original article

Retrospective review of invasive pediatric pneumococcal diseases in a military hospital in the southern region of Saudi Arabia

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BACKGROUND AND OBJECTIVES: Invasive pneumococcal disease (IPD) is associated with high case-fatality rates and serious chronic sequelae. The objective of this study was to assess the magnitude of invasive pneumococcal infections in a pediatric population without universal vaccination during childhood in a single hospital.
DESIGN AND SETTING: Retrospective review of all pediatric cases of invasive pneumococcal infection during a 7-year period.
PATIENTS AND METHODS: We reviewed the microbiological and clinical records of cases of IPD in children <13 years of age admitted to the Armed Forces Hospital, Southern Region, Saudi Arabia.
RESULTS: We identified 41 patients with IPD; 27 (66%) were <2 years of age. Four (50%) of those with pneumoccal meningitis were <2 years of age. The case fatality was 3 of 41 (7.3%) due to meningitis and 2 of 41 (5%) due to sepsis, with a case fatality of 5 (12%) due to meningitis and sepsis. Nine patients developed sequelae; of those with meningitis, 5 (73%) developed sequelae. Only 15 (41%) patients had predisposing medical conditions. The overall intermediate and high levels of pneumococcal resistance to penicillin and ceftriaxone were found to be 48.5%, 2.4% and 2.4%, 0%, respectively. None of the pneumococcal isolates were serotyped, and none of the patients had been vaccinated against pneumococcal infections in our hospital.
CONCLUSIONS: Despite the presence of a targeted immunization program, a considerable number of cases of invasive pneumococcal infections were reported among our pediatric population over a period of 7 years. Prospective studies in serotypes and antibiotic resistance from the southern region are needed to provide baseline information for the formulation and evaluation of a national prevention and control program.

Streptococcus pneumoniae infections are caused by 90 serotypes grouped into 46 serogroups based on immunological similarities.[1] *S pneumoniae* remain a leading cause of serious illness among young children worldwide and are the most frequent cause of pneumonia, bacteremia, sinusitis and acute otitis media.[2-5] It has been reported that age is clearly a risk factor for invasive infections, with such infections being most frequent in the initial years of life.[6] A high incidence of pneumococcal bacteremia has been repeatedly documented in children less than 2 years of age. The incidence is generally low among teenage children and young adults, but tends to increase in middle age, and peaks again among men and women in their 70s. Host-related factors also contribute to susceptibility to pneumococcal infection. Underlying heart and central nervous system conditions, as well as malignancies, are frequently identified in patients who develop invasive pneumococcal infections.[7] Individuals with underlying immune abnormalities, like human immunodeficiency virus (HIV) infection, are also at increased risk of invasive pneumococcal infections.[8] In this study, we reviewed records of invasive pediatric *S pneumoniae* infections at the Armed Forces Hospital, Southern Region, Saudi Arabia, over a 7-year period. The objective of this study was to assess invasive pneumococcal infections in a pediatric population without universal vaccination during early childhood in a single hospital.

PATIENTS AND METHODS

This study retrospectively identified all pediatric cases of invasive pneumococcal infection during a 7-year pe-

Table 1. Distribution of invasive pneumococcal infections by age group.

Age (years)	No. (%) of cases
<1	16 (39)
1<2	11 (27)
2-5	5 (12)
6-12	9 (22)
Total	**41 (100)**

Table 2. Distribution of invasive pneumococcal infections and their outcome by age and body site.

Age (years)	No bacteremia		Bacteremia with			Total (n= 41)
	Meningitis	Arthritis	No focus	Sepsis	Pneumonia	
	S (D)	S (D)	S (D)	S (D)	S (D)	S (D)
<1	3 (3)	1 (0)	5 (0)	0 (1)	3 (0)	12 (4)
1<2	1 (0)	0 (0)	5 (0)	0 (0)	5 (0)	11 (0)
2-5	1 (0)	0 (0)	0 (0)	0 (0)	4 (0)	5 (0)
6-12	3 (0)	0 (0)	3 (0)	0 (1)	2 (0)	8 (1)
Total	**8 (3)**	**1 (0)**	**13 (0)**	**0 (2)**	**14 (0)**	**36 (5)**

S: number of survivors, D: number of deaths.

riod at the Armed Forces Hospital, Southern Region. This hospital serves military personnel and their immediate family members. During this study period, the pneumococcal immunization program at this hospital targeted only children at high risk of invasive infection.

The electronic laboratory information system at the Central Microbiology Laboratory at the Armed Forces Hospital, Southern Region, was used to identify all pediatric patients between 0 and 12 years of age with positive *S pneumoniae* culture from any sterile body site, spinal fluid, pleural fluid or ascitic fluid) between January 2001 and December 2007. Strains isolated from sputum or mucosal sites such as the conjunctiva, middle ear or sinus cavities were not included in this study. A medical chart review was subsequently performed on each case.

