A Bi-centre Study of the Pattern and Evolution of readily detectable Neurological Sequelae of Acute Bacterial Meningitis

GO Akpede*, SO Dawodu**, GEA Iyassere***, SC Olomu****

Summary

Akpede GO, Dawodu SO, Iyassere GEA, Olomu SC. A Bi-centre Study of the Pattern and Evolution of readily detectable Neurological Sequelae of Acute Bacterial Meningitis. Nigerian Journal of Paediatrics 2003;30(1):27. The pattern and evolution of obvious post-meningitic sequelae were determined in 187 post-neonatal children followed up at two tertiary centres. The pattern of sequelae was classified using previously described schemes, as well as by the number of deficits per child. One hundred and eighty-seven children were assessed on discharge, 157 after six weeks of discharge and 134 after three months. The incidence of sequelae was 40/187 (21.4 percent) on discharge versus 23/157 (14.7 percent) after six weeks (p = 0.106) and 18/134 (13.4 percent) after three months (p = 0.069) of follow up. Two (1.4 percent) of the 147 children who were apparently normal on discharge had sequelae on follow up, while two (7.4 percent) of the 27 children discharged with major sequelae, died. Among 17 children who were followed up for at least six months, three (18 percent) at ≥6 weeks to <6 months and ten (59 percent) at ≥6 months (p = 0.034) had persistent deficits. Among the 42 children with sequelae, 29 (69 percent) had major deficits alone (n = 15) or with minor deficits (n = 14). Fifteen (36 percent) had one, 14 (33 percent) two and 13 (31 percent) ≥3 deficits. There was full or partial resolution of deficits in 15/19 (79 percent) children with sequelae who were treated with and in 6/15 (40 percent) (p <0.05) who were not treated with dexamethasone on admission. There was no significant relationship between the pattern and evolution of sequelae and selected characteristics of the acute illness including its severity, pattern of aetiological agents and response to initial antibiotic therapy. However, characteristics of the acute illness were significantly (p <0.01) associated with a high incidence of sequelae.

Introduction

MOST reports on acute bacterial meningitis in developing countries have focussed on the incidence, presentation, the pattern and susceptibility of aetiological agents to antimicrobial drugs, and their influence on the incidence of an adverse outcome. This focus is relevant; first, the severity of illness at diagnosis is the principal determinant of the incidence of neurological sequelae;1,3 secondly, the risk of sequelae differs according to the aetiological agents;4 and thirdly, treatment failure is associated with an increased incidence of adverse outcome.5,6 However, knowledge of the pattern and evolution of deficits, and their relationship to aspects of the acute illness is also important, but has received only limited attention. This can determine the need for preferential management practices and rehabilitation. Some data on the pattern of sequelae are available in the form of studies of the general pattern of neurologic diseases.7 This may not be representative of children who have had meningitis.
More specific reports\(^8\) on post-meningitic sequelae have methodological limitations which might limit the interpretation of the data and the conclusions. First, the pattern of sequelae is not described beyond providing a glossary of the individual deficits. Secondly, only the resolution of individual deficits, which might not be representative of the resolution of deficits in children with multiple deficits, nor indicative of the evolution of the pattern of deficits, is described. Thirdly, some of the studies are based on referrals of children with post-meningitic sequelae and not on a cohort followed up from discharge. There is also a paucity of data from tropical Africa on the benefits and constraints to the use of dexamethasone in meningitis.

The aims of the present study were (a) to define the pattern and evolution of neurological deficits in a cohort of children followed up from discharge, (b) to determine the effect of selected indices of the acute illness, such as severity, on the pattern and evolution of deficits, and (iii) to determine the impact of dexamethasone therapy on the incidence, pattern and evolution of sequelae.

