ORIGINAL RESEARCH

Mortality Risk among Pregnant Women during COVID-19 Pandemic: A Case–Control Study in Rajasthan

Aditi Bansal[1], Sapna Choudhary[2], Pushpa Nagar[3], Nivesh Lal[4], Preeti Gupta[5]

Received on: 23 July 2022; *Accepted on*: 12 October 2022; *Published on*: 16 November 2022

Abstract

Objective: To analyze the risk factors associated with mortality in COVID-positive pregnant women.

Material and methods: The study was designed as a case–control study and was conducted at COVID-designated tertiary care hospital. It included 42 deceased and 96 RT-PCR-positive surviving pregnant women who developed severe forms of disease. All the affected patients were admitted and managed according to Indian national guidelines. Risk factors – age, residence, socioeconomic status, gestation age, parity, and comorbidities were evaluated for their association with mortality.

Results: Advanced maternal age (>28 years), rural residence, diabetes, and comorbidities were found to be associated with increased risk of mortality among the COVID-affected pregnant women, the respective adjusted odds ratio was 15.45, 12.61, 2.65, and 4.77, respectively.

Conclusion: Pregnant women are vulnerable to COVID infection. They were at higher risk of mortality with comorbidities, advanced age, and low access to healthcare in the rural areas.

Keywords: Comorbidity, COVID-19, Mortality risk, Pregnant women.

Journal of South Asian Federation of Obstetrics and Gynaecology (2022): 10.5005/jp-journals-10006-2130

Introduction

Coronavirus disease 2019 (COVID-19) is the most dreadful pandemic of the 21st century. The second wave affected the world in a more drastic way in terms of increase in morbidity, mortality rates, and higher post-COVID complications.

A shift from TH1 to TH2 immunity[1] is postulated to be responsible for altered responses to respiratory viral infections or autoantigens during pregnancy and increased severity of respiratory viral infections.[2–4]

Pregnancy itself, being an immunocompromised state in comparison with nonpregnant state, is ingenuous to higher risk of obstetric complications and unfavorable fetal outcomes.[5,6] Th2 cells stimulate B lymphocytes, increase antibody production, and suppress the cytotoxic T lymphocyte response, decreasing the robustness of cell-mediated immunity.

In women with other viral infections like Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV), the case fatality was also found to be higher when compared with general population.[7] However, despite various studies, the exact spectrum of COVID-19 disease and risk factors associated with the severity of disease still remains a mystery.

Limited healthcare facilities for non-COVID pregnant women during the pandemic in lower socioeconomic countries further aggravated these rates. Pregnant women presented to healthcare facilities at advanced stages of the disease, and moreover, their preexisting comorbidities were also not identified and treated timely.

We have conducted a case–control study in COVID-19-positive pregnant women admitted to a COVID-designated tertiary care maternity hospital during the pandemic in Jaipur, the Rajasthan State capital. The aim of the study was to assess the risk factors associated with increased risk of mortality among the hospitalized RT-PCR-positive pregnant women.

[1–3]Department of Obstetrics and Gynecology, SMS Medical College, Jaipur, Rajasthan, India

[4]Department of Obstetrics and Gynecology, JNU Medical College, Jaipur, Rajasthan, India

[5]Department of Radiology, Command Hospital, Kolkata, West Bengal, India

Corresponding Author: Sapna Choudhary, Department of Obstetrics and Gynecology, SMS Medical College, Jaipur, Rajasthan, India, Phone: +91 9799610530, e-mail: dreamzheaven11@gmail.com

How to cite this article: Bansal A, Choudhary S, Nagar P, *et al*. Mortality Risk among Pregnant Women during COVID-19 Pandemic: A Case–Control Study in Rajasthan. J South Asian Feder Obst Gynae 2022;14(5):602–605.

Source of support: Nil

Conflict of interest: None

Methodology

The study was conducted at the Department of Obstetrics and Gynecology, SMS Medical College, Jaipur, during the second wave of COVID-19 pandemic. A total of 440 COVID-positive pregnant women were admitted to hospital during the 6-months' time period. This study was conducted on 138 COVID-positive pregnant women (out of a total of 440 women) who developed severe disease. In this study, 42 COVID RT-PCR-positive pregnant women who succumbed to the disease at our center were taken as cases, and 96 RT-PCR-positive pregnant women who survived the disease, were taken as controls.

All the patients were examined thoroughly, and data were collected on age, socioeconomic characteristics, residence, parity, gravida, gestational age, comorbidity, obstetric complications, treatment, and outcomes. All the necessary precautions were taken by healthcare professionals like PPE kit protection, appropriate use

of N95 face mask, hand-washing, etc. All the patients were also advised to follow all necessary guidelines.

