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Clinical presentations, pregnancy complications, and maternal outcomes in pregnant women with COVID-19 and tuberculosis: A retrospective cohort study

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To date, a large number of pregnant women have been infected with Severe Acute Respiratory Syndrome Corona virus 2 (SARS-CoV-2) and these patients are at higher risk of developing certain pregnancy complications. Out of 10 million people infected globally with tuberculosis (TB), a quarter of the disease burden is contributed by India. Pregnant and postpartum women are at increased risk of developing TB, and this is associated with poor outcomes including premature birth, intrauterine growth retardation, and an increase in maternal mortality.

Tuberculosis and coronavirus disease 19 (COVID-19) primarily involve the lungs, share common risk factors, and present with similar symptoms. Increased susceptibility to SARS-CoV-2 infection has been observed in individuals with latent or active TB.³ However, at present there is a lack of information on TB with concurrent COVID-19 in pregnant woman. The present study aims to assess the clinical presentations and maternal outcomes in pregnant and/or postpartum women with active pulmonary TB (PTB) and/or previous TB with concurrent COVID-19.

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Conflicts of Interest

The authors have no conflicts of interest.

Author Contributions

RG and NM were responsible for the study concept and design. SB, GP, NK, and AB contributed to the acquisition of data. All authors contributed to analysis and/or interpretation of data. RG, NM, and NK were responsible for the drafting of the manuscript. RG, NM, SM, DM contributed to critical revision of the manuscript for important intellectual content. RG, NM, and AB were responsible for statistical analysis. SM, RG, and NM were responsible for administrative and technical or material support.

Trial Registration

PregCovid study is registered with Clinical Trial Registry of India (Registration no: CTRI/2020/05/025423).

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A total of 879 pregnant and/or postpartum women with COVID-19 were admitted to BYL Nair Hospital⁴ from April to September, 2020. Six pregnant women were diagnosed with concurrent PTB and COVID-19. Eleven pregnant women and one postpartum woman had previous history of TB, which was subsequently cured. Ethical approval for the present study was granted by the Institutional Ethics Committee of BYL Nair Hospital (ECARP/ 2020/63 dated May 27, 2020) and ICMR-NIRRH (D/ICEC/Sci-53/55/2020 dated June 4, 2020). A waiver of consent was granted as the study involved retrospective data collection from medical case records.

The study demonstrates the adverse impact of TB and COVID-19 in pregnant women. Of the six women with PTB, three were recently diagnosed with PTB and were on a course of anti-tubercular treatment, while the other three patients were serendipitously diagnosed with TB while being investigated for COVID-19-related symptoms (Table 1). Since TB has an insidious onset, it is likely that TB already existed in these patients and SARS-CoV-2 infection subsequently aggravated the condition, thus leading to a severe presentation. The diagnosis of TB could have otherwise been delayed if these women had not been evaluated for COVID-19. Oxygen saturation at the time of admission in patients with active PTB and COVID-19 was comparatively lower than patients with previous TB and COVID-19 (p =0.04). The clinical presentation was mild in women with past TB and COVID-19. Of the six women with PTB, there was one case of maternal mortality and one spontaneous abortion (early fetal demise at 11 weeks of gestation) observed. Additionally, 4 (67%) patients with PTB and SARS-CoV-2 co-infection were symptomatic, whereas only 2 (17%) patients with past TB and COVID-19 were symptomatic. Two women with active PTB and COVID-19 developed ARDS and required ICU admission (Table S1). One woman with extensively drug-resistant TB, who underwent treatment therapy for 4 months, developed severe complications including ARDS, preeclampsia, and fetal growth restric-tion, and she died 18 days after COVID-19 diagnosis. These results suggest that the combination of PTB and SARS-CoV-2 infection would possibly result in severe presentation with adverse outcomes in pregnant women.