**Patients and Methods**

The study involved children aged one month to 15 years who were treated for acute bacterial meningitis at the University of Maiduguri Teaching Hospital, Maiduguri, from January 1, 1993 to June 18, 1996 and at Irrua Specialist Teaching Hospital, Irrua, from May 17, 1993 to June 30, 2000. Minimum criteria for the diagnosis of acute bacterial meningitis included cerebrospinal fluid (CSF) white blood cell count \(\geq 10/\text{mm}^3\) with neutrophils \(\geq 50\%\), CSF/blood glucose ratio \(\leq 50\%\) and CSF protein \(\geq 80\text{ mg/dl}\). Children with an identified pathogen (from CSF culture, Gram stain or latex particle agglutination (only three cases were diagnosed using latex test) or blood culture) were taken as having confirmed bacterial meningitis (CBM), and children without an identified pathogen as having apparent bacterial meningitis (ABM). A standard course regimen of dexamethasone\(^9\) was used. Other aspects of the management and outcome of children in the study have been described elsewhere.\(^5\) The patients were followed up at the Neurology Clinic fortnightly to bi- or tri-monthly. Assessment was by history and physical examination, but the clinical impression of deafness was confirmed audiometrically.

**Classification:** Severity of the acute illness was classified using a previously described method.\(^5\) A score of one point each was given for age \(\leq 2\) years, illness \(\geq 7\) days, convulsions, pre-treatment with antibiotics, presence of shock, coma, abnormal posturing, abnormal muscle tone, abnormal respiration, and focal neurological deficit. Children with a total score of at least 3/10 were classified as having severe illness, while those with lower scores had illnesses of moderate and mild severity.\(^5\) Dexamethasone therapy was classified as appropriate if commenced at diagnosis, preferably before the first dose of antibiotics, in children who had not received antibiotics before diagnosis.\(^10\) It was inappropriate if given to children with a history of antibiotic therapy before diagnosis. Delayed sterilization of the CSF was defined as persistent CSF turbidity and depression of CSF/blood glucose ratio with or without repeat isolation of the causative organism after 96 hours of treatment.\(^6\) Neurological deficits were classified into 'major' and 'minor' as described by Herson and Todd:\(^1\) major sequelae included quadriplegia, blindness, seizures, among others, while minor sequelae included ataxia, deafness, hypekinesia, hemiplegia, etc. Deficits were also classified according to their number per child.

**Statistical analysis:** Frequencies were compared between dichotomous events using Yates' corrected \(\chi^2\) test, or Fisher's exact test as appropriate, and between groups in an \(n \times n\) table using group \(\chi^2\) test. Two-tailed \(p\) values \(< 0.05\) were taken as significant. Epi Info Version 6\(^{11}\) was used for statistical analysis.

**Results**

Two hundred and forty three children were treated for pyogenic meningitis at the two centres. Differences in clinical profile, aetiological agents, initial therapy and outcome between children in Maiduguri and Irrua, and between children with CBM and ABM are shown in Table I. The incidence, pattern, and resolution of sequelae are shown in Table II in relation to study centre and diagnosis. A significantly higher number of children in Maiduguri attended follow-up for \(\geq 6\) weeks (\(p < 0.05\)). Other differences between the two centres or between CBM and ABM were not significant. All the children with sequelae were therefore pooled together for further analysis of the pattern and evolution of deficits to allow for the small numbers involved from each centre and diagnostic group.

**Incidence of neurologic sequelae**

Overall, 187 children were assessed on discharge, 157 after six weeks of discharge and 134 after three months. The incidence of sequelae was 40/187 (21.4 percent) on discharge versus 23/157 (14.7 percent) after six weeks (\(p = 0.106\)) and 18/134 (13.4 percent) after three months (\(p = 0.069\)) of follow up.
### Clinical Profile, Aetiological Agents, Initial Treatment and Outcome in Children with Meningitis

