

Streptococcus pneumoniae-associated hemolytic uremic syndrome among children in North America

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on behalf of the Emerging Infections Network Hemolytic-Uremic Syndrome Study Group

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ABSTRACT

Background: *S. pneumoniae* – associated hemolytic-uremic syndrome (pHUS) is being increasingly recognized. To better characterize this disease, we report the largest series of pHUS among children in North America

Results: 37 cases were submitted by 15 EIN members. 34 cases (92%) were culture– confirmed while 3 (8%) were diagnosed clinically by the presence of pneumonia, microangiopathic hemolytic anemia, acute renal failure, and thrombocytopenia.

The median patient age was 2 years and 76% of patients were up-to-date on their PCV7 vaccinations. The majority of patients presented with pneumonia (92%) and bacteremia (78%) while other clinical manifestations such as pericardial effusion (15%), and meningitis (11%) were less common. 21% of patients with bacteremia had *S. pneumoniae* concurrently isolated from CSF or pleural fluid. Severe illness was common with 95% requiring admission to the intensive care unit, 59% requiring mechanical ventilation, 54% undergoing chest tube placement or video-assisted thorascopic surgery, and 73% requiring dialysis during hospitalization.

Among 30 patients with a median follow up of 6 months after hospitalization, 23% remained dialysis-dependent, 10% had undergone renal transplantation, 13% had neurologic sequelae, and 3% died. Among 24 serotyped isolates, 96% were non-PCV7 serotypes. Serotype 19A was most common (51%) followed by serotypes 7F (17%), 3 (12%), 1 (8%), 22 (8%), and 14 (4%). Among 32 isolates with susceptibility results available, 10% were penicillin non-susceptible (MIC > 2 mcg/ml).

Conclusions: pHUS among North American children was caused by non-PCV7 serotypes, had severe clinical manifestations, and was associated with significant morbidity.

METHODS

•Members of the Emerging Infections Network (EIN) were polled for clinical and laboratory features of pediatric cases of pHUS between 1997 and 2009.

RESULTS

•37 cases were submitted by 15 EIN members

- 33(89%) culture confirmed
- 4 (11%) diagnosed clinically

•All patients had microangiopathic hemolytic anemia, renal injury, and thrombocytopenia (<150,000/ml) within 7 days.

•Most cases occurred in the winter months and after year 2005.

•Most patients were previously healthy and up to date on PCV7 immunizations.

•The majority of patients had pneumonia and bacteremia

•Most patients required ICU admission, mechanical ventilation, invasive procedures, and dialysis.

•1 patient with meningitis died.

•3 patients underwent renal transplantation.

•Nearly half of 30 patients with follow-up had evidence of renal insufficiency.

•Most *S. pneumoniae* isolates were PCN susceptible, are not included in PCV7, but are included in PCV 13.

Table 1. Clinical characteristics

CLINICAL CHARACTERISTIC	N =37
	No. (%)
Median age (y)	2 (range 0.75-7)
PCV up to date	28 (76)
Co-morbidities	5 (13)
Fever on admission	33 (89)
Duration of fever (d)	5
Length of stay (d)	22
ICU admission (d)	35 (95)
Duration of ICU stay (d)	11
Dialysis	27 (73)
Duration of dialysis (d)	15
Mechanical ventilation	22 (59)
Duration of ventilation (d)	6.5
Pneumonia/pulmonary infiltrate	34 (92)
Mod-large pleural effusion	23 (68)
Cavitary PNA	10 (29)
Pericardial effusion	5 (15)
Meningitis	
Possible	12 (32)
Culture-confirmed	4 (11)
Sterile site culture with <i>S. pneumoniae</i>	34 (92)
Blood	22 (65)
Blood+pleural fluid	3 (9)
Blood + CSF	3 (9)
Pleural fluid	3 (9)
Blood +urine	1 (3)
CSF	1 (3)
Sputum (BAL)	1 (3)

