ORIGINAL ARTICLE

COVID-19 Infection in Reproductive Age Group Females: Experience of a Tertiary Care Urban Teaching Hospital

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Abstract

Background The objective of this study was to find out the effect, course of disease and management of the COVID-19 infection in pregnant women and compare it with non-pregnant population.

Method This is a retrospective study done at Sardar Vallabhbhai Patel Institute of Medical Science and Research (SVPIMSR), Smt. NHL MMC, Ahmedabad, from April 1, 2020, to September 30, 2020. All COVID-19-positive patients were divided into two groups: group A was comprised of pregnant/postpartum and group B of non-pregnant patients.

Result A total of 709 women (Group A-205, Group B-504) were included in the study, In group A 90% of patients were asymptomatic, while in group B 48% asymptomatic patients. Group A had 5.9% and group B had 13.1% patients having comorbidities. In group A, smaller number of patients had raised inflammatory markers as compared to group B. Only 4% patients of group A showed significant changes on chest X-ray as compared to 16% in group B. Only 2.9% patients of group A required intensive care unit admission as compared to 10.31% patients of group B. Mean hospital stay of group A was 10.6 days, and that of group B was 12.1 days.

Conclusion In pregnancy, due to the physiological alterations in cardiovascular, respiratory and immune system, the pregnant women are vulnerable to infections. Although pregnancy is immunocompromised state, the severity of Coivd-19 disease is milder as compared to non-pregnant COVID-19-positive patients.

Keywords COVID-19 · Disease course · Inflammatory markers · Reproductive age · Pregnancy

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Introduction

Since the whole world is facing novel Covid crisis, it is imperative to know its effect and progression of disease in pregnant females as compared to general population. The corona virus disease 2019 (COVID-19), caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), is a global public health emergency. Corona viruses are enveloped, non-segmented, positive-sense RNA viruses belonging to the family Coronaviridae [1]. It causes illness such as respiratory diseases or gastrointestinal diseases. A novel corona virus (nCoV) is a new strain that has not been identified in humans previously. COVID-19 infection is highly contagious, and this must be taken into consideration during management of pregnancy [2]. Among those who will become infected, some will show no symptoms and those who develop symptoms may have a mild to moderate, but self-limiting disease with symptoms similar to the seasonal flu. A minority group of people will present with more

severe symptoms and will need to be hospitalized, most often with pneumonia, and in some instances, the illness can include acute respiratory distress syndrome, sepsis and septic shock. The mean incubation period (from exposure to the appearance of clinical features) is 5 to 7 days. Most people who are infected will show features latest by 11th day of exposure [3].

Pregnancy is physiologically immunocompromised state. It increases susceptibility to infections in general [4]. Reproductive age group of women comprises the large part of world's population. If we are able to know the effect of COVID-19 viral disease in pregnancy, we can take the appropriate steps and combat against the disease in pregnancy.

There is a difference in pathophysiology of immune response towards SARS-CoV-19 in both non-pregnant and pregnant women which affects their disease course [5].

In non-pregnant women, due to SARS-CoV-19 infection, activation of Th1 immunity which elevates pro-inflammatory cytokines (IFN GAMMA,IL 1 Beta, IL 6,IL 12) leads to lung damage. There is dominance of Th1 immunity over Th2 immunity. So there are more pro-inflammatory cytokines than anti-inflammatory cytokines [6].

In pregnancy, both Th1 and Th2 immunity are activated. That's why anti-inflammatory markers of Th2 immunity (IL4, IL 10) counteract effects of pro-inflammatory markers. In addition, pregnancy hormones (estrogen, progesterone, prostaglandins, corticosteroids, adiponectin) cause immune modulation resulting into enhancement of Th2 immunity and suppression of Th1 immunity. Cumulative effects may explain the reason for reduction in the inflammatory reaction responsible for severe pneumonia and systemic damage [7].