<table>
<thead>
<tr>
<th>Clinical profile</th>
<th>Maiduguri</th>
<th>Irrua</th>
<th>p</th>
<th>a+b vs c+d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CBM* Na (%)</td>
<td>ABM* Na (%)</td>
<td>CBM* No. (%)</td>
<td>ABM* No. (%)</td>
</tr>
<tr>
<td>Age ≤2 years</td>
<td>29 (42) (n = 69)</td>
<td>33 (61) (n = 54)</td>
<td>11 (22) (n = 51)</td>
<td>19 (28) (n = 59)</td>
</tr>
<tr>
<td>Illness &gt;5 days</td>
<td>8 (12) (n = 69)</td>
<td>21 (39) (n = 54)</td>
<td>27 (53) (n = 51)</td>
<td>43 (62) (n = 59)</td>
</tr>
<tr>
<td>Partial treatment</td>
<td>18 (26) (n = 69)</td>
<td>22 (41) (n = 54)</td>
<td>18 (35) (n = 51)</td>
<td>30 (44) (n = 59)</td>
</tr>
<tr>
<td>Convulsions</td>
<td>42 (61) (n = 69)</td>
<td>30 (56) (n = 54)</td>
<td>18 (35) (n = 51)</td>
<td>22 (32) (n = 59)</td>
</tr>
<tr>
<td>Shock</td>
<td>12 (17) (n = 69)</td>
<td>9 (17) (n = 54)</td>
<td>3 (6) (n = 51)</td>
<td>1 (2) (n = 59)</td>
</tr>
<tr>
<td>Unconscious coma</td>
<td>19 (28) (n = 69)</td>
<td>6 (11) (n = 54)</td>
<td>11 (22) (n = 51)</td>
<td>6 (9) (n = 59)</td>
</tr>
<tr>
<td>Severely ill</td>
<td>32 (46) (n = 69)</td>
<td>24 (44) (n = 54)</td>
<td>20 (39) (n = 51)</td>
<td>21 (30) (n = 59)</td>
</tr>
</tbody>
</table>

**Aetiologic agents:**
- *N. meningitidis* / GNDC
  - 45 (65) (n = 69) NA 8 (16) (n = 54) NA NA NA <0.01
- *S. pneumoniae* / GPDC
  - 12 (17) (n = 69) NA 20 (39) (n = 54) NA NA NA <0.05
- *H. influenzae* / GNCB
  - 3 (4) (n = 69) NA 2 (4) (n = 54) NA NA NA 1.00
- Miscellaneous
  - 9 (13) (n = 69) NA 21 (30) (n = 54) NA NA NA <0.01

**Initial therapy:**
- Monotherapy with Pen, Amp, or Chl
  - 14 (20) (n = 69) 10 (19) (n = 54) 23 (45) (n = 51) 39 (57) (n = 59) 0.987 0.292 <0.01
- Therapy with Pen or Amp + Chl
  - 47 (68) (n = 69) 36 (67) (n = 54) 21 (41) (n = 51) 21 (30) (n = 59) 0.981 0.305 <0.01
- Other regimens
  - 7 (10) (n = 69) 9 (17) (n = 54) 7 (14) (n = 51) 9 (13) (n = 59) 0.426 0.871 0.909
- Dexamethasone
  - 42 (61) (n = 69) 24 (44) (n = 54) 19 (37) (n = 51) 23 (33) (n = 59) 0.103 0.801 0.005
- Outcome:
  - 16/63 (25) 9/46 (20) 10/50 (20) 4/67 (6) 0.628 0.043 0.045

GNDC = Gram negative diplococci, GPDC = Gram positive diplococci, GNCB = Gram negative cocco-bacilli, NA = not applicable, Pen = penicillin, Amp = ampicillin, Chl = chloramphenicol.

@: Excludes children discharged against advice.
### Table II

**Incidence, Manifestations, Pattern and Resolution of Sequelae in Survivors**

<table>
<thead>
<tr>
<th></th>
<th><strong>Maiduguri</strong></th>
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</thead>
<tbody>
<tr>
<td></td>
<td><strong>CBM</strong> (%)</td>
<td><strong>ABM</strong> (%)</td>
<td><strong>CBM</strong> (%)</td>
<td><strong>ABM</strong> (%)</td>
<td><strong>a vs b</strong></td>
<td><strong>c vs d</strong></td>
<td><strong>a+b vs c+d</strong></td>
<td></td>
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<td></td>
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<tr>
<td><strong>Incidence of sequelae:</strong></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>No. with sequelae/no. survived</td>
<td>11/47 (23)</td>
<td>11/37 (30)</td>
<td>10/40 (25)</td>
<td>10/63 (16)</td>
<td>0.586</td>
<td>0.376</td>
<td>0.354</td>
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</tbody>
</table>

