Pneumococcal Meningitis in Jamaican Children

H Trotman[1], O Olugbuyi[1], M Barton[1], D McGregor[2], S Thomas[2]

ABSTRACT

Objective: *To describe the clinical features and outcome of pneumococcal meningitis in Jamaican children.*

Methods: *All patients admitted to the Bustamante Hospital for Children, during the period 1995–1999, who had pneumococcus isolated from cerebrospinal fluid (CSF) or pleocytosis in association with a blood culture isolate of pneumococcus were selected. Demographic, clinical and laboratory data were collected.*

Results: *Twenty-five (23%) of 111 patients with pneumococcal infections satisfied criteria for meningitis. The median age was 8 months (range 0.5–60 months). There were 4 (16%) cases of sickle cell disease, 2 (50%) of whom were first diagnosed during the current illness. This represents a 53-fold increased risk of pneumoccocal meningitis in patients with Sickle-cell disease based on population prevalence rates. Oxacillin resistance occurred in 3 (12%) patients, one of whom died. Mortality rate was 12% (3) with all deaths occurring in infants < 1 year. Poor outcome occurred in 36% (9) of the patients. Of the (35%) 8 survivors who had follow-up evaluation, (38%) 3 had documented hearing loss.*

Conclusions: *Meningitis is a common clinical syndrome of invasive pneumococcal disease, occurring in 23% of cases resulting in mortality and high morbidity among Jamaican children. Local seroepidemiological studies are urgently needed to inform national vaccine decisions. As an interim plan, policymakers should consider a risk-based strategy to vaccine prophylaxis that will ensure that high risk groups such as children with sickle cell disease are offered currently available conjugate pneumococcal vaccines.*

La Meningitis Pneumocócica en Niños Jamaicanos

H Trotman[1], O Olugbuyi[1], M Barton[1], D McGregor[2], S Thomas[2]

RESUMEN

Objetivo: *Describir las características clínicas y evolución de la meningitis meningocócica en niños jamaicanos.*

Métodos: *Se escogieron todos los pacientes que ingresaron al Hospital Infantil Bustamante, durante el período de 1995-1999, y que tuvieron pneumococos aislados del líquido cefalorraquídeo (LCR) o pleocitosis asociada con un aislado de pneumococos en un cultivo de sangre. Se recogieron los datos demográficos y clínicos, así como los datos de laboratorio.*

Resultados: *Veinticinco (23%) de los pacientes con infecciones pneumocócicas correspondían a los criterios de la meningitis. La edad promedio fue de 8 meses (rango 0.5 – 60 meses). Hubo 4 (16%) casos de anemia falciforme, 2 (50%) de los cuales fueron diagnosticados primeramente durante la enfermedad corriente. Esto representa un aumento de riesgo de meningitis meningocócica 53 veces mayor en pacientes con anemia ciclémica, teniendo en cuenta las tasas de prevalencia poblacional. Se halló resistencia a la oxacilina en 3 (12%) pacientes, uno de los cuales murió. La tasa de mortalidad fue del 12% (3), correspondiendo todas las muertes a infantes < 1 año. Resultados pobres se produjeron en (9) 36% de los pacientes. De los 8 (35%) supervivientes que tuvieron evaluación de seguimiento, 3 (38%) tuvieron pérdida de la audición documentada.*

From: [1]Department of Obstetrics, Gynaecology and Child Health, The University of the West Indies, Kingston 7, Jamaica and [2]Bustamante Hospital for Children, Arthur Wint Drive, Kingston 5, Jamaica, West Indies.

