

# Overview on the Causes and Management of Neonatal Meningitis

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## Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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## ABSTRACT

In comparison to other ages, neonatal meningitis is more prevalent. Because the immature immune system lacks humoral and cellular immunological responses in phagocytic and complement functions, the newborn is especially vulnerable to infection. According to the World Health Organization, almost 5 million newborn fatalities occur each year. The great majority of them (98%) take place in underdeveloped countries. Meningitis is diagnosed through a physical examination and a study of the patient's medical history for any of the symptoms listed above. Although patients with viral meningitis normally do not require hospitalisation, antipyretics, antiemetics, and analgesics that may be used at home should be offered.

**Keywords:** Neonatal bacterial meningitis; very low birth weight; lumbar puncture; cerebrospinal fluid; antibiotics; vaccine.

## 1. INTRODUCTION

The major burden of neonatal sepsis and meningitis happens in the developing world, but most of the evidence derives from the wealthy

countries although the range of disease, etiology and prognosis may differ. According to the WHO, there are approximately 5 million neonatal deaths each year. The vast majority (98 percent) occur in developing countries [1-3]. Neonatal meningitis

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donates significantly to the burden of neonatal morbidity and death, and other causes include other infection, prematurity and birth asphyxia. The true occurrence of neonatal bacterial meningitis may be undervalued, particularly in resource-poor settings for multiple reasons. These include trouble in diagnosing neonatal meningitis, differences between hospital-based and public studies, regional differences and unregistered deaths in areas where admission to health care is poor [4]. There is no consensus on the meaning of the neonatal or early infant period. Many studies define the neonatal retro as up to 30 or 90 days of age, and WHO defines 'young infant', as  $\leq 60$  days. Within these boundaries, it is estimated there are 126 000 cases of neonatal meningitis yearly, and more than 50 000 deaths [1-3]. Mortality rates vary by area, e.g. 0.7–1.9/1000 live births in sub-Saharan Africa, 0.33–1.5 in the Middle East and North Africa and 0.4-2.8 in the Americas and Caribbean [1].

Meningitis is more common in the neonatal historical than at any other time [5]. The newborn is particularly susceptible to infection as the undeveloped immune system is deficient in humoral and cellular immune replies in phagocytic and in complement functions [6]. In developed republics, mortality has dropped from nearly 50% in the 1970s to <10% [7-9], but morbidity leftovers substantial, and 20–58% of survivors will have serious neurological sequelae, such as deafness [7,6,10,9-11]. Death in the developing world remains unacceptably high, inconsistently reported as 40–58% [12-13]. Morbidity is under reported but supposed to be considerable.

Neonatal meningitis is a serious problem with a high death and frequent neurological sequelae. The prevalence rate of neonatal meningitis was intended, and the aetiology, clinical and laboratory features, and management of cases documented prospectively over a 7 year 8 month period were predictable. It was further investigated whether secondary meningitis had arisen after lumbar puncture. The estimated occurrence of bacterial, viral, and fungal meningitis was 0.25, 0.11, and 0.02 per 1000 live births correspondingly [14].

Despite the rapid development of new pathogen diagnosis and antibiotics, neonatal meningitis (NM) contributes to worldwide infant mortality and morbidity. Neonatal meningitis is an inflammation of the lining of the brain during the

first 28 days of life [15]. Depending on when it was diagnosed, it was either early-onset meningitis (EOM) or late-onset meningitis (LOM). In EOM, the clinical topography emerges during the first weeks of life. LOM occurs 8 to 28 times after birth [16,17]. The incidence of bacterial meningitis in neonates ranges from 0.25 to 1 per 1000 live births and occurs in 25% of neonates with sepsis [18,19]. In established countries, group B streptococcus (GBS) is the most common cause of bacterial meningitis, accounting for 50% of all cases. Escherichia coli (E. coli) accounts for an additional 20%.

Therefore, identifying and treating maternal urogenital tract infections is an important prevention strategy [20]. In emerging countries, gram-negative bacilli such as Klebsiella and E. Coli may be more common than GBS, especially in LOM [21,22]. In addition, other organisms considered to cause meningitis include Enterobacter spp., Citrobacter spp. and Serratia spp. Meningitis is several times more severe with gram-negative bacteria and has a higher morbidity and mortality rate [23]. Diagnosis of NM is based on both clinical presentation and examination of cerebrospinal fluid (CSF). Cerebrospinal fluid culture is an excellent test to demonstrate meningitis. Evaluation of white blood cell counts, glucose, and cerebrospinal fluid protein levels can aid in the diagnosis [24]. This school study evaluated infants diagnosed with meningitis between 2008 and 2012 at our high school. We evaluated the maternal and neonatal risk aspects, clinical presentation, pathogenetic and neurologic complications of neonatal meningitis cases.