Aims and Objectives

The aim of the study is to observe the course of the disease, changes in inflammatory markers and management of pregnant patients with COVID-19 infection and compare it with non-pregnant COVID-19-positive patients.
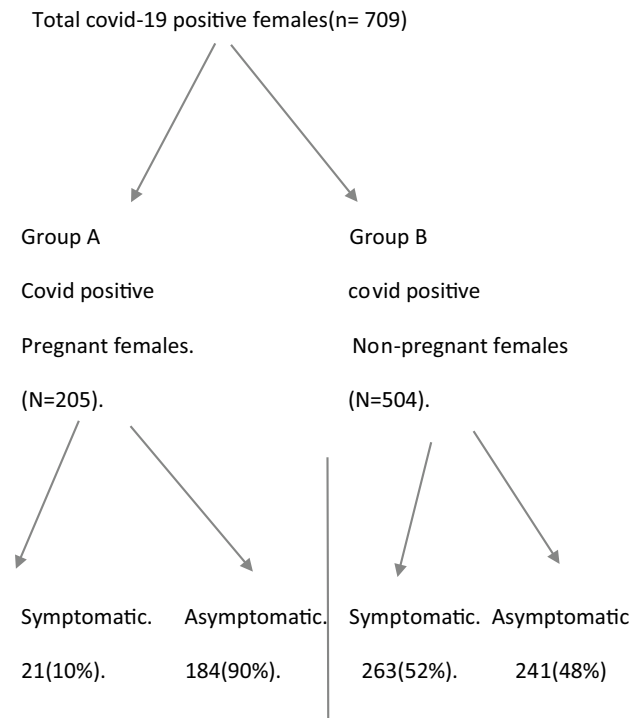
Materials and Methods

This is a retrospective, observational comparative study done at Sardar Vallabhbhai Patel Institute of Medical Science and Research (SVPIMSR), Smt. NHL Municipal Medical College run by Ahmedabad Municipal Corporation (AMC) in western India from April 1, 2020, to September 30, 2020. Study was started after taking due permission from Institutional Review Board (IRB).

Inclusion criteria: Confirmed COVID-19 RT-PCR-positive female patients. Age group of 18 years to 44 years with or without comorbidities.

Exclusion criteria: Patients less than 18 years and more than 44 years.

All patients fitting into inclusion criteria were divided into two groups as follows (Total $N = 709$).

Total covid-19 positive females(n= 709)

Group A
Covid positive
Pregnant females.
(N=205).

Group B
covid positive
Non-pregnant females
(N=504).

| Symptomatic. | Asymptomatic. | Symptomatic. | Asymptomatic |
| 21(10%). | 184(90%). | 263(52%). | 241(48%) |

All patients were examined thoroughly, all necessary hematological and radiological investigations were done and treatment was started according to guidelines of hospital core committee for COVID-19 infection.

All the patients were monitored throughout their hospital stay, and their investigations were repeated as and when required. All babies were admitted in NICU to rule out COVID-19 infection, those who came negative were discharged, and the positive ones were kept in NICU.

Statistical Analysis

1. The data were analyzed using MS Excel and R-3.5.1 software.
2. All the tests of significance were carried out at 5% level of significance.
3. The statistical methods used were:

   a. Frequency distribution and percentage

Table 1 Symptomatology distribution in study group

	Group A ($n = 205$)	Group B ($n = 504$)
Asymptomatic	184 (90%)	241 (48%)
Symptomatology	21 (10%)	263 (52%)

$Z = 49.91$; $p < 0.00001$

Table 2 Distribution on basis of comorbidity

	Comorbid	Non-comorbid
Group A ($n = 205$)	12 (5.9%)	193 (94.1%)
Group B ($n = 504$)	66 (13.1%)	438 (86.9%)

**Table 3** Distribution on the basis of pre-existing comorbidity

	Group A ($n = 205$)	Group B ($n = 504$)
Hypertension	8 (3.9%)	38 (7.53%)
Diabetes mellitus	4 (1.95%)	22 (4.4%)
Respiratory disorder	3 (1.5%)	8 (1.59%)
Cardiac disorder	0	2 (0.4%)

   b. Descriptive statistics (minimum, maximum, mean, pie chart, bar diagram)
   c. Paired t-test for comparative variables (Chi-square test)

