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STORCH Infections Among Very Low Birth Weight and Preterm Infants in the United States, 2018–2020

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Introduction

Syphilis, toxoplasmosis, other infections (varicella zoster virus, parvovirus B19), rubella, cytomegalovirus (CMV), and herpes simplex (STORCH) infections may result in neonatal disease and neurological sequalae[1]. Population-based prevalence rates of STORCH infections among very low birth weight (VLBW) and/or preterm infants in the U.S. are lacking.

Methods

Vermont Oxford Network (VON) is a voluntary worldwide community of practice. VON members submitted standardized data on live born infants 401 to 1500 grams or 22 to 29 completed weeks' gestational age who were inborn or transferred to the reporting hospital within 28 days of birth from January 1, 2018 to December 31, 2020[2]. Infant data were collected during the initial birth hospitalization. Transferred infants were tracked to

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Contributors' Statement Page

Dr. Edwards conceptualized and designed the study, conducted the analyses, drafted the initial manuscript, and reviewed and revised the manuscript.

Ms. Greenberg conducted the analyses and reviewed and revised the manuscript.

Drs. Ehret, Soll, Lanzieri, and Horbar conceptualized and designed the study and reviewed and revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Conflict of Interest Disclosures:

Dr. Edwards and Dr. Ehret receive salary support from Vermont Oxford Network. Ms. Greenberg is a Vermont Oxford Network employee. Dr. Soll is Vice President, Director of Clinical Trials and Follow-up, Director of Cochrane at VON, and an unpaid member of the Vermont Oxford Network Board of Trustees. Dr. Horbar is the President, Chief Executive and Chief Scientific Officer of Vermont Oxford Network, and an unpaid member of the Vermont Oxford Network Board of Trustees.

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determine their ultimate disposition and length of stay. The Institutional Review Board at the University of Vermont determined that use of the VON database for this study was not human subjects research.

A STORCH infection was defined as acquired *in utero* or during birth from a list that included: toxoplasmosis; rubella; syphilis; CMV; herpes simplex; parvovirus B19; Zika; varicella zoster. Maternal race and ethnicity were determined by personal interview with the mother or review of the birth certificate or medical record, in that order of preference[2]. Congenital anomalies included an anomaly on a specific list, or, if not on the list, an anomaly that was the primary cause of death or required surgical or medical therapy prior to discharge[2]. Small for gestational age (SGA) was defined as birth weight <10th percentile and microcephaly was defined as head circumference <3rd percentile for gestational age and sex[3]. Isolated microcephaly was defined as microcephaly without SGA. Statistical analyses were performed using SAS 9.4.

Results

Data were reported by 777 hospitals in the U.S. Overall, 944 of 128,133, or 7.37/1,000 VLBW and/or preterm infants were diagnosed with STORCH infections. CMV (3.37/1,000), syphilis (2.01/1,000), and herpes simplex (1.82/1,000) were the infections reported most frequently (Table 1). Eleven infants had >1 infection.

Infants with CMV had the lowest birth weights and were nearly twice as likely to be SGA or microcephalic as infants without infections, although infants with CMV were least likely to have isolated microcephaly (Table 2). Survivors with CMV also had the longest lengths of stay. Only 70.5% of mothers of infants diagnosed with syphilis received any prenatal care compared with 96.1% of infants without infections.

Infants with STORCH infections had similar rates of survival (86.3%) as infants without STORCH infections (87.4%).

Discussion

Prevalence of STORCH infections was 7.37/1,000 among VLBW and/or preterm infants. In a population of VLBW and/or preterm infants in California from 2005 to 2016, prevalence of CMV infection was 2.7/1,000[4], lower than in the current study.

In this cohort, a large proportion of infants with CMV were SGA or microcephalic. In a study using health care data from 2000 to 2015 in the U.S., congenital CMV diagnosis was associated with a seven-fold increased birth prevalence of microcephaly[5]. A report from a single center found the yield of routinely testing SGA infants for STORCH infections was extremely low[6]. A survey of neonatologists found that most frequent reasons for pursuing STORCH testing were pathologic findings of physical and ophthalmologic examinations, such as microcephaly[7].

In 2019, the VON VLBW database included over 90% of U.S. live births, making this study nearly population-based and the largest report of STORCH infections among VLBW

and/or preterm infants. VON does not have population-based data on moderate preterm, late preterm, or term populations. We do not know whether NICUs performed universal screening for STORCH infections or routine testing based on clinical criteria such as SGA or microcephaly, so we have underestimated the exact incidence. We do not know what testing was used to diagnose STORCH infections. Understanding testing practices may be important to assess differences in ascertainment and to develop strategies to increase identification of STORCH infections. STORCH infections tests may not be covered by health insurance; therefore, identifying high-risk populations in which testing is cost-effective is an important public health issue. These data might be useful to monitor trends and identify health disparities in STORCH infections among infants in the U.S.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We thank our colleagues who submit data to VON on behalf of infants and their families. The list of centers contributing data to this study are in the Supplemental Table.