All patients were examined for clinical status and obstetric conditions. Risk factors were identified and treated in accordance with the standard treatment protocol as per national clinical management protocol for COVID-19.[8] Treatment included antibiotics, dexamethasone, methylprednisolone, low-molecular-weight heparin, remedesivir, tocilizumab, etc. Those who required higher modes of ventilation were kept in specialized ICUs and monitored very closely. All the pregnancies were terminated irrespective of the gestational age in favor of maternal health. All the newborns were admitted for monitoring and were tested for COVID infection within 24 hours of birth.

A univariate, bivariate, and multivariate analysis was conducted. The risk was measured by odds ratio and confidence intervals. Statistical software SPSS 21 was used for analysis.

Results

The mean age of the case group (deceased) was 28.74 + 4.89 years which was significantly higher as compared with that of the control group (survivors). The mean age of the survivors was 26.73 $\pm$ 4.73 years. Sixty-two percent of the deceased women were older than 28 years as compared with 34% of surviving pregnant women (Table 1).

Women belonging to rural areas (83.3%) witnessed a significantly high mortality as compared with their urban counterparts (χ^2 = 15.11, p = 0.003). We found statistically significantly higher mortality among cases who had diabetes, barotrauma, and comorbidities. We also analyzed COVID mortality associated with gravida, obstetric complications, etc., and found no statistically significant difference between cases and controls. The mean gestational age of the case group was 30.83 + 8.54 weeks, while for the control group, it was 32.94 + 6.86 weeks. There was not a statistically significant difference in mortality with gestational age.

Table 2 shows the multivariate analyses of the association of various risk factors with increased risk of mortality due to COVID among pregnant women. We included all significant risk factors in logistic regression model. The final model retained only age, rural residence, and comorbidities.

Age higher than 28 years was highly significantly associated (p-value 0.02). The risk of dying was fifteen times higher, the

Table 1: Demographic variables and risk factor assessment

Characteristics	*Cases (n = 42)*	*Controls (n = 96)*	*Significance level*
Mean age (years + SD)	28.74 + 4.89	26.73 + 4.73	t = 2.27, p = 0.02
Age years (category)			
≤27	16 (38.09)	62 (64.58)	χ^2 = 9.32, p <0.009
≥28	26 (61.53)	34 (35.41)	
Residence			
Urban	7 (16.66)	50 (52.08)	χ^2 = 15.11, p <0.003
Rural	35 (83.33)	46 (47.91)	
Mean gestation (weeks + SD)	30.83 + 8.54	32.94 + 6.86	t = −1.54, p >0.05
Mean gravida (+SD)	2.19 + 1.19	2.03 +1.11	t = 0.74, p >0.05
Gravida			
Multi	28 (66.66)	57 (59.37)	χ^2 = 0.657, p >0.05
Primi	14 (33.34)	39 (40.62)	
APH			
Present	0 (0.0)	5 (5.20)	χ^2 = 2.28, p >0.05
Not present	42 (100.00)	91 (94.79)	
Obst. complications		29 (30.20)	
Present	9 (21.42)	67 (69.79)	χ^2 = 1.129, p >0.05
Not present	33 (78.57)	67 (69.79)	
Diabetes			
Present	4 (9.52)	95 (98.95)	χ^2 = 4.38, p <0.031
Not present	38 (90.48)	95 (98.95)	
Other comorbidity			
Present	18 (42.85)	73 (76.04)	χ^2 = 4.99, p <0.025
Not present	24 (57.14)	73 (76.04)	
Barotrauma			
Present	3 (7.14)	95 (98.5)	χ^2 = 3.864, p <0.049
Not present	39 (92.85)		

Cases – COVID-19-affected pregnant women who died in the hospital. Controls – COVID-19-affected pregnant women who survived during hospitalization

Table 2: Multivariate logistic regression: Risk factors associated with high mortality among pregnant women affected with COVID-19

Variable	*β coefficient*	*Standard error*	*Significance (p-value)*	*Odds ratio 95% CI: LL–UL*
Age 28 +	2.738	1.205	0.02	15.45, 1.45–16.87
Residence	2.535	0.592	0.000	12.61, 3.95–40.27
Diabetes	0.975	0.472	0.04	2.65, 1.05–6.68
Comorbidity	1.562	0.466	0.001	4.77, 1.91–11.89
Constant	–4.031	1.290	0.002	0.018

adjusted OR being 15.45 (95% CI: 1.45–16.87). The effect of age was independent of all other risk factors.

