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Co-infection of malaria and dengue in pregnant women with SARS-CoV-2

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Keywords

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Many low- and middle-income countries (LMICs) experience high rates of malaria and other neglected tropical diseases (NTDs), such as dengue.[1] The COVID-19 pandemic complicates these matters further as COVID-19 in pregnant women is associated with an increased risk of preterm birth, and in some LMICs it is associated with a higher risk of maternal death.[2] Furthermore, the clinical presentations of malaria and dengue strongly overlap with that of COVID-19, therefore posing an additional challenge for differential diagnosis. The PregCovid registry (https://pregcovid.com), registered with Clinical Trials Registry India (no. CTRI/2020/05/025423), is currently accumulating data from various regions in Maharashtra, India. The present study reports the clinical presentations, management, and outcomes of three pregnant women with COVID-19 who also had co-infections of malaria, and one with dengue, admitted to BYL Nair Hospital in Mumbai, India.[3] Baseline characteristics, clinical presentation, hematological parameters, and subsequent management are shown in Tables 1 and 2. The study was approved by the Ethics Committees of TNMC (No. ECARP/2020/63) and ICMR-NIRRH (IEC no. D/ICEC/Sci-53/55/2020). Informed consent was waived for this study.

The results of this study raise concerns pertaining to the health of pregnant women with co-infections of malaria and dengue in endemic regions. Our observations reveal that pregnant

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Author Contributions

RG and NM were responsible for the study concept and design. SK, SS, AN and NM contributed to the acquisition of the study data. RG, NM, SK and DM were responsible for the drafting of the manuscript. Critical revision of the manuscript for important intellectual content was performed by RG, NM and DM. NM and RG contributed to statistical analysis. BG, NM and SM provided administrative and technical or material support. All authors contributed to the analysis and interpretation of the data, and reviewed and approved of the final version of the manuscript.

Conflicts of Interest

The authors have no conflicts of interest.

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women with suspected COVID-19 infection can present with the same clinical symptoms associated with dengue or malaria. However, in cases of co-infection, the symptoms do not aggravate or present differently. This is clinically challenging because laboratory results take time to acquire; therefore, management is highly dependent on the presenting symptoms. With the availability of universal screening for SARS-CoV-2 in pregnant women nearing delivery, cases of asymptomatic pregnant patients with COVID-19 are being reported increasingly in our hospital. Some of these women may remain asymptomatic throughout their pregnancy, while others might show mild to moderate symptoms at some point of their pregnancy. The present case series shows that patients with mild to moderate symptoms of COVID-19 are problematic because co-infections can be misdiagnosed easily as late-onset COVID-19 presentation, whereas they may be presentations of dengue or malaria, which require a completely different clinical management protocol to that of COVID-19. Misdiagnosis could have life-threatening consequences for the patient and their fetus. Indeed, one of the patients who had both SARS-CoV-2 and malaria experienced fetal demise and had to undergo abortion (Patient 2). If malaria had been diagnosed earlier, the pregnancy might have been saved. In the other three cases, the co-infections were not life-threatening and had no major complications. This could be attributed to the fact that the patients presented in a timely manner and were under constant observation. Although COVID-19 is generally regarded as having little to no impact on pregnancy outcomes, the present study points towards the need to evaluate outcomes in the first, second, and third trimester of pregnancy.

Currently, healthcare systems are overburdened by the management of COVID-19, especially in low-resource settings. The strain on healthcare systems is further exacerbated when infections such as malaria or dengue occur concurrently with SARS-CoV-2 infection. Because COVID-19 is continuing to spread to the tribal and rural parts of India, the management and diagnosis of co-infections is of high clinical importance.

We recommend that physicians and obstetricians be vigilant in order to enable early identification of co-infections such as malaria and dengue with COVID-19. All symptomatic COVID-19 cases with fever should be investigated for other common infections in endemic regions, both in the general population and in pregnant women, to avoid complications. Healthcare centers should have appropriate and ample provisions of medicine and equipment to manage cases of co-infection. Referral links should also be established with neighboring tertiary hospitals that treat pregnant women with COVID-19.

Currently, there is no definitive treatment for COVID-19 and many clinical trials are ongoing using old and new treatment regimens. Further prospective studies are required to address the burden of co-infection in pregnancies complicated by COVID-19 and to determine the prognosis and outcomes of such cases in LMICs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Socio-demographic, clinical characteristics, and treatment of pregnant women with COVID-19 and dengue/malaria.