Correspondence: Dr Helen Trotman, Department of Obstetrics, Gynaecology and Child Health, The University of the West Indies, Kingston 7, Jamaica, West Indies. Fax: 876-927-1446 Email: helen.trotmanedwards@uwimona.edu.jm

Conclusiones: *La meningitis es un síndrome clínico común de la enfermedad pneumocócica invasiva, que tiene lugar en 23 % de los casos, y que trae por consecuencia mortalidad y una alta morbilidad entre los niños jamaicanos.*

Se requieren con urgencia estudios seroepidemiológicos locales a fin de tener información para las decisiones nacionales sobre las vacunas. A modo de plan provisional, los encargados de trazar las políticas deben considerar una estrategia de riesgo para la profilaxis de vacuna, a fin de asegurar que los grupos de alto riesgo, tales como los niños con anemia falciforme, puedan tener a su alcance las vacunas pneumocócicas conjugadas actualmente disponibles.

West Indian Med J 2009; 58 (6): 586

INTRODUCTION

Prior to the introduction of the conjugate pneumococcal vaccine, pneumococcal invasive disease was one of the leading causes of morbidity and mortality in young children with serious acute bacterial infections in developed and developing countries alike. Although dramatic reductions in disease incidence have occurred in several developed countries following vaccine introduction, the disease continues to contribute to childhood morbidity and mortality in many developing countries where no vaccine prophylaxis programmes have been implemented. (1–4) Most of the morbidity and mortality related to this disease occurs in patients with meningitis. Case-fatality rates of 6–20% have been reported for first world countries and even higher rates occur in developing countries where onset of disease occurs very early in infancy and medical attention is usually sought later in the course of illness (2, 5).

Studies describing clinical, laboratory and prognostic features of pneumococcal meningitis originate mainly from developed countries and very scant data exist for developing countries (5, 6).

We describe the demographic, clinical and laboratory features associated with pneumococcal meningitis in patients with this disease who were admitted to The Bustamante Hospital for Children over a five-year period.

SUBJECTS AND METHODS

The Bustamante Hospital for Children serves children living in Jamaica's capital city of Kingston, in addition to accepting referrals from all over the island. Using laboratory records, all patients admitted to the Bustamante Hospital for Children from January 1, 1995 to December 31, 1999, in whom pneumococcus had been cultured from a normally sterile body fluid were identified. Information on patient's age, gender, clinical features, laboratory findings, resistance pattern, treatment and outcome were obtained using a precoded questionnaire. Patients with meningitis were then selected for detailed review.

Pneumococcal meningitis was defined as the isolation of *Streptococcus pneumoniae* (*S pneumoniae)* from cerebrospinal fluid or the presence of more than 10 white blood cells in the CSF associated with *S pneumoniae* in the blood. Poor outcome was defined as mortality or significant morbidity detected at the time of discharge or in the first 3 months of follow-up. A patient was considered to have significant morbidity if abnormal neurological findings such as focal signs, hydrocephalus, deafness or other cranial nerve deficits were noted.

STATISTICAL ANALYSIS

Descriptive analyses were performed using the SPSS statistical programme, version 11. Ethical approval for the conduct of this study was granted by The Bustamante Hospital for Children and Faculty of Medical Sciences, The University of the West Indies/The University Hospital of the West Indies Ethics Committee.

RESULTS

Twenty-five children were documented to have pneumococcal meningitis during the study period. Their ages ranged from two weeks to five years with a median age of eight months. There were 13 (52%) males and 12 (48%) females.

Homozygous sickle cell (SS) disease was documented in four (16%) children (age range 9 months – 4 years), two of whom were diagnosed at the time of the present illness (aged 9 and 18 months respectively). Of the two children previously diagnosed with Hb SS disease neither had received any type of pneumococcal vaccine and only one was on penicillin prophylaxis. No child with Hb SS disease died. Given the proportion of patients with Hb SS disease in this series, this represents a 53-fold increased risk of pneumoccocal meningitis in patients with sickle cell disease based on population prevalence rates.

Nine (36%) children were documented as having poor nutritional status with a weight for age below the 5th centile on the National Center for Health Statistics (NCHS) growth chart; 2 (22%) of these children died. There was one child who had recurrent meningitis and was investigated for an underlying immunodeficiency disorder.

