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Research Article

# Neonatal meningitis: Preterm and term infants evaluated by magnetic-resonance-imaging-based score analysis

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**Abstract**

*Objectives*: To investigate the difference of brain damages between preterm and term infants with bacterial meningitis by using MRI-based score analysis.
*Methods*: The clinical information and MRI dataset of 65 newborns with meningitis were reviewed, including 18 preterm infants and 47 term ones. There were 13 basic brain injury patterns identified on cranial MRI. And the severity of these injuries was graded from score 1 to 3. These 13 patterns were further classified into three major groups − white matter abnormalities (WMA), gray matter abnormalities (GMA) and non-parenchyma abnormalities (NPA).
*Results*: Of all the newborns, 63% presented with cerebral lesions (41/65) and 3% presented with cerebral plus cerebellar damages (2/65). The incidence and MRI-based score of abnormal myelination of the posterior limb of internal capsules, ventricular dilatation and periventricular white matter volume loss were significantly higher in the preterm than the term group. Regarding WMA, GMA and NPA, the score of WMA in the preterm group was significantly higher than that of the term group ($p = .000$). While, the differences of GMA and NPA scores between the preterm and the term groups were not significant ($p = .076$, .224, respectively).
*Conclusion*: White matter abnormalities were more frequently seen in the preterm infants with meningitis.


*Keywords:* Newborn; Preterm; Term; Meningitis; Magnetic resonance imaging

## 1. Introduction

Neonatal bacterial meningitis is a serious disease globally, the incidence of which is described as 0.25−6.1 per 1000 live births (developed countries 0.3; Asia 0.48−2.4; Africa and South Africa 0.81−6.1) [1] and frequently leads to severe neurological impairment and potentially devastating consequences with a high mortality rate [2,3]. Mortality from neonatal meningitis in developing countries is estimated to be 40−58%, against 10% in developed countries [4]. Experience in the developed world suggests that even if mortality can be greatly reduced, the burden of continuing morbidity from meningitis in infancy remains high [5−7]. It is therefore important to study neonatal meningitis sin order to optimize treatment and prevention strategies.

Magnetic resonance imaging (MRI) is an important assessment tool that can be safely used for neonates. It is increasingly used to safely provide high resolution images of the brain parenchyma in premature newborns. In recent

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**Key points**

- Cerebral abnormalities are the most common nervous system abnormalities in neonatal meningitis.
- White matter abnormalities are common in neonatal meningitis.
- Preterm infants with meningitis are susceptible to more severe brain damage as compared to term ones.
- Preterm infants with meningitis are more inclined to develop white brain matter abnormalities.

studies, researchers used MRI to determine the spectrum of white matter injuries in premature newborns, they found that cystic periventricular leukomalacia (PVL) was distinctly uncommon, whereas non-cystic white matter injury was very common, which was not accurately detected by cranial ultrasound [8–12].

It is known that the cumulative incidence of meningitis is highest in the first month of life and its incidence is higher in preterm neonates than term ones [10–13]. For premature infants with meningitis, the neurodevelopmental consequences are often profound [11–14]. Despite the relatively high incidence and substantial morbidity, few published studies assess the MRI findings and their implications in infants with meningitis. Identifying brain injury early in life in infants with meningitis is crucial to effectively counseling parents of premature newborns regarding prognosis, as well as targeting these high-risk newborns for appropriate rehabilitation services. Thereby, we are interested in whether there are different brain injury patterns on MRI findings between preterm and term infants with bacterial meningitis. We reviewed and analyzed the brain MR images of both the preterm and term infants with bacterial meningitis at our hospital in the past two and half years. The results of this study provided further evidence implicating the brain damage and its structural abnormalities which might explain some of the functional deficits found in preterm infants.

## 2. Methods

### 2.1. Patients

We reviewed the cases of patients who were admitted to the neonatal intensive-care unit in Children's Hospital of Fudan University, between July 1, 2011, and Dec 31, 2013, with a final diagnosis of neonatal meningitis or purulent meningitis. Each patient's clinical history was collected including gestational age at birth, date of the onset, Gram staining of cerebrospinal fluid (CSF), composition