## 2. SYMPTOMS OF MENINGITIS IN BABIES

The symptoms of meningitis can come on very quickly. Your baby may be hard to comfort, especially when they're being held. Other symptoms in a baby may contain:

- Developing a abrupt high fever
- Neonates not accepting breastfeeding
- Vomitings
- Being less active or energetic than usual
- Being very sleepy or hard to wake up
- Being more irritable than usual
- Bulging of the soft spot on their head (the anterior fontanelle)

Other symptoms may be hard to notice in a baby, such as:

- Severe headache
- Neck stiffness
- Sensitivity to bright light

Irregularly, a baby may have a seizure. Many times this is due to the high fever and not the meningitis itself.

### 3. CAUSES OF MENINGITIS IN BABIES

Bacteria, viruses, or a fungus can cause meningitis in a baby. Viral meningitis has long been the most common cause of meningitis. Since the development of vaccines to prevent bacterial meningitis, this type of meningitis has developed increasingly uncommon. Fungal meningitis is occasional.

#### 1-Viral meningitis:

Meningitis is an inflammatory condition that affects the three protective membranes that cover the brain and spinal cord, called the meninges [25]. The outermost layer of the meninges is called the dura mater, followed by the arachnoid and meninges. The two inner layers (arachnoid and fibula) are also called meninges and are separated by the subarachnoid space, which stores cerebrospinal fluid (CSF) [26]. Aseptic meningitis, also known as delayed viral disease, was of interest in the early 1950s when it was considered as a possible model for chronic diseases of the nervous system [27]. Bacteria are the most common cause of meningitis. However, viruses, fungi, and non-infectious mediators such as drugs can also cause meningitis [26]. Pathogens can move through the CSF by hematogenous spread by two main mechanisms: 1) by infecting immune cells, where the fissure transports the pathogen to the nervous system, and 2) by migrating through blood capillaries and entering the CSF as a free pathogen [28]. The term aseptic meningitis is used to define meningitis caused by pathogens other than pyogenic bacteria [29]. Viral meningitis is the most common type of aseptic meningitis and usually affects young children [25]. Enterovirus (EV) is the major causative agent of viral meningitis, with approximately 75,000 new cases each year in the United States [30]. In the following, we provide an overview of viral meningitis and its main common pathogens and their pathogenesis. We also consider the epidemiological, diagnostic, and clinical aspects of the disease.

Viral meningitis usually isn't as thoughtful as bacterial or fungal meningitis, but some viruses do cause a severe infection. Common viruses that typically cause mild disease include:

- 1- Non-polio enterovirus. These viruses cause most cases of viral meningitis in the United States. They cause many types of infections, including colds. Many people get the disease, but very few people get meningitis. The virus is spread when your child comes in contact with sick stools or oral secretions.
- 2- Flu. This virus causes the flu. It is a feast caused by contact with secretions from the lungs or mouth of a person with the condition.
- 3- Measles and the mumps virus. Meningitis is a rare condition of these highly contagious viruses.

Viruses that can cause very severe meningitis contain are:

**1-Varicella:** This virus causes chickenpox. It's easily blowout by contact with a person infected with it.

**2-Herpes simplex virus:** A baby usually gets it from their mother in the womb or during birth.

**3-West Nile virus:** This is conveyed by a mosquito bite.

Children under 5, including babies, have a higher risk of receiving viral meningitis. Babies between birth and 1 month of age are more likely to mature a severe viral infection.

#### 2-Bacterial meningitis:

Bacterial meningitis is a dangerous infection that is associated with high mortality and morbidity in infants. Prompt diagnosis and management are essential for successful outcomes in affected neonates. Although overall morbidity and mortality have decreased over the past decades, the incidence of neonatal meningitis has remained largely unchanged [31,32]. Neonatal meningitis is a rare disease. Although morbidity and mortality have decreased in recent decades, morbidity among survivors remains high. The nature and distribution of pathogens is related to gestational age at birth, postpartum age and geographic region. Confirming the discovery of meningitis can be difficult. Clinical signs are often

subtle and lumbar puncture is often delayed in clinically unstable neonates. When informed consent is obtained, cerebrospinal fluid (CSF) cultures are often facilitated by prenatal or postnatal antibiotic exposure. While blood cultures and CSF boundaries can be helpful in uncertain diagnoses, bacterial meningitis can occur in neonates without sepsis and a normal CSF border. . Newer trials such as polymerase chain reaction show promise but more research is needed. Prompt action with appropriate antibiotics is essential to optimize outcomes. Successful efforts to prevent neonatal meningitis have included the use of prophylactic antibiotics in childbirth against group B streptococcus (GBS) [33].

