increased risk of respiratory distress in pregnant women especially in the third trimester.

However, as the Covid-19 wave in 2021 has taken over the world by its deadly probable mutant strains, as researched in regions outside India, early data suggest that pregnant and peripartum women are experiencing more severe illness in the second wave of the COVID-19 pandemic than was observed in the first wave. The preliminary studies conducted in the UK and Spain have shown that covid in pregnancy has a severe outcome^{4,5}.

However, there has been sparse data regarding the second wave of this pandemic and more research needs to be done in this direction. Through our study, we aim to contribute to the vast ongoing research regarding the implications of covid in pregnancy in India during the sudden resurgence of COVID-19 in 2021.

Objectives -

1. Categorisation of disease severity in pregnant covid patients.
2. Evaluation of disease progression and severity in different trimesters of pregnancy.
3. Correlation of severity with laboratory parameters, treatment protocol and pregnancy outcome at our tertiary care centre.

Methodology

This retrospective observational study was carried out at a tertiary care hospital in Ahmedabad, Gujarat from 1st January 2021 to 30th June 2021 after taking relevant approval from Institutional Review Board (IRB).

Inclusion criteria: Confirmed rapid antigen positive or RT-PCR positive pregnant patients with or without comorbidities who were admitted at our tertiary care hospital.

Electronic medical records were retrieved in retrospect. All admitted patients were thoroughly assessed in terms of detailed history regarding symptom onset, medical treatment received at home and other parameters relevant to COVID-19 infection. The patients were evaluated for obstetric history and examination. Necessary laboratory and radiological investigations of Pregnancy and COVID-19 were enumerated. Detailed assessment was done based on their oxygen requirement and clinical presentation taking into account the treatment received by multidisciplinary approach. Patients were then classified for severity according to the guidelines of severity classification issued by AIIMS - ICMR in 2021 as follows -

- a) Mild - Upper respiratory tract symptoms and/or fever without shortness of breath
- b) Moderate - any one of : RR \geq 24/min , spo2 < 94% on room air
- c) Severe - any one of : RR > 30/min , spo2 < 90% on room air

Various parameters were studied and compiled to extract a significant association or correlation with severity to focus on the treatment and outcome of pregnancy and Covid-19 in pregnancy. Extensive data on mortality was also studied so as to aid in contributing to better health care for covid positive patients at our hospital.

Statistical analysis: All data was analysed for categorisation and comparison of severity, management protocol and disease outcome. The collected data were analysed using SPSS software. Pearson's chi square test was used to assess whether pregnancy and clinical severity of Covid -19 infection were related. A p value obtained less than 0.05 was considered significant.

Results

As shown in the above table, 36 of 122 (29.44%) patients of the affected were in the age group of 18-28 years. 76 of 122 (62.3%) of the affected were in the age group of 29-39 years. 10 of 122 (8.22%) of all the affected patients were in the age group of \geq 40 years. Mean age of the patients affected was 31.5 years All patients who were moderately and severely affected needed oxygen support. All patients who were severely affected were admitted in ICU.

Table 1: Correlation of age distribution and severity of Covid pregnant patients

Age in years	Mild	Moderate	Severe
18 - 28	23 (18.85%)	6 (4.9%)	7(5.7%)
29 - 39	49 (40.16%)	12 (9.8%)	15 (12.3%)
\geq 40	4 (3.3%)	1 (0.8%)	5 (4.1%)

None of the asymptomatic patients were severely affected. Amongst the symptoms, out of those admitted with shortness of breath, 38.29% were severely affected. Thus, out of the 122 patients studied, 26 were asymptomatic and none of them were severely affected. Of the remaining 96 patients who were symptomatic, more than half were severely affected.

CRP was elevated above 50 mg/dl in 50 out of 122 patients (40.9%) and was found to be significantly associated with the severity of disease (p <0.00001). Out of the 15 patients with D-Dimer less than 0.5, one of the patients

suffered from severe consequences of covid-19. Out of the 12 patients with D-Dimer more than 3.5, 2 patients had severe disease. However, D-Dimer has not been found to be significantly associated with disease severity. 12(9.8%) of the 122 patients had LDH above 600. LDH is significantly ($p=0.00001$) associated with severity of disease (table 2).

