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Maternal and fetal outcomes of COVID-19 infection in pregnant women with chronic rheumatic heart disease in a South Asian population: A case series

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Abstract

Rheumatic heart disease (RHD) is associated with an increased risk of adverse maternal, fetal, and neonatal outcomes, particularly in developing countries. The current COVID-19 pandemic has also affected pregnant women, probably increasing the adverse effects. It is speculated that COVID-19 infection in pregnant women would further increase the risk of complications. However, factual data is still lacking, especially from resource-constrained countries. We conducted a case series of 20 pregnant women with RHD and COVID-19 infection and compared their outcomes with 40 with RHD but without COVDI-19. We observed a high risk of adverse cardiac and pregnancy effects across the whole cohort of 60 patients. However, the comparative study between the two groups failed to show any incremental risk of complications due to COVID-19 infection. Although the sample size was limited; the results are encouraging, particularly for developing countries.

Key words: cardiovascular disease, developing country, pregnancy outcomes, SARS-CoV-2 infection, valvular heart disease.

Introduction

Rheumatic heart disease (RHD) continues to be a significant cause of maternal morbidity and mortality, especially in the low- and middle-income countries (LMICs).[1,2] Pregnant women with RHD have adverse fetal outcomes, including preterm birth, low birth weight (LBW), intrauterine growth retardation (IUGR), and perinatal death.[3] The poor outcomes may be particularly pronounced in the LMICs due to inadequate healthcare facilities, delayed access, poor education level, and suboptimal antenatal visits, among other factors. However, large prospective data on pregnancy outcomes in LMICs, including India, are lacking.

The coronavirus disease 2019 (COVID-19) pandemic presents a significant challenge for these patients, who are likely to encounter interruptions in secondary prophylaxis, access to care, and adequate antenatal visits. Moreover, the ongoing COVID-19 pandemic itself is believed to cause a higher risk of adverse pregnancy outcomes.[4,5] Unfortunately, most data on the impact of COVID-19 infection on pregnancy is restricted to high-income countries (HICs). This is concerning because pregnant women from LMICs are supposed to be at higher risk of maternal and neonatal complications from COVID-19 infection.[5–7]

Consequently, pregnant women with RHD and COVID-19 infection in LMICs may pose an augmented risk of maternal and fetal adverse events. At the onset of the pandemic, World Heart Federation (WHF) recognized RHD as a risk factor for severe COVID-19 disease in low-income countries.[8] However, data to support this speculation is still entirely lacking. Thus, the objective of this study was to

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delineate the impact of COVID-19 infection in pregnant women with RHD in a resource-poor setting.

Case Report

This case series was conducted at a COVID-19 referral center in Northern India between May 2020 and July 2021. Twenty pregnant women admitted for delivery with RHD and COVID-19 infection were included in the study. Their pregnancy outcomes were compared with 40 age-matched pregnant women with RHD and without COVID-19 infection during the same period. The study was approved by the Institutional Ethics Committee (ECR/526/Inst/UP/2014/RR-20). Written informed consent was obtained from all the participants. The diagnosis of RHD was confirmed in all cases by 2D echocardiography and the COVID-19 infection by RT-PCR (reverse transcriptase-polymerase chain reaction). Adverse cardiac events were defined as cardiac complications, including cardiac death, heart failure, cerebrovascular accident, infective endocarditis, or new-onset atrial fibrillation. Fetal and neonatal adverse events were defined as preterm delivery, premature rupture of membranes, small for gestational age, respiratory distress syndrome, stillbirth, or neonatal death. The independent means were compared by unpaired Student *t*-test and proportions by the chi-square test. All tests were two-sided, and a statistically significant difference was considered at p-value <0.05.

The clinical characteristics of the participants are shown in Table 1, and the outcomes of pregnancy are described in Table 2. The mean gestational age of pregnant women with RHD in the COVID-19 positive group was 36.3 ± 2.1 and 34.8 ± 3.7 weeks in the COVID-19 negative group ($p = 0.09$). Both the groups were comparable in terms of comorbidities, including hypertension, diabetes mellitus, and hypothyroidism, except lower hemoglobin in the COVID-19 negative group (9.4 ± 2.7 vs. 10.9 ± 1.3 g/dL, $p = 0.02$). Mitral valve was most commonly affected, and there was no significant difference between the two groups in the pattern and severity of valvular involvement. The obstetric outcomes were similar in the COVID-19 positive and negative groups including premature rupture of membrane (5% vs. 10%, $p = 0.51$), preterm birth (50% versus 67.5, $p = 0.19$), and stillbirth (10% vs. 15%, $p = 0.59$). The mean birth weight in the COVID-19 positive group was 2357.8 ± 449.9 g versus 2377.9 ± 687.8 in the COVID-19

