Caspian J Reprod Med, 2023, 9 (1): 16-21

Caspian Journal of Reproductive Medicine

Journal homepage: www.caspjrm.ir

Original article

Inflammatory markers in covid-19 positive pregnant women: Insights from a comparative study

Neelima Shah [1, *], Sonali Ranade [1], Prashant Shah[1], Varun Damle [1]

[1] Department of Obstetrics and Gynaecology, Kolhapur Maharashtra, India

Received: 17 Dec 2022 Accepted: 20 June 2023

Abstract

Background: The COVID-19 pandemic has wrought significant repercussions on lives worldwide. Pregnancy, a period marked by profound physiological changes, renders women susceptible to fluctuations in various biological parameters. The study aimed to fill this void by examining the levels of inflammatory markers, as well as liver and renal function tests, in pregnant women suffering from COVID-19.

Methods: This study was conducted to investigate inflammatory markers such as C-reactive protein (CRP), D-dimer, lactate dehydrogenase (LDH), white blood cell (WBC), as well as liver function tests (LFT) and renal function tests (RFT) in pregnant women afflicted with COVID-19. We enrolled 52 COVID-19-positive women (cases) alongside 48 COVID-negative women (controls) who underwent delivery at Dr. D. Y. Patil Hospital and Research Institute in Kolhapur, India. All participants underwent COVID-19 testing via reverse transcription polymerase chain reaction (RT-PCR) methodology.

Results: The findings revealed that a majority of cases exhibited elevated WBC counts compared to controls (78.8% versus 27.1%), with D-dimer levels higher in 61.5% of cases versus 12.5% of controls. LFT and RFT abnormalities were observed in 51.9% of cases versus 20.8% of controls. Moreover, LDH and CRP levels were elevated in 71.2% and 90.4% of cases, respectively, in contrast to 16.7% and 10.4% of controls, respectively. Statistical analysis underscored a significant association between deranged laboratory parameters and COVID-19 positivity.

Conclusion: The study underscores the potential exacerbation of inflammatory responses to COVID-19 among pregnant women with preexisting chronic conditions, which may precipitate liver damage. Thus, prioritizing inflammation and liver health management in the treatment regimen for pregnant women with COVID-19, especially those with chronic comorbidities, emerges as imperative.

Keywords: COVID-19, Inflammatory markers, Liver function, Maternal health, Pregnancy

Introduction

The emergence of the COVID-19 virus, which triggers severe acute respiratory syndrome, originated in the Wuhan province of China and swiftly escalated into a global pandemic (1). Particularly concerning was its impact on pregnant and postpartum women, given the intricate physiological changes and immune adaptations their bodies undergo during pregnancy (1). While pregnancy itself does not inherently increase susceptibility to COVID-19 infection, there exists a heightened risk of adverse maternal and fetal outcomes among infected mothers (2,3). Notably, the immunological landscape of pregnant women undergoes significant shifts, particularly in anticipation of delivery, marked by elevated levels of pro-inflammatory cytokines in cervical tissue, myometrium, and blood (4).

*Correspondence author: Neelima Shah, Department of Obstetrics and Gynaecology, Kolhapur Maharashtra, India

Email: neelimapshah@gmail.com Tel: +918257818954

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[DOI: 10.22088/caspjrm.9.1.16]

Various studies aimed at furnishing empirical evidence for the prevention and management of COVID-19 have been conducted, highlighting the heightened vulnerability of pregnant women owing to their immunocompromised status (5). Pneumonia, regardless of its infectious origin, stands as a significant cause of morbidity and mortality in pregnant women (6).. Hence, it is imperative to classify pregnant women, especially those with pre-existing chronic conditions, as a high-risk group during the ongoing COVID-19 pandemic (7).

Concurrently, COVID-19 infection prompts the release of a plethora of inflammatory cytokines within the body, correlating with disease severity (5). However, the specific role of these markers, including C-reactive protein, D-dimer, lactate dehydrogenase (LDH), and leukocyte counts, in pregnant and postpartum women infected with SARS-CoV-2 remains underexplored. Consequently, this study aims to bridge this gap by investigating the levels of these inflammatory markers, alongside liver and renal function tests, in pregnant women afflicted with COVID-19.