The most common presenting symptoms were fever in 22 (88%), irritability in 14 (56%), vomiting in 13 (52%), drowsiness in 8 (32%) and seizures in 5 (20%). In 10 (40%) patients, there was also evidence of pneumonia; in 8 (32%), there was evidence of an otitis media and 1 (4%) patient also had a septic arthritis. These findings were not mutually exclusive of each other. The mean duration of illness prior to presentation was 2.4 ± 0.8 days (range 1–7 days). No seasonal variation in presentation was noted in this study (Fig. 1).

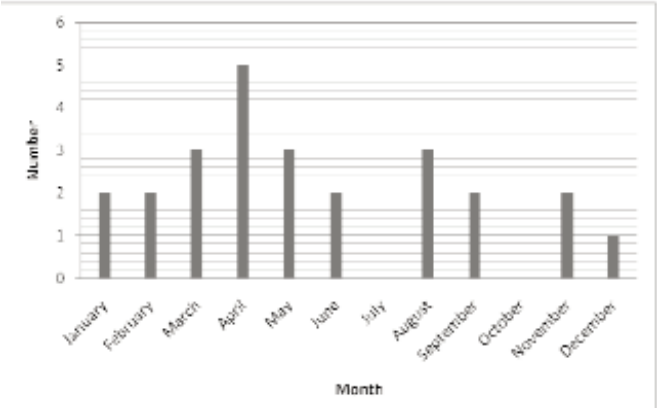

Fig. 1: Seasonal presentation of Jamaican children with pneumococcal Meningitis.

Eighteen (72%) children received a course of dexamethasone within the first 48 hours of admission. Twenty-one (84%) children had a haemoglobin (Hb) level at presentation of less than 10g/dL with a modal Hb level of 7 g/dL (range 5.3 – 13.7 g/dL). Three (12%) children had thrombocytopaenia (platelet < 150 x 10^9/L) at presentation and 8 (32%) had thrombocytosis (platelet > 450 x 10^9/L). White blood cell counts ranged from 4.2 – 35.8 x 10^9/L and 12 (48%) children had an abnormal band count.

S pneumoniae was isolated from both blood and cerebrospinal fluid (CSF) in 19 (76%) children. It was isolated from CSF alone in 4 (16%) children and from blood alone in 2 (8%) children who had associated CSF pleocytosis. Empiric treatment consisted of a penicillin (crystalline penicillin or ampicillin) in combination with chloramphenicol in 23 (92%) cases. On receipt of cultures, therapy was narrowed to monotherapy consisting of penicillin for an average of 10 days duration.

Oxacillin resistance was noted in 3 of 44 isolates (blood and CSF combined). Death occurred in 1 patient with documented oxacillin resistance. This was a 7-month old female infant with dysmorphic features who was < 5th centile for weight for age, she had been premature at birth with a birth weight of < 2.5 Kg. At presentation, she was both anaemic (Hb 7.1 g/dl) and leucopaenic (WBC 4.2 x 10^9/L.) She was commenced on crystalline penicillin and chloramphenicol but died within a week of admission. No resistance to the cephalosporins was noted among the isolates in this study.

The majority of patients 17 (68%) had a hospital stay of 10–14 days, 3 (12%) stayed for 21 days and 2 (8%) stayed for greater than 21 days. Nine (36%) children had documented poor outcome, 3 (12%) children died (2 females and 1 male). All three were less than 9 months of age. Complications were seen in 6 (24%) children; two developed hydrocephalus with spastic hemiparesis, one suffered profound hearing loss as well as focal seizures and one had an isolated hemiparesis. Audiometry was performed in 8 of 15 children (including the child with profound hearing loss), three (38%) had abnormal results. Of the children receiving audiometry testing, 5 (33%) received dexamethasone during the first 48 hours of admission; of these, 2 (40%) had abnormal results. Fig. 2 shows the age distribution by outcome.