TABLE 1 Clinical characteristics of women with rheumatic heart disease at delivery admission

Demographic	COVID positive ($n = 20$)	COVID negative ($n = 40$)	p-value
Age (years)	25.5 ± 3.2	26.5 ± 4.6	0.36
Parity	2.1 ± 0.9	1.9 ± 0.8	0.43
Primigravida	6 (30)	13 (32.5)	0.84
Gestational age (weeks)	36.3 ± 2.1	34.8 ± 3.7	0.09
Hemoglobin (gm/dL)	10.9 ± 1.3	9.4 ± 2.7	0.02
Hypertension	2 (10)	5 (12.5)	0.78
Diabetes mellitus	1 (5)	3 (7.5)	0.71
Hypothyroidism	3 (15)	4 (10)	0.57
NYHA functional class III/IV	4 (20)	11 (27.5)	0.53
Prosthetic heart valve	2 (10)	3 (7.5)	0.74
Mitral stenosis	16 (80)	27 (67.5)	0.31
Severe[a]	10 (50)	19 (47.5)	0.86
Mitral regurgitation	17 (85)	31 (77.5)	0.49
Severe[a]	9 (45)	12 (30)	0.25
Aortic stenosis	1 (5)	4 (10)	0.51
Severe[a]	0	1 (2.5)	0.48
Aortic regurgitation	7 (35)	18 (45)	0.46
Severe[a]	3 (15)	7 (17.5)	0.81
Tricuspid regurgitation	10 (50)	22 (55)	0.71
Severe[a]	3 (15)	9 (22.5)	0.49
Pulmonary hypertension	5 (25)	9 (22.5)	0.83
Severe[a]	1 (5)	6 (15)	0.26
Modified WHO risk score III/IV	10 (50)	23 (57.5)	0.58

Note: Data presented as numbers (percentages) or mean ± SD unless otherwise specified.; Abbreviations: NYHA, New York Heart Association; WHO, World Health Organization. and [a]The severity of valvular lesions were defined according to the 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines.

TABLE 2 Outcomes of pregnant women with rheumatic heart disease

Outcomes	COVID positive ($n = 20$)	COVID negative ($n = 40$)	p-value
Obstetric outcomes			
Gestational diabetes mellitus	0	2 (5)	0.31
Preeclampsia/eclampsia	2 (10)	5 (12.5)	0.78
APH (antepartum hemorrhage)	1 (5)	0	0.15
PPH (postpartum hemorrhage)	2 (10)	3 (7.5)	0.74
HELLP	0	1 (2.5)	0.48
Oligohydramnios	2 (10)	3 (7.5)	0.74
Premature rupture of membrane	1 (5)	4 (10)	0.51
Caesarean delivery	13 (65)	19 (47.5)	0.20
Preterm birth	10 (50)	27 (67.5)	0.19
Stillbirth	2 (10)	6 (15)	0.59
Fetal and neonatal outcomes	$n = 18$	$n = 34$	
Birthweight (gm)	2357.8 ± 449.9	2377.9 ± 687.8	0.90
Low birth weight (<2.5 kg)	8 (44.4)	18 (52.9)	0.56
Very low birth weight (<1.5 kg)	2 (11.2)	5 (14.7)	0.72
Small for gestational age	6 (33.3)	10 (29.4)	0.77
Apgar score <7 at 5-min	2 (11.1)	4 (11.8)	0.94
Respiratory distress syndrome	2 (11.1)	3 (8.8)	0.79
ICU admission	4 (22.2)	7 (20.6)	0.89
Neonatal death	0	1 (2.9)	0.47
Adverse cardiac events	3 (15)	11 (27.5)	0.28
Fetal and neonatal adverse events	13 (65)	33 (82.5)	0.13

Note: Data presented as numbers (percentages) or mean ± SD unless otherwise specified. and Abbreviations: HELLP, hemolysis, elevated liver enzymes, low platelet count; ICU, intensive care unit.

negative group ($p = 0.9$). Moreover, both the groups had statistically similar fetal and neonatal outcomes. The adverse cardiac events were seen in 15% of the COVID-19 and 27% in the COVID-19 negative group ($p = 0.28$). The adverse fetal and neonatal events occurred in 65% of the COVID-19 positive and 82.5% of the COVID-19 negative group ($p = 0.13$).

