

Epidemiology of neonatal meningitis in Qatar

Mahmoud F. El-Said, MBBCH, CABP, Mohammed S. Bessisso, DCH, MD, Mohammad A. Janahi, MD, FAAP, Lina H. Habob, MBBCH, CBBP, Sittana S. El-Shafie, MSc, FRCP(Path).

ABSTRACT

Objective: Neonatal meningitis is responsible for thousands of neonatal deaths annually all over the world. Our study was conducted to determine the epidemiology, management and best preventive measures for neonatal meningitis in Qatar.

Methods: A retrospective study reviewed the records of bacterial meningitis patients under the age of one month. The study was carried out at Hamad Medical Hospital, the only hospital that provides health care at Qatar and the study period was between January 1998 to December 2000.

Results: Thirteen patients were included. Sixty percent of patients had early onset meningitis. Causative organisms were group B *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Pseudomonas species*, *Neisseria meningitidis*, *Staphylococcus epidermidis* and *Flavibacterium meningococcus septicum*. A bacterial

resistance to the usual combination of ampicillin and gentamicin were noticed (as initial treatment before culture sensitivity results), which affected negatively on some patients. Complications of cerebral palsy, mental retardation and epilepsy occurred in 3 patients (23%). None of the patients died during the study period.

Conclusion: Emphasis is placed on the importance of correct early diagnosis and appropriate antibiotic therapy. It is suggested that the identification and appropriate treatment of any maternal bacterial infection is an important measure in preventing neonatal sepsis and meningitis.

Keywords: Neonatal meningitis, bacterial, antibiotics, prevention.

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First reports of neonatal meningitis appeared in the European and American literature in the late 1890s.^{1,2} Non-specific symptoms of neonatal meningitis can be misdiagnosed as metabolic errors, respiratory disease, cardiac illness or neurological disease. Early diagnosis and prompt management are essential, not only to save life but also to prevent further complications. The correct early diagnosis of neonatal meningitis depends primarily on a high degree of suspicion leading to the obtaining of a sample of spinal fluid for microscopic examination, chemical analysis, and culture. The infecting

organisms are quite different from those that infect other age groups. Maternal colonization with group B beta-hemolytic *Streptococci* or *Escherichia coli* (*E. coli*) and maternal genito-urinary infections constitute high risk factors for neonatal meningitis. In addition, complications of labor such as premature rupture of membranes and prolonged labor also increase the risk of neonatal meningitis. Preventive measures can be effective. The overall mortality ranges from 20% to 30% in most centers and neurological sequelae of some degree persist in 30% to 50% of survivors. Our study aimed to determine

From the Department of Pediatrics, Hamad Medical Corporation, Doha, Qatar.

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Address correspondence and reprint request to: Dr. Mahmoud F. El-Said, Department of Pediatrics, Hamad Medical Corporation, PO Box 3050, Doha, Qatar. Tel. +974 5545295. Fax. +974 4392204. E-mail: fawzi59@hotmail.com

the epidemiology, management and best preventive measures for neonatal meningitis in Qatar.

Methods. A retrospective study conducted between January 1998 through December 2000 reviewed the medical records of all patients under one month of age diagnosed with bacterial meningitis based upon a positive cerebrospinal culture. Similar patients with abnormal blood biochemistry (glucose and protein) or an abnormal cytology count and with negative culture were excluded. Case records included prematurity, duration of illness before admission, signs and symptoms on admission, laboratory test results, antibiotic use, acute and chronic complications and subsequent death. Clinical signs considered were hypothermia, fever, tense anterior fontanel, neck rigidity, level of consciousness, convulsions and neurological deficits. Drugs used initially and drugs used after sensitivity testing were recorded. Tests on blood included total and differential leukocyte counts, erythrocyte sedimentation rates, and cultures. The cerebro-spinal fluid was examined cytologically and biochemically was cultured for antibiotic sensitivity and was tested by the latex agglutination method.