Materials & Methods

Upon securing ethical approval, our retrospective study commenced. We enrolled 52 COVID-19-positive women (cases) and 48 COVID-negative women (controls) who had delivered at Dr. D. Y. Patil Hospital and Research Institute, Kolhapur. All participants underwent COVID-19 testing via reverse transcription polymerase chain reaction (RT-PCR) methodology and informed consent was obtained before enrollment.

A detailed case record proforma was completed, capturing demographic and antenatal details, alongside inflammatory markers such as C-reactive protein (CRP), D-dimer, lactate dehydrogenase (LDH), white blood cell (WBC), as well as liver function tests (LFT) and renal function tests (RFT) in pregnant women afflicted with COVID-19.

For statistical analysis, we utilized SPSS (Statistical Package for Social Sciences) version 20 (IBM SPSS Statistics [IBM Corp. released 2011]). Data were meticulously entered into an Excel spreadsheet. Descriptive statistics, such as mean and standard deviation for quantitative variables, and frequency with proportions for qualitative variables, were calculated. Inferential statistics, including the Chi-square test for qualitative variables and independent sample t-test for quantitative variables (such as age and gestational age between the groups - Cases and Controls), were employed. The significance level was set at 5%.

Results

In our study, we enrolled 52 cases (pregnant women positive for COVID-19) and 48 controls (pregnant women negative for COVID-19). The majority of both cases and controls fell within the age group of 21 to 25 years, accounting for 51.9% and 37.5%, respectively. This was followed by 32.7% of cases and 29.2% of controls from the age group of 26 to 30 years. The mean age of the cases was 24.15±3.41 years (ranging from 19.0 to 35.0 years), while controls had a mean age of 26.46±4.83 years (ranging from 19.0 to 36.0 years). Notably, a statistically significant difference was observed between the mean ages of the cases and controls (p= 0.007).

Table 1 reveals that the majority of cases (84.6%) had a gestational age between 37 to 40 weeks, with only 5 cases (9.6%) falling between 32 to 36 weeks. Similarly, most controls (72.9%) had a gestational age between 37 to 40 weeks, while 9 cases (18.8%) were in the 32 to 36 weeks range. The mean gestational age for cases was 37.2 ± 4.2 weeks (ranging from 19 to 40 weeks), whereas for controls, it was 38.6 ± 1.6 weeks (ranging from 32 to 42 weeks). Notably, no significant difference was observed between the mean gestational ages of cases and controls.

Table1. Distribution of the participants based on gestational age (n = 100)

Gestational age	Cases N=52 N (%)	Control N=48 N (%)	Total
< 32 weeks	3 (5.8)	0 (0.0)	3 (3.0)
32 to 36 weeks	5 (9.6)	9 (18.8)	14 (14.0)
37 to 40 weeks	44 (84.6)	35 (72.9)	79 (79.0)
> 40 weeks	0 (0.0)	4 (8.3)	4 (4.0)

Chi-square value= 9.02, p value = 0.029

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Figure 1 illustrates the gravida status of the subjects. It reveals that the majority of cases, comprising 33 individuals (63.5%), were primigravida, while most controls, totaling 30 subjects (62.5%), were multigravida. Significantly, a notable difference was observed between the two groups (p= 0.009).

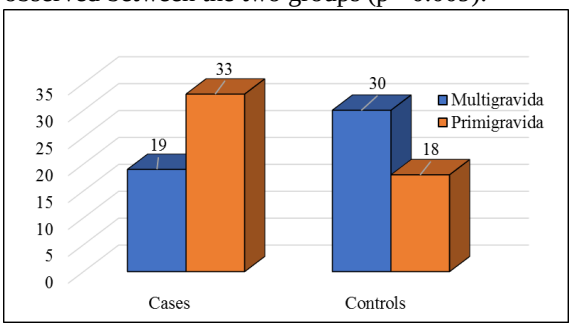


Figure 1. Distribution of the subjects based on gravida

Figure 2 illustrates the presenting symptoms of the patients. Notably, 90% of cases (47 out of 52) reported no complaints, while only 8% of controls (4 out of 48) were asymptomatic. Among the symptomatic cases, fever was reported in 2 instances, cough in 1, and fever with cough in 1, and fever with chills in 1. Conversely, the most prevalent symptoms among controls were cough, cold, fever, and myalgia, observed in 12, 6, 4, and 4 patients respectively.