**Manifestations of sequelae:**

<table>
<thead>
<tr>
<th>Deficit Type</th>
<th><strong>Maiduguri</strong></th>
<th></th>
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<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td><strong>CBM</strong> (%)</td>
<td><strong>ABM</strong> (%)</td>
<td><strong>CBM</strong> (%)</td>
<td><strong>ABM</strong> (%)</td>
<td><strong>Motor deficits</strong></td>
<td>7 (64)</td>
<td>10 (91)</td>
<td>6 (60)</td>
<td>8 (80)</td>
<td>0.311</td>
<td>0.629</td>
<td>0.854</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Visual or hearing loss</strong></td>
<td>6 (55)</td>
<td>4 (36)</td>
<td>2 (20)</td>
<td>3 (30)</td>
<td>0.669</td>
<td>1.00</td>
<td>0.29</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td><strong>Deficit of other cranial nerves</strong></td>
<td>1 (9)</td>
<td>1 (9)</td>
<td>2 (20)</td>
<td>2 (20)</td>
<td>1.00</td>
<td>1.00</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Afebrile seizures</strong></td>
<td>2 (18)</td>
<td>1 (9)</td>
<td>3 (30)</td>
<td>2 (20)</td>
<td>1.00</td>
<td>1.00</td>
<td>0.445</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Hydro- or micro-cephaly</strong></td>
<td>1 (9)</td>
<td>1 (9)</td>
<td>2 (20)</td>
<td>3 (30)</td>
<td>1.00</td>
<td>1.00</td>
<td>0.229</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Ataxia</strong></td>
<td>2 (18)</td>
<td>1 (9)</td>
<td>2 (20)</td>
<td>2 (20)</td>
<td>1.00</td>
<td>1.00</td>
<td>0.40</td>
</tr>
</tbody>
</table>

**Pattern of sequelae:**

<table>
<thead>
<tr>
<th>Deficit Type</th>
<th><strong>Maiduguri</strong></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>CBM</strong> (%)</td>
<td><strong>ABM</strong> (%)</td>
<td><strong>CBM</strong> (%)</td>
<td><strong>ABM</strong> (%)</td>
<td><strong>Motor deficits</strong></td>
<td>6/11 (55)</td>
<td>8/11 (73)</td>
<td>6/10 (60)</td>
<td>9/10 (90)</td>
<td>0.659</td>
<td>0.303</td>
<td>0.645</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Visual or hearing loss</strong></td>
<td>4/11 (36)</td>
<td>2/11 (18)</td>
<td>2/10 (20)</td>
<td>5/10 (50)</td>
<td>0.635</td>
<td>0.35</td>
<td>0.836</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Deficit of other cranial nerves</strong></td>
<td>11/11 (100)</td>
<td>10/11 (91)</td>
<td>6/10 (60)</td>
<td>7/10 (70)</td>
<td>1.00</td>
<td>1.00</td>
<td>0.018</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Afebrile seizures</strong></td>
<td>6/11 (55)</td>
<td>7/10 (70)</td>
<td>3/6 (50)</td>
<td>2/7 (29)</td>
<td>0.659</td>
<td>0.592</td>
<td>0.328</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Hydro- or micro-cephaly</strong></td>
<td>6/11 (55)</td>
<td>7/10 (70)</td>
<td>3/6 (50)</td>
<td>2/7 (29)</td>
<td>0.659</td>
<td>0.592</td>
<td>0.328</td>
</tr>
</tbody>
</table>

* Summation of the frequencies is greater than the total number with sequelae because the deficits were multiple (>1 type) in some subjects (n = 21): motor deficits + visual or hearing loss, delayed speech or other cranial nerve deficits 6, hydrocephaly or microcephaly + motor deficits +/- seizures, visual loss or other cranial nerve deficit 5, ataxia + hearing loss 3, motor deficits + seizures 3, miscellaneous combinations 4.

