

## **The Contribution of delayed Diagnosis to the Outcome in Pyogenic Meningitis**

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### **Summary**

**Akpede GO and Ighogboja SI. The Contribution of delayed Diagnosis to the Outcome in Pyogenic Meningitis. *Nigerian Journal of Paediatrics* 1996; 23 : 4.** Meningitis was unsuspected following initial admission work-up in 25.8 percent of 66 infants and children with pyogenic meningitis managed at the University of Maiduguri Teaching Hospital. Eleven of the 17 were infants of whom nine were aged six months and under. Diarrhoea with dehydration, pre-admission treatment with antibiotics, focal infections, malaria parasitaemia and absence of seizures on or before admission were associated with delayed diagnosis of meningitis. A major subsequent development which led to diagnosis was seizure which occurred in 58.8 percent of the patients; other additional developments included alteration of consciousness in 23.5 percent and appearance of signs of meningitis in 35.3 percent. Case fatality rate of 47.1 percent was higher in patients with delayed diagnosis than the 17.4 percent in those without ( $P = 0.024$ ), whereas sequelae rates were comparable.

### **Introduction**

PYOGENIC meningitis is often unsuspected at the initial clinical evaluation of acutely ill young infants in whom the onset of the disease is frequently insidious,<sup>1</sup> or, as a result of inadequate evaluation, the diagnosis may be missed.<sup>2</sup> The decision as to which ill child should undergo a lumbar puncture (LP) so as

to establish a diagnosis of meningitis, is often difficult because of the non-specific clinical features of the disease in young children and the fact that the initial cerebrospinal fluid (CSF) specimen may be normal,<sup>3</sup> while meningitis may be a complication of LP, particularly in a child with existing bacteraemia.<sup>4</sup> Delay by parents to seek medical care for most childhood diseases, including meningitis, is usually given as an important contributory factor to poor outcome in these diseases in developing countries.<sup>5,6</sup> Yet, delayed diagnosis of an illness may make as much, or even greater contribution to the outcome of disease than delayed hospital admission. The aim of the present prospective study was to examine those factors that

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contributed to delay in the diagnosis and outcome of pyogenic meningitis among hospitalized children.

### Patients and Methods

The patients consisted of children with pyogenic meningitis who were admitted into the emergency room, department of Paediatrics, University of Maiduguri Teaching Hospital (UMTH), over a period of 16 months (August 1991 - November 1992). Diagnosis of meningitis was based on the criteria that have been previously reported.<sup>7</sup> By these criteria, definite diagnosis of pyogenic meningitis was made if the gram-stain or culture of the CSF, or blood culture was positive and typical biochemical changes in the CSF were present. If no organisms were identified, the condition was described as probable meningitis. Final diagnosis was based on a combination of the CSF appearance (turbid, cloudy or purulent), pleocytosis (white cell count, mainly polymorphs, of more than 10 cells per ml of CSF), protein concentration greater than 0.8gm/ml and CSF/blood glucose ratio less than 50 percent. In the present study, delayed diagnosis of meningitis was defined as the non-inclusion of this disease in the provisional diagnosis on admission of a child, leading to either a delay to perform an LP, or administration of appropriate therapy.

Statistical analysis of the data was undertaken using chi-square test with Yates' correlation for continuity. Fisher's exact test was undertaken where assumptions for chi-square tests were not fulfilled. P value less than 0.05 was considered significant.

### Results

Lumbar puncture was performed on 341 (27.8 percent) of the 1227 patients, aged between one and a half months and 15 years, who were admitted during the period of the study. Sixty-six (19.4 percent) of the 341 patients had pyogenic meningitis and of these 66, 20 (30.3 percent) had no typical clinical features of the disease at the time the procedure was carried out, while the diagnosis of meningitis was delayed in 17 (25.8 percent). Six (35.3 percent) of the 17 patients had no signs of meningitis compared with 14 (28.6 percent) of the remaining 49 patients in whom the diagnosis was promptly made ( $P > 0.05$ ). Later indications for diagnostic LP in the 17 cases of delayed diagnosis, included the development of repeated seizures in five patients (29.4 percent), meningeal signs in four patients (23.5 percent), seizures with coma in three (17.6 percent), seizures and meningeal signs in two (11.8 percent), and seizures in a patient with bronchopneumonia (5.9 percent); other indications were deterioration in the level of consciousness in one (5.9 percent) and persistent fever in one other patient (5.9 percent). Absence of diagnostic features was significantly ( $P = 0.01$ ) more common in children aged less than two years of age (16/47) compared to those older (1/19).

