

Sodium valproate increases the level of γ -aminobutyric acid in the brain, inhibiting the enzymes that catabolize γ -aminobutyric acid. It has a direct membrane-stabilizing effect by affecting potassium channels. Phenytoin prevents seizures as a non-specific sodium-channel blocker; it targets almost all voltage-gated sodium-channel subtypes. These two mechanisms may partially explain the decreased FHR variability in our patient's infant.

The International League Against Epilepsy Task Force on Women and Pregnancy recommends that multiple doses of AEDs should be avoided if possible.³ Sodium valproate and phenytoin increase fetal anomalies.⁴ Our patient's neurologist continued to prescribe these AEDs during her pregnancy as a last resort because of her severe side effects with the other AEDs. There was minimal FHR variability without deceleration, no neonatal asphyxia, and no other reasons for decreased FHR variability in this case, which led to the hypothesis that this rare combination of AEDs might have suppressed the FHR variability. Our observations may help to estimate fetal well-being when similar cases are encountered.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

AUTHOR CONTRIBUTIONS

MM, KO, MK, KN, and TI were involved in study design and data interpretation. MM, KO, MK, KN, and TI were involved in the data analysis. All authors critically revised the report, commented on drafts of the manuscript, and approved the final report.

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Obstetrics

The lethal effect of the second wave of COVID-19 on pregnant women: a matter of concern

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Since December 2019, coronavirus disease (COVID-19) has resulted in major transformations to day-to-day life and the socioeconomic workings of the entire world. During this period, India has faced the wrath of the pandemic which continues to cripple healthcare and finances. At the time of writing, India has faced two waves of COVID-19. A total of 31 064 908 confirmed cases and 413 091 deaths have been reported as of July 17, 2021.¹ The sudden surge of

cases during the second wave in India might be ascribed to a highly infectious double mutant strain of SARS-CoV-2 (B.1.617 lineage), as well as public ignorance towards social distancing measures.² The second wave was remarkably worse than the first wave with higher morbidity and mortality rates, countrywide. There was a shortage of oxygen beds and ventilators, and the amount of health resources available to combat the second wave was grossly insufficient. Amidst

TABLE 1 Maternal baseline, disease-specific, and pregnancy characteristics during the first and second wave of the COVID-19 pandemic

Variables	First wave (n = 60)	Second wave (n = 68)	P value [*]
Age ^a	27.82 ± 5.10	28.25 ± 4.84	0.62
Parity ^a	2.37 ± 1.25	0.95 ± 1.09	<0.00001
Gestational age ^a	34.23 ± 7.98	33.35 ± 8.09	0.54
Trimester wise prevalence ^b			
1st trimester	4 (6.7%)	3 (4.41%)	0.70
2nd trimester	3 (5%)	11 (16.18%)	0.02
3rd trimester	53 (88.3%)	54 (79.41%)	0.23
COVID-19 related symptoms ^b			
Absent (asymptomatic)	49 (81.7%)	37 (54.41%)	0.001
Present (symptomatic)	11 (18.3%)	31 (45.59%)	
COVID-19 related symptoms at the time of presentation ^b			
Cough	7 (11.7%)	21 (30.88%)	0.01
Fever	5 (8.3%)	19 (27.94%)	0.005
Pneumonia	1 (1.7%)	16 (23.52%)	0.0002
Fatigue	2 (3.4%)	15 (22.05%)	0.001
Breathlessness	2 (3.4%)	16 (23.52%)	0.0009
Disease severity ^b			
Mild	9 (15%)	16 (23.53%)	0.26
Moderate	0	0	-
Severe	2 (3.3%)	15 (22.06%)	0.001
Obstetric outcomes ^b			
Early pregnancy loss	3 (5%)	3 (4.41%)	1
Ectopic pregnancy	1 (1.7%)	-	0.46
PIH/preeclampsia	7 (11.7%)	7 (10.29%)	1
Gestational diabetes	-	4 (5.89%)	0.12
Hypo/hyperthyroidism	13 (21.7%)	10 (14.7%)	0.36
IHCP	2 (3.3%)	2 (2.94%)	1
FGR	3 (5%)	9 (13.23%)	0.13
IUFD	1 (1.7%)	9 (13.23%)	0.01
Oligohydramnios	13 (21.7%)	14 (20.59%)	1
Obesity	2 (3.3%)	-	0.21
APH	1 (1.7%)	3 (4.41%)	0.62
Anemia			
Mild	19 (31.7%)	35 (51.47%)	0.03
Moderate	8 (13.3%)	10 (14.7%)	1
Severe	1 (1.7%)	1 (1.47%)	1
Thrombocytopenia	21 (35%)	17 (25%)	0.24
Deranged LFT	12 (20%)	19 (27.94%)	0.31
Deranged KFT	4 (6.7%)	3 (4.41%)	0.7
Preterm birth	19 (31.7%)	31 (45.59%)	0.14
Vaginal delivery	19 (31.7%)	11 (16.18%)	0.06
Rate of cesarean delivery	32 (53.3%)	39 (57.35%)	0.72
Received LMWH ^b	24 (40%)	50 (73.53%)	0.0002
Received dexamethasone therapy ^b	2 (3.34%)	21 (30.88%)	0
Requirement of nasal oxygen therapy ^b	1 (1.67%)	3 (4.41%)	0.62
Non-invasive ventilation ^b	0	2 (2.94%)	0.49

