Long-term Outcome for Children with Bacterial Meningitis in Rural Papua New Guinea

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Summary

This study was undertaken to evaluate the long-term neurological outcome for survivors of bacterial meningitis in rural Papua New Guinea. Children who were discharged from Nonga Base Hospital in Rabaul with a diagnosis of bacterial meningitis between 1992 and 2000 were evaluated in their home villages or on review at hospital. Neurological and developmental complications were documented. The outcomes for 80 of 121 eligible children were determined; eight had died following hospital discharge and 41 were lost to follow-up. Major neurological sequalae were found in 50 (63 per cent) of surviving children, and 27 (34 per cent) had multiple severe complications. In rural Papua New Guinea meningitis causes high rates of mortality and severe long-term disability in a high proportion of survivors. High-level resistance to chloramphenicol is likely to be part of the reason for this, but widespread availability of third-generation cephalosporins for the treatment of meningitis, although urgently required, will not overcome the other problems of delayed presentation with established complications. There is a need for the introduction of conjugate *Haemophilus influenzae* vaccine, and affordable vaccination strategies against *Streptococcus pneumoniae*. Richer countries could sponsor these vaccines in developing countries, and apply pressure on vaccine producers to lower the costs.

Introduction

Meningitis is a major cause of death and disability among children worldwide. With the advent of conjugate vaccines against the three major pathogens and availability of third generation cephalosporins, the burden is increasingly concentrated in developing countries that cannot afford the vaccines and where expensive antibiotics are not readily available.[1] Follow-up studies in high income countries where case fatality rates from meningitis are low, show that up to one-quarter of survivors have a single significant impairment, such as intellectual disability, spasticity, blindness, deafness or epilepsy, or multiple minor impairments such as educational deficits and behaviour problems.[2] Much less is documented of the long-term outcome for survivors of bacterial meningitis in developing countries, where hospital-case fatality rates range from 18 to 47 per cent.[3–10] We investigated the medium- to long-term outcomes for 80 survivors of childhood meningitis in East New Britain Province in Papua New Guinea.

Papua New Guinea has a population of approximately 5 million, and infant and child mortality rates estimated at 77 and 92 per thousand live births, respectively. Mortality is unevenly distributed, with mortality rates in the capital being half the mortality rate in some remote rural provinces. Nonga Base Hospital is in Rabaul, the main town in the East New Britain Province. The case fatality proportion for childhood meningitis at Nonga Base Hospital throughout the late 1990s averaged about 40 per cent (unpublished Hospital Annual Report).

Materials and Methods

Case finding was done by review of the medical records of all children who had a diagnosis of 'bacterial meningitis' or 'meningitis' and were discharged from hospital between 1 January 1992 and 31 December 2000. The following information was retrieved: name, address, age, sex, dates of admission and discharge, duration of illness prior to admission, clinical signs and symptoms at presentation, cerebrospinal fluid (CSF) results, antibiotics and anticonvulsants given, and the clinical status of

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TABLE 1
Organisms causing meningitis and frequency of neurological complications

Organism	Number	Mean age (months)	Number (%) with any complication at follow-up	Number (%) with multiple severe complications at follow up
No bacteria identified	34	30	21 (62)	12 (35)
S. pneumoniae[a]	26	34	17 (65)	8 (31)
H. influenzae[b]	13	7	7 (54)	4 (31)
N. meningitidis[c]	3	22	3 (100)	2 (67)
E. coli	3	0.3	1	0
S. aureus	1	143	1	1
Total	80	27.4 (SD 40)	50 (63)	27 (34)

Multiple severe complications were defined as two or more major deficits (e.g. a motor deficit such as hemiplegia or spasticity plus a major sensory deficit, e.g. deafness, or communication deficit such as speech delay).
[a]Culture positive ($n = 10$) or identification of Gram-positive diplococci.
[b]Culture positive ($n = 9$) or identification of Gram-negative coccobacilli.
[c]Culture positive ($n = 1$) or identification of Gram-negative diplococci.

the patient on discharge. Children were included in the study if one of the following criteria was met: CSF culture or Gram stain positive for pathogenic bacteria, or CSF white cell count >20 per mm^3 in neonates and >10 per mm^3 in the older children, and CSF protein elevated or glucose low. Children with pre-existing diseases of the central nervous system were excluded from the study.