Discussion

To our knowledge, this is the largest case series on the effect of COVID-19 infection in pregnant women with RHD. Our study showed a high incidence of adverse maternal and fetal outcomes in pregnant women with RHD. The overall incidence of adverse cardiac events among 60 patients in this study was 23.3%. This is comparable to an incidence of 15%–40% reported in earlier studies from India.[9,10] This is concerning because India is among the most developing countries with RHD prevalence in women of childbearing age.[1]

The ongoing COVID-19 pandemic has hit maternal and fetal health, particularly in resource-constrained countries. Pregnant women are considered at risk for COVID-19-related complications due to alterations in cell-mediated immunity and cardiopulmonary function.[10] Accruing evidence also suggests an increased risk of adverse maternal and fetal outcomes due to SARS-CoV-2 infection.[4,11] We thus hypothesized that COVID-19 infection in pregnant women with RHD would further increase the negative consequences. However, our study did not find an incremental risk of adverse pregnancy outcomes in women with RHD. The maternal obstetric, fetal, and neonatal outcomes and the adverse cardiac events were statistically similar between the groups with or without COVID-19 infection. Unfortunately, clinical data related to this issue is very limited/lacking. However, in a small case series of three patients of RHD and COVID-19, only one woman had preterm birth but with a good neonatal outcome.[12]

Despite being limited by a small sample size, the results of our study seem to be quite encouraging. However, following a COVID appropriate behavior is still advisable. Furthermore, early detection, close antenatal follow-up, and secondary prevention of RHD are highly recommended in developing countries.

Disclosure

None declared.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. Watkins DA, Johnson CO, Colquhoun SM, Karthikeyan G, Beaton A, Bukhman G, et al. Global, regional, and national burden of rheumatic heart disease, 1990-2015. *N Engl J Med*. 2017;**377**(8):713–22. doi:10.1056/NEJMoa1603693 PMID: 28834488.
2. van Hagen IM, Thorne SA, Taha N, Youssef G, Elnagar A, Gabriel H, et al. ROPAC investigators and EORP team. Pregnancy outcomes in women with rheumatic mitral valve disease: results from the registry of pregnancy and cardiac disease. *Circulation*. 2018;**137**(8):806–16. doi:10.1161/CIRCULATIONAHA.117.032561
3. Liaw J, Walker B, Hall L, Gorton S, White AV, Heal C. Rheumatic heart disease in pregnancy and neonatal outcomes: a systematic review and meta-analysis. *PLoS One*. 2021 Jun 29;**16**(6):e0253581. https://doi.org/10.1371/journal.pone.0253581
4. Wei SQ, Bilodeau-Bertrand M, Liu S, Auger N. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. *CMAJ*. 2021;**193**(16):E540–8. https://doi.org/10.1503/cmaj.202604
5. Gajbhiye RK, Sawant MS, Kuppusamy P, Surve S, Pasi A, Prusty RK, et al. Differential impact of COVID-19 in pregnant women from high-income countries and low- to middle-income countries: a systematic review and meta-analysis. *Int J Gynaecol Obstet*. 2021 Oct;**155**(1):48–56. https://doi.org/10.1002/ijgo.13793
6. Hopman J, Allegranzi B, Mehtar S. Managing COVID-19 in low- and middle-income countries. *JAMA*. 2020;**323**(16):1549–50. https://doi.org/10.1001/jama.2020.4169
7. Chmielewska B, Barratt I, Townsend R, Kalafat E, van der Meulen J, Gurol-Urganci I, et al. Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis. *Lancet Glob Health*. 2021;**9**(6):e759–72. https://doi.org/10.1016/S2214-109X(21)00079-6.
8. Thienemann F, Pinto F, Grobbee DE, Boehm M, Bazargani N, Ge J, et al. World heart federation briefing on prevention: coronavirus disease 2019 (COVID-19) in low-income countries. *Glob Heart*. 2020 Apr 9;**15**(1):31. https://doi.org/10.5334/gh.778
9. Baghel J, Keepanasseril A, Pillai AA, Mondal N, Jeganathan Y, Kundra P. Prediction of adverse cardiac events in pregnant women with valvular rheumatic heart disease. *Heart*. 2020;**106**(18):1400–6. https://doi.org/10.1136/heartjnl-2020-316648
10. Khanna R, Chandra D, Yadav S, Sahu A, Singh N, Kumar S, et al. Maternal and fetal outcomes in pregnant females with rheumatic heart disease. *Indian Heart J*. 2021;**73**(2):185–9. https://doi.org/10.1016/j.ihj.2021.01.012
11. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the INTERCOVID multinational cohort study. *JAMA Pediatr*. 2021;**175**(8):817–26. https://doi.org/10.1001/jamapediatrics.2021.1050
12. Tilve A, Mahajan NN, Pandey A, Jnanananda B, Gadekar S, Mahale SD, et al. Impact of COVID-19 on pregnant women with rheumatic heart disease or Peripartum cardiomyopathy. *Eur J Obstet Gynecol Reprod Biol*. 2021 Mar;**258**:459–61. https://doi.org/10.1016/j.ejogrb.2021.01.024