The COVID-affected pregnant women who resided in the rural areas were also at a significantly higher risk of dying of COVID-19 as compared with their urban counterparts. They were at 12-times higher risk of succumbing to COVID, the adjusted OR being 12.61 (3.95–40.27). The mortality risk associated with rural residence was independent of age, diabetes and other comorbidities, a grave indicator of inequity, and poor access to healthcare in the rural areas.

Almost 10% of pregnant women had diabetes as a comorbidity in the case group, while only 1% were diabetic in the control group. This difference was statistically significant (*p*-value <0.031). The risk of dying of COVID-19 due to diabetes was more than two-and-a-half times, and the effect was independent of all risk factors with an adjusted OR of 2.65 (95% CI: 1.05–6.68).

Other comorbidities like hypertension, hypothyroidism, anemia, etc. were present in 42.8% of patients in case group and in 23.9% patients in the control group, the difference being statistically significant (*p*-value <0.025). The presence of other comorbidities significantly increased the risk of dying about five times (adjusted OR (aOR) 4.77, 95% CI: 1.91–11.89). Seven percent of patients suffered from barotrauma because of mechanical ventilation in the case group, and only 1% in the control group. Barotrauma significantly increased the risk of dying (*p*-value = 0.049).

Discussion

Our study has shown that the pregnant women are highly vulnerable to COVID-19. They are at higher risk of mortality in the presence of diabetes, comorbidity, and barotrauma. The women with higher age were at greater risk of dying with COVID infection. According to some studies, advanced maternal age >35 years is associated with adverse outcomes in COVID-19-positive pregnant women in high-income socioeconomic countries. In our study, women >28 years of age had risk of mortality 15.45 times higher than the women in younger age group. Allotey et al.[9] concluded that the relative risk of mortality in COVID-positive pregnant women was much more in comparison with the nonpregnant women in terms of increased maternal age.

The rural areas of our country are underdeveloped. Higher incidence of low literacy levels, lack of knowledge of preventive measures, delay in seeking medical advice, poor socioeconomic status, etc., proclaims rural areas as a major risk factor for mortality. Nwafor et al.[10] conducted a study in a low-resource African setting and concluded that the adjusted odds ratio for rural residence as a risk factor for inadequate knowledge was 9.11 (aOR 9.11; 95% CI: 5.67–20.01, *p* <0.001). Our multivariate regression analysis manifested that the risk of the rate of mortality was 12.61 times higher in women belonging to the rural area than the women residing in the urban area.

India is one of the diabetic capitals of the world. Vouga et al.[11] conducted a study to assess risk factors of severity in COVID-19-positive women. The adjusted OR was 2.2 (aOR 2.2, 95% CI: 1.1–4.5), which is comparable to OR – 2.65 (OR – 2.65, 95% CI: 1.05–6.68). In our study, in terms of maternal diabetes, 9.5% of patients of case group succumbed to death pertaining to diabetes as a comorbidity. The exact pathophysiology of diabetes to cause severity of disease is not known. Two main theories are:

(1) Fuso et al.[12] postulated that in diabetic patients there is pulmonary dysfunction that adversely affects lung volume, pulmonary diffusion capacity, bronchomotor tone, and neuroadrenergic bronchial innervation, leading to poor outcomes in patients with COVID infection and diabetes.

(2) Hoffmann et al.[13] presumed that Coronavirus uses angiotensinogen-converting-enzyme 2 (ACE2) to bind and gain entry into infected cells, leading to overactivation of the renin–angiotensin system in diabetics.[14,15]

Pre-existing medical conditions make COVID-positive pregnant women more vulnerable to increased severity of the disease.[16–19]

Allotey et al.[9] conducted a study to conclude that the risk of increased severity was 1.81 times greater (aOR 1.81, 95% CI: 1.49–2.20) in COVID-positive pregnant women. Such increased risk leads to serious complications like intensive care unit admission, need of intubation, and maternal mortality. Similar results were obtained in multivariate regression analysis that showed 4.7-times higher chances of maternal death.

In our study, there is also association of barotrauma with increased mortality. Barotrauma develops as a result of the need of invasive mechanical ventilation in severe cases of COVID.

Conclusion

One of the systemic reviews suggested that the risk of maternal mortality, stillbirth, and neonatal death is in around 1% of pregnant women infected with COVID virus.[14]

All pregnant women, irrespective of the age, residential area, and living standards should be advised to seek medical advice as soon as possible to avoid complications. Increased maternal age, rural residence, illiteracy, diabetes, pre-existing maternal comorbidities, and barotrauma add up the burden of severity on COVID-19-positive pregnant women.