Results

The main purpose of this study was to observe the course of the disease, severity of the disease, effect of COVID-19 on pregnancy and effect of pregnancy on COVID-19 disease.
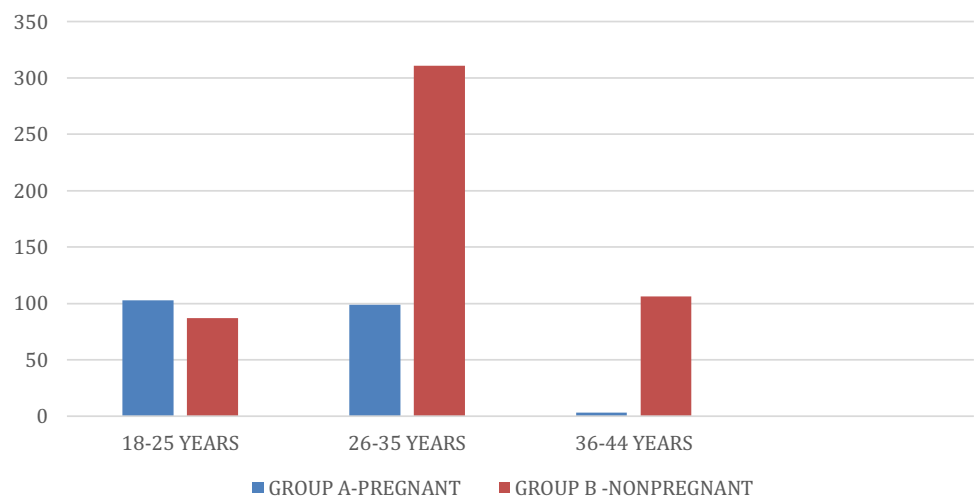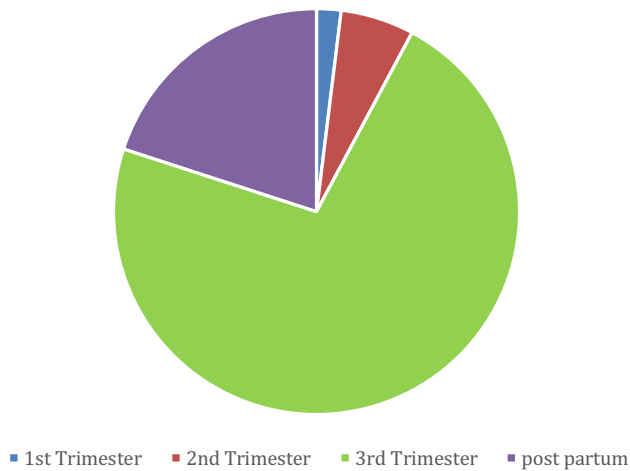
In our study, age group is 18–44 years. Table 1 shows symptomatic distribution. Only 10% of patients of group A were symptomatic as compared to 52% patients of group B. Table 2 shows distribution on basis of comorbidities like hypertension, diabetes mellitus, respiratory disorders and cardiovascular disorders. Only 5.9% patients of group A were found to be comorbid as compared to 13.1% in group B. Table 3 shows that hypertension was present in 3.9% and 7.53%, diabetes in 1.95% and 4.4%, respiratory disorder in 1.5% and 1.59%, respectively, in group A and group B. Figure 1 shows comparison of inflammatory markers in both the groups, and in group A the number of patients having raised inflammatory markers was less as compared to group B. Figure 2 shows radiological comparison between two groups, and only 4% of patients from group A had abnormal changes in X-ray as compared to 16% of patients in group B. Figure 3 shows comparison of treatment plan between two groups, and group B patients required more meticulous treatment. Table 4 shows comparison of ICU admissions between two groups, and group B (10.31%) patients required more ICU admissions as compared to group A (2.9%). Table 5 shows comparison of hospital stay between two groups, and group A patients required shorter hospital stay as compared to group B.

Discussion

The clinical course of COVID-19 disease during pregnancy appears to be mild in the present study. After applying Chi-square test to Table 1, $Z = 49.91$ and p value was less than 0.00001 which is statistically significant concluding that COVID-19-positive pregnant patients are relatively asymptomatic as compared to COVID-19-positive non-pregnant patients. Symptoms mainly were cough without expectoration, fever, shortness of breath and sore throat. Another study

Fig. 1 Demographic distribution

Fig. 2 Gestation-wise distribution

Table 4 Distribution on the basis of intensive care unit admission

	ICU	Stable ward
Group A ($n = 205$)	6 (2.9%)	199 (97.1%)
Group B ($n = 504$)	52 (10.31%)	452 (89.7%)
$Z = 10.597$; p value $= 0.001$		

