

Clinical outcomes and respiratory virus detections in children with neurologic/neuromuscular disorders hospitalized for acute respiratory infection, 2013 – 2015

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BACKGROUND

- Neurologic/neuromuscular disorders (NNMD) can aggravate respiratory viral infections, such as influenza, and lead to severe illness.
- Children with NNMD may have impaired lung or muscle function, resulting in a diminished capacity to clear respiratory secretions from their airway or complete swallowing function.
- The Minnesota Department of Health in collaboration with the CDC and CSTE developed surveillance for patients hospitalized with severe acute respiratory illness (SARI) to improve the understanding of the health impact of respiratory pathogens.
- We describe clinical outcomes and respiratory pathogen detections in children with NNMD.

METHODS

- From September 2013 through June 2015, surveillance for patients with SARI was conducted at three large sentinel hospitals with diverse populations in the Minneapolis/St. Paul metropolitan area.
- Respiratory specimens collected from hospitalized patients with acute respiratory illness were tested by the state public health laboratory for 22 respiratory pathogens.
- Medical chart abstractions were performed by MDH personnel on all identified patients to record demographic, admitting symptoms, clinical course, and underlying/chronic condition data.
- We compared severe outcomes (intensive care unit admission, mechanical ventilation, or death) and length of stay (LOS) by pathogen detected among three SARI patient groups: NNMD, other comorbidities, and no comorbidities.
- We used a multinomial logistic regression model to evaluate severe outcome. The LOS was evaluated by group and among children with NNMD alone using a negative binomial regression model adjusting for variables significant in univariate analysis.
- Pathogen testing at MDH was conducted using individual and multiplexed real-time RT-PCR assays for the following pathogen:
 - Influenza A, B and A/B subtypes (FLU)
 - Respiratory syncytial virus (RSV)
 - human metapneumovirus (MPV)
 - Rhinovirus (RV)
 - Enterovirus (EV)
 - Adenovirus (ADV)
 - Parainfluenza viruses (PIV) 1-4
 - Coronaviruses 229E, OC43, NL63, and HKU1 (COV)
 - Bacterial pathogens: *Legionella* species, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae* (MYCO), and *Bordetella pertussis*, *B. parapertussis*, and *B. holmesii*

Figure 1 – Hospital admission time series of children with SARI hospitalization by co-morbid condition category

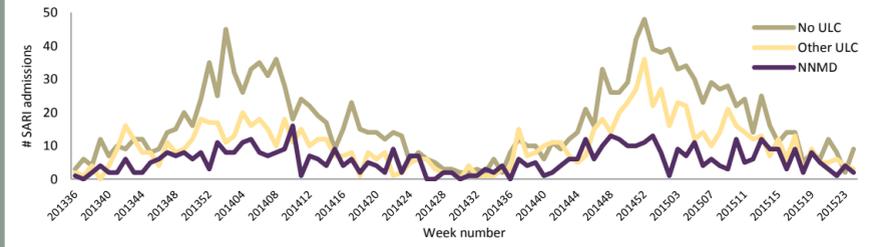


Table 1 – Demographic and clinical characteristics of children with SARI hospitalization by co-morbid condition category

	NNMD (n=530)	Other ULC (n=970)	No ULC (n=1628)	P-value
Median Age (years, IQR)	2.9 (1.1–7.0)	1.6 (0.6–5.0)	0.6 (0.2–1.7)	<0.0001
Age Group				
0 – 11 months	121 (22.8)	358 (36.9)	995 (61.1)	<0.0001
12 – 23 months	90 (17.0)	178 (18.4)	286 (17.6)	
2 – 4 years	135 (25.5)	205 (21.1)	209 (12.8)	
5 – 17 years	184 (34.7)	229 (23.6)	138 (8.5)	
Race/Hispanic Ethnicity				
White, non-Hispanic	244 (46.0)	408 (42.1)	706 (43.4)	<0.0001
Black, non-Hispanic	119 (22.5)	270 (27.8)	325 (20.0)	
Asian or Pacific Islander	63 (11.9)	100 (10.3)	203 (12.5)	
Hispanic (any race)	62 (11.7)	72 (7.4)	164 (10.1)	
Onset <2 days prior to admission	101 (19.1)	177 (18.2)	226 (13.9)	<0.0001
Admission Reasons				
Acute respiratory illness	301 (56.8)	651 (67.1)	1148 (70.5)	<0.0001
Fever	328 (61.9)	521 (53.7)	934 (57.4)	0.0152
Pneumonia	120 (22.6)	159 (16.4)	232 (14.3)	<0.0001
Other respiratory/cardiac	203 (38.3)	273 (28.1)	437 (26.8)	<0.0001
Other non-respiratory/cardiac	172 (32.5)	218 (22.5)	411 (25.2)	0.0002
Symptoms at Admission				
Fever (>100.4F)	209 (39.4)	358 (36.9)	651 (40.0)	NS
Respiratory distress	316 (59.6)	579 (59.7)	927 (56.9)	NS
Shortness of breath	50 (9.4)	134 (13.8)	194 (11.9)	0.0374
Cough	372 (70.2)	718 (74.0)	1209 (74.3)	0.0876
Wheezing	115 (21.7)	352 (36.3)	407 (25.0)	<0.0001
Discharge Diagnosis				
Pneumonia	231 (43.6)	299 (30.8)	443 (27.2)	<0.0001
Bronchiolitis	117 (22.1)	349 (36.0)	839 (51.5)	<0.0001
Seizures	22 (4.2)	9 (0.9)	29 (1.8)	0.0003
Acute respiratory distress syndrome	1 (0.2)	3 (0.3)	1 (0.1)	NS
Clinical Course				
Median length of stay (days, IQR)	4 (2–7)	3 (2–4)	3 (2–4)	<0.0001
ICU admission	169 (31.9)	153 (15.8)	210 (12.9)	<0.0001
Median ICU length of stay (days, IQR)	5 (2–10)	3 (2–6.5)	3 (2–7)	<0.0001
Mechanical Ventilation	74 (14.0)	44 (4.5)	78 (4.8)	<0.0001
Death	7 (1.3)	1 (0.1)	5 (0.3)	0.0014