During the first 28 days of life, bacterial meningitis is most often produced by bacteria called:

1. Group B Streptococcus. It is usually transmitted from the mother to the baby at birth.
2. Gram-negative bacilli such as *Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae*. *E. coli* can be transmitted from the mother to the baby during childbirth, whether it is dirty food, food made by someone who used the toilet without washing their hands at the time.
3. *Listeria Monocytogenes*. Newborns usually get these from their mother in utero. Babies rarely get it at birth. Mothers get it by eating contaminated foods, especially refrigerated foods.

In children under 5 years, including babies over 1 month old, the most mutual bacteria that cause meningitis are:

- 1- Streptococcal pneumonia. This bacteria is found in the sinuses, nose, and lungs. It is spread by breathing air that an infected person has sneezed or coughed on. It is the most common cause of bacterial meningitis in infants younger than 2 years of age.
- 2- *Neisseria meningitidis*. It is the second most common cause of bacterial meningitis. It is spread by contact with secretions from the lungs or mouth of an infected person. Infants under 1 year of age are most at risk of being affected.
- 3- *Haemophilus influenzae* type b (Hib). It is spread by interacting with secretions from the mouth of a carrier. Carriers of the

bacteria usually don't get sick, but can make you tasteless. Babies need to be in close contact with pathogens for several days to grow up. Even then, most babies will just become carriers and not develop meningitis.

### 3-Fungal meningitis:

Fungal meningitis is rare because it usually only affects people with weakened immune systems. Certain fungi can cause meningitis. Three types of fungi live in the soil and one lives around bat and bird droppings. The fungus enters the body through the respiratory tract. Unbalanced premature babies are at increased risk for contamination in the blood from a fungus called *Candida*. A baby often gets this fungus in the hospital after birth. It can then be transported to the brain, causing meningitis. Although overall survival in low-birth-weight (VLBW) infants has improved over the past period, nosocomial infections continue to have a negative impact on clinical outcomes for impaired hosts. immunodeficiency develops [34]. Among these infections, disseminated or disseminated candidiasis is a major cause of morbidity and mortality. An alteration of the pathogenic classes of *Candida* causing systemic neonatal disease has recently been reported, with more infections caused by non-albicans species [35,36]. CNS involvement as a complication of sporadic *Candida* infections may be associated with increased morbidity, and the number of cases of *Candida* meningitis in TPN children appears to be increased [36,37]. However, little is known about the risk factors, clinical features, laboratory findings, management, and outcomes of *Candida* meningitis in these neonates.

### 4-Aseptic meningitis:

When a toxic infant or young child presents with fever and is lethargic or irritable, it is important to consider the diagnosis of acute meningitis in the absence of classic focal signs and symptoms. Cerebrospinal fluid will be obtained (unless lumbar puncture is clinically contraindicated) to enable initial treatment planning. Initial CSF findings may not definitively distinguish aseptic meningitis from bacterial meningitis, and antibacterial rehabilitation of all likely organisms should be instituted. until a definitive culture result is available. Comprehensive treatment, including antiseptics and antiviral agents, should continue until the cause is identified and more specific treatment is initiated, eliminating the

cause or the patient's condition improves. significant and complete course of antibiotic treatment. Group B streptococcus is the most common bacterial agent in cases of meningitis occurring during the first month after birth. The etiologies of aseptic meningitis include viral infections, partially treated bacterial meningitis, congenital infections, drug responses, post-vaccination complications, systemic disease, and malignancies. Long-term sequelae of meningitis include neuromuscular deficits, learning disabilities, and hearing loss. Prompt diagnosis and treatment are essential to improve outcomes [38].

#### 4. DIAGNOSIS

##### 1-Diagnosis of viral meningitis:

The diagnosis of meningitis begins with an ancient patient health overview of one of the physical examinations and the above-mentioned signs. Recently accepted physical methodologies developed to evaluate the stimulus of Meningeal are known as stimuli. Systematic review made by Iguchi and his colleagues showed that emergency accents can remove meningitis using emergencies. However, the sensitivity of this test and the associated sensitivity and specificity (65.3%, 70.4%, respectively), respectively (respectively) is considered to be low, and more research is required to evaluate its exploration [39]. Poke the lumbar puncture and CSF collection to check the pathogenic agent. The surgery is performed by placing the patient in a supine or sitting position and aspiration of CSF by inserting a hollow needle into the subarachnoid space between the L3, L4, or L5 vertebrae [40]. The cerebrospinal fluid is then tested to control the number of red and white blood cells, as well as glucose and protein levels. The number of cells usually helps distinguish the different types of meningitis. For example, bacterial meningitis usually presents with a high white blood cell count ( $\geq 500$  cells/ $\mu\text{L}$ ) along with a high neutrophil count ( $>80\%$ ).

##### 2-Diagnosis of bacterial meningitis:

To confirm the diagnosis of neonatal meningitis, a PL is sought to collect cerebrospinal fluid. Active growth on CSF cultures helps identify the offending organism and allows for fine-tuning therapy [41,42,43].