Figure 1: Time of presentation

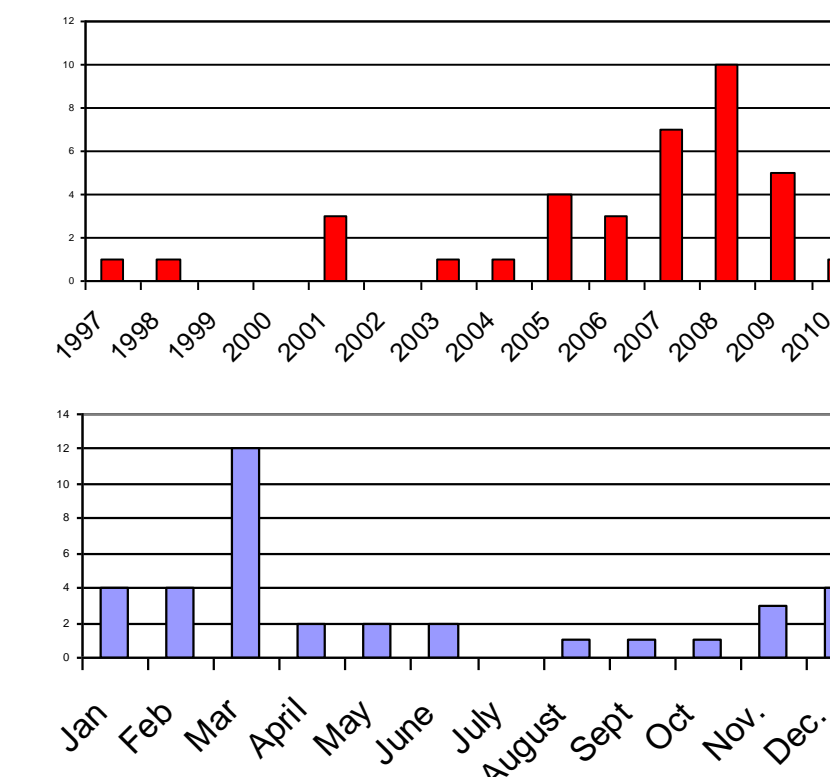


Table 2. Microbiology

*PCN MIC (mcg/ml) reported	NO. (%)
S < 0.06	32
I 0.12-1	10 (31)
R > 2	2 (10)

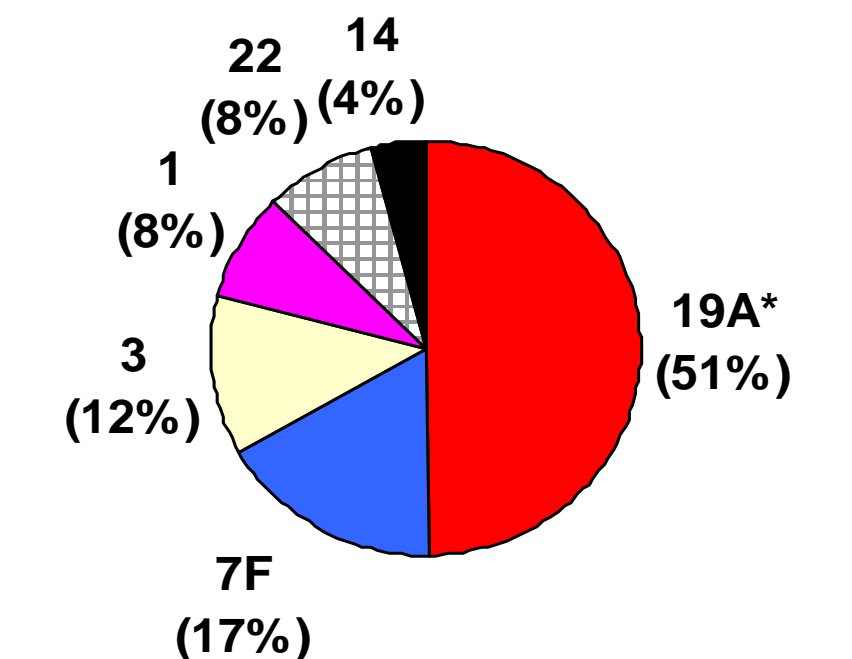
* Meningitis breakpoints, CLSI, 2008

Table 3. Outcomes

OUTCOME	HOSPITAL DISCHARGE (N=37)	FOLLOW-UP (N=30)
Death	1 * (3)	0
Dialysis	8 (22)	7 (23)
Elevated creatinine	17 (46)	11 (37)
Proteinuria	16 (43)	6 (20)
Hypertension	16 (43)	9 (30)
Neurologic deficits	2 (5)	4 (13)
Renal transplantation	-	3 (10)

* Patient had meningitis.

Figure 2: Distribution of *S.pneumoniae* serotypes



Serotypes were available for 24 patients. Isolates included in PCV13 are solid colors; isolate not included in PCV13 is shown in hatched pattern. Serotype 14 is a PCV7 serotype and was isolated in 2001 from a patient with unknown PCV7 history. * Includes 1 isolate reported as 19 nonF.

CONCLUSIONS

- This is the largest case series of pHUS among North American children and the largest collection of serotyped *S. pneumoniae* isolates associated with pHUS.
- Patients with pHUS required high acuity of care, had prolonged hospitalizations, and significant morbidity.
- pHUS was caused by serotypes that are not in PCV7 but are in PCV13.
- PCV13 has potential to reduce the incidence of pHUS.

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