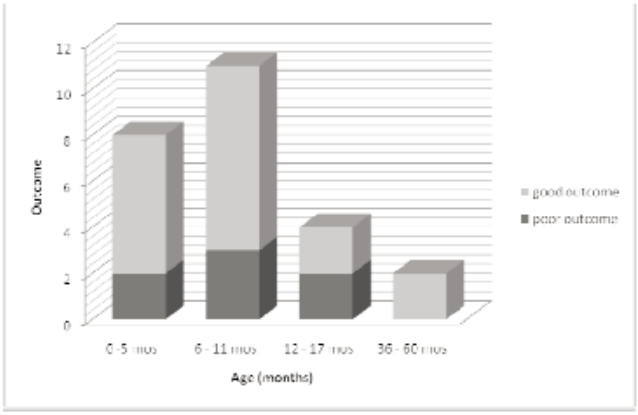

Fig. 2: Age specific distribution by outcome for Jamaican children with pneumococcal meningitis.

Eight out of twenty-two (36%) children defaulted from follow-up, 3 (14%) were followed-up for less than 6 months and 11 (50%) were followed-up for greater than a year.

DISCUSSION

Pneumococcal meningitis accounts for significant morbidity and mortality in young children worldwide (1). Mortality ranges from 7.7% in developed countries to 48% in developing countries. The mortality rate of 12% in this study is comparable with rates reported from developed countries in the pre-vaccine era. The proportion of children with abnormal neurological outcome seen in this study however is far higher approaching the rates reported from developing countries. The very young are particularly prone to the disease because of their limited ability to mount an appropriate response to infection. This is illustrated in this study where the majority of patients were under 1-year of age.

Patients with sickle-cell disease are at increased risk for pneumococcal sepsis because of their functional asplenia. The incidence of haemoglobin SS disease in Jamaica is 315 per 100 000 (7) and given the proportion of patients with SS disease in this series, there is a 53-fold increased risk of pneumoccocal meningitis in patients with sickle cell disease. However, despite their increased risk of acquiring disease, complete recovery without development of sequelae occurred in all patients with sickle cell disease in this study.

Clinical resistance to penicillin (oxacillin) was associated in one case with mortality in this study. Several studies have looked at the impact of penicillin resistance on mortality in pneumococcal meningitis; these studies quote a rate of resistance of 4% to 5% which is comparable to this study (8, 9).

The development of a pneumococcal conjugate vaccine which is immunogenic in young children was a landmark

achievement on the road to successful disease reduction and prevention in young children. In 2000, this heptavalent pneumococcal conjugate vaccine was included in the recommended immunization programme for children in the United States of America (USA) and since then has been introduced to several other countries. (10) The seven serotypes contained in the vaccine have been estimated to represent over 80% of invasive isolates in North America. (10, 11). Given this close correlation, the vaccine has been found to be efficacious with 80% reduction in invasive disease documented in large efficacy trials conducted in the USA (12). In many developed countries, successful reduction in disease rates has occurred since the introduction of the pneumococcal conjugate vaccine (13).

Although the incidence of this disease is reported to be much higher in the developing world, the vaccine has not yet been included in the routine immunization schedules of many developing countries, like Jamaica. The lack of published data on disease epidemiology and serotype distribution in many developing countries has delayed proper economic analysis. Concerns have been raised about the applicability of this vaccine to developing countries, where it is felt that these seven serotypes may not always represent the pattern of invasive disease. However, given the higher rates of invasive pneumococcal disease in these countries as well as the increasing prevalence of HIV, one may argue that even if the vaccine serotype match is 50% which is significantly lower than the 80% match documented for North American countries, there may be benefits given the burden of disease.

Recent concerns with the emergence of disease caused by non-vaccine serotypes such as 19A in countries like the USA, highlight the challenges faced with changing seroepidemiology (14, 15). Nine and thirteen valent vaccines have been developed in an attempt to provide protection against more of the serotypes that commonly cause disease. However, while the conjugate vaccines have been efficacious in reducing disease, the phenomenon of serotype switching now highlights the importance of ultimately developing protein vaccines that will offer protection against *Streptococcus pneumoniae*, regardless of serotype.

