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A possible outbreak of *Streptococcus pneumoniae* invasive infection in children in Ibadan, Nigeria

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Summary

Streptococcus pneumoniae is an important aetiological agent of infections in children worldwide. The isolation rate of the bacteria has been strikingly low in the recent past in Nigeria. In a study of 1000blood samples from patients, out of which 642 were from children in Ibadan between May 1999 and December 2000, 14 isolates of *Streptococcus pneumoniae* were obtained (a prevalence rate of 1.4%). All the isolates were from children and clustered between 13th September and 22nd October 1999, period of 40 days and thereafter no more organisms were isolated. Antibiotic sensitivity testing of all isolates by disc diffusion method showed resistance to cotrimoxazole, tetracycline and penicillin to be 14%, 21% and 36% respectively. All the isolates were sensitive to chloramphenicol and erythromycin. No fatalities were recorded among the children. This may have indicated an outbreak and underscores the urgency for an epidemiological database in Nigeria to ascertain the exact clinical burden of *S. pnemoniae* infections so as to determine the appropriate vaccine strategies required for Nigerian children.

Keywords: *Streptococcus pneumoniae aetiological, infections, worldwide.*

Résumé

Le streptococcies Pneumonie est un agent étiologique important d'infection chez les enfants du monde entier. Le taux d'isolation était tellement inférieur dans ces derniers temps. A travers une étude de prélèvement de sang auprès des 1000 malades dont 642 était des enfants à Ibadan entre la période de mai 1999 et décembre 2000, 14 isolés de streptococcies pneumonie sont prises (1,4% taux prévalent). Tous les isolés venaient des enfants rassemblés entre 13 septembre et 22 octobre 1999; une période de 40 jours. Après ces jours aucun organisme n'étaient isolé. L'expérimentation de la sensibilité antibiotique de tous les isolés par méthode de la diffusion de disque a montré une résistance de 14%, 21% et 36% respectivement Cotomaxazole, Tétracycline, Pénicilline. Tous les isolés avait la sensibilité au Chloramphenicol et Erythromycin. Il n'y avait pas de morts parmi les enfants. Il se peut que cela indique un épidémie et mettre en évidence le besoin urgent pour entreprendre une base de donné épidémiologie au Nigeria pour déterminer le problème clinique exact des infections de S. pneumonie afin de déterminer la stratégie de vaccination requise pour les enfants nigérians.

Introduction

Streptococcus pneumoniae (*S. pneumoniae*) is an important aetiological agent of invasive infections in children worldwide [1-4]. Pneumonia and meningitis caused by the encapsulated strains of *S. pneumoniae* and *Haemophilus influenzae* are major causes of morbidity and mortality in children less than 5years old in developing countries [4]. It is estimated that nearly 4million of the 15million deaths worldwide each year in children younger than 5years old are caused by pneumonia [5-7]. Case–fatality rates of between 5 and 32% have been reported for pneumococcal infections [8]. Benzyl-penicillin used to be drugs of choice for the treatment of pneumococcal disease up to the 1960s [9,10]. By the 1970s there were occasional reports of resistant strains, and by the 1980s pneumococci resistant to penicilin and other antibiotics had become a global problem [11,12]. Because of the high rate of complications and death associated with *S. pneumoniae* infection [13] and rapidly increasing antibiotic resistance in the bacteria [14], development and use of effective pneumococcal vaccines is of high priority [15].

Isolation rates in the recent past have been low in many hospitals in Nigeria [6,17]. The reasons for this are not fully known but may be due in part to poor laboratory techniques and high level of self-medication on the part of patients before presenting at the hospital. This study was therefore designed to determine the number of children seen with invasive pneumococcal disease in hospital in Ibadan.

Materials and methods

Between May 1999 and December 2000, venous blood was aseptically collected from 1000 patients with fever from two major hospitals in Ibadan. Brain-heart infusion broth (lab M), 5% blood agar and heated blood agar (brain heart infusion as a base and 5% horse blood) were used to isolate *S. pneumoniae* from the blood of patients. Ten–fifteen millilitres of blood were collected from adults and 5ml from children. Each 5ml aliquot of blood was inoculated into a separate bottle containing 50ml of brainheart infusion broth with 0.05% sodium polyanetholesulphonate. Subculture unto fresh sheep blood agar and chocolate agar plates was performed at 24, 48 and 96hr and whenever there was visible growth in the bottles. A terminal subculture was done on the 7th day for all bottles with no evidence of growth. The plates were incubated at 37°C in air (blood agar) or 5% CO (chocolate agar) for 48hrs.*S. pneumoniae* was identified by standard method [18].

Antibiotic sensitivity of the isolates was carried out on Mueller Hinton Agar (Oxoid) supplemented with sheep blood by disc diffusion method using mastrings (Mast Diagnostics, Merseyside, England) with disc containing antibiotic concentrations specified by the National Committee for Laboratory Standards (NCCLS) [19]. Diameter of zones of inhibition was measured and interpreted by NCCLS standard.

Results

During the study period, no *S. pneumoniae* was isolated from the adults. Six hundred and forty-two of the 1000 patients screened were children between 0 and 7years of age. Four hundred and four of the children were from a tertiary hospital and 238 from a general hospital. *S. pneumoniae* was isolated from 14 (1.4%) of the 1000 screened patients, all of whom were children translating into 14(2.1%) of the 642 children, 10 from a general hospital and 4 from a tertiary hospital. All the isolation were from children between 6months and 7years of age with most

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isolates, 10 (71%), isolated from children below the age of 2years (Table 1). Six isolates were from male children, a male female ratio of 1:1.34. Six (43 %) of the 14 patients had pneumonia, and the rest had septicaemia. Four of the *S. pneumoniae* positive children had sickle cell anaemia. All the children recovered and were discharged.