Table 2: Correlation of laboratory parameters and disease severity in pregnancy

CRP (p value<0.00001)	No of patients
<20	46 (37.7%)
20-50	26 (21.3%)
>50	50 (40.9%)
LDH (p value = 0.00001)	No of patients
<250	54 (44.26%)
250-600	56 (45.9%)
>600	12 (9.8%)
D Dimer (p value= 0.5)	No of patients
<0.5	15 (12.3%)
0.5-3.5	95 (77.9%)
>3.5	12 (9.8%)

Of patients under 12 weeks of gestation, none were severely affected. Patients between 13-28 weeks of gestation, 9 (34.6%) patients needed remdesevir. Patients between 28-34 weeks of gestation, 8(38.1%) of the 21 patients needed remdesevir. None of the 4 patients above 34 weeks of gestation needed remdesevir. Remdesevir was given to severely affected patients only (table 3). 53 patients were admitted within 5 days of symptom onset out of which only 8 suffered from severe consequences of covid. Rest of them suffered from mild disease. 26 patients presented to the hospital after 5 days of symptom onset, were admitted and out of them, 14 were severely affected. There is a strong statistical significance between severity of Covid-19 infection and time taken to admit after symptom onset. In 65 mildly affected patients, 19 patients took less than 7 days to recover (sent for home isolation), 42 patients recovered within 7-14 days of symptom onset and only 4 patients recovered after 14 days. Amongst 13 severely affected patients, only 3 patients recovered within less than 7 days, 5 patients out of 13 took more than 14 days after symptom onset to recovery. There is statistical significance between

severity of infection and time taken to recovery amongst pregnant covid patients.

Table 3: Correlation of the need of treatment to disease severity at various gestational age

Gestational age	Treatment	Mild	Moderate	Severe
Upto 12 weeks	LMWH	0	0	0
	Heparin	0	0	0
	Oral anticoagulants	0	0	0
	Steroids	3	0	0
	Remdesevir	0	0	0
	None	4	0	0
13-28 weeks	LMWH	13	3	6
	Heparin	0	0	2
	Oral anticoagulants	0	0	0
	Steroids	10	7	9
	Remdesevir	8	7	9
	None	5	0	0
28-34 weeks	LMWH	5	5	5
	Heparin	0	0	0
	Oral anticoagulants	0	0	0
	Steroids	8	4	8
	Remdesevir	6	2	8
	None	4	0	0
>34 weeks	LMWH	9	5	0
	Heparin	0	0	4
	Oral anticoagulants	0	0	0
	Steroids	12	5	0
	Remdesevir	5	4	0
	None	20	0	0

Table 4: Termination at various stages of severity

Gestational age at termination	Mild	Moderate	Severe
0-12 Weeks	2	0	0
12-28 Weeks	5	0	1
28-32 weeks	2	2	4
32-34 Weeks	2	4	1
>34 Weeks	34	5	1

Out of the 63 antenatal patients terminated, 40 patients (63.49%) were above 34 weeks of gestation when terminated. 30% of pregnancies were preterm on termination. 15 (12.5%) of 63 patients were terminated between 28-34 weeks of gestation. Rest were before 28 weeks of gestation (table 4). Only one of the patients terminated above 34 weeks of gestation suffered from severe disease (2.5%), whereas 33.33% i.e. 5 out of 15 patients terminated between 28-34 weeks of gestation were severely affected during termination. Of the term patients who suffered from mild disease, 4 patients had to be terminated at 32-34 weeks of gestation, due to IUGR, PROM and preterm labour i.e. obstetric indications. About 74.60% of the patients who terminated pregnancies underwent cesarean section in our study. 7.4% of patients were terminated by vaginal delivery (table 5).

Table 5: Outcome of termination

Outcome of termination	No. of patients	Percentage
Ectopic	1	1.59
Abortion /D and E	7	11.11
Hysterotomy	4	6.35
Vaginal delivery	4	6.35
Cesarean delivery	47	74.60

All of the 7 antenatal patients that expired were between 12-28 weeks of gestation. Of the 14 patients that died, 11 patients had symptoms for more than 10 days. 10 patients died after 10 days of admission. 9 patients of 14 were admitted after 9 days of symptom onset. Of the 63 patients terminated, 53 (84%) pregnancies were liveborn. 2 fetus died in utero. Materno-fetal transmission of Covid-19 was seen in only two of the terminated pregnancies.