Table 2 displays the laboratory parameters of both cases and controls. It reveals notable disparities between the two groups: the majority of cases exhibited elevated white blood cell (WBC) counts

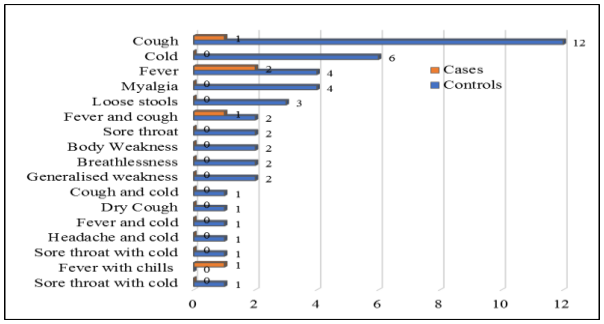


Figure 2. Presenting symptoms of cases and Controls

Compared to controls (78.8% and 27.1% respectively), while D-dimer levels were higher in 61.5% of cases compared to 12.5% of controls. Additionally, liver function tests (LFT) and renal function tests (RFT) were found to be deranged in 51.9% of cases and 20.8% of controls. LDH) and C-reactive protein (CRP) levels were observed in 71.2% and 90.4% of cases respectively, in contrast to 16.7% and 10.4% of controls respectively.

Moreover, the statistical analysis revealed a significant correlation between abnormal laboratory parameters and COVID-19 positivity, as all p-values were <0.01, indicating statistical significance.

Table 2. Distribution of the laboratory parameters of cases and controls

Lab parameters		Cases N=52 N (%)	Controls N=48 N (%)	Total N=100 N (%)	Chi-square value	p value
WBC count	Normal	11 (21.2)	35 (72.9)	46 (46.0)	26.92	0.001
	Raised	41 (78.8)	13 (27.1)	54 (54.0)		
D - dimer	Normal	20 (38.5)	42 (87.5)	62 (62.0)	25.47	0.001
	Raised	32 (61.5)	6 (12.5)	38 (38.0)		
LFT, RFT**	Normal	25 (48.1)	38 (79.2)	63 (63.0)	10.35	0.001
	Raised	27 (51.9)	10 (20.8)	37 (37.0)		
LDH***	Normal	15 (28.8)	40 (83.3)	55 (55.0)	29.94	0.001
	Raised	37 (71.2)	8 (16.7)	45 (45.0)		
CRP****	Normal	5 (9.6)	43 (89.6)	48 (48.0)	63.94	0.001
	Raised	47 (90.4)	5 (10.4)	52 (52.0)		

* WBC: White blood cell, **LFT: Liver function tests and RFT: Renal function tests, *** LDH: Lactate dehydrogenase, ****CRP: C-reactive protein

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[DOI: 10.22088/caspjrm.9.1.16]

Discussion

We conducted a prospective hospital-based study to evaluate inflammatory markers in pregnant women with COVID-19. Our findings revealed fever and cough as the predominant symptoms among pregnant patients with COVID-19, while a majority exhibited no respiratory symptoms. These observations align with previous studies by Chen L. et al., 2020 and Guan et al., 2020 (8,9). Zaigham and Andersson (2020) (10). also noted a significant proportion of COVID-19 patients presenting with no symptoms upon admission, suggesting the potential for asymptomatic infections (11,12). Thus, it becomes imperative to distinguish COVID-19-infected patients from non-infected ones upon hospital admission through laboratory indicators.

Furthermore, there is a need for comprehensive research on maternal symptoms of COVID-19 during the first or second trimester of pregnancy. In comparison to pregnant women without COVID-19, pregnant patients with COVID-19 exhibited significantly higher lymphocyte counts and CRP levels, indicative of typical clinical characteristics of pneumonia. Chen L. et al. (2020) [8] reported lymphopenia in 51 out of 116 pregnant women diagnosed with COVID-19, while Liu D. et al. (2020) (7). found decreased lymphocyte counts in 12 out of 15 pregnant COVID-19 patients, along with increased CRP values. It is recommended to closely monitor blood indices in pregnant COVID-19 patients, as changes in inflammatory markers have been correlated with patient prognosis (8).

Furthermore, the long-term effects of COVID-19 infection and its treatment on blood indices of pregnant patients warrant further investigation. Lymphocytes play a crucial role as the primary immune barrier against viral infections, and their dysregulation can be indicative of an invasive pathogen. Consistent with previous reports (13), our study demonstrated normal or increased peripheral lymphocyte counts and percentages in pregnant patients during the early stages of COVID-19 infection.