A thorough systemic protocol needs to be developed so as to encourage timely medical advice at even initial trimesters of pregnancy. Thorough antenatal checkup, wise investigation panel, and correct treatment regime will allow pregnant women to recover without the aid of intensive care or oxygenation.

Pregnancy being a high-risk state if contracts a severe form of disease has lower threshold for the requirement of ICU care, has higher needs for assisted ventilation, and has greater risk of maternal mortality.[15–19]

Orcid

Sapna Choudhary https://orcid.org/0000-0003-3698-2360

References

1. Wegmann TG, Lin H, Guilbert L, et al. Bidirectional cytokine interactions in the maternal fetal relationship: Is successful pregnancy a Th2 phenomenon. Immunol Today 1993;14(7):353–356. DOI: 10.1016/0167-5699(93)90235-D.
2. Jamieson DJ, Theiler RN, Rasmussen SA. Emerging infections and pregnancy. Emerg Infect Dis 2006;12(11):1638–1643. DOI: 10.3201/eid1211.060152.
3. Pazos M, Sperling RS, Moran TM, et al. The influence of pregnancy on systemic immunity. Immunol Res 2012;54(1–3):254–261. DOI: 10.1007/s12026-012-8303-9.
4. Forbes RL, Gibson PG, Murphy VE, et al. Impaired type I and III interferon response to rhinovirus infection during pregnancy and asthma. Thorax 2012;67(3):209–214. DOI: 10.1136/thoraxjnl-2011-200708.
5. Zambrano LD, Ellington S, Strid P, et al. Update: Characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status – United States, January 22-October 3, 2020. MMWR Morb Mortal Wkly Rep 2020;69(44):1641–1647. DOI: 10.15585/mmwr.mm6944e3.
6. Royal College of Obstetricians and Gynaecologists. Coronovirus (COVID-19) Infection in Pregnancy. Information for Healthcare Professionals. RCOG: London 2020;1(1):148–150.
7. Samji P, Manoj KR. Effect of COVID-19 on pregnancy and childbirth. Indian J Obstet Gynecol Res 2020;7(2):296–299. DOI: 10.18231/j.ijogr.2020.065.
8. Ministry of Health and Family Welfare. Clinical Management Protocol for COVID-19. Available from: https://www.mohfw.dated27062020.pdf. Accessed on: May 21, 2021.
9. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: Living systematic review and meta-analysis. BMJ 2020;370:m3320. DOI: 10.1136/bmj.m3320.
10. Nwafor JI, Joseph KA, Anozie BO, et al. Pregnant women's knowledge and practice of preventive measures against COVID-19 in a low-resource African setting. Int J Obstet Gynecol 2020:1–3. DOI: 10.1002/ijgo.13186.
11. Vouga M, Favre G, Martinez-Perez O, et al. Maternal outcomes and risk factors for COVID-19 severity among pregnant women. Sci Rep 2021;11(1):13898. DOI: 10.1038/s41598-021-92357-y.
12. Fuso L, Pitocco D, Antonelli-Incalzi R. Diabetic lung, an underrated complication from restrictive functional pattern to pulmonary hypertension. Diabetes Metab Res Rev 2019;35(6):e3159. DOI: 10.1002/dmrr.3159.
13. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 2020;181(2):271–280.e8. DOI: 10.1016/j.cell.2020.02.052.
14. Papapanou M, Papaioannou M, Petta A, et al. Maternal and neonatal characteristics and outcomes of COVID-19 in pregnancy: An overview of systematic reviews. Int J Environ Res Public Health 2021;18(2):596. DOI: 10.3390/ijerph18020596.
15. Nakamura-Pereira M, Betina Andreucci C, de Oliveira Menezes M, et al. Worldwide maternal deaths due to COVID-19: A brief review. Int J Gynaecol Obstet 2020;151(1):148–150. DOI: 10.1002/ijgo.13328.
16. Agarwal N, Garg R, Singh S, et al. Coronavirus disease 2019 in pregnancy: Maternal and perinatal outcome. J Educ Health Promot 2021:10(1)194. DOI: 10.4103/jehp.jehp_954_20.
17. Malhotra J, Agarwal P, Garg R, et al. Corona virus disease (COVID-19) and pregnancy: What obstetrician should know. JSAFOG 2019;11(6):337–339. DOI: 10.5005/jp-journals-10006-1744.
18. Malhotra N, Garg R, Singh S, et al. Pregnancy management in coronavirus disease – Challenges in developing countries. J Reprod Healthcare Med 2021;2:18. DOI: 10.25259/JRHM_58_2020.
19. Malhotra N, Malhotra N, Garg R. COVID and women's health in India. J Indian Med Assoc 2022;119(3).