Variables	First wave (n = 60)	Second wave (n = 68)	P value ^a
Invasive mechanical ventilation ^b	1 (1.67%)	12 (17.64%)	0.002
Maternal death ^b	1 (1.67%)	11 (16.18%)	0.005
Neonatal COVID-19 positivity within 24h ^b	0	11 (16.18%)	0.005

Abbreviations: APH, antepartum hemorrhage; FGR, fetal growth restriction; ICU, intensive care unit; IHCP, intrahepatic cholestasis of pregnancy; IUFD, Intrauterine fetal death; KFT, kidney function test, LFT, liver function test; LMWH, low molecular weight heparin; PIH, pregnancy induced hypertension.

^aValues presented as mean \pm SD.

^bValues presented as n (%).

*Statistical significance at $P < 0.05$.

this crisis, there was one subset of patients that suffered heavily—pregnant women. The present study aimed to compare disease severity, maternal morbidity and mortality, and pregnancy outcomes with regards to the first and second wave of the COVID-19 pandemic and its effect on pregnant women infected with SARS-CoV-2.

The present study was a prospective observational study conducted at a tertiary care institute in India. A total of 128 pregnant women infected with COVID-19 were hospitalized at our institution—60 during the first wave (July–December 2020) and 68 during the second wave (March–June 2021) of the pandemic. The study was registered with the Clinical Trial Registry of India (CTRI/2020/09/027617) and approved by the AIIMS institutional ethics committee (AIIMS/IEC/20/559).

Overall, more pregnant women were infected with SARS-CoV-2 during the second wave (particularly primiparas and early gestation pregnancies). The number of pregnant women presenting with COVID-19-related symptoms and occurrence of severe disease was significantly higher during the second wave ($P = 0.001$ and 0.001 , respectively). No statistical difference was noted in pregnancy outcomes in either wave except for the incidence of intrauterine fetal demise (1 [1.7%] vs. 9 [13.23%]). The need for low molecular weight heparin (24 [40%] vs. 50 [73.53%]; $P = 0.0002$), dexamethasone therapy (2 [3.34%] vs. 21 [30.88%]), and invasive ventilation (1 [1.67%] vs. 12 [17.64%]; $P = 0.002$) was proportionately higher during the second wave of the pandemic. The maternal mortality rate was remarkably higher in the second wave when compared to the first wave ($P = 0.005$). No neonate was found to be infected during the first wave, while 11 neonates were diagnosed with SARS-CoV-2 infection within 24 h during the second wave—the difference was statistically significant ($P = 0.005$). Table 1 describes maternal baseline, disease-specific, and pregnancy characteristics during both waves of the COVID-19 pandemic.

The present study reveals that the second wave hit pregnant women more severely than the first wave in terms of disease severity, intensive care unit admission and invasive ventilation, and maternal mortality. Similar results were reported from the UK, along with increased referral for extracorporeal membrane oxygenation.^{3,4} Additionally, Spain documented low severity of COVID-19 infection in pregnant women during the first wave, whilst reporting a 10-fold

rise in the amount of pregnant women hospitalized due to COVID-19 infection during the second wave.⁵

Considering the higher frequency of severe COVID-19-related disease and maternal mortality in the second wave, vaccination during pregnancy has become crucial for combatting the devastating effects of the pandemic, in addition to other preventive measures. A total of 399 695 879 Indians have been vaccinated at the time of writing.⁶ Recently, the Ministry of Health and Family Welfare of India approved the vaccination of pregnant and breastfeeding women by acknowledging that pregnancy with COVID-19 may result in the rapid deterioration of maternal health and may have deleterious effects on the fetus too. Further data is required to ascertain the amount of protection vaccination can offer for pregnant populations. With India's new vaccination strategy, there is hope that pregnant women with COVID-19 infection will not suffer the same dismal fate as others did during the lethal second wave.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest.

AUTHOR CONTRIBUTIONS

KK proposed the idea for the analysis. AM and AA collected the data. AA and KK drafted the manuscript with direction from JC and AB. AG, LC, and RM critically evaluated the manuscript. All authors (KK, AA, AM, AG, LC, RM, AB, and JC) contributed to and approved of the final version of the manuscript.

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