Abbreviations:

CMV	Cytomegalovirus
SGA	small for gestational age
STORCH	syphilis; toxoplasmosis, other, rubella, cytomegalovirus, herpes simplex virus
U.S.	United States
VLBW	very low birth weight
VON	Vermont Oxford Network

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Table 1.

Incidence of specific STORCH infections among very low birth weight and preterm infants, U.S. VON member hospitals, 2018–2020

	# of infections[a]	Rate per 1000 (99% CI)
Overall	956	7.37 (6.78, 8.01)
Cytomegalovirus	432	3.37 (2.98, 3.82)
Syphilis	257	2.01 (1.71, 2.35)
Herpes simplex	233	1.82 (1.54, 2.15)
Parvovirus B19	16	0.12 (0.07, 0.24)
Toxoplasmosis	10	0.08 (0.04, 0.17)
Rubella[b]	5	0.04 (0.01, 0.12)
Varicella zoster	2	0.02 (0.00, 0.08)
Zika	1	0.01 (0.00, 0.07)

[a]A total of 933 were diagnosed with 1 infection, 10 were diagnosed with two infections, and one was diagnosed with three infections.

[b]Infections may have been suspected; only 2 cases of congenital rubella have been reported in the U.S. during 2018–2019 [Annual statistics from the National Notifiable Diseases Surveillance System (NNDSS). (cdc.gov)].

Table 2.

Characteristics of very low birth weight and preterm infants with and without STORCH infections, U.S. VON member hospitals, 2018–2020

	Cytomegalovirus (n=424)	Syphilis (n=253)	Herpes Simplex (n=227)	Additional[a] (n=40)	None (n=127,197)
Maternal Characteristics					
Maternal Race and Ethnicity					
Black[b], n (%)	141 (33.8)	109 (43.3)	82 (36.3)	12 (30.0)	39380 (31.3)
Hispanic, n (%)	98 (23.5)	67 (26.6)	42 (18.6)	7 (17.5)	24647 (19.6)
White[b], n (%)	142 (34.1)	66 (26.2)	98 (43.4)	16 (40.0)	51501 (40.9)
Asian/Pacific Islander[b], n (%)	24 (5.8)	2 (0.8)	1 (0.4)	2 (5.0)	6411 (5.1)
American Indian/Alaska Native[b], n (%)	3 (0.5)	4 (1.6)	1 (0.4)	3 (7.5)	1008 (0.8)
Other[b], n (%)	10 (2.4)	4 (1.6)	2 (0.9)	0 (0.0)	2789 (2.2)
Prenatal Care, n (%)	411 (97.6)	177 (70.5)	216 (95.2)	37 (92.5)	121782 (96.1)
Multiple Gestation, n (%)	59 (13.9)	38 (15.0)	35 (15.4)	6 (15.0)	30588 (24.0)
Vaginal Delivery, n (%)	101 (23.8)	82 (31.9)	83 (36.6)	10 (25.0)	34341 (27.0)
Infant Characteristics					
Birth Weight, g – median (Q1, Q3)	896 (660, 1248)	1190 (928, 1380)	1100 (790, 1335)	1081 (750, 1373)	1085 (790, 1330)
Gestational Age, weeks – median (Q1, Q3)	28 (25, 31)	29 (27, 30)	28 (26, 30)	28 (26, 30)	28 (26, 30)
1 Minute Apgar – median (Q1, Q3)	5 (3, 7)	5 (3, 7)	6 (3, 7)	3 (1, 7)	5 (3, 7)
Male, n (%)	239 (56.4)	120 (47.4)	110 (48.5)	16 (40.0)	64305 (50.6)
Congenital Anomaly, n (%)	45 (10.6)	19 (7.5)	7 (3.1)	8 (20.0)	7956 (6.3)
Small for Gestational Age, n (%)	182 (43.4)	38 (15.2)	30 (13.3)	10 (25.0)	24378 (19.5)
Microcephaly, n (%)	117 (30.7)	29 (12.2)	21 (9.9)	6 (15.8)	10612 (9.1)
Isolated Microcephaly, n (%)	9 (7.7)	8 (27.6)	9 (42.9)	3 (50.0)	1992 (18.8)
Outcomes					
Survivors, n (%)	363 (87.3)	223 (89.91)	185 (82.2)	31 (77.5)	110,415 (87.4)
Total Length of Stay among Survivors, days – median (Q1, Q3)	81 (50, 121)	64 (48, 95)	68 (47, 99)	74 (53, 98)	66 (45, 96)

Footnotes:

[a] Due to small numbers rubella, parvovirus B19, toxoplasmosis, Zika, and Varicella zoster were combined in the “additional” group. Eleven infants with >1 infection are also in this group.

[b] Non-Hispanic.