@ Motor deficits = quadripleasis 20, hemiparesis 10, monoparesis 2, delay or regression of motor milestones 3, loss of neck control 3, hyperactivity 1, choreiform movements 1, rolling movements of the head 1, coarse tremors 1, delayed speech development 1; hearing loss = 8, visual loss = 9; other cranial nerve palsies = 6, 7th 4; hydrocephalus = 6, microcephalus = 2.
### Table III
Clinical and Laboratory Profile and the Incidence, Pattern and Resolution of Deficits in Children treated with Dexamethasone

<table>
<thead>
<tr>
<th>Clinical and laboratory</th>
<th>Children with previously untreated meningitis</th>
<th></th>
<th>Children with partially treated meningitis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DEX +VE (n = 54) %</td>
<td>DEX -VE (n = 65) %</td>
<td><em>p</em></td>
</tr>
<tr>
<td><strong>Age ≤2 years</strong></td>
<td>17 (32)</td>
<td>20 (31)</td>
<td>0.908</td>
</tr>
<tr>
<td><strong>Severely ill</strong></td>
<td>15 (28)</td>
<td>12 (19)</td>
<td>0.323</td>
</tr>
<tr>
<td><strong>Confirmed bacterial meningitis</strong></td>
<td>33 (61)</td>
<td>29 (45)</td>
<td>0.107</td>
</tr>
<tr>
<td><strong>No. with “usual” organisms/total no. with +ve culture or serology</strong></td>
<td>18/20 (90)</td>
<td>14/16 (88)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Delayed sterilization of CSF</strong></td>
<td>5 (9)</td>
<td>8 (12)</td>
<td>0.813</td>
</tr>
</tbody>
</table>

**Incidence, pattern and resolution of deficits:**

<table>
<thead>
<tr>
<th></th>
<th>DEX +VE</th>
<th>DEX -VE</th>
<th><em>p</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. with deficits</td>
<td>12 (22)</td>
<td>12 (19)</td>
<td>0.78</td>
</tr>
<tr>
<td>No. with major deficits/no. with deficits</td>
<td>8/12 (67)</td>
<td>9/12 (75)</td>
<td>1.00</td>
</tr>
<tr>
<td>No. with ≥3 deficits/no. with deficits</td>
<td>3/12 (25)</td>
<td>2/12 (17)</td>
<td>1.00</td>
</tr>
<tr>
<td>No. with full or partial resolution/no. followed up</td>
<td>9/11 (82)</td>
<td>4/8 (50)</td>
<td>0.319</td>
</tr>
</tbody>
</table>

DEX +VE = children treated with dexamethasone, DEX -VE = children not treated with dexamethasone.

Note: The number of DEX +VE children is <108 as in Table I because of the exclusion of children who died or were discharged against advice (n = 28).
Follow up status of children who were apparently normal on discharge

Of the 147 children who were apparently normal on discharge, 33 did not attend for follow-up or kept only the first appointment, 49 attended for <3 months, and 65 for three to ten months. Seventeen of those who attended for ≤2 weeks and 25 of those who attended for <3 months were seen later for other reasons after defaulting; they remained normal. Thus, overall, 107 children had a known status at ≥3 months after discharge. Two (1.9 percent) had neurological sequelae that were not evident at discharge. The first, a 14-year-old boy with pneumococcal meningitis, presented seven months after discharge with generalised tonic clonic afebrile seizures. This child earlier had five episodes of 'febrile seizures' as an under-5. The second, a five-week-old male infant with ABM, had focal afebrile seizures precipitated by non-compliance with phenobarbitone at the age of four months and generalised status epilepticus associated with bronchopneumonia at the age of 11 months. The dose of phenobarbitone had been overdue for review to allow for growth but the mother had defaulted from follow-up. Compared to the twin brother, this child also had delayed motor milestones.

