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Impact of COVID-19 on pregnant women with Rheumatic heart disease or Peripartum cardiomyopathy

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Title: Impact of COVID-19 on pregnant women with Rheumatic heart disease or Peripartum cardiomyopathy

Title: Heart Disease with COVID-19

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Highlights

- Countries with endemic RHD should make provision of cardiac assessment to improve RHD diagnosis and strengthen system.
- Significant challenges faced by these women with Heart Diseases during COVID-19 pandemic,
- Difficulties in secondary prophylaxis and access to health care leading to additional risk for adverse pregnancy and neonatal outcomes.
- Holistic approach is needed to medically complicated pregnancies with COVID-19 and multidisciplinary coordination resulted in excellent maternal outcomes despite the trying conditions of the early stages of the pandemic.

Keywords: Rheumatic Heart disease; Cardiomyopathy; COVID-19; Peripartum period; SARS-CoV-2 infection.

Dear Editor,

We observed that, little is still known about the impact of the SARS-CoV-2 infection on pregnant women with heart disease (HD). Aim of our study was to investigate the impact of COVID-19 on pregnancy and neonate retrospectively at BYL Nair Charitable Hospital (NH), a dedicated COVID-19 hospital [1] in women with HD in Mumbai, India. In the initial phase of COVID-19 pandemic of 6 months, NH received five RT-PCR confirmed COVID-19 pregnant women with heart disease [Rheumatic HD (RHD; n=3), Peripartum Cardiomyopathy (PPCM; n=2)], out of 879 COVID-19 pregnant and post-partum women (Table 1). To address if COVID-19 poses additional risk in pregnancy with HD, we compared outcomes in uninfected pregnant women with HD (n=43) in pre-pandemic period from the same center (Table S1). We found around 1% of heart disease in pregnant women with COVID-19. Adverse

outcomes such as preterm delivery, PPRM, low birth weight, neonatal death were observed in pregnant women with HD (RHD/PPCM) and COVID-19. Pre-term delivery was nearly three times higher in women with HD and COVID-19 (95% CI 0.33-20.48). PPRM/PROM was observed 14 times higher in women with HD and SARS-CoV-2 infection (95% CI 0.69-283.79). Preterm vaginal delivery was reported in one woman with RHD and COVID-19 (Case-2) and her new-born required neonatal intensive care due to low birth weight.

Pregnant woman with RHD and COVID-19 presented with fever, cough with expectoration, breathlessness, tachycardia with normal oxygen saturation. This suggests some diagnostic overlap between SARS-CoV-2 infection and new or recurrent acute respiratory failure with HD.[2] Two women with RHD were on secondary prophylaxis with penicillin in our study group. During the period of lockdown when there were transportation restrictions, the pregnant women with RHD faced several challenges in accessing the healthcare. Therefore, secondary prophylaxis must be ensured to all patients with RHD and more specifically to pregnant women by the public and private healthcare providers. Pregnancy is a state that is particularly susceptible to respiratory diseases like COVID-19 due to a compensated respiratory alkalosis with metabolic acidosis.[3] Despite this, both the cases with PPCM described in this report did not have worsening of PPCM due to COVID -19.

We faced multiple challenges because of COVID-19 status and comorbidities of the women presented in this report. During the early phase of pandemic, there was a delay in receiving appropriate treatment as all these women were denied treatment in multiple hospitals before being referred to our dedicated COVID-19 facility at NH. This observation suggested the significant challenges faced by these women, who are also likely to face difficulties in secondary prophylaxis and access to health care leading to additional risk for adverse pregnancy and neonatal outcomes.

One woman with PPCM (Case-5) had multiple congenital anomalies at 21-weeks pregnancy but was denied medical termination of pregnancy (MTP) in multiple hospitals. MTP Act in India permits the termination until 20-weeks. For a woman with less than average means and education there still exists considerable difficulty to get the adequate and appropriate medical assistance so as to terminate a grossly anomalous pregnancy. This lacuna in the health care system (time sensitive abortion services) resulted in the emotional trauma of not only carrying the pregnancy to term but which was later complicated by the development of PPCM and getting infected with SARS-CoV-2.

In the context of the COVID-19 pandemic, our study generated an evidence of impact of COVID-19 on pregnant women with RHD with COVID-19. Therefore, countries with endemic RHD with higher COVID-19 burden should make provision of cardiac assessment on ultrasound to improve RHD diagnosis and strengthen the healthcare system for multi-speciality management of pregnant women with RHD and COVID-19.

Declaration of Competing Interest

The authors have no conflicts of interest relevant to this article.

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Author Contributions:

NM and RG had full access to all data and take responsibility for data integrity and the accuracy of the analysis. NM and RG were responsible for study concept and design. NM, RG, SM supervised the study. AT, BJ, NK and SG acquired the data. All authors interpreted the data. RG and NM performed statistical analysis. NM, SM, and RG provided administrative, technical and material support. NM and AT drafted the manuscript. RG, NM and DM revised the manuscript. All authors approved the manuscript.