Pneumococcal meningitis causes significant morbidity and mortality in Jamaican children particularly in infants. Pneumococcal prophylaxis is the most important way of reducing disease incidence and would require early administration of an efficacious vaccine that appropriately offers protection against the pneumococcal serotypes commonly seen in Jamaica. Further studies to define the local seroepidemiology will need to be done to determine conjugate vaccine applicability. Such studies in conjunction with vaccine cost-effectiveness analyses will provide policy-makers with the needed information to identify the best and most cost-effective strategy for pneumococcal prophylaxis in Jamaican children.

REFERENCES

1. Teele D. Pneumococcal Infections. Textbook of Paediatric Infectious Disease. Elsevier Science Health USA. Feigin-Cherry; 1998://1129–35
2. Usen S, Adegbola R, Mulholland K, Jaffar S, Hilton S, Oparaugo A et al, Epidemiology of invasive pneumococcal disease in the Western Region, The Gambia. Paediatr Infect Dis J 1998; **17:** 23–8
3. Lim LH, Lee WS, Parasakthi N. Childhood invasive pneumococcal disease: a hospital-based study from Malaysia. J Paediatr Child Health 2007; **43:** 366–9.
4. Holliman RE, Liddy H, Johnson JD, Adjei O. Epidemiology of invasive pneumococcal disease in Kumasi, Ghana. Trans R Soc Trop Med Hyg 2007; **101:** 405–13. Epub 2006 Nov 28.
5. Kaplan S. Bacterial Meningitis: Clinical Presentations, Diagnosis and Prognostic Factors of Bacterial Meningitis. Infectious Disease Clinics of North America, (1999) **13:** 1–19
6. Knight-Madden J, Serjeant GR. Invasive Pneumococcal Disease in Homozygous Sickle Cell Disease: Jamaican Experience 1973–1997. J Pediatr 2001; **138:** 65–70.
7. Serjeant GR, Serjeant BE, Forbes M, Hayes RJ, Higgs DR, Leighmann H. Sickle Cell Disease. Brit J Haematol 1986; **64:** 253–62.
8. Arditi M, Mason EO Jr, Bradley JS, Tan TQ, Barson WJ, Schutze GE et al, three-year multicenter surveillance of pneumococcal meningitis in children: clinical characteristics, and outcome related to penicillin susceptibility and dexamethasone use. 1998; **102**: 1087–97.
9. Urwin G, Yuan MF, Hall LM, Brown K, Efstratiou A, Feldman RA. Pneumococcal meningitis in the North East Thames Region UK: epidemiology and molecular analysis of isolates. 1996; **117:** 95–102.
10. Preventing pneumococcal disease among infants and young children. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep, 2000. **49** (RR-9): p. 1–35.
11. Henrichsen, J. Six newly recognized types of Streptococcus pneumoniae. J Clin Microbiol 1995; **33**: 2759–62.
12. Black S. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. Northern California Kaiser Permanente Vaccine Study Center Group. Pediatr Infect Dis J 2000; **19:** 187–95.
13. Whitney CG. Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. N Engl J Med 2003; **348:** 1737–46.
14. Centers for disease Control and Prevention (CDC). Emergence of antimicrobial-resistant serotype 19A Streptococcus pneumoniae-Massachusetts, 2001–2006. MMWR Morb Mortal Wkly Rep 2007 19; **56:** 1077–80.
15. Hicks LA, Harrison LH, Flannery B, Hadler JL, Schaffner W, Craig AS et al. Incidence of pneumococcal disease due to non-pneumococcal conjugate vaccine (PCV7) serotypes in the United States during the era of widespread PCV7 vaccination, 1998–2004. J Infect Dis 2007; **196:** 1346–54. Epub 2007 Oct 4.