Discussion

As shown in table 1, in our study, mean age of pregnancies affected was 31.5 years. Majority of patients affected were young (29-39 years of age), which goes in accordance with Arora et al ². 46 out of 122 antenatal patients (37.70%) needed oxygen support. Unlike studies conducted by Blitz et al and Khalil et al, there was no correlation of comorbidities in pregnant women with severity in our study ^{6,9}. The rate of ICU admission was higher than mild disease in pregnancy affected by covid 19 ^{6,7,10,11}. This could also probably be the consequence of our hospital being one of the few government tertiary hospitals. Majority of cases were referred from other hospitals for high demand and low availability of oxygen equipment and ventilators at other hospitals owing to the exhaustion against the rapidly rising Covid-19 cascades in the city. Majority of the patients had shortness of breath, bodyache and weakness as the presenting symptoms as the most common, asymptomatic patients were all mildly affected. In a study by Khalil et al, The most commonly reported clinical symptoms were fever (63.3%), cough (71.4%) and dyspnoea (34.4%) ⁶. Whereas, according to studies by Blitz et al, the most commonly reported symptoms were fever (40%) and cough (39%). According to a study by V Peyronnet et al, the most common symptoms at the onset of illness were fever (98%), cough (76%) fatigue or myalgia (44%), sputum (28%) and headache (8%) ¹⁰.

As shown in table 2, CRP showed a significant association ($p < 0.00001$) with severity of affected pregnant patients and so did LDH ($p = 0.00001$), which goes in accordance with Sun G et al ⁵. D-Dimer was not significantly associated ($p = 0.5$) to severity of the patients affected. A probable reason for this is because pregnancy, already being

a procoagulant state, D-Dimer is likely to be elevated even in a normal pregnancy not affected by covid-19.

As shown in table 3, majority of the severely affected patients were between 14-34 weeks of gestation i.e. second trimester and early third trimester. None of the patients above 34 weeks of gestation were severe enough to need remdesevir. This goes in accordance with study by Tug N et al, effect was more prominent in pregnant women at >20 weeks gestation ($p < 0.001$) ⁷. As in the article of Blitz et al, all pregnant patients affected with Covid-19 were treated with prophylactic anticoagulants ⁹. In our study majority of affected patients were treated with oral or parenteral anticoagulants. The majority of the patients being affected were in the second trimester of pregnancy, which is believed to be related to the increasing hemodynamic changes and resulting cardiac workload, hypercoagulability occurring in the second trimester of pregnancy.

As shown in table 4 and 5, we have a higher rate of preterm birth in covid pregnancies at our institute (approximately 30%). As in a study by Khalil et al, 73.9% were in their third trimester; 52.4% had delivered, 48.3% by cesarean section. The rate of preterm birth (<37 weeks) was found as 21.8%, which were mostly (18.4%) iatrogenic ⁶. Approximately 75% patients in our study underwent cesarean section owing to the scant studies of trial of vaginal delivery in covid positive patients. As in studies by Tug N et al, 11 (18.3%) had vaginal deliveries and 49 (81.7%) were by cesarean section. Of these 60 deliveries, 40 (66.7%) were <37 weeks gestation ⁷. Studies in the UK and Spain also show that rate of preterm birth has increased in covid 2021 in pregnancy ^{5,11}.

Most of the deceased were already severe at the time of admission, majority of the reasons being a longer interval between symptom onset and admission. Materno-fetal transmission of Covid-19 was seen in only two of the terminated pregnancies and none of the babies were symptomatic. They were discharged soon after supportive care and after a negative covid report.

Limitations of our study: This study has been performed retrospectively on a limited sample size in a single tertiary care centre. Hence the results may be biased and have various confounding factors related to a single-centre study. It shows only the tip of the iceberg of the massive number of patients affected all over the country.

Conclusion

Based on the findings of our study, we observed that covid infection led to more adverse pregnancy outcomes than those who were not affected by Covid-19 in view of

preterm deliveries and maternal respiratory distress that led to increase maternal mortality. However, we need more data in order to confirm or refute the findings of this study.

Conflict of interest: None. **Disclaimer:** Nil.

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