Parameters	Patient 1	Patient 2	Patient 3	Patient 4[a]
Age, years	22	32	27	25
Socio-economic status	Low	Low	Low	Low
Gravida (G)/parity (P)/ living children (L)	Primigravida	G4P3L2	G2P1L1	G2P1L1
Gestational age	37 weeks 6 days	24 weeks 3 days	40 weeks 1 day	37 weeks 2 days
Dengue/malaria reports	Positive for dengue NS1 antigen	Positive for plasmodium vivax	Positive for plasmodium vivax	Positive for plasmodium vivax
Indication for COVID-19 RT-PCR testing	Universal testing	ILI symptoms	Universal testing	Universal testing
Comorbidities	None	Pre-eclampsia	Post-datism, previous CS	Previous CS, Rh-negative, bicytopenia (thrombocytopenia and leucopenia), extra hepatic portal venous obstruction, chronic liver disease × 3years,
Obstetric outcome	PROM x 2 days, labor augmentation, VD, low birth weight (2.2 kg)	IUFD, termination of pregnancy, retained POC – evacuation under anesthesia	Uneventful emergency CS for scar tenderness, healthy newborn, CS wound healed	PROM on 16th day of admission, emergency CS for meconium-stained liquor with previous CS, CS wound healed
Complication	None	IUFD, retained POC	None	None
Ultrasonography	Intrauterine fetal growth restriction	D1-Reversal of diastolic flow in umbilical artery, heterogeneous liver echotexture and moderate ascites D2-IUFD		Portal cavernoma, extra hepatic portal venous obstruction, liver parenchymal disease, caudate lobe hypertrophy, moderate splenomegaly
Symptoms and signs of Dengue/Malaria/ COVID-19	Mild fever for 4 days, no petechiae, No bleeding tendencies	Abdominal pain, headache and blurring of vision for 10 days, breathing difficulty for 7 days, fever with chills for 3 days	Fourth day post-CS: fever for 7 days	On 11th day of admission: fever and breathing difficulty for 3 days
Blood transfusion	No	No	No	1 PCV transfused at 20 weeks of gestation
Treatment	Antibiotics, hydration therapy	Antibiotic, tab labetalol, tab nifedipine, tab chloroquine	Antibiotic, inj artesunate (120 mg, twice a day followed by 120 mg, once a day for five days), tab chloroquine 500 mg, once a week	Antibiotic, inj low molecular weight heparin, tab chloroquine
Chest X-ray changes, oxygen requirement, ICU admission, mortality	No	No	No	No
Duration of hospital stay	9 days	13 days	15 days	25 days

Abbreviations: COVID-19, coronavirus disease 2019; CS, Cesarean section; ICU, Intensive care unit; ILI, Influenza-like illness; IUFD, intrauterine fetal demise; PCV, Packed cell volume; POC, products of conception; PROM, premature rupture of membranes; RT PCR, Reverse transcriptase polymerase chain reaction; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; VD, Vaginal delivery.

[a]The patient suffered from extra hepatic portal venous obstruction, chronic liver disease, and multiple splenic artery pseudo-aneurism with mild portal biliopathy after a 3-year history with bicytopenia (thrombocytopenia and leucopenia). She had undergone endoscopic variceal ligation at 20 weeks of gestation for persistent hematemesis.

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Table 2

Laboratory findings of the pregnant women admitted with COVID-19 and dengue/malaria.

Laboratory parameter	Patient 1 (Day 1)	Patient 1 (Day 7)	Patient 2 (Day 1)	Patient 2 (Day 3)	Patient 2 (Day 10)	Patient 3 (Day 1)	Patient 3 (Day 5)	Patient 4 (Day 1)	Patient 4 (Day 5)	Patient 4 (Day 8)	Patient 4 (Day 11)	Patient 4 (Day 15)	Reference value
Hemoglobin (g/dl)	12.7	12.9	11.2	10.9	11.4	10.4	10.8	11.4	10.9	10.5	10.1	11.3	>11
Total leucocyte count (mL)	16 800	12 000	4200	6700	8200	11 400	7800	4500	3800	2700	2600	2800	4000–9000
Platelet count (mL)	197 000	343 000	130 000	140 000	351 000	308 000	247 000	84 000	75 000	57 000	64 000	71 000	150 000–350 000
Aspartate transaminase (U/L)	–	–	75	130	59	–	–	28	33	–	21	29	5–40
Alanine aminotrans-ferase (U/L)	–	–	150	178	97	–	–	11	19	–	16	15	5–40
Serum bilirubin (mg/dl)	–	–	0.2	0.3	0.3	–	–	1.0	1.5	–	0.5	1.0	0–1
D-dimer (ug/ml)	–	–	0.73	–	–	–	–		2.5	–	–	–	<0.4
Blood group and Rh type	A positive	–	AB positive	–	–	A positive	–	O negative	–	–	–	–	–