In India, Bacillus Calmette-Guérin (BCG) vaccination is part of the country's Universal Immunization Programme, with BCG vaccinations being administered at birth. Although controversial, the BCG vaccine has been proposed as a potential method for protection against SARS-CoV-2. However, our series, similar to other epidemiological studies, ^{5,6} does not support this notion as all 18 patients in our study had either active TB or past exposure to TB in spite of receiving the BCG vaccine at birth and were infected with SARS-CoV-2. Coinfections are likely to be a greater challenge in low- and middle-income countries with a high burden of both diseases. A 26% decline in reported cases of TB within the national surveillance system was reported due to the COVID-19 pandemic, which has adversely affected the National Tuberculosis Elimination Program in India.2 The present study highlights the opportunities for integration of healthcare services for the treatment of TB and COVID-19. Therefore, based on the results of our study, we recommend that pregnant women with respiratory symptoms should be tested for both COVID-19 and TB in countries with a high burden of TB. Additionally, this represents an opportunity to engage the infrastructure and trained manpower of the TB Program for the control of COVID-19, and vice versa.

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Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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$\label{table Table 1} \mbox{ Table 1}$ Details of six pregnant women with COVID-19 and active PTB

Treatment given	Antibiotics, HCQ	Antibiotics, corticosteroids	Antibiotics	Antibiotics, low molecular weight heparin, labetalol	Antibiotics
Oxygen	Š.	HFNO	°Z	Mechanical ventilation	°N
ARDS	N _o	Yes	o N	Yes	Š.
Lowest oxygen saturation	94%	%08	%86	% 09	%86
Pregnancy outcomes	Ongoing pregnancy	Early fetal demise at 11 weeks of gestation	Ongoing pregnancy	Maternal death, pre-eclampsia FGR and oligohydramnios	Oligohydramnios, emergency LSCS, surgical site infection,
Duration of ATT	Newly started	Newly started	Newly started on AKT-4 for MDR TB	Started on ATT for XDR TB four months prior to COVID-19 infection	ATT for 4 months
Auscultation results	Left-sided crepitation	Bilateral	Normal	Bilateral	Normal
HRCT	QN	Bilateral consolidation with cavitation. Features atypical of COVID-19 pneumonia. More likely superaded infection	Q.	QX	Q.
CXR changes/USG findings	CXR: left lower lobe consolidation USG: mild right-sided pleural effusion	Bilateral heterogeneous opacities	Patchy shadows and pleural effusion. Inhomogeneous shadows and fibro-calcific densities s/o old infective etiology	Patchy opacities in both lungs. Consolidation. Bilateral Bilateral So old infective etiology. Widening of upper mediastimm (enlarged lymph nodes)	Normal
Clinical presentation	Fever, cough	Breathing difficulties	Fever, cough	Cough, breathing difficulties	Asymptomatic
Gestational age (week)	=	=	26	33	38
Gravidity/ parity	G3P1	G4P2	15	G4P3	G1
Age (years)	26	28	29	46	24
Case no.	-i	%	લ ં	4	rç.

Treatment given		Antibiotics
Oxygen		N _o
ARDS		o N
Lowest oxygen saturation		%66
Pregnancy outcomes	prolonged hospital stay	Vaginal delivery at term, induction of labor
Duration of ATT		ATT for 5 months
Auscultation results		Normal
HRCT		NO
CXR changes/USG findings		Normal
Clinical presentation		Asymptomatic
Gestational Clinical age (week) presenta		39
Gravidity/ parity		G4P2
Case Age no. (years)		24
Case no.		.9

hydroxychloroquine; HFNO, high frequency nasal oxygen; HRCT, high-resolution computed tomography; LSCS, lower segment cesarean section; MDR, multi-drug-resistant; MTB, mycobacterium TB; ND, not done; P, Parity; PTB, pulmonary tuberculosis; SARS-CoV-2, Severe Acute Respiratory Syndrome Corona virus 2; S/O, suggestive of; TB, Tuberculosis; USG, ultrasonography; XDR, extensively drug-resistant.