Table 2 – Factors associated with severe outcomes among children with SARI hospitalization by co-morbid condition category

Comorbidity Group	Severe outcomes (ICU admission or death)					
	Univariate			Multivariate (Reduced Model)		
	Odds Ratio	95% CI	P-value	Odds Ratio	95% CI	P-value
NNMD	3.1	(2.5,3.9)	<0.0001	2.9	(2.2,3.8)	<0.0001
Other ULC	1.3	(1.1,1.6)	0.0502	1.2	(1.1,1.6)	0.0853
No ULC	ref					
Age Group						
0-11m	ref					
1-<2y	0.9	(0.7,1.2)	NS			
2-4y	1.1	(0.9,1.5)	NS			
5-17y	1.7	(1.3,2.1)	<0.0001			
Pathogen detection	0.74	(0.6,1)	0.0185	0.7	(0.5,0.9)	0.0116
Onset <2 days	1.6	(1.2,2)	0.0003	1.4	(1.1,1.8)	0.0048
Admission Reason						
Pneumonia	1.8	(1.4,2.2)	<0.0001	1.8	(1.3,2.3)	<0.0001
Fever	0.6	(0.5,0.7)	<0.0001	0.5	(0.4,0.7)	<0.0001
Acute respiratory illness	0.7	(0.6,0.9)	0.0032			
Other respiratory/cardiac	1.5	(1.2,1.8)	<0.0001			

Figure 2 – Severe outcomes by age and comorbidity group

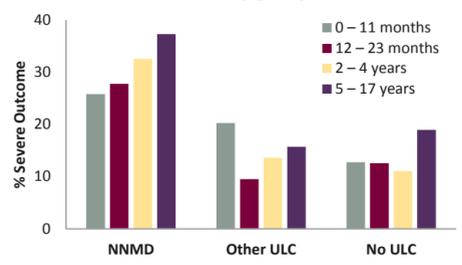


Figure 3 – Median age by comorbidity group and pathogen detection

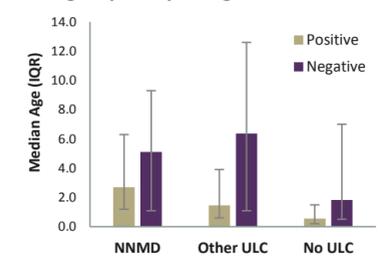
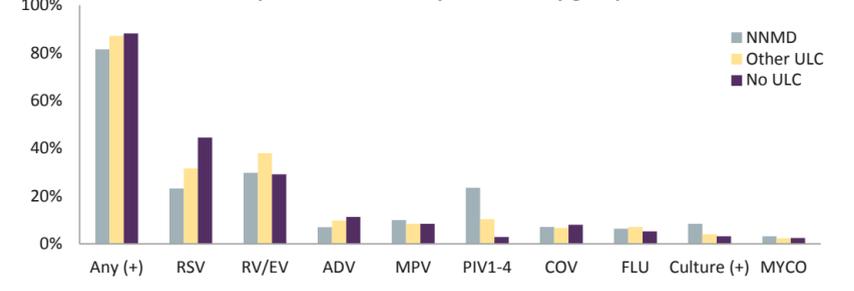


Figure 4 - Respiratory pathogen detections among children hospitalized for SARI by comorbidity group



RESULTS

- The MN SARI Surveillance Program identified 3,128 children <18 years with SARI (Table 1): 530 (16.9%) had NNMD, 970 (31.0%) had other comorbidities (Other ULC), and 1,628 (52.0%) had no identified comorbidities (No ULC).
- The presence of comorbidities increased with age.
- Children with NNMD were significantly older than those with other or no comorbidities (median age 2.9, 1.6 and 0.6 years, respectively, p<0.0001, Table 1).
- Severe outcomes were more frequent among children with NNMD and increased with increasing age (Figure 2)
- Pathogen detection was slightly less frequent among children with NNMD (79.5%) compared with those with other or no comorbidities (87.2% and 86.3%, respectively, p<0.0001, Figure 3).
- Among children with NNMD, most commonly detected pathogens were rhinovirus/enterovirus (29%), respiratory syncytial virus (23%), metapneumovirus (10%), and parainfluenza viruses (8%, Figure 4).
- In multivariable analysis, compared to children with no or other comorbidities, children with NNMD had a longer LOS (6.1 vs. 4.5 and 3.7 days, respectively, p<0.0001), and were more likely to have a severe outcome (Table 2).
- Detection of a respiratory pathogen was not independently associated with comorbidity group; however, among children with NNMD, LOS was 26.2% longer among children with a pathogen detected (95% CI: 16.7-35.6% p<0.0001).

CONCLUSIONS

- Children with SARI who have NNMD are at greater risk for severe outcome and a longer LOS, which may be further prolonged when a pathogen is detected.
- Children with NNMD represented 16% of the patient-population hospitalized for SARI and presented at an older age.
- A better understanding of the impact of respiratory-specific pathogens in patients with NNMD may help target preventive measures.

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