**Perform or delay LP:** Because LP is an invasive technique with risks, it is difficult to

determine which infants should receive this drug as part of septic management [44,45]. Among children who receive a positive blood culture, up to 30% will have a positive CSF culture simultaneously [46]. However, in neonates with meningitis, 15-38% will have a negative blood group [47-49].

**Interpretation of CSF parameters:** Neonates are often exposed to antibiotics during birth or empirically prior to receiving PL, which may lead to false-negative CSF philosophy in those with meningitis [50] In these cases, CSF restrictions are used to help determine the likelihood of meningitis.

**Secondary Tests:** Polymerase chain reaction (PCR) has been used as a diagnostic tool for meningitis. In addition to better sensitivity and specificity, PCR also allows for faster pathogen detection than conventional culture [51].

#### 5. MANAGEMENT OF MENINGITIS

##### 1-Treatment of the viral meningitis:

Patients with viral meningitis do not need to be hospitalized, but they must provide treatment, such as repellents, antimicrobial agents, and analgesics that can be deduced at home. However, some patients, such as those who wound from attacks, should be under medical management [52]. In order to reduce inflammation effects involved in this disease, it is generally given in corticosteroids in the case of bacterial meningitis, but there is a need for evidence of the effectiveness of the effectiveness of viral brain salts, and more training is still needed [53]. Pleconaril is an antiviral drug that acts as an entertainer copier inhibitor aiming for a structure of viral capsid [54]. It is adopted as a cure for a cold, but it is a potential treatment for divine diseases such as meningitis, because it leads to a slightly higher interest in CNS [55]. Pleconaril has been found to be a matter of studying the stroke of symptoms, especially in reducing the stroke of headaches [56]. However, according to a further study, there was no significant difference between the control group and the placebo [57]. Because the FDA causes the activity of the CYP3A enzyme, it has not approved the oral communication of the drug, so it leads to drug connection, especially oral contraceptula [58].

In a study in England, students have found that students stayed at the hospital in hospitals were

4 days for 9 days during patients with viral meningitis and antiviral treatment. They also decided that the delay of the puncture and unnecessary guidelines is related to long hospitals and long-term wetting rates [59]. In the case of sterile meningitis, accurate treatment is not prescribed and the drug is generally provided with minimal diseases such as fever and headache and in most cases from 5 to 14 days [60]. Regarding HSV leadership, according to one study, the antiviral rehabilitation of the immune bond patients containing the rare suspension should be almost started, and the delay of the treatment of the recipient may lead to the development of financial complications [61]. It also evaluated the use of Acyclovir for the HSV2Sided municipality with better results observed in patients with treated patients. However, one tolerance caused a problem of concentration as a symptom of meningitis lasting for about three months [62]. In recent years, PRSV1 and HSV2 are suppressed by Proteases and DNA polymerase to suppress HSV 1 and HSV2 to be prepared as possible to treat meningitis by HSV [63]. Valaciclovir has also been tested in clinical trials for its antiviral ability to inhibit the recurrence of meningitis. However, treatment with valaciclovir (twice daily) does not prevent meningitis recurrence and is not recommended for this definition [64,65]. Some vaccines have been developed against some microorganisms, such as EV71 [66].

## 2-Treatment of the bacterial meningitis:

**Antibacterial therapy:** It is important to start antibiotic treatment in a timely manner. Treatment discontinuation is associated with increased mortality and morbidity [67]. Empirical antimicrobials used for suspected meningitis require adequate CSF penetration and sensitivity with the most probable pathogens [68]. Once pathogens and their susceptibility are documented, antimicrobial reporting should be adjusted accordingly.

**Duration of antibiotic treatment:** In the case of simple meningitis, the minimum selective treatment period is as follows [69-71].

- 14 days for GBS, *L. monocytogenes* and *S. pneumonia*
- 21 days for gram-negative gut bacteria such as *Pseudomonas* and *E. coli*.

A longer course of treatment is optional for meningitis infants who have delayed clinical

improvement after healing has begun or who have complications such as brain abscesses, ventriculitis, or cerebral infarction [72].

**Adjuvant therapy:** There are several adjuvant therapies using.

Intra-ventricular antibiotics, dexamethasone, intravenous immunoglobulin, granulocyte or granulocyte-macrophage colony stimulating factor, and oral glycerol have been studied to improve punishment in infants with meningitis [73]. None of the suggested adjuvant therapies are currently used in routine practice.

## 6. CONCLUSION

Meningitis is more common in the neonatal period than at any extra time. In developed countries, mortality has dropped, but morbidity leftovers are substantial, with serious neurological sequelae. Patients with viral meningitis usually do not need to be hospitalized, but they should be given home-based antibiotics, antipyretics, antiemetics, and pain relievers.

## CONSENT AND ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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