The isolates were determined to be *S pneumoniae* by colonial morphology, optochin susceptibility and bile solubility.[9] The susceptibility of *S pneumoniae* strains was determined using broth microdilution methods consistent with the guidelines of National Committee for Laboratory Standards[10] (Sensititre HPB; Trek Diagnostic Systems, UK) using Muller-Hinton broth (SPML, Saudi Arabia) supplemented with 5% lysed horse blood. The quality control strains *S pneumoniae* ATCC 49619 were included in each run. Clinical Laboratory Standard Institute (CLSI) (2001) breakpoints for penicillin, ceftriaxone, vancomycin, cotrimoxazole, tetracycline, clindamycin, rifampin, lenozolid and other antibiotics were used to interpret susceptibility results.[11] For analysis, the study population was divided into 4 age groups (**Table 1**).

RESULTS

Over the 7-year period, we had 41 patients with invasive pneumococcal diseases with ages ranging from 2 months to 12 years. Almost two thirds of the severe cases were in patients within the first two years of life, which is consistent with published data in the literature. The disease spectrum included meningitis in 11 (27%) cases; bacteremias in 13 (32%); sepsis in 2 (05%); bacteremia with pneumonia in 14 (34%) cases, and 1 (2.3%) case with arthritis of the left elbow. Seven of 11 (63%) patients with meningitis were less than 2 years of age, 16 of 41 patients were less than 1 year of age (**Table 1**), and the case fatality was 3 of 41 (7.3%) due to meningitis and 2 of 41 (5%) due to sepsis (**Table 2**). Seventy-five percent of the patients with meningitis who survived had chronic sequelae, including bilateral sensorineural hearing loss in 3 (37.5%) cases; sixth nerve palsy in 1 (12.5%) case, convulsion in 2 (25%) cases, hydrocephalus with ventriculoperitoneal shunt insertion in 1 (12.5%) case, delayed motor development in 2 (25%) cases, and some patients had more than one morbid condition. Apart from age as the major factor, other predisposing medical conditions were present in 15 (36.6%) cases (**Table 3**).

A total of 31 (75.6%) cultures out of 41 demonstrated intermediate or full resistance to at least one antibiotic. Of patients with meningitis, 45% were intermediately resistant to penicillin, and none was resistant to ceftriaxone or to vancomycin. Of patients without meningitis, 52% were intermediately resistant to penicillin, and only 1 (3.5%) patient was fully resistant. One (3.45%) culture was intermediately resistant to ceftriaxone, and none was resistant to vancomycin. Out of all resistant cultures, resistance to individual antibiotics is shown in **Table 4**.

DISCUSSION

The incidence of pneumococcal infection varies widely worldwide and even varies within countries.[12] The incidence of invasive pneumococcal disease is influenced by age, immunization status and ethnic background.[13] According to the medical chart review, none of our patients had received any form of the pneumococcal vac-

cines. Invasive pneumococcal disease was found to be most prevalent early in life, with 39% of the patients aged 12 months. Our results further confirm the presence of a considerable number of cases of pneumococcal infections in young children, which has also been observed in other studies.[14,15]

The number of cases was relatively small, probably because this hospital serves families of military recruits only and a vaccination program for high-risk patients was implemented only 3 years ago with the 7-valent conjugated pneumococcal vaccine; and 10 years ago, with the 23-valent pneumococcal vaccine for those older than 2 years of age. Another reason may that the population served by our hospital is also eligible to be treated at the Ministry of Health hospitals.

The case fatality was 12.2%; and for those who survived the disease, mainly meningitis, 75% had chronic sequelae affecting his/her quality of life, mostly because of a delay in seeking medical help and nature of the disease. Although the number of isolates was low, the results of antibiotic-susceptibility testing from this study are similar to those of several previous studies from Saudi Arabia and the region except for penicillin, which is more sensitive in our study.[16-19] Unfortunately, serotyping was not done for any of the isolates because of the lack of facility to do so, but a recent study by Shibl et al (personal communication) showed that 83% of the pneumococcal isolates found in the southern region are covered by the 7-valent conjugated pneumococcal vaccine program.

In conclusion, although in this study the small number of isolates and lack of serotyping are major limiting factors, it showed very obviously the high magnitude and impact of invasive pneumococcal infections in our pediatric population despite the presence of a targeted immunization program. Therefore, adding the 7-valent conjugated pneumococcal vaccine to the national immunization program is a highly justifiable and welcome decision. Prospective studies in serotypes and antibiotic resistance from the southern region are needed to fill in the information gap in our study and to make an important information baseline for the formulation and evaluation of a national prevention and control program.

Table 3. Predisposing medical conditions in different age groups.

Age (years)	Chronic lung disease	Congenital heart diseases	Renal diseases	Splenic dysfunction	Immuno-deficiency state	Previous history of pneumococcal diseases
<1	1	2				
1 < 2		1			1	1
2-5	1	1		2		1
6-12		1	1[a]	2[b]	1[c]	
Total	**2**	**4**	**1**	**4**	**2**	**2**

[a]Nephrotic syndrome; [b]Sickle cell disease; [c]Non-Hodgkin lymphoma (post bone marrow transplant).

Table 4. Antimicrobial resistance.

Antibiotic	Total sensitivity tests	Resistance (n, %)
Cotrimoxazole	38	24 (63.2)
Tetracycline	39	15 (38.5)
Erythromycin	48	16 (33.3)
Penicillin	49	1 (2.0)

χ^2=40.5; *P*<.0001

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