During 2001 we attempted to follow-up all survivors of meningitis. Radio announcements were made throughout the province requesting children to attend hospital. Children were reviewed through outpatient clinics and home visits. Visits were made to the home village of those who did not attend hospital review. Children were assessed with a full neurological examination and developmental assessment. Developmental milestones were assessed using the Denver Developmental Screening Test. Visual loss was defined as an inability to fix and follow in an age-appropriate way. Hearing loss was defined as no response to sound. Multiple severe complications were defined as two or more major deficits (e.g. a motor deficit such as hemiplegia or spasticity, plus a major sensory deficit, e.g. deafness, or communication deficit such as speech delay). Data was entered into an Excel spreadsheet and analysed using Stata Version 7.

Results

One hundred and twenty-one children were discharged from hospital fulfilling the criteria for a diagnosis of meningitis and were eligible for the study. The long-term outcome for 80 children was determined: eight (10 per cent) had died in the years following their initial infection and 41 (33 per cent) were lost to follow-up. Of the 80 whose outcome was known at follow-up, 48 (60 per cent) were male. The median age at the time of illness was 7 months (IQR 3–31 months). Fifty-eight per cent were under 12 months of age and 66 per cent were under 24 months of age. The mean duration of follow-up was 3.2 years (SD 2.2 years).

During the acute illness, 54 per cent of children were treated with chloramphenicol as the sole antibiotic, while the remainder received various combinations of chloramphenicol with penicillin (10), anti-tuberculous agents (7), gentamicin (5), or a third generation cephalosporin (4). No child received corticosteroids.

Table 1 shows the bacterial aetiology, the ages of children, and the rates of complication according to causative organism. Some neurological sequelae were found in 50 (63 per cent) children, and 27 (34 per cent) had multiple severe complications (Tables 1 and 2).

Discussion

Meningitis causes only about 2 per cent of hospital admissions but 13 per cent of all child deaths in hospitals in Papua New Guinea. The high hospital mortality and the very high rate of long-term neurological complications in survivors demonstrate the generally poor outcome from bacterial meningitis. Rates of adverse outcome in this rural study were substantially worse than were reported from the only tertiary referral hospital in Papua New Guinea in 1992,[11] and greater than in other provincial hospitals where diagnostic facilities, drug supplies and supportive care are better resourced.[12] Rates of early neurological sequelae from meningitis reported from other developing countries are between 22 and 46 per cent.[5,10,13–16]

Poor outcomes occur from meningitis in developing countries because of advanced disease at the time of presentation, co-existing malnutrition, antibiotic resistant bacteria, shortages of effective antibiotics

TABLE 2
Types of neurological complications in children with bacterial meningitis, and the proportion that had multiple complications

Late complication	Number	Number (%) complicated by multiple sequelae
Deafness	23 (29)	11 (48)
Severe speech delay	20 (25)	15 (75)
Delayed developmental milestones	18 (23)	11 (61)
Cerebral palsy	14 (18)	14 (100)
Hemiparesis	9 (11)	8 (89)
Late death	8 (10)	
Ataxia	6 (8)	6 (100)
Epilepsy	5 (6)	3 (60)
Hydrocepalus	2 (3)	2 (100)
Squint	1 (1)	0 (0)

and deficits in case management and staffing. Although antibiotic susceptibility testing was not possible in this study other studies in Papua New Guinea around the same time suggest that over 20–30 per cent of *Haemophilus influenzae* are resistant to chloramphenicol.[9,12,17,18] There is now emerging chloramphenicol resistance among *Streptacoccus pneumoniae* isolates.[17]

Third-generation cephalosporins are difficult to afford in many countries: only 5 per cent of children in this study received these antibiotics. Outcomes are overwhelmingly poor when chloramphenicol-resistant meningitis is treated with chloramphenicol, and worldwide, resistance rates are rising.[12,19,20] Third-generation cephalosporins to treat meningitis in hospitals in Papua New Guinea are urgently required. However, this will not overcome the problems of late presentation and established acute brain injury. Difficult access to hospitals means that expensive antibiotics, which can only be available in hospitals, may make only a small impact on the overall mortality burden. The major long-term solutions to these problems in Papua New Guinea will be preventative, particularly the availability of *H. influenzae* type b (Hib) vaccine and strategies for vaccinating against *S. pneumoniae*.[21] There is an urgent need for developed countries and international agencies to assist in making Hib and pneumococcal conjugate vaccine available to poorer countries.

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