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Table 1: Demographic, epidemiological, clinical characteristics and management of pregnant women with RHD or PPCM and COVID-19

Parameters	RHD1	RHD2	RHD3	PPCM1	PPCM2
Heart Disease history	RHD since childhood	RHD diagnosed during first pregnancy	RHD since childhood	PPCM	PPCM
No. of referrals before reaching NH	2	1	2	4	5
Demographic					
Age in years	27	31	26	26	21
Gravida (G) /Parity (P)	Primigravida	G3P2L2	G4P2L2	G3P2L2	Primigravida
BMI kg/m²	22.6	23.1	Not available	34.5	23
Containment/Sealed zone	No	Yes	No	No	Yes
Indication for COVID-19 RT-PCR testing	Symptomatic	Universal Testing	Universal Testing	Symptomatic	Universal Testing
Clinical					
Asymptomatic/Symptomatic (Mild/Moderate/Severe)	Symptomatic Mild cough with expectoration and breathlessness ^b	Asymptomatic	Asymptomatic	Symptomatic Mild (palpitations and dyspnoea)	Asymptomatic
Fever	No	No	No	No	No
Cough	Yes	No	No	Yes	No
Breathing Difficulty	Yes	No	No	Yes	No
Investigations					
Hemoglobin, g/dL (Reference range - >11.0)	12.1	11.1	9.9	12	10.6
White blood cell count, /μL (Reference range - 3500-9500)	7300	6700	9800	10900	6000
Platelet count, $\times 10^3/\mu$L (Reference range - 125-350)	1.21	1.20	1.3	3.09	4.11
Serum Creatinine, mg/dL (Reference range - 0.84 to 1.21)	2.3	1.0	0.9	0.4	0.9
Echocardiogram	Moderate MS, moderate MR, mild TR, dilated LA with mildly dilated LV, Moderate PAH, MVOA 1.3cm ² LVEF-65%	Severe MS, moderate MR, trivial AR Severe TR	Moderate MS severe PAH LVEF 60%	Dilated LV, severe generalised LV hypokinesia, LVEF 20%, LV diastolic dysfunction, LV non-compaction, Mild MR, Mild PAH, Mild TR, RVSP 48mmhg	Global LV Hypokinesia, LVEF of 30-35%, LV non-compaction, Mild MR, Moderately Compromised LV Systolic Function
Blood Pressure in mmHg	100/70	110/70	100/70	130/80	110/70
Oxygen Saturation %	95	99	98	96	99
Chest X-ray changes	Yes	Not done	Not done	Normal	Not done
Consolidation	Yes	No	No	No	No
ARDS	No	No	No	No	No
Arterial blood gas analysis	Normal	Normal	Normal	Normal	Normal
Relevant Ultrasound	Ultrasound - bilateral bright kidney.	-	-	-	Level-II ultrasound at 21 weeks - severe oligohydramnios, bilateral hydro-nephrosis, hydro-ureter,

					key-hole bladder, posterior urethral valves..
Weeks of Gestation at delivery	39 weeks	36 weeks	37 weeks at admission	36weeks 5days	38weeks 1day
Mode of delivery	Vaginal Delivery	Vaginal Delivery	Undelivered	Cesarean section	Vaginal Delivery ^a
PROM/PPROM	No	No	-	Yes	No
Preterm labour	No	Yes	-	Yes	No
Neonatal Outcome	Good	NICU admission, Baby survived	-	Good	Multiple congenital anomalies, poor APGAR, NICU admission, NND
Birth Weight in Kg	2.470	1.790	-	2.240	2.229
Complications intrapartum & postpartum	No	No	-	No	No
Treatment	frusemide, laciactone (with-held) and metoprolol	spironolactone, frusemide, metoprolol, penicillin	atenolol, frusemide, penicillin	frusemide, bisoprolol, isosorbide dinitrate, digoxin	carvedilol, ramipril
Hospital Stay	14	17	4	13	5
Mortality	No	No	No	No	No

^a presented in the labour suite with a fully dilated cervix and delivered vaginally immediately on arrival, on the stretcher; ^b increased in intensity since 5 days but she had similar complaints since long before pregnancy

SARS-CoV-2, Severe Acute Respiratory Syndrome Corona virus 2; RT-PCR, Reverse Transcriptase Polymerase Chain Reaction; COVID-19, coronavirus disease 2019; PROM, premature rupture of membranes ; PPRM, preterm premature rupture of membranes; NICU , neonatal intensive care unit; NND, neonatal death; RHD, rheumatic heart disease ; PPCM, peripartum cardiomyopathy; MS, mitral stenosis; MR, mitral regurgitation; TR, tricuspid regurgitation; LA- Left Atrium, LV-Left ventricular; PAH, pulmonary artery hypertension; MVOA, Mitral Valve Orifice Area; LVEF, left ventricle ejection fraction; AR, aortic regurgitation; RVSP, right ventricular systolic pressure; ARDS, Acute Respiratory Distress Syndrome.