Results. Thirteen patients (8 males and 5 females) with a mean age of 7 days (0.5 - 30 days) were included in the study. Eight of these had early onset in the first week of life, 5 had late onset of meningitis. The incidence was 0.5\1000 live births (term 0.3\1000, preterm 2\1000). Symptoms at presentation were mainly change in behavior (hypo-activity, drowsiness, irritability) 7\13 (53%); followed by vomiting 5\13 (38%), fever 4\13, seizures 4\13 (30%) and bulging fontanel 1\13 (8%). Results of cerebrospinal fluid (CSF) hematology and biochemistry are shown in **Table 1**, cultures, sensitivities and other tests in **Table 2**. Causative

organisms were group B *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Pseudomonas species*, *Neisseria meningitidis*, *Staphylococcus (Staph.) epidermidis* and *Flavibacterium meningococcus septicum*. Treatment was started with ampicillin and gentamicin and was changed to other combinations according to the results of culture sensitivity of the CSF. Complications of cerebral palsy, mental retardation and epilepsy meningitis occurred in 3 patients (23%). None of the patients died during the study period.

Discussion. Bacterial meningitis in the neonatal period has characteristic clinical symptoms, signs, causative organisms and management that are definitely different from the other age groups. The incidence of neonatal meningitis in our study of 0.5\1000 live births was similar to other reported incidence ranging from 0.13 to one per 1000 live births.^{2,3-5} The risk for premature infants in our study is 2\1000 live premature birth which is similar to the reported rate of 2.24\1000 live premature births. Male babies appear to be more at risk than females (1.6\1) although studies over the past 10 to 15 years had shown that the sexes are equally affected.⁶ Early-onset meningitis begins within the first week of life and results usually from vertical maternal-fetal infection during fetal or intra-partum periods. Late-onset meningitis develops 7 days or more after delivery and is caused by bacteria acquired horizontally from the mother or other caretakers. Most of our patients (60%) had early onset meningitis (8/13) possibly due to preventive measures against group B *Streptococci* not being taken until the end of 1999 (personal communication). The clinical course in the early onset form is often rapidly progressive with death occurring in 3 to 4 days. No deaths occurred in our patients possibly due to the high standard of free health care in our hospital. An experienced pediatrician examines all babies at least twice in the first 48 hours of life. In addition, most of our patients were admitted in the first day of their illness. Late-onset meningitis is associated with a less fulminant clinical course and a lower mortality rate. Thirty percent of infections in our patients were caused by group B *Streptococci*, 30% by *Staph. epidermidis* and 40% by Gram negative organisms (*Klebsiella*, *Pseudomonas* and *Neisseria meningitidis*). None of our patients had infections with *Listeria species* or *E. coli*. Other studies have shown *E. coli* accounting for 30%-35%, group B beta-hemolytic *Streptococci* for 30%-35%, and *Listeria monocytogenes* for 10% of neonatal meningitis cases.⁷⁻⁹ Antenatal care, sexual activity and social level may explain those bacterial variations between different communities. Fortunately, only one percent of infants colonized with group B *Streptococcus* develop symptomatic infections and approximately 0.5% of infants

Table 1 - Cerebrospinal fluid cytology and biochemistry.

Test	CSF WBC	CSF Polys %	Protein (gm/1)	CSF sugar/ blood glucose ratio	Blood WBC/ mm ³	Polys %	ESR
Minimum	5	70	0.6	0.01	2700	12	1
Maximum	9500	90	9.8	0.7	27000	70	55
Mean	868	88	3.4	0.3	12000	50	10

CSF - cerebrospinal fluid, WBC - white blood cell, Polys - polymorphs, ESR - erythrocyte sedimentation rate.

Table 2 - Bacterial gram stain, latex, culture sensitivity and outcome.

Organism	Sensitivity	Resistance	Positive Gram stain	Positive latex	Blood Culture	Complication
<i>GBS</i> (4/13)	Penicillin	No	Gram positive cocci	Positive	3/4	1 patient
<i>Staph. epidermidis</i> (4/13)	Gentamicin and cloxacillin	Penicillin	Negative	Negative	None	None
<i>Pseudomonas</i> (2/13)	Gentamicin and ceftazidim	Ampicillin	Gram negative bacilli	Negative	None	None
<i>Klebsiella pneumonia</i> (1/13)	Ceftriaxone	Gentamicin	Negative	Negative	None	None
<i>Flavibacterium meningococcus</i> (1/13)	Ceftriaxone	Ampicillin Gentamicin Cefazidim	Gram negative rods	Negative	None	1 patient
<i>Neisseria meningitidis</i> (1/13)	Penicillin	No	Gram negative diplococci	Positive	None	1 patient