Pattern of neurologic sequelae

There was an average of 2.1 deficits per child, and a total of 89 individual deficits: motor 49 (55 percent), special senses 17 (19 percent; visual loss 9, hearing loss 8), other cranial nerve palsies, six (7 percent; 6\textsuperscript{th} cranial nerve-2, 7\textsuperscript{th} cranial nerve - 4), afebrile seizures, eight (9 percent), abnormal growth in head circumference, eight (9 percent; hydrocephalus 6, microcephaly 2) and delayed speech development one (1 percent). Details of these deficits are contained in Table II. The motor deficits included quadriparesis 20, hemiparesis 10, monoparesis 2, ataxia 7, delay or regression of motor milestones 3, loss of neck control 3, and one each of hyperactivity, choreiform movements, rolling movements of the head, and coarse tremors. Fifteen (36 percent) children had major and 13 (31 percent) minor deficits only, while 14 (33 percent) had major plus minor deficits.

Evolution of deficits

The status of deficits in eight children (two, five and one with major, major+minor, and minor deficits, respectively, at or within two weeks of discharge) was uncertain because they did not attend for follow-up, attended for <6 weeks or died before the 6\textsuperscript{th} week follow-up. Overall, the deficits in nine (27 percent) of the 34 children with sequelae followed up for at least six weeks had fully resolved. These included 2/13, 2/9 and 5/12 children with major, major + minor and minor deficits, respectively. The deficits evolved from major or major plus minor to minor in a further two (6 percent) children and from multiple to single in six (18 percent). Seven of 16 children with single vs 2/18 with multiple deficits (p = 0.052) and 5/12 with minor vs 4/22 with major +/- minor deficits (p = 0.22) had fully resolved deficits.

Satisfactory control of seizures was achieved in three of five children, one of whom was seizure-free for a period of one year. Hydrocephalus became arrested within a few months in four of the five children while one was referred for neurosurgery because of pressure symptoms/signs. Full resolution was observed in 4/5 children with ataxia, 2/8 with visual loss, 3/8 with hearing loss, and 7/22 with hemi- or quadriparesis. Seventeen (40 percent) children were followed up for at least six months, ten (24 percent) for three to <6 months, and seven (17 percent) for at least six weeks, while eight (19 percent) attended for shorter periods or not at all, or died before six weeks (one child only). Five of the eight children followed up for <6 weeks showed partial resolution of their deficits before defaulting. Three (18 percent) of 17 children who attended for ≥6 weeks to <6 months and 10/17 (59 percent) who attended for ≥6 months (p = 0.034) had non-resolving deficits.

Two of the 40 children who had sequelae on discharge are known to have died. The first had coliform meningitis, was discharged with spastic quadriparesis, 7\textsuperscript{th} nerve palsy and afebrile seizures, and died at a traditional healer's home following prolonged seizures five weeks after discharge. The second had ABM, was discharged with quadriparesis and afebrile seizures, and died of bronchopneumonia 16 months after discharge.

Relationship between selected characteristics of the acute illness, including dexamethasone therapy, and the incidence, pattern and resolution of deficits

Among the 187 children who recovered, 64 (34 percent) were ≤2 years of age and 60 (32 percent) were severely ill on admission. Eighty seven (47 percent) had CBM. The aetiological agent was identified in 64 children; 13 had "unusual agents" (Gram negative bacilli 10, and Staphylococcal aureus 3) and 51 usual agents (Neisseria meningitidis, Streptococcus pneumoniae, and Haemophilus influenzae). Thirty-five (19 percent) had delayed sterilization of the CSP.
The incidences of sequelae were 28/64 (44 percent) in the young and 14/123 (11 percent) in the older children (p < 0.01), and 28/60 (47 percent) in severely ill vs 14/127 (11 percent) in non-severely ill children (p < 0.01). It was 8/13 (62 percent) in children with "unusual agents" vs 12/51 (24 percent) in those with usual agents (p = 0.016), and 14/35 (40 percent) in children vs 28/152 (18 percent) in those without delayed sterilization of the CSF (p = 0.011). The incidence did not differ significantly between CBM and ABM (21/87 vs 21/100, p = 0.736). There was no significant relationship between the pattern or resolution of sequelae and characteristics of the acute illness.

