Neonatal Meningitis: Risk Factors, Causes, and Neurologic Complications

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Abstract

Objective
Neonates are at greater risk for sepsis and meningitis than other ages and in spite of rapid diagnoses of pathogens and treatments, they still contribute to complications and mortality. This study determines risk factors, causes, and neurologic complications of neonatal meningitis in hospitalized neonates.

Material & Methods
In this descriptive, cross sectional study, we evaluated 415 neonates with sepsis and meningitis admitted to the neonatal intensive care unit at our center between 2008 and 2012. The data that was recorded was age, sex, birth weight, prenatal risk factors, clinical features, blood and cerebrospinal fluid analysis, and brain sonographic findings and outcomes.

Results
Twenty patients had meningitis. Eleven cases (55%) were male. The mean age was 8.41 days and mean birth weight was 2891.5±766 grams. Poor feeding, seizures, and tachypnea were detected in 12 (60%), 11 (55%), and 6 (30%) patients, respectively. Prenatal risk factors were prolonged rupture of membranes, maternal vaginitis, asymptomatic bacteriuria, prematurity, low birth weights, and asphyxia. Four patients had positive cerebrospinal fluid cultures with klebsiella pneumoniae 2 (50%), Enterococcus spp. 1 (25%), and Group B streptococcus 1 (25%) cases, respectively. Two cases had positive blood cultures with klebsiella pneumoniae. Neurologic complications were brain edema, subdural effusion, and brain abscesses with hydrocephaly. One neonate (5%) died.

Conclusion
Our study provides some information about risk factors, pathogens, and neurologic complications for neonatal meningitis. Prenatal assessments help to diagnose and reduce risk factors of this hazardous disease.

Keywords: Neonatal meningitis; Risk factor; Complication

Introduction
In spite of the development of the rapid diagnosis of pathogens and new antibiotics, neonatal meningitis (NM) contributes to neonatal mortality and morbidity worldwide. Neonatal meningitis is the inflammation of the meninges during the first 28 days of life (1). According to the time of diagnosis, it is classified as early-onset (EOM) or late onset meningitis (LOM). In EOM, clinical features appear during the first weeks of life. LOM occurs between 8–28 postnatal days (2,3). The incidence of neonatal bacterial meningitis ranges from 0.25 to 1 per 1000 live birth...
and occurs in 25% of neonates with bacteremia (4,5). In
developed countries, group B streptococci (GBS) are the
most common causes of bacterial meningitis, accounting
for 50% of all cases. Escherichia Coli (E. Coli) accounts
for another 20%. Thus, identification and treatment of
maternal genitourinary infections is an important
prevention strategy (6). In developing countries, gram-
negative bacilli such as Klebsiella and E. Coli may be
more common than GBS especially in LOM (7,8). In
addition, other organisms that have been implicated as a
cause of meningitis include Enterobacter spp., Citrobacter
spp., and serratia spp. Meningitis is often more severe
with gram-negative bacteria and with a higher rate of
mortality and morbidity (9). Diagnosis of NM is based
on both clinical manifestations and cerebrospinal fluid
(CSF) examination. CSF culture is an excellent exam for
demonstration of meningitis. Evaluation of leukocyte
count, glucose, and protein levels in the CSF may help
in the diagnosis (10). This study evaluates neonates who
were admitted with meningitis from 2008 to 2012 in
our tertiary center. We evaluated maternal and neonatal
risk factors, clinical manifestations, pathogens, and
neurologic complications of neonatal meningitis cases.

Materials & Methods
In this retrospective cross-sectional study, we included
all admitted neonates with diagnosis of sepsis and
meningitis in Ali-Asghar Training Children’s Hospital,
Tehran, between 2008 and 2012. Medical records of the
neonates who were referred to our center for a sepsis
work up were investigated. Infants older than 28 days,
congenital infections (TORCHs syndromes), central
nervous system anomalies, and severe intraventricular
hemorrhage were excluded. Lumbar punctures were
routinely performed on every patient as part of the
sepsis work up before starting empirical antibiotics to
rule out meningitis. A definitive diagnosis of meningitis
was based on the growth of a pathogen from primary
CSF culture and supportive clinical manifestation
(seizures, thermal instability, and feeding intolerance,
among others). Suspected meningitis was diagnosed if
no organism was obtained from the CSF culture and
CSF characteristics (Leukocyte count > 32/mm3 and
> 29/mm3; glucose level < 34 mg/dl and < 24 mg/dl;
and protein level > 170 mg/dl and > 150 mg/dl as the
criteria of meningitis in term and premature neonates,
respectively) was suggestive for NM (11). Gestational
age (GA), gender, birth weight, onset of infection
(EOM, LOM), risk factors, clinical findings, CSF
analysis, CSF, and blood cultures were recorded. Risk
factors such as prolonged rupture of membranes (> 18
hours), mother’s vaginitis and asymptomatic bacteriuria,
prematurity (GA <37 week), low birth weight (LBW; i.e.
a birth weight <2500gr), multiple birth pregnancy, and
asphyxia were investigated. Clinical findings such as
fever, poor feeding, seizures, and tachypnea were noted.
Laboratory finding such as CSF analysis, blood, and CSF
cultures were evaluated. All patients with meningitis
were evaluated by brain sonography. Neonates with an
abnormal brain sonography were examined with brain
magnetic resonance imaging (MRI). Mortality rate was
recorded. Data were analyzed using SPSS (ver. 14). This
study was approved by ethics committee of the Iran
University of Medical Science.