While WBC may vary during pregnancy, it often returns to levels comparable to nonpregnant patients postpartum (14). However, its correlation with WBC percentage suggests a potentially poor prognosis, as lymphocyte percentage has been associated with the severity of COVID-19 (15). It's worth noting that all enrolled patients in our study had recovered by the study's conclusion.

D-dimer serves as an indicator of fibrinolysis and is commonly utilized to assess thromboembolism. Prior research has linked elevated levels of D-dimer with COVID-19 occurrence in adult patients (16). Our study observed higher D-dimer levels in pregnant patients with COVID-19, although its clinical application in this population may be limited due to physiological elevation during delivery. Nonetheless, elevated D-dimer levels in pregnant women with COVID-19 indicate a potential risk of venous thromboembolism and/or pulmonary embolism.

Additionally, our findings revealed significantly higher values of LFTs in pregnant women with COVID-19, suggesting potential liver function impairment. A cohort study by Guan et al., 2020 (9), comprising 1,099 COVID-19 cases, reported abnormalities in bilirubin (10.5%), ALT elevation (21.3%), and AST elevation (22.2%). Moreover, it has been reported that 2–11% of COVID-19 patients exhibit liver comorbidities and 14–53% show abnormal AST and ALT levels during disease progression (17). However, due to the limited number of pregnant COVID-19 patients in our study, detecting changes in ALT and AST may have been constrained. Additionally, the majority of COVID-19 patients in our study experienced mild infection, and liver injury was not readily apparent. Hence, further research is warranted to elucidate the extent of liver damage caused by COVID-19 during pregnancy.

The significance of these markers in patients with COVID-19 necessitates further research for a comprehensive understanding of their clinical implications.

There are several limitations that should be acknowledged: The study enrolled a relatively small sample size of 52 COVID-19-positive women (cases) and 48 COVID-negative women (controls). A larger sample size would enhance the generalizability of the findings and provide more robust statistical power. Second, the study was conducted at a single hospital, and Research Institute in India. This may limit the generalizability of the findings to other settings or populations with different demographics or healthcare systems. Third, the study employed a retrospective design, which may introduce bias and limitations in data collection, accuracy, and completeness.

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Prospective studies would offer more control over data collection and minimize potential biases. Fourth, the study provides cross-sectional data on inflammatory markers at a single time point. Longitudinal data would provide insights into the dynamic changes in inflammatory markers over time and their correlation with disease progression and outcomes. Fifth, the study did not account for potential confounding factors such as gestational age, pre-existing medical conditions, medication use, and socioeconomic status, which could influence the inflammatory response and outcomes. Finally, while the study focused on inflammatory markers and liver function tests, other relevant outcome measures such as maternal and neonatal outcomes, severity of COVID-19 illness, and long-term health effects were not assessed. Including these outcome measures would provide a more comprehensive understanding of the impact of COVID-19 on pregnant women.

Given that the study was conducted at a single center in a specific geographical location, caution should be exercised when generalizing the findings to other populations or regions with different healthcare settings and sociodemographic characteristics. Overall, while the study contributes valuable insights into the inflammatory response among pregnant women with COVID-19, these limitations should be considered when interpreting the findings and designing future research studies.

Conclusion

In conclusion, our study investigated 52 pregnant patients with COVID-19, shedding light on the unique clinical characteristics and laboratory findings of this disease during pregnancy. Our findings suggest that pregnant individuals with COVID-19 exhibit distinct clinical features and laboratory profiles compared to their nonpregnant counterparts. It is imperative to provide tailored medical guidance and proactive treatment to ensure optimal recovery for these patients. Additionally, our results underscore the potential exacerbation of inflammatory responses and liver damage in pregnant women with preexisting chronic conditions. Hence, emphasizing the management of inflammation and liver health is crucial in the management of pregnant women with COVID-19, particularly those with underlying chronic diseases.

Acknowledgements

We express our sincere gratitude to all the participants who generously contributed their time and effort to this study. We also extend our appreciation to the staff and healthcare professionals at Dr. D. Y. Patil Hospital and Research Institute in Kolhapur, India, for their invaluable support and assistance throughout the research process. This study would not have been possible without their cooperation and dedication.

Conflicts of Interest

No conflict of interest as declared by the author.

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