

Invasive *Haemophilus Influenzae* Infections in Children: A Ten Year Study

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Abstract

Background: The rate of *Haemophilus influenzae* type b (HIB) infections has decreased dramatically since the use of HIB vaccines in infants and children. The current prevalence of invasive HIB infections and those due to non-type b *H. influenzae* is not fully known. The objective was to describe the cases of all invasive *H. influenzae* infections and describe the spectrum and severity of clinical disease.

Methods: Retrospective study of all hospitalized patients with culture-proven invasive *Haemophilus influenzae* infections at Nationwide Children's Hospital, Columbus, Ohio, from 2009 to 2018. The electronic health records were reviewed for pertinent demographic, clinical, laboratory data, and outcomes.

Results: There were a total of 59 culture-proven *H. influenzae* infections of which 12 were excluded due to insufficient patient data. The remaining 47 patients (32 [68%] male; 30 [64%] white, 8 [17%] African-American) and their culture results are provided in Table 1. There were 14 (30%) patients with pneumonia and bacteremia, 6 (13%) with meningitis and bacteremia, 2 (4%) with only meningitis, 1 (2%) with bacteremia/meningitis and septic hip, 2 (4%) septic arthritis with bacteremia, 1 (2%) with periorbital cellulitis and bacteremia, and 21 (45%) with only bacteremia. Of the 3 cases of *H. influenzae* type b, 2 had not been vaccinated while 1 received only 1 dose of HIB vaccine.

Conclusion: Invasive *H. influenzae* infections were associated with substantial morbidity and a 2% case-fatality rate.

Background

- ❖ The rate of *Haemophilus influenzae* type b (HIB) infections has decreased dramatically since the use of HIB vaccines in infants and children.
- ❖ The current prevalence of invasive HIB infections and those due to non-type b *H. influenzae* is not fully known.

Objective

- ❖ To describe the cases of all invasive *H. influenzae* infections and describe the spectrum and severity of clinical disease

Methods

- ❖ Retrospective study of all hospitalized patients with culture-proven (from normally sterile sites) invasive *H. influenzae* infections at Nationwide Children's Hospital (NCH), Columbus, OH, from 2009 to 2018
- ❖ The electronic health records were reviewed for pertinent demographic, clinical, laboratory data, and outcomes.
- ❖ Capsular serotyping was performed by the NCH Microbiology Laboratory using monovalent (type b) and polyclonal (types a, c, d, e, f) antisera. Strains were classified by capsular type as encapsulated type b or non-b (a, c, d, e, f), non-typeable (negative for any serotypes a-f), or not typed.
- ❖ The study was approved by the NCH IRB.

Results

- ❖ 59 cases of culture-proven *H. influenzae* infections during the 10 year study period; 12 cases excluded due to insufficient patient data.
- ❖ 47 patients: study population (Table 1, 2), all hospitalized
 - 32 (68%) male; 30 (64%) White, 14 (30%) Black (5, Somalian), 2 (4%) Hispanic, 1 (2%) Asian
- ❖ 18 (38%) patients: none (previously healthy)
- ❖ 29 (61%) patients with underlying medical condition (Table 2)
- ❖ Clinical diagnoses are provided in Figure 1. 2 (4%) patients had septic shock, 7 (15%) acute hepatic failure, 4 (8%) hepatitis, 2 (4%) pancreatitis, 1 (2%) peritonitis with pseudocyst (VP shunt infection)
- ❖ 3 cases of *H. influenzae* type b infection (Table 2): 2, not vaccinated, 1 had received 1 dose of HIB vaccine
- ❖ 30% (14/45) of *H. influenzae* strains were β -lactamase positive.
- ❖ Of 30 β -lactamase negative *H. influenzae* invasive strains tested (1, not done), all were susceptible to ampicillin (one additional β -lactamase negative strain from endotracheal aspirate culture was ampicillin-resistant).

