# Neonatal Meningitis in Northern Jordan

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## Summary

**A two-and-a-half year prospective study of neonatal meningitis in the two main referral hospitals in Northern Jordan was carried out to determine the clinical spectrum and particular characteristics of meningitis in the newborn. The 53 cases studied represented an incidence of 1.1 per 1000 live births. The commonest bacterial pathogen isolated was *Klebsiella* species (40 per cent) followed by Enterobacter (19 per cent). The mortality rate and neurological sequelae among surviving children were 32 and 39 per cent, respectively, with higher rates among preterm/low birth weight and early onset meningitis groups. Of the presenting clinical features, there was a highly positive association between two risk factors and outcome. A bulging anterior fontanelle was the only significant predictor of mortality ($P = 0.009$) and altered sensorium was the only predictive of post-meningitis sequelae ($P = 0.016$). The need to recognize that *Klebsiella* species is an increasingly important pathogen; cefotaxime or ceftazidime plus ampicillin are the most appropriate antibiotics to be used initially, and continuous surveillance thereafter have been stressed.**

## Introduction

Neonatal meningitis continues to be a significant problem with an estimated mortality rate of 20–40 per cent and permanent neurological sequelae complicating 30–50 per cent of the patients afflicted.[1] The micro-organisms causing neonatal meningitis not only vary between different countries, but show temporal changes within the same country.[2,3] Despite the increased availability of neonatal intensive care units, considerable advances in the speed of diagnosis and the use of highly effective antibiotic regimens, mortality and morbidity figures remain at an unacceptable level.[1–5] Thus, it is essential for each neonatal unit to record infection rates, note the micro-organisms concerned and to regularly review the situation as local variations in bacterial pathogens may necessitate modifications of the antibiotic regimen used as an initial therapy. The majority of studies published on neonatal meningitis have emanated from either America or Europe, few being reported from the Middle East.[6,7]

This is the first report on neonatal meningitis from this region in which the incidence, bacteriology, clinical features, risk factors, and outcome are described.

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## Patients and Methods

All neonates with meningitis admitted to the two main referral hospitals in the city of Irbid in Northern Jordan (Princess Badia'a and Prince Rashid Military hospitals) during the period of 30 months between January 1992 and June 1994 were included in this study. The following data were recorded for each patient, age at presentation, gestational age, birth weight, the time between the onset of illness and diagnosis, clinical presentation, laboratory findings, culture results, treatment, and outcome.

A diagnosis of neonatal meningitis was made either when microorganisms were cultured from the cerebrospinal fluid (CSF) or, in cases where the CSF was sterile, the presence of a positive blood culture and CSF pleocytosis with a cell count of more than 100/mm$^3$. Nineteen patients were excluded from this study because they either had associated central nervous system congenital anomalies (neural tube defects) or had cultures which were deemed to be contaminated (cultures grew more than one organism). Antibiotic susceptibility tests were determined by the standard Kirby–Bauer method.[8] No viral cultures were taken.

A combination of ampicillin (300 mg/kg/day) and gentamicin (5–7.5 mg/kg/day) was used initially until mid-1993, when the antibiotic combination was altered due to the detection of a high bacterial resistance rate, cefotaxime or ceftazidime (150 mg/kg/day) being substituted for gentamicin. On the basis of the results of culture and sensitivity tests, therapy was modified and continued for a period of

  

2–3 weeks. Survivors were examined at regular intervals for a period of 8–30 months to determine any persistent neurological sequelae.

## Results

During the two-and-a-half-year study period there were 47 669 live births in the catchment areas of the two hospitals and 53 infants with neonatal meningitis were seen, an incidence of 1.1 per 1000 live births. Forty-two patients had micro-organisms cultured from their CSF, whilst the remaining 11 had positive blood cultures and significant pleocytosis despite their CSF cultures being sterile. Twenty-nine were boys and 24 were girls with a male to remale ratio of 1.2:1. There were 24 preterm and/or low birth weight infants, while the rest were born at term. The mean age at presentation was 7 days (range 1–28). Fifteen neonates were seen within 48 h of birth (early onset), the remaining 38 patients presenting more than 48 h after birth (late onset).