GBS - group B streptococcus, *Staph.* - *Staphylococcus*,

colonized with *E. coli* develop symptomatic infection.^{9,10} The risk factors for neonatal meningitis are prematurity, maternal infection, prematurely ruptured membranes, prolonged labor, endotracheal intubation, intravenous catheters, birth trauma and meningomyelocele.¹¹

The symptoms and signs of neonatal bacterial meningitis are non-specific and indistinguishable from those seen with sepsis, systemic viral infections, cardiopulmonary disorders and metabolic errors.^{3,12} Irritability, temperature instability, apnea, and respiratory distress are the most common early signs. Neurologic symptoms are a decreased level of alertness, a tense fontanel, and intermittent opisthotonic posturing. Seizures have been reported in a wide range (20%-70%) of patients¹²⁻¹³ which might mean that the more subtle types of seizure such as apnea, automatism and pedaling movements go unnoticed. General laboratory abnormalities such as leukopenia, leukocytosis, increased sedimentation rate, are not reliable indicators although some studies have shown that very low white blood cell counts indicate a poor prognosis.³ Spinal fluid examination is essential both for diagnosis and management. Cerebrospinal fluid should be examined for protein and sugar, by Gram stain, cell count, latex agglutination and culture. In bacterial meningitis not all aspects of the spinal fluid analysis need be abnormal to provide evidence for bacterial infection. In culture-proven group B beta-hemolytic *Streptococcal meningitis*, the spinal fluid cell count is normal in 25% to 30% of patients and protein and glucose values are normal in up to 50%.¹⁴ However, if all components of spinal fluid examination are considered in a given patient, the chances that the cell

count, protein and glucose concentrations, and Gram stain will all be normal is less than one percent.¹⁴ Antibiotic susceptibilities should be determined on all organisms so that the most appropriate antibiotic therapy can be used. Initial empirical antimicrobial therapy consists of ampicillin plus either gentamicin, or a 3rd generation cephalosporin, such as cefotaxime or ceftriaxone.^{3,9-16} Cultures of our patients were sensitive to the above combinations. However, *Klebsiella* was resistant to gentamicin, *Staphylococci* were resistant to ampicillin and *Flavibacterium meningococcus* was resistant to ceftazidim, gentamicin and ampicillin. Some authors use ampicillin and gentamicin or ceftriaxone in early onset meningitis and for those who have late onset, they use oxacillin and gentamycin or vancomycin and ceftazidim or ticoplanin and ceftazidim if the patients has nephrogenic toxicity or the drug cannot be monitored.¹⁷ Once the antibiotic sensitivities of an organism are known, specific drug therapy can be selected. In most cases of gram-negative meningitis 2-drug therapy is recommended for 3 weeks, whereas single-drug therapy is usually sufficient for gram-positive meningitis for 2 weeks. Complications of bacterial meningitis result primarily from impaired cerebral blood flow, vascular occlusion, and metabolic-toxic injury of neurons. Chronic and permanent disabilities include severe cognitive deficits, hydrocephalus, seizures, ataxia, visual impairment, language disorders, and motor deficits. Complications occurred in 22% of our patients, which included epilepsy, motor disability, and mental retardation. Twenty percent of patients with group B *Streptococcus* infection compared to 40% of patients with gram-negative meningitis reflects the severity of

the causative organism. Neurological complications have been reported in 10 to 15% of meningitis patients infected by group B beta-hemolytic and in 70 to 75% of patients infected by gram-negative organisms. The overall rate of complications is 30% to 50%.¹⁸⁻²⁰ Neonatal meningitis is responsible for thousands of neonatal deaths annually all over the world. Group B *Streptococcal meningitis* alone accounts for more than 6,000 neonatal deaths each year in the United States of America (USA).³ In most major pediatric centers where antibiotic therapy and aggressive supportive care is given the overall mortality rate is approximately 20-30%. Mortality specifically for *E. coli* has been reported to be as high as 70%, whereas that for group B beta-hemolytic *Streptococci* is frequently reported to be below 20%.^{18,20} The principal means of prevention is reducing exposure of neonates to potential sources of bacteria. Intravenous administration of ampicillin or penicillin during delivery to women colonized with group B beta-hemolytic *Streptococci* markedly reduces the risk of neonate infection.^{10,11,21} Identifying and appropriately treating any maternal bacterial infection is an important measure in preventing neonatal sepsis and meningitis.

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