Figure 1. Laboratory-confirmed clinical diagnoses in the 47 patients

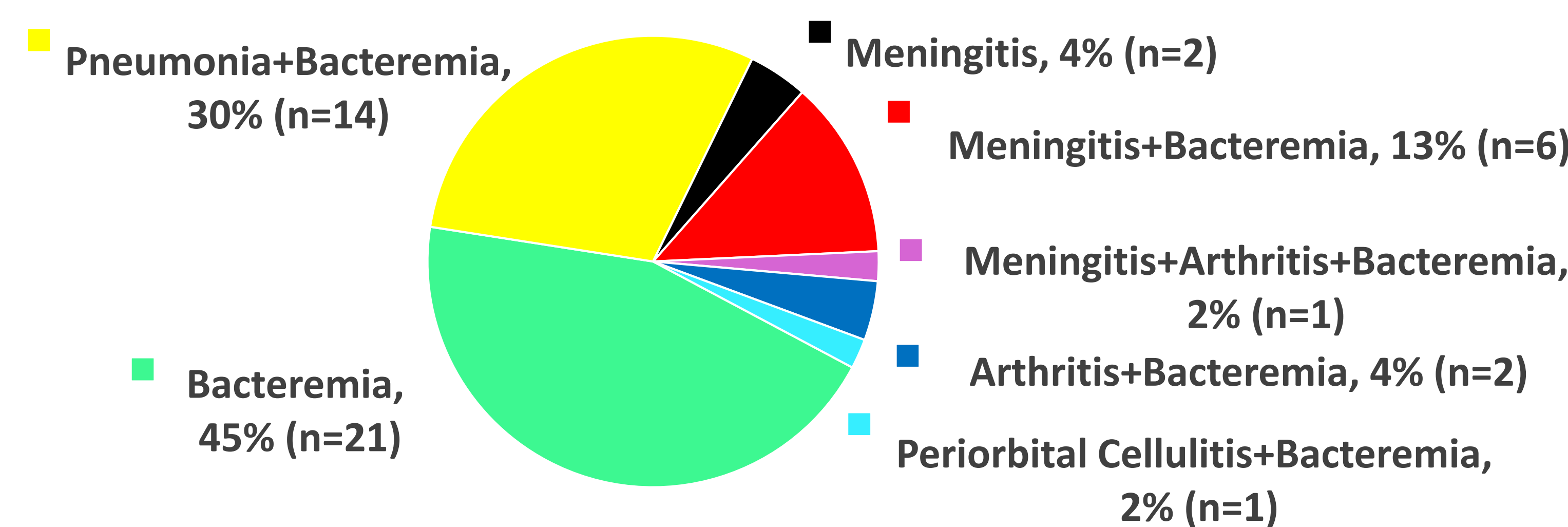


Table 1. Culture source of *Haemophilus influenzae* by serotype distribution and bacterial/viral co-detection among the 47 patients

	Encapsulated		Non-typeable n=30	Not typed n=2	Total n=47
	Type b n=3	Non-b n=12			
Culture source:					
Blood only	1 (33) ^a	5 (41)	27 (90)	2 (100)	35 (75)
CSF only	1 (33)	0	0	0	1 (2)
Blood and CSF	1 (33)	5 (41)	0	0	6 (13)
CSF and peritoneal fluid	0	0	1 (3)	0	1 (2)
Blood and synovial fluid	0	2 (16)	0	0	2 (4)
Blood and eye discharge	0	0	2 (6)	0	2 (4)
Bacterial coinfection ^b	1 (33)	0	5 (16)	2 (100)	8 (17)
Viral detection ^c	3 (100)	4 (33)	14 (46)	1 (50)	22 (47)

^a Number in parentheses, percent

^b Methicillin-resistant *Staphylococcus aureus* (n=1), methicillin-sensitive *S. aureus* (n=1), *Escherichia coli* (n=3), *Klebsiella pneumoniae* (n=2), *Mycobacterium avium* (n=1), *Toxoplasma gondii* (n=1), *Clostridium difficile* (n=1)

^c Adenovirus (n=4), coronavirus (n=4), rhinovirus/enterovirus (n=10), influenza A (n=2) and B (n=1), herpes simplex virus (n=2), respiratory syncytial virus (n=6), human metapneumovirus (n=1)

Table 2. Clinical characteristics of the 47 patients

	Encapsulated		Non-typeable n=30	Not typed n=2	Total n=47
	Type b n=3	Non-b n=12			
Age:					
<6 months	0	0	7 (23) ^a	1 (50)	8 (17)
6-12 months	2 (67)	8 (66)	7 (23)	0	17 (36)
1-5 years	1 (33)	4 (33)	6 (20)	1 (50)	12 (25)
6-8 years	0	0	8 (26)	0	8 (17)
9-17 years	0	0	0	0	0
≥18 years	0	0	2 (6)	0	2 (4)
Underlying medical conditions:					
Prematurity	0	0	8 (26)	1 (50)	9 (19)
Congenital heart disease	0	2 (16) ^b	4 (13) ^{c,d}	0	6 (12)
Asthma	0	2 (16)	3 (10)	0	5 (10)
Cerebral palsy	1 (33)	0	3 (10)	0	4 (8)
Down syndrome	0	2 (16)	2 (6)	0	4 (8)
Laryngotracheomalacia / Pierre Robin syndrome	0	0	3 (10)	0	3 (6)
Splenectomy / Spleen dysfunction	0	2 (16)	1 (3)	0	3 (6)
Acute lymphoblastic leukemia (ALL)	0	0	1 (3)	0	1 (2)
Metabolic disorder	0	0	1 (3)	0	1 (2)
Restrictive lung disease	0	0	1 (3) ^d	0	1 (2)
PICU	2 (67)	3 (25)	20 (66)	1 (50)	26 (55)
NICU	0	0	3 (10)	1 (50)	4 (8)
Clinical diagnoses:					
Bacteremia	1 (33)	3 (25) ^e	15 (50)	2 (100)	21 (45)
Pneumonia + Bacteremia	0	1 (8)	13 (43) ^f	0	14 (30)
Meningitis	1 (33) ^g	0	1 (3)	0	2 (4)
Meningitis + Bacteremia	1 (33)	5 (41)	0	0	6 (13)
Meningitis + Arthritis + Bacteremia	0	1 (8)	0	0	1 (2)
Arthritis + Bacteremia	0	2 (16)	0	0	2 (4)
Periorbital Cellulitis + Bacteremia	0	0	1 (3)	0	1 (2)
Death	0	0	1 (3)	0	1 (2)

^a Number in parentheses, percent

^b Down's syndrome with atrioventricular canal defect (2, encapsulated non-b; 1, non-typeable)

^c 2, DiGeorge syndrome

^d Trisomy 18

^e 1, pericarditis

^f 2, pleural effusion

^g 1, hydrocephalus, status epilepticus, and unilateral sensorineural hearing loss

Conclusions

- ❖ The majority of patients with invasive *H. influenzae* infections were ≤5 years of age (79%) and had underlying medical conditions (61%).
- ❖ The majority of infections were due to capsular serotypes other than b (27%) and to non-typeable strains (67%).
- ❖ *H. influenzae* infections were associated with substantial morbidity (meningitis, 19%; PICU admission, 55%) and a 2% case-fatality rate.

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