A total of 119 (64 percent) children had no history of treatment with antibiotics before diagnosis. Thirty-two of 61 such children in Maiduguri and 22/58 in Iruua (p = 0.159) were treated with dexamethasone. Sixty-eight children (36 percent) had partially treated meningitis; 12 of 23 such children in Maiduguri and 14/45 in Iruua (p = 0.154) received dexamethasone. Characteristics of the acute illness, and the incidence, pattern and resolution of sequelae in children treated with dexamethasone are shown in Table III in comparison with those of untreated children. There were no significant differences between children who had dexamethasone therapy and those who did not, whether they had partially treated or previously untreated meningitis. However, in the pooled population, that is, all children treated with dexamethasone vs those not treated, the incidence of full or partial resolution of sequelae was significantly higher in those given dexamethasone [15/19 vs 6/15, relative risk (95% confidence interval) = 1.97 (1.02, 3.83), p = 0.049].

Discussion

There is a wide variation (10-47.4 percent) in the incidence of post-meningitis sequelae in developing countries.10,15-17 The incidences of 15.9 to 29.7 percent in this study, depending on the study location (Maiduguri vs Iruua) and the nature of the diagnosis (CBM vs ABM), are within this range. The overall incidence of permanent neurological sequelae (sequelae persisting >3 months)18 of 14.9 percent is also within this range, and compares with the 13.4 percent reported recently in Libyan children.18 The pattern of sequelae has not, to our knowledge, been reported from developing countries as major and minor with respect to individual children, although it is possible to deduce the information with respect to individual deficits from previous reports. Working in a developed country, Herson and Todd1 reported that in children with H. influenzae meningitis, four of 15 with sequelae at discharge and six of 16 on subsequent follow-up had major deficits. Compared to this, the corresponding rates of 29/42 and 25/34 in the present study were high. Differences in the pattern of organisms and severity of illness may account for the difference in rates.3

Previous reports from African countries do not contain enough data to help in determining the pattern of sequelae at discharge, but enough data is available to determine the proportion of major sequelae among the individual deficits. In earlier reports, 68 percent deficits reported from Lusaka, Zambia,19 67 percent from Ibadan, Nigeria4 and 35 percent in Enugu, Nigeria20 were major. In more recent reports, six percent deficits in Accra, Ghana,17 47 percent in Benghazi, Libya15 and 37 percent in Enugu, Nigeria10 were major. Thus, as with the incidence of sequelae, the proportion with major deficits is also variable, although mostly high. The 50 percent deficit rate obtained in the present study falls within this range.

Reduction of the risk of sequelae in survivors is an important objective in the management of meningitis.21 Dexamethasone has been recommended for this purpose, but this is controversial.5,22-25 However, dexamethasone might also have beneficial effects on the evolution of sequelae.22 This is supported by the results of this study. Although a reduction in the incidence of sequelae could not be demonstrated in this study, this has been shown in other studies from developing countries.26 This, plus the beneficial effect on the evolution of sequelae,22 which is also supported by results of this study, suggest that dexamethasone therapy may also be worthwhile in developing countries. Another issue is the selection of patients for preferential treatment with dexamethasone or other agents. Although there are reports which suggest that dexamethasone may be more beneficial in mildly ill patients,27 it has also been shown to be beneficial in severely ill patients.27 One conclusion from the results of this study is that unlike the risk of sequelae,13 the pattern and evolution might not be predictable from the characteristics of the acute illness. Therefore, illness severity may not be a sufficient basis for the selection of patients. An important limitation to the use of dexamethasone in developing countries may be the problem of partial treatment with antibiotics. Misuse of antibiotics is common in developing countries28 and dexamethasone therapy might not be beneficial in partially treated meningitis.13 Other limitations to its use have been discussed by Tefuwarani and Vince.16 The evolution of sequelae in this study is encouraging, even allowing for the limited follow-up attendance. First, although 67 percent of the sequelae were major
or mixed initially, those in 30 percent of evaluable patients evolved from major/mixed to minor or none. Second, 62 percent of evaluable patients had fully (29 percent) or partially (32 percent) resolved deficits. This is similar to reports of other series, including those on individual deficits.5,10