Table 1: Age distribution of *S. pneumoniae* positive patients

Age (months)	Number (%) positive
6-11	4 (29)
12-23	6 (43)
24-59	2 (14)
>60	2 (14)
Total	14(100)

All the isolates were recovered between September and October 1999, a period of 40 days only. The sensitivity of all the isolates to penicillin, chloramphenicol, tetracycline, erythromycin and cotrimoxazole was determined. A total of 9 (64%) were sensitive to all antibiotics tested (Table 2). All the isolates were sensitive to chloramphenicol and erythromycin while 2 (14%) isolates were resistant to penicillin only and 2 (14%) of the isolates were resistant to three antibiotics (penicillin, tetracycline and cotrimoxazole). Resistance to penicillin, tetracycline and cotrimoxazole occurred in 36%, 21%, and 14% of the isolates, respectively (Table 3).

Table 2: Antibiotic resistant patterns of the 14 *S. pneumoniae*

Patterns	Number (%)
All sensitive	9 (64)
Pen^R	2 (14)
$Pen^RTet^RCot^R$*	2 (14)
Pen^RTet^R	1 (7)

**Pen = penicillin; Tet=tetracyclin; Cot=cotrimoxazole; R=resistance*

Table 3: Antibiotic resistant of the 14 *S. pneumoniae* isolates

Antibiotics	Number (%) resistance
Penicillin	5 (36)
Chloramphenicol	0 (0)
Tetracycline	3 (21)
Erythromycin	0 (0)
Cotrimoxazole	2 (14)

Discussion

Studies have shown that the bacterium is an important cause of pneumonia, meningitis and septicaemia in children [4,20,21]. This study shows *S. pneumoniae* is also an important aetiological agent of infection in Nigerian children. The blood culture isolation rate of 2.1% from the children is comparable to that from some developing countries. For example, an isolation rate of 3.5% has been reported from Gambia [22] and 1.3% from the Philippines [4]. The apparent clustering of *S. pneumoniae* isolates (fourteen) obtained within a short period of time (40 days) between September and October may be indicative of an outbreak. Unfortunately no typing of the isolates was done to confirm this. Also the seasonal variation that has been reported for pneumococcal infections may have been responsible though less likely because the isolates were obtained at an off peak season for pneumococcal infections. *S. pneumoniae* exhibits peak incidences during the cold rainy months July-September) and the cold months (January/February) of the dry season in Lagos, Nigeria [23]. But the incidence is generally higher during the dry season than rainy season. Temperature and humidity appear to influence prevalence of pneumonia, and in countries where the most abrupt and severe changes occur, the incidence of the disease is correspondingly high during such times [24,25]. Many of the *S. pneumoniae* patients (43%) had pneumonia. Pneumonia is an important cause of morbidity and mortality in children in developing countries. It is estimated that nearly 4 million of the 15 million deaths worldwide each year in children younger than 5 year of age are caused by pneumonia [5-7]. Several studies have demonstrated the significant role played by *S. pneumoniae* in the aetiology of pneumonia [4,26]. Approximately 71% of the *S. pneumoniae* disease in this study occurred in children less than 2 years of age, which is at a clearly higher age than in some developing countries [4,20]. This coupled with the fact that close to one-third of the disease was observed during the first 12months of life, probably indicates requirement for early vaccination, if the new conjugate vaccines against this pathogen are to be used to prevent *S. pnuemoniae* disease in Nigeria.

Antibiotic resistance in *S. pneumoniae* appears to be a problem in our environment. The observed resistance rate of between 14% for cotrimoxazole and 36% for penicillin is much higher than that from some developing countries [4,27] and this may be attributed to the high rate of antibiotic abuse in the country. Resistance of *S. pneumoniae* is an emerging problem worldwide [14] including some African countries like South Africa [28] and Zambia [29]. There is the need therefore for constant monitoring of antibiotic resistance in *S. pneumoniae* as the treatment of multiple resistant strains is becoming a major challenge globally [14].

The poor isolation rate of *S. pneumoniae* in many laboratories in Nigeria may be due to poor laboratory techniques [30] and prior antibiotic usage in patients which leads to resistance to these organisms [4,31,32]. Almost all antibiotics can be bought over the counter in Nigeria without prescription for individual usage at convenience. This emphasizes the need for an easier method such as detection of antigen in clinical specimens by latex agglutination or counterimmuno electrophoresis, other than the blood culture method to determine the aetiology of bacterial infection [4,26,33].

It is interesting that 4 (29%) of the *S. pneumoniae* patients were homozygous for sickle cell haemoglobin. It has been observed that patients homozygous for sickle cell haemoglobin are at a higher risk for pneumococcal infections than those with other haemoglobin types in the population [34,35].

This study shows therefore that *S. pneumoniae* is still an important cause of invasive disease in Nigeria and underscores the need for full epidemiological data to identify the prevalent serotypes associated with disease, monitor the antibiotic resistance profile of the organism and identify the high- risk populations. These are all necessary for the formulation of vaccination strategies [4,36].

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