Maternal and neonatal outcomes of COVID-19 co-infection in pregnant women with chronic hepatitis B virus infection: A prospective cohort study

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The coronavirus disease 2019 (COVID-19) pandemic has caused significant global morbidity and mortality. With the emergence of a more contagious Omicron variant (B.1.1.529), the epidemic is expected to continue. SARS-CoV-2 infection is known to cause an increased risk of adverse pregnancy outcomes, including pre-eclampsia, stillbirth, preterm deliveries, and maternal mortality. Moreover, the risk of maternal and neonatal complications may be higher in mothers from low- and middle-income countries (LMICs). There is some evidence to suggest that HBV and COVID-19 co-infection may not cause more severe outcomes in most cases. However, at present, there are no studies in the existing literature on the impact of co-infection in pregnant women. We conducted a prospective observational study to delineate the effect of this co-infection on maternal and neonatal outcomes. This study was performed at a tertiary care hospital in Northern India between May 2020 and July 2021. Twenty pregnant women with COVID-19 and hepatitis B virus co-infection, admitted for delivery, were included in the present study. The pregnancy outcomes of these patients were compared with 40 HBV mono-infected pregnant women. The study was approved by the BHU Institutional Ethics Committee (ECR/526/Inst/UP/2014/RR-20). Written informed consent was obtained from all participants in this study.

The mean age of pregnant women in the HBV group was 26.1 ± 3.9 years and was comparable to the co-infected group (25.7 ± 5.5 years, P = 0.83) (Table 1). Obstetric outcomes were similar except for prematurity deliveries, which were more common in women with COVID-19 and HBV co-infection (35% vs. 12.5%, P = 0.04). No statistical difference in fetal outcomes, comprising fetal distress and intrauterine growth retardation (IUGR), occurred between the two groups. However, the mean birth weight in the co-infected group was significantly less than the HBV-only group (2482.2 ± 661.8 g vs. 2630 ± 242.1, P = 0.03). The neonatal outcomes of both groups were also comparable.

This prospective study found that co-infection caused a significantly higher proportion of preterm deliveries and lower mean birth weight. These results are particularly problematic in a resource-poor setting like ours with a background of a high prevalence of chronic HBV infection (3%-4.2%). However, our study is limited by the small sample size and limited work-up of HBV infection. Robust data is urgently required for this group of pregnant women due to the continuing pandemic and the possibility of adverse maternal outcomes.

CONFLICT OF INTEREST
The authors have no conflicts of interest.

AUTHOR CONTRIBUTIONS
MR, SS, AA conceptualized the study. MR, SS, AA, BV collected the data. BV and DY drafted the manuscript and did the analysis. MR, BV, DY critically evaluated the manuscript. All authors reviewed and approved the final version of the manuscript.
TABLE 1  Pregnancy outcomes of COVID-19 co-infection with chronic HBV infection

| Parameters                                      | HBV     | HBV + COVID-19 (n = 40) | P value * (n = 20) |
|------------------------------------------------|---------|-------------------------|-------------------|
| Age (years), mean ± SD                          | 26.1 ± 3.9 | 25.7 ± 5.5              | 0.83              |
| Primigravida                                    | 14 (35) | 8 (40)                  | 0.14              |
| Gestational age (days), mean ± SD               | 269.1 ± 18.8 | 262.3 ± 10.8           | 0.14              |
| Obstetric outcomes                              |         |                         |                   |
| Severe anemia (Hb < 7 g/dl)                     | 3 (7.5) | 1 (5)                   | 0.71              |
| Gestational diabetes mellitus                   | 2 (5)   | 2 (10)                  | 0.46              |
| Pre-eclampsia/eclampsia                         | 4 (10)  | 3 (15)                  | 0.57              |
| APH                                             | 2 (5)   | 0                       |                   |
| PPH                                             | 1 (2.5) | 1 (5)                   | 0.61              |
| Cholestasis of pregnancy                        | 3 (7.5) | 3 (15)                  | 0.36              |
| Oligohydramnios                                 | 2 (5)   | 2 (10)                  | 0.46              |
| Premature rupture of membrane                   | 4 (10)  | 1 (5)                   | 0.51              |
| Caesarean delivery                              | 15 (37.5) | 10 (50)               | 0.35              |
| Preterm birth                                   | 5 (12.5) | 7 (35)                 | 0.04              |
| Fetal outcomes                                  |         |                         |                   |
| Fetal distress                                  | 12 (25) | 7 (35)                  | 0.69              |
| Intrauterine growth retardation                 | 9 (22.5) | 5 (25)                  | 0.83              |
| Small for gestational age                       | 2 (5)   | 2 (10)                  | 0.46              |
| Stillbirth                                       | 1 (2.5) | 2 (10)                  | 0.21              |
| Birthweight (g), mean ± SD                      | 2630 ± 242.1 | 2482.2 ± 661.8         | 0.03              |
| Low birth weight (<2.5 kg)                      | 9 (22.5) | 7 (35)                 | 0.30              |
| Neonatal outcomes                               |         |                         |                   |
| Apgar score < 7 at 5 min                        | 4 (10.3) | 2 (11.1)                | 0.92              |
| Respiratory distress                            | 5 (12.8) | 2 (11.1)                | 0.69              |
| ICU admission                                    | 8 (20.5) | 3 (16.6)               | 0.73              |
| Neonatal death                                  | 1 (2.5) | 0                       |                   |

Note. Values are shown as number (percentage), except where otherwise stated.
Abbreviations: APH, antepartum hemorrhage; HBV, Hepatitis B virus; ICU, Intensive care unit; PPH, postpartum hemorrhage.
*Statistical significance was considered as P value <0.05.

DATA AVAILABILITY STATEMENT
Research data are not shared.

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