Two findings in this study were of a low incidence, but their occurrence is, nonetheless, a cause for concern: First, 6.9 percent of the 29 children with major sequelae died from morbidities arguably related to the sequelae. The problem of delayed mortality associated with major sequelae may, therefore, be important. Second, two children who were initially assessed as normal, subsequently developed afebrile seizures. One had a preceding history of recurrent febrile seizures, a risk factor for afebrile seizures.21 The second child subsequently manifested with other deficits. Afebrile seizures as a complication of meningitis are usually associated with other deficits,29 but this is not invariable.29 Thus, the absence of clinical abnormalities on discharge, an assessment which may not be infallible, might not preclude the subsequent development of seizures. Whatever the explanation, the phenomenon of delayed appearance of sequelae is rare but not unknown,20 and underlies the need for follow-up of even apparently normal patients.

Other than the overall pattern of sequelae, the incidence of individual sequelae may also be of interest. Hearing loss has in particular been emphasized.21,52 The 3.7 percent incidence among 187 survivors in this study is within the 1 to 4 percent range of profound or total impairment reported from developed countries.32 Afebrile seizures have also been reported in 5 to 44 percent of survivors.21 The incidence of 4.3 percent in the present study may represent an underestimation for two reasons: First, its apparent rarity contrasts with the high incidence of seizures at diagnosis and during treatment.31 Seizures during the illness are a strong predictor of the risk of major sequelae.13,20 Second, many families still believe that traditional or spiritual therapy is better for seizure disorders and might not have taken their children to formal health facilities. In this study, one of those with sequelae who subsequently died was taken to the traditional healer on the insistence of the grandmother.

Certain aspects of the methodology in this study merits further discussion. First, only “readily detectable sequelae” were reported because full assessment of all the children could not be done. For example, whereas all children should have a hearing assessment post-meningitis,50 only those who were deaf on clinical assessment had formal audiometric assessment for confirmation. This was due to lack of facilities. Formal psychometric assessment for cognitive deficits was also not performed, but non-formal assessment of most of those who recovered fully, during presentations for other reasons, indicated that they were doing well. In addition, we adopted the classification of Herson and Todd1 because the degree of functional impairment expected from the deficits seems to have been the basis for the classification. However, other studies50,51 have shown that the pathological basis for some “minor” deficits such as hemiparesis might be no less gross than that of major deficits. Also, some “minor” deficits may be no less important. Thus, hearing loss has important effects on speech development and education.31 We added the number of deficits as an additional method of classification because a child with multiple deficits would be expected to suffer more functional impairment, as well as require more resources for rehabilitation, than one with fewer deficits. Another aspect is the poor compliance with follow-up appointments which was a major problem as only 40 percent of the patients with sequelae attended for upwards of six months. The speed of resolution of sequelae may be a factor, and children who attended for ≥6 months were less likely to have fully or partially resolved sequelae. Neuroimaging other than plain skull radiography was not done, mainly because of lack of facilities. Nonetheless, none of the children had a course of illness suggestive of mass lesions as a complication. These are also quite rare as complications of meningitis.2 Finally, children with ABM were included because they fulfilled other criteria for the diagnosis of bacterial meningitis. There were only a few significant differences between CBM and ABM, as discussed in previous reports.52

We conclude that most patients with post-meningitic sequelae in developing countries have major or major plus minor deficits and deficits may resolve partially or fully in about two-thirds of affected children; the pattern and evolution of sequelae are not clearly predictable from the characteristics of the acute illness on admission, but dexamethasone therapy may be associated with a more favourable evolution of deficits.

References


