



Short Communication

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Neonatal Outcomes by Pandemic Wave Among Pregnant Individuals with COVID-19 Infection



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Abstract

Background: The impact of COVID variants on neonatal outcomes is not well understood. The objective of this study is to compare neonatal outcomes by wave of the pandemic.

Materials and methods: Single center retrospective cohort of neonates born to individuals infected with COVID in pregnancy from 3/2020-2/2022. Primary outcome was a neonatal composite of NICU admission, intubation/CPAP, NEC, IVH, sepsis, and death. Secondary outcomes included components of composite. Outcomes were compared between pandemic “waves,” including wildtype (WT) (5/2020-9/2020), alpha (11/2020-3/2021), delta (8/2021-10/2021), omicron (12/2021-2/2022).

Results: Of 527 pregnant individuals, 133 (25.3%) were infected with WT, 99 (18.8%) with alpha, 62 (11.8%) with delta, and 157 (29.8%) with omicron. Maternal race and ethnicity, insurance status, and symptomatic COVID differed by wave. Gestational age at delivery, mode of delivery, and IAI did not differ. Neonatal composite was similar across waves (Table), as were secondary neonatal outcomes. No neonates were infected with COVID. When controlling for race and ethnicity, insurance status, symptomatic COVID, cesarean delivery, vaccination, and gestational age at delivery, neonates in alpha, delta, and omicron waves had lower odds of adverse outcomes and NICU admission compared to those born to individuals infected with COVID during WT wave.

Conclusion: Odds of adverse neonatal outcome and NICU admission were lower among those born in the alpha, delta, and omicron waves compared to those born in WT wave.

Keywords: COVID-19, neonatal outcomes, viral variants

Introduction

Pregnancy is associated with increased risk for severe COVID-19 and higher rates of maternal morbidity and mortality [1]. Neonatal infections are less common, thus data are sparse investigating perinatal transmission, as well as the impact of severe maternal infection on neonatal outcomes. Maternal disease severity varied across pandemic waves for all populations, yet limited data exist on neonatal morbidity and mortality across viral variants [1]. This study aims to describe neonatal outcomes by COVID-19 pandemic waves.

Materials and Methods

Retrospective cohort study of pregnant individuals delivered in single healthcare system (3/2020-2/2022) performed after IRB approval (Pro00105162). Individuals included if diagnosed with COVID-19 infection with positive PCR or antigen test at any point during pregnancy. Demographic information, pregnancy,

delivery, neonatal, COVID-19 infection, and vaccination details were abstracted from the electronic medical record (EMR).

The primary outcome was a neonatal composite including neonatal intensive care unit (NICU) admission, intubation or continuous positive airway pressure (CPAP) therapy, necrotizing enterocolitis (NEC) (grade 2/3), intraventricular hemorrhage (IVH) (grade 3/4), sepsis, and death. Secondary outcomes included individual components of the composite, and neonatal SARS-CoV-2 infection. The exposure of interest was pandemic “wave.” Pandemic waves were defined using Department of Health and Human services data to identify community peaks in Durham County, North Carolina [2]. Waves defined as wildtype (5/2020-9/2020), alpha (11/2020-3/2021), delta (8/2021-10/2021), and omicron (12/2021-2/2022). Individuals with infections between defined waves were excluded. Bivariate statistics used to analyze the data, with regression models used to control for potential confounders identified using $p < 0.05$ on univariate analysis.

Results

Five-hundred twenty-seven pregnant individuals were included. One-hundred thirty-three (25.3%) patients were infected with wildtype, 99 (18.8%) with alpha, 62 (11.8%) with

delta, and 157 (29.8%) with omicron. Maternal race and ethnicity, insurance status, and symptomatic COVID-19 differed by wave. Gestational age at delivery, mode of delivery, and intraamniotic infection did not differ by wave (Table1).

Table 1: Demographics of individuals infected with COVID-19 during pregnancy.