Results
Between April 2008 and August 2012, out of 415 neonates
were hospitalized for sepsis work up, 20 patients (4–8%)
were diagnosed with meningitis. A total of 55% of the
patients were male. A total of 16 patients (80%) were
term. The mean birth weight was 2891.5±766 grams.
A total of 13 patients (65%) had EOM and 7 patients
(35%) had LOM. Maternal risk factors were included
PROM, mother’s vaginitis during third trimester, and
asymptomatic bacteriuria. Neonatal risk factors for
NM were prematurity, LBW, multiple birth pregnancy,
and asphyxia (Table 1). Clinical findings included
poor feeding 12 (60%), seizures 11 (55%), tachypnea 6
(30%), fever 6 (30%), decreased Moro reflex 5 (25%),
irritability 2 (10%), icter 2 (10%), bulging of fontanelle
1 (5%) of cases. The mean CSF leukocyte count was
741±473 cells/mm3. Mean glucose and protein levels in
CSF were 49±39 mg/dl and 120±93 mg/dl, respectively.
CSF cultures were positive in 4 (20%) patients and
pathogens included klebsiella pneumoniae, GBS,
and Enterococcus spp (Table 2). Blood cultures were
performed for all patients and two patients had positive
blood cultures with klebsiella pneumoniae with the same
results in CSF cultures (Table 2).
All patients with meningitis were evaluated by brain
similar to Gerdes et al (15). The presenting signs and symptoms of NM are nonspecific. Common symptoms include poor feeding, lethargy, vomiting, respiratory distress, and temperature instabilities (11). In our study, the most common clinical manifestations were poor feeding, seizures, and tachypnea.

In our study, CSF culture confirmed meningitis contributed to 20% of the cases and klebsiella pneumoniae were the most commonly detected pathogens. Other pathogens were GBS and Enterococcus spp. In Aletayeb, which was similar to our study, klebsiella pneumoniae was the common cause of EOM and LOM. Other isolated pathogens were Enterobacter, E.coli, Enterococcus spp., Pseudomonas aeruginosa, and Staphylococcus aureus. With this proportion, it is suggested to pay greater attention to other pathogens than GBS in prenatal cares in our country. In our investigation, the rate of positive CSF culture was lower than other references. It may be due to maternal antibiotic prophylaxis or delayed LP in antibiotic treated neonates and in these situations, clinicians have to rely on the CSF parameters specially WBC and clinical features to determine NM (10).

In this study, positive blood cultures were detected in 2 cases (50%) of patients that had positive CSF cultures with the same microorganism (klebsiella pneumoniae). It is suggested that meningitis frequently occurs in the absence of bacteremia and lumbar punctures as an important part of the diagnostic evaluation in suspected cases (10). A total of 58% of the NM cases in Aletayeb et al had a positive blood culture for the same organisms isolated from the CSF (2). A positive blood culture in their study was higher than for our study and this difference may be due to a higher rate of antibiotic prescribing during labor and a lower quality of culture techniques at our center.

In the present study, neurologic complications were detected in 20% of cases in brain sonography, including hydrocephaly with and without abscess formation, subdural effusion, and brain edema. A brain MRI confirmed our data and neurosurgical consultations were performed to evaluate these cases. In Kavuncoglu et al, pathological sonographic findings were ventricular dilatation, hydrocephalus, and intracranial hemorrhage.

Discussion
In this study, we identified 20 cases of neonatal meningitis. Our data indicated that NM is found predominantly in boys and our results confirmed the findings of Laving et al and Kavuncoglu et al (2, 14). They have mentioned that there is a gender–linked susceptibility to meningitis. In our survey, according to reported age of the patients at the time of admission (in their medical records), 65% of neonates were younger than 7 days as EOM and it is similar to the findings of Chang et al, which among 85 patients treated with diagnosis of NM, 51 (60%) had EOM. It is worth mentioning that the prevalence of NM is higher in late onset sepsis but, according to our findings, maternal risk factors that contribute to EOM were more common in our patients. It is suggested to place greater attention on maternal and prenatal care especially during the third trimester to early diagnosis and treatment of genitourinary infections.

According to this study, maternal risk factors for NM were PROM, mother’s third trimester vaginitis, and asymptomatic bacteriuria. In a study in Turkey, PROM was involved in 12.5% of cases with EOM and 8.6% of these patients had positive bacterial growth in maternal urinary or cervical cultures (14). Neonatal risk factors of meningitis in our study were prematurity, LBW, asphyxia, and multiple birth pregnancy, which was similar to Gerdes et al (15).
It is recommended that brain sonography be performed as a baseline study in every infant with suspicion of bacterial meningitis. In patients with complicated bacterial meningitis, an MRI should be the next study of choice (16).