The organisms cultured from the CSF/blood in 40 (60.6 percent) of the 66 patients with meningitis consisted of *Streptococcus pneumoniae* (*Strep pneumoniae*) in 12 (30.0 percent), *Neisseria meningitidis* (*N meningitidis*) in 14 (35.0 percent), *Haemophilus influenzae* (*H influenzae*) in five (12.5 percent) and others, including coliform spp and *Staphylococcus aureus* (*Staph aureus*) in nine (22.5 percent). There was no difference in

the pattern of isolated organisms between patients with delayed diagnosis and the others.

Three (4.5 percent) of the 66 patients with meningitis were discharged against medical advice; 31 (47.0 percent) survived without neurological sequelae, 16 (24.2 percent) survived with neurological sequelae and 16 (24.2 percent) died. In the remaining 63 patients who were not dis-

charged against advice, mortality was significantly higher at 47.1 percent among the 17 patients with delayed diagnosis than the 17.4 percent among the 46 other patients who were diagnosed on admission (P=0.024). The proportion (2/17) of the patients with delayed diagnosis who survived with sequelae, was not significantly different from that (14/46) of those diagnosed without delay (P=0.195).

**TABLE 1**

*Relationship between presenting Clinical Features and the relative Risk of delayed Diagnosis in Meningitis*

<i>Feature</i>	<i>Percent of patients (n = 49) diagnosed on admission with Features</i>	<i>Percent of Patients (n = 17) with delayed diagnosis with Features</i>	<i>Relative Risk (95 percent Confidence Limits) of delayed diagnosis in patients with the Feature *</i>	<i>P Value</i>
Age ≤ 6 months	32.7	52.9	1.84(0.82, 4.16)	0.232
Male sex	55.1	58.8	1.12(0.49, 2.58)	0.986
Duration of fever ≤ 3 days	44.9	47.1	1.07(0.47, 2.42)	0.898
Seizures before or on admission	53.1	17.7	0.27(0.09, 0.86)	0.024
Diarrhoea	24.5	70.6	4.20(1.68, 10.48)	0.002
Previous antibiotic therapy	26.5	58.8	2.67(1.17, 6.08)	0.035
Temperature >38.0°C	61.2	76.5	1.74(0.64, 4.72)	0.400
Severe malnutrition	12.2	11.8	0.97(0.27, 3.47)	1.000
Focal extracranial infections	26.5	52.9	2.25(1.01, 5.02)	0.091*
Coma	55.1	70.6	1.66(0.66, 4.17)	0.405
Dehydration	8.2	52.9	4.59(2.20, 9.56)	0.0003
Malaria parasitaemia	2.0	11.8	2.80(1.12, 6.98)	-

\*Relative risk of delayed diagnosis in patients with the stated feature versus those without it.

The relationship between presenting clinical features and the relative risks of delayed diagnosis of meningitis is shown in Table I. Absence of seizures on/or before admission, a history of diarrhoea, home treatment with antibiotics and the presence of signs of dehydration in patients with diarrhoea were significantly associated with an increased risk of delayed diagnosis. Although the association did not attain statistical significance, delayed diagnosis was also more likely in infants aged six months and under, as well as in those with focal infections and malaria parasitaemia.

The diagnosis on admission, duration of delay in diagnosis, indications for the diagnostic

LP, result of blood and CSF cultures and the outcome in individual patients with delayed diagnosis of meningitis are shown in Tables II and III. Among the 17 patients with delayed diagnosis, initial diagnosis included bronchopneumonia and other focal infections in seven (41.2 percent), gastroenteritis in five (29.4 percent) (one had dysentery and one dysentery plus malaria parasitaemia) and malaria in another five (29.4 percent). All the patients with gastroenteritis were aged two years and under as were eight (88.9 percent) of the nine with focal infections, seven (87.5 percent) of the eight with dehydration and two (40.0 percent) of the five patients with malaria.

Table II

*Serial Numbers, Age, Initial Diagnosis and Duration of Delay in Diagnosis in 17 Patients with Meningitis*

No	Age (months)	Initial diagnosis	Duration of delay (hours)
1 *	3	Bronchopneumonia	12
2	3	Malaria	92
3	3	Malaria	60
4	4	Bronchopneumonia, Gastroenteritis	16
5	4	Measles, Bronchopneumonia	18
6	6	Gastroenteritis	48
7	6	Gastroenteritis with dehydration	48
8	6	Bronchopneumonia	72
9	6	Marasmus, Gastroenteritis with dehydration	72
10	10	Bronchopneumonia, Gastroenteritis with dehydration	144
11	10	Marasmus, Gastroenteritis with dehydration	84
12	16	Bronchopneumonia, Febrile seizures	48
13	18	Dysentery, Malaria	24
14	30	Malaria	48
15	60	Malaria	12
16	60	Malaria, Febrile seizures	18
17	156	Septicaemia with bronchopneumonia and multiple septic arthritis	8