The presenting signs and symptoms, and their relationship to mortality and neurological sequelae among survivors are detailed in Table 1. They were non-specific and fairly typical of sepsis. The most common being temperature instability and reluctance to feed. The main specific neurological signs were altered sensorium and bulging anterior fontanelle. Altered sensorium was defined as a change in the level of consciousness (lethargy, drowsiness or coma).

The relationship between the causative pathogens isolated, and gestational age, birth, weight the time of onset of the disease, and outcome are detailed in Table 2. Gram-negative organisms were isolated most frequently (87 per cent) with a predominance of *Klebsiella* species (40 per cent). Careful evaluation of their antimicrobial susceptibility revealed that the majority of Gram-negative organisms were sensitive to cefotaxime and ceftazidime, whilst only half of them were sensitive to gentamicin (Table 3). All Gram-positive organisms detected were sensitive to gentamicin, cefotaxime and ceftazidime.

TABLE 1
*Mortality and neurological sequelae rates in relation to presenting clinical features*

| Presenting clinical features | No. | Mortality | Neurological sequelae |
|---|---|---|---|
| Hypo/hyperthermia | 39 | 11 | 10 |
| Reluctance to feed | 38 | 10 | 13 |
| Altered sensorium | 22 | 8 | 9 |
| Convulsions | 17 | 8 | 6 |
| Respiratory distress | 15 | 4 | 3 |
| Vomiting | 15 | 5 | 3 |
| Bulging anterior fontanelle | 10 | 7 | 2 |
| Cyanosis | 8 | 3 | 2 |
| Neonatal jaundice | 6 | 1 | 1 |

Most symptoms and signs occurred in combination.

Seventeen of the neonates died and 22 survived without any residual disability. Of the 14 with disabilities, nine were left with cerebral palsy and five with hydrocephalus. The mean duration of follow up was 16.4 months (range 8–30 months) with only 30 of the surviving 36 patients attending regularly. Rates of mortality and neurological sequelae were higher among the preterm/low birth weight patients when compared to full term/normal birth weight group (38 *v.* 28 per cent) and (53 *v.* 29 per cent), respectively. There were also higher rates of mortality and neurological sequelae in patients with early onset meningitis than in those with late onset meningitis; 40 per cent mortality compared with 29 per cent and 56 per cent neurological sequelae compared with 33 per cent. These differences in mortality and neurological sequelae were not statistically significant.

Multiple logistic regression was used to assess the prognostic value of each of the different clinical manifestations after adjustment for the effect of all others. Results showed that, bulging anterior fontanelle was the only significant predictor of mortality after adjustment for all others variables ($P = 0.009$). Newborns with meningitis and bulging anterior fontanelle were about eight times more likely to die compared to those without (OR = 7.7, 95 per cent CL 1.7–35.4). On the other hand, an altered sensorium was highly predictive of post-meningitis sequelae. The risk of sequelae was six times more likely among newborn with altered sensorium than those without (OR = 6.1, 95 per cent CL 1.4–26.9, $P = 0.016$) after adjustment for all other clinical manifestations.

## Discussion

The findings in this prospective study provide interesting baseline data on the spectrum of neonatal meningitis in Northern Jordan. Gram-negative pathogens constituted 87 per cent of all isolates, *Klebsiella* species being the commonest organism detected (40 per cent) followed by the *Enterobacter* species (19 per cent) as shown in Table 2. These findings are similar to those in our previous study on neonatal septicaemia,[9] and to some other reports from Africa.[3,10] Group B Streptococci was an uncommon isolate as only two cases occurred in this study. A similar finding has been reported from many developing countries.[2,11,12] This difference may be attributed to the low prevalence of Group B Streptococci in the birth passages of pregnant women in some areas.[13,14] It may be due to the low incidence of early onset meningitis (28 per cent) in this study. However, it is well documented that the type of organisms causing neonatal meningitis vary among