In our study, the mortality rate was 5%, because of the association of asphyxia with NM. In Aletayeb et al, the mortality rate was 30%. This difference may be due to higher rate of low birth weight (60%) in their study, which has an important role in mortality (2).

There were some limitations in our study including a small sample size and lack of technical facilities for a culture of viruses in suspected cases of nonbacterial meningitis.

**In conclusion**, we found that in our center, EOM was more common than LOM and klebsiella pneumoniae was the most common cause of neonatal meningitis. Hydrocephaly, brain edema, and subdural effusion were neurologic complications of patients with NM. More emphasis on prenatal assessments may reduce maternal risk factors and neurologic complications of this hazardous disease.

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**Author Contribution:**

Dr Khalessi has collected and analyzed data and dr Afsharkhas has written and edited the paper.
Table 3. Neurologic Complications Observed in Brain Sonography

| Brain sonography findings                      | No. (%) |
|------------------------------------------------|---------|
| Hydrocephaly                                   | 1(25%)  |
| Hydrocephaly and Abscess formation             | 1(25%)  |
| Brain edema                                    | 1(25%)  |
| Subdural Effusion                              | 1(25%)  |

References

1. Volpe JJ. Bacterial and fungal intracranial infections. In: Neurology of the Newborn. 5th Edition. Philadelphia, Pa: Saunders Elsevier. 2008. Pp: 916–56.
2. Aletayeb M, Farajzadeh S, Dehdashtian M. Eleven-year study of causes of neonatal bacterial meningitis in Ahvaz, Iran Pediatrics International 2010; 52, 463–466.
3. Edwards MS, Baker CJ. Sepsis in the newborn. In Gershon AA, Hotez PJ, Katz SL, editors. Krugman’s Infectious Diseases of Children, 11th edition. Philadelphia: Mosby. 2004. Pp: 545-561.
4. Hristeva L, Booy R, Bowler I, Wilkinson AR. Prospective surveillance of neonatal meningitis. Arch. Dis. Child. 1993; 69: 14–8.
5. Klein JO. Bacterial meningitis and sepsis. In: Remington JS, Klein JO (eds.). Infectious Diseases of the Fetus and Newborn Infant. 4th edition WB Saunders, Philadelphia, PA. 2006. Pp: 943–98.
6. Klinger G, Chin CN, Beyene J, et al. Predicting the outcome of neonatal bacterial meningitis. Pediatrics. Sep 2000; 106(3):477-82.
7. Tiskumara R, Fakharee SH, Liu C-Q, Nuntnarumit P, Lui K-M, Hammoud M, et al. Neonatal infections in Asia. Arch Dis Child Fetal Neonatal Ed. March 2009; 94: 144-8.
8. Zaiedi AK, Thaver D, Ali SA, Khan TA. Pathogens associated with sepsis in newborns and young infants in developing countries. Pediatr Infect Dis J. 2009 Jan; 28 (Suppl. 1):S10-8.
9. Muhe L, Tilahun M, Lulsegd S et al. Etiology of pneumonia, sepsis, and meningitis in infants younger than three months of age in Ethiopia. Pediatric. Infect. Dis. J. 1999; 18(Suppl): 56–61.
10. Garges HP, Moody MA, Cotten CM, et al. Neonatal meningitis: what is the correlation among cerebrospinal fluid cultures, blood cultures, and cerebrospinal fluid parameters? Pediatrics. Apr 2006; 117(4):1094-100.
11. Edwards MS. Neonatal sepsis. In Martin RJ, Fanaroff AA, Walsh MC, editors. Fanaroff and Martin’s Neonatal-Perinatal Medicine. Diseases of the fetus and infant, 9th edition. Philadelphia: Elsevier Mosby. 2010. Pp: 606-809.
12. Laving AM, Musoke RN, Wasunna AO, Revathi G. Neonatal bacterial meningitis at the newborn unit of Kenyatta National Hospital. East Afr. Med. J. 2003; 80: 456–62.
13. Chang Chien HY, Chiu NC, Li WC, Huang FY. Characteristics of neonatal bacterial meningitis in a teaching hospital in Taiwan from 1984–1997. J. Microbiol. Immunol. Infect. 2000; 33: 100–4.
14. Kavuncuoglu S, Gursoy S, Turel O, Aldemir E, Hosaf E. Neonatal bacterial meningitis in Turkey: epidemiology, risk factors, and prognosis J Infect Dev Ctries 2013; 7(2):073-081.
15. Gerdes JS Diagnosis and management of bacterial infections in the neonate. Pediatr Clin Nam. 2004; 51: 939-959.
16. Yikilmaz A and Taylor AG. Sonographic findings in bacterial meningitis in neonates and young infants. Pediatric Radiology 2008; 38: 129-137.