Table 5 Duration of hospital stay

Duration of stay (days)	Group A ($n = 205$)	Group B ($n = 504$)
≤ 7	57 (28%)	81 (16%)
8–10	92 (45%)	247 (49%)
11–14	47 (23%)	115 (23%)
> 14	9 (4%)	61 (12%)

conducted by Hu Z also has similar findings that pregnant patients have only mild symptoms like cough, cold and fever and lesser need for hospital admission [8]. Pregnant women do not appear to be more susceptible to COVID-19 infection or to serious complications compared to non-pregnant women [9]. In the present study, more than one comorbidity coexisted in some patients of both the groups. Pregnant women with COVID-19 who have pre-existing medical conditions such as diabetes or high blood pressure are more likely to suffer severe health complications due to COVID-19 infection [10]. In our study, inflammatory markers (CRP, d-dimer, ferritin and ESR) and radiological changes (chest X-ray) were more significant in group B as compared to group A. As the disease is novel, management plan changes from time by time, inflammatory markers like LDH and IL-6 were not compulsory in hospital management protocol during this study period and were only done in patients with severe disease. Yates Chi-square test when applied to Fig. 2 ($Z = 15.9$. p value < 0.0001) showed

that Covid non-pregnant patients develop significant X-ray changes like B/L consolidations, ground glass opacities compared to COVID-19-positive pregnant patients. Study conducted by Zhiqiang Wang and colleagues also suggests that in pregnant Covid-positive females, severity of symptoms, X-ray changes and duration of hospital stay are less as compared to the non-pregnant females which is similar to our study [11].

Many patients with moderate to severe disease required specific treatment in the form of broad-spectrum antibiotics given intravenously, antivirals as and when required with steroids (methylprednisolone), low molecular weight heparin and oral hydroxychloroquine. After applying Chi-square test for hospital stay > 14 days in both the groups, $Z = 10.46$ and p value is < 0.001 which is statistically significant, indicating that patients belonging to group B needed longer hospital stay as compared to group A. Mean hospital stay of patients in group A was 10.6 days, whereas that of group B was 12.1 days. In the present study, pregnant patients had milder signs and symptoms, normal to mildly deranged

Fig. 3 Comparison of serum inflammatory markers in group A and group B
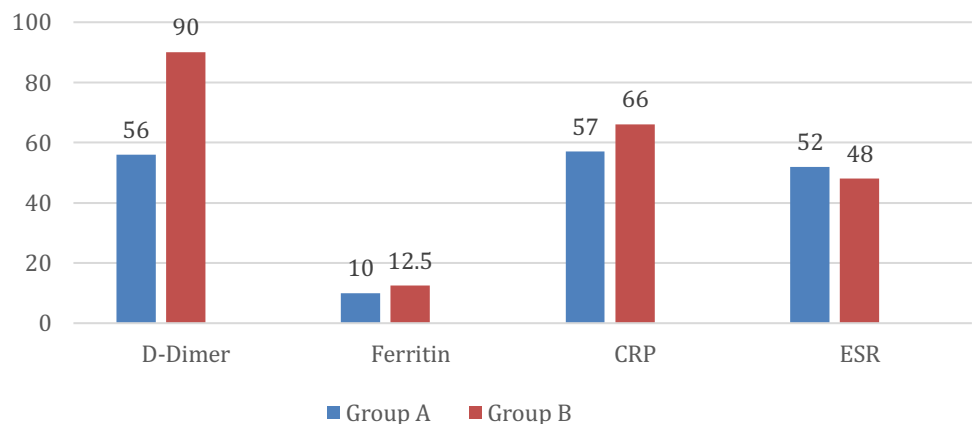
hematological and radiological investigations, lesser need for complex treatment, less need for intensive care facility, and shorter duration of hospital stay as compared to non-pregnant COVID-19-positive patients.

Conclusion

In pregnancy, due to the physiological alterations in cardiovascular, respiratory and immune system, the pregnant women are vulnerable to infections and are at greater risk of any complication, especially in this global pandemic of SARS-CoV-2.

Though pregnancy is immunocompromized state, they might have higher level of endogeneous steroids which might be supporting milder symptoms in the pregnancy with COVID-19 cases [12]. This can be explained by shifting of immunity from helper T cell-1 to helper T cell-2. The hospitalization of all pregnant women with confirmed COVID-19 infection, the provision of an individualized approach, the appropriate use of medications, and the management of cases within the framework of a multidisciplinary team seem to be associated with favorable outcomes.

As the disease is novel and due to emergence of newer strains time by time, the meta-analysis of more research work is required to establish universal protocol for management of the disease. The present study suggests that the severity is more in non-pregnant females, which gives us a ray of hope amid the global pandemic. More research can prove it better, till then we should follow the government-approved guidelines in the population only.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Ethical approval has been taken from Institutional Review Board (IRB) of Smt. N.H.L Municipal Medical College, Ellisbridge, Ahmedabad.

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