TABLE 2
*Organisms isolated in relation to gestational age/birth weight, onset of meningitis and outcome*

| Organism | No. | Preterm/LBW | Full term | Early onset | Late onset | Mortality | Neurological sequelae |
|---|---|---|---|---|---|---|---|
| *Klebsiella pneumoniae* | 19 | 9 | 10 | 7 | 12 | 4 | 4 |
| *Enterobacter* spp. | 10 | 5 | 5 | 2 | 8 | 5 | 3 |
| *Acinetobacter* spp. | 4 | 1 | 3 | 1 | 3 | 1 | |
| *Staphylococcus aureus* | 4 | 2 | 2 | 2 | 2 | 1 | 1 |
| *Escherichia coli* | 3 | 2 | 1 | 1 | 2 | 2 | 1 |
| *Meningococci* | 3 | 1 | 2 | | 3 | 1 | 2 |
| Group B *Streptococci* | 2 | 1 | 1 | | 2 | | 1 |
| *Salmonella* species | 2 | 1 | 1 | 1 | 1 | 2 | |
| *Klebsiella oxytoca* | 2 | 1 | 1 | | 2 | | |
| *Proteus mirabilis* | 2 | 1 | 1 | | 2 | 1 | 1 |
| *Staphylococcus epidermidis* | 1 | | 1 | 1 | | | |
| *Pseudomonas aeruginosa* | 1 | | 1 | | 1 | | 1 |
| Total | 53 | 24 | 29 | 15 | 38 | 17 | 14 |

LBW: low birth weight.

TABLE 3
*Antibiotic susceptibility testing of the most common organisms isolated*

| | *Klebsiella* spp. | | *Enterobacter* spp. | |
|---|---|---|---|---|
| Antibiotics | No. | R | No. | R |
| Ampicillin | 21 | 21 | 10 | 10 |
| Chloramphenicol | 21 | 21 | 10 | 10 |
| Gentamicin | 20 | 10 | 8 | 5 |
| Amikacin | 20 | 7 | 8 | 0 |
| Ceftazidime | 18 | 0 | 8 | 0 |
| Cefalexin | 10 | 7 | 5 | 4 |
| Cefotaxime | 18 | 1 | 7 | 0 |

R = resistance.

different countries and show temporal changes within the same country. *Listeria monocytogenes* predominates in Spain and Kuwait, Group B Streptococci in North America, *Escherichia coli* in the Netherlands, and *Klebsiella* in Nigeria.[2,4,6,15,16] The reason for these differences is unknown. They may either reflect local conditions[16,17] or be due to other causes such as hereditary factors or maternal genitourinary tract hygiene.[2]

The incidence of neonatal meningitis (1.1/1000) reported in this study is higher than that found by others[3,17,18] with a predominance of Gram-negative pathogens and may be related to the high rates of infection and bacteraemia which prevail in this part of the developing world or it could be due to problems with hospital hygiene, since most of the cases are of late onset (72 per cent). The sex ratio of 1.2 males to each female is similar to the findings in other reports,[4,11,15] as is the noticeable rise in the mortality rates in preterm/low birth weight patients (38 per cent) and for early onset meningitis in 40 per cent.[16,17] The overall mortality rate of 32 per cent and neurological sequelae rate of 39 per cent are comparable to that in other developing countries.[1,2,11]

The findings in this and a recent report on neonatal septicaemia[9] indicate that the initial antimicrobial therapeutic regimen should include the use of one of the third generation Cephalosporins like cefotaxime or ceftazidime (Table 3). Other authors have reported similar findings.[3,19]

The presence of bulging anterior fontanelle was significantly associated with high mortality rate, a finding which confirmed the observation of other workers.[2] Altered sensorium was significantly related to neurological sequelae which is one of the known poor prognostic indicator in neonates and older children with bacterial meningitis.[17,20,21] These signs may be attributed to the presence of brain oedema which has previously been recognized as an important contributory factor to the mortality and permanent neurological sequelae in meningitis.[17,22] This finding has led to the suggestion that aggressive treatment may be crucial for survival in those cases of meningitis in which features of increased intracranial pressure are evident.[22]

In conclusion, the findings in this study have highlighted the importance of the *Klebsiella* species as a cause of neonatal meningitis in Northern Jordan. The presence of bulging anterior fontanelle and altered sensorium are poor prognostic indicators. The use of third generation cephalosporins initially is stressed and continuous surveillance of the prevalent organisms that cause neonatal meningitis and improvement in hospital hygiene is therefore recommended.

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