	WT N=133(%)	Alpha N=99(%)	Delta N=62(%)	Omicron N=157(%)	p
Median maternal age at delivery, years, [IQR]	28.5 [24.0, 33.0]	27.0 [23.0, 32.0]	28.0 [22.0, 32.0]	28.0 [24.0, 33.0]	0.48
Race					<0.001
Asian	3 (4.5)	3 (3.8)	1 (1.9)	5 (4.0)	
Black	30 (44.8)	37 (47.4)	29 (55.8)	60 (47.6)	
Native American	0 (0.0)	1 (1.3)	0 (0.0)	2 (1.6)	
White	16 (23.9)	36 (46.2)	20 (38.5)	57 (45.2)	
Other	18 (26.9)	1 (1.3)	2 (3.8)	2 (1.6)	
Hispanic	87 (65.4)	21 (21.6)	12 (19.7)	32 (20.9)	<0.001
Private insurance	26 (19.5)	42 (42.4)	36 (58.1)	107 (68.2)	<0.001
Symptomatic COVID infection	87 (65.4)	53 (53.5)	41 (66.1)	70 (44.6)	0.001
Gestational age at delivery, weeks [IQR]	39.0 [37.3, 39.7]	39.3 [37.4, 39.9]	38.8 [37.1, 39.6]	39.1 [37.3, 39.6]	0.63
Intraamniotic infection	5 (3.8)	4 (4.0)	1 (1.6)	1 (0.6)	0.22
Cesarean section	35 (26.3)	38 (38.4)	22 (35.5)	39 (24.8)	0.07
Neonatal composite	20 (15.0)	13 (13.1)	7 (11.3)	17 (10.8)	0.73
Admitted to NICU	17 (12.8)	9 (9.1)	7 (11.3)	15 (9.6)	0.77
Median NICU LOS, days, [IQR]	12.0 [3.0, 23.0]	12.0 [5.0, 61.0]	9.0 [4.5, 17.5]	9.0 [5.0, 24.0]	0.74
IVH grade 3 or 4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	>0.99
Neonatal death	3 (2.3)	5 (5.1)	1 (1.6)	2 (1.3)	0.27
Neonatal NEC grade 2/3	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0.31
Need for neonatal intubation/mechanical ventilation	1 (0.8)	1 (1.0)	2 (3.2)	0 (0.0)	0.15
Neonatal sepsis (confirmed)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0.49
Adjusted odds of neonatal composites with WT as comparison group					
		Alpha*	Delta*	Omicron*	
		aOR (95%CI)	aOR (95%CI)	aOR (95%CI)	
Neonatal composite		0.28 (0.09, 0.90)	0.24 (0.07, 0.88)	0.24 (0.07, 0.79)	
Admitted to NICU		0.17 (0.05, 0.54)	0.24 (0.07, 0.88)	0.25 (0.08, 0.83)	

WT, wildtype wave; IQR, inter-quartile range; LOS, length of stay

*controls for race, ethnicity, insurance status, intraamniotic infection, cesarean delivery, vaccination status, and gestational age at delivery.

Neonatal composite did not differ between waves (p=0.73), nor did secondary neonatal outcomes (Table 1). Median NICU length of stay was 12 days for wildtype (IQR:3,23) and alpha (IQR:5,61) waves and 9 days for delta (IQR:4.5,17.5) and omicron (IQR:5,24)

(p=0.77). Overall, neonatal NEC occurred in one neonate, neonatal intubation in four neonates, and death in 11. No neonates tested positive for SARS-CoV-2, had IVH grade 3 or 4, or had confirmed cases of sepsis. In adjusted analyses, neonates born to individuals

with COVID-19 infection during pregnancy had lower odds of composite adverse outcome during the alpha (adjusted odds ratio (aOR) 0.28, 95% confidence interval (CI):0.09,0.90)), delta (aOR 0.24, 95%CI:0.07,0.88), and omicron (aOR 0.24, 95%CI:0.07,0.79), when compared to those born to individuals infected during wildtype wave. Neonates had lower odds of being admitted to the NICU during alpha (aOR 0.17, 95%CI:0.05,0.54), delta (aOR 0.28, 95%CI:0.09,0.95), and omicron (aOR 0.25, 95%CI:0.08,0.83) when compared to those born to individuals infected during the wildtype.

Discussion

In this population, neonates born to individuals following COVID-19 infection in pregnancy had higher risk of adverse neonatal outcome in the wildtype wave compared to alpha, delta, or omicron pandemic waves. This is consistent with the illness severity observed for the general population in the wildtype wave. Interestingly, neonatal outcomes were not worse during the delta wave, despite increased maternal disease severity in that wave [3]. This is also consistent with recent findings that the omicron wave was associated with reduced risk of maternal and neonatal outcomes in intensive care unit admission, preterm birth, and low birth weight [4].

This study is limited by several factors. We only included individuals who delivered in a single health system in the Southeast United States, limiting generalizability. Additionally, individuals who fell outside of our specifically defined waves were excluded. While we adjusted for vaccination status in our analyses, we did not look at impact of vaccination status on neonatal outcomes. Recent studies into safety of COVID-19 vaccination are reassuring for low risk of adverse neonatal outcomes following vaccination

during pregnancy [5]. Lastly, we did not assess long-term infant adverse outcomes. Despite these limitations, our findings emphasize the importance of understanding neonatal impacts by wave as we anticipate ongoing COVID-19 variants, as well as the potential need for long term follow-up in neonates born to individuals with COVID-19.

Conflict of Interest

The authors report no conflicts of interest. Julia Moyett was awarded a Travel Scholar grant by the Infectious Diseases Society for Obstetrics & Gynecology to attend the 2022 annual meeting where this data was presented in preliminary form.

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