\* Patient No 1 also presented with seizures

**Table III**

*Serial Numbers, Indications for LP, Organisms and Outcome in 17 Patients with delayed diagnosis of Meningitis*

<b>No</b>	<b>Indications for LP</b>	<b>Organisms from blood \ CSF</b>	<b>Outcome</b>
1	Meningeal signs	None	Survived
2	Repeated seizures	<i>H influenzae</i>	Sequelae
3	Persistent fever after clearance of malaria parasitaemia, irritability	<i>H influenzae</i>	Survived
4	Seizures	None	Survived
5	Repeated seizures	<i>N meningitidis</i>	Died
6	Repeated seizures	None	Died
7	Prolonged multifocal seizures, meningeal signs; ecchymotic rash	<i>N meningitidis</i>	Died
8	Seizures	<i>H influenzae</i>	Sequelae
9	Repeated seizures in a patient with respiratory distress	Coliform spp	Died
10	Coma; seizures, persistent fever	<i>Strep pneumoniae</i>	Died
11	Coma	<i>Strep pneumoniae</i>	Died
12	Coma; repeated seizures	<i>Strep pneumoniae</i>	Died
13	Coma; seizures	None	Survived
14	Meningeal signs	None	Survived
15	Meningeal signs	<i>Strep pneumoniae</i>	Survived
16	Repeated seizures, meningeal signs	<i>N meningitidis</i>	Survived
17	Equivocal meningeal signs	<i>Staph aureus</i>	Died

LP = Lumbar puncture

### Discussion

The size of the problem of delayed diagnosis of meningitis as shown in the present study was unexpected. However, meningitis can be missed on initial evaluation even in optimal settings where LP has been omitted from the initial management of acutely ill patients.<sup>1</sup> It is also easy for meningitis to be missed where certain basic rules of care are neglected.<sup>2</sup> The latter is most likely where experienced manpower is scarce, the level of supervision of junior physicians is low and the patient-load is high, all of which situations are common in many developing countries.

In the present series, it is noteworthy that the presence of focal infections increased the likelihood of delayed diagnosis of meningitis although the sequelae rate was lower than expected in patients with delayed diagnosis. Delayed diagnosis might be contributory to the higher case fatality rate in patients with meningitis and concomitant focal extracranial infections.<sup>8</sup> Pre-treatment with antibiotics, which is more likely in patients with focal infections,<sup>1</sup> could contribute to delayed diagnosis by creating a false sense of security and delaying the appearance of meningeal signs.<sup>3</sup> It might, however, partly lower the sequelae rate by reducing the antigen load and associated inflammatory response, an important determinant of the occurrence and severity of sequelae<sup>9</sup> on the institution of effective therapy.

About one third of our patients with meningitis lacked typical meningeal signs, an observation which is not unusual in patients under 18 months of age.<sup>10</sup> In addition, the fact that there is a large number of diseases whose

presentations mimic that of meningitis,<sup>11</sup> emphasizes the significant risk of both over- and under-diagnosis of meningitis, if reliance is placed on the presence of clinical features alone without undertaking confirmatory LP.

It is an established fact that LP can have significant risks in patients with meningitis who have raised intracranial pressure.<sup>10 12 13</sup> However, the case for more, rather than fewer LPs is, in our opinion, justifiable in the tropics, because of the high prevalence of malaria parasitaemia in endemic areas<sup>11</sup> and the frequent co-existence of meningitis with acute respiratory infection<sup>8 14</sup> which may constitute potential red herrings. The large number of patients with seizures associated with fever in the tropics,<sup>15</sup> the non-specificity of clinical features of meningitis, plus their frequent absence in patients with meningitis<sup>10</sup> and the association between the syndrome of seizures with fever and meningitis<sup>2 16</sup> are further justifiable reasons for readily undertaking LPs in the tropics. The occurrence of seizures in young patients underscores its importance as a presenting feature of meningitis and thus the need for LP in such patients with seizures and fever.<sup>2</sup>

Delay in diagnosis in hospitalised patients in the present study was partly contributory to the relatively high case fatality rate of meningitis. Delay was more likely to occur in infants, in patients without seizures before or on admission and in those with concomitant gastroenteritis, focal infections and malaria parasitaemia. The subsequent occurrence of seizures and coma were useful features of the disease that indicated the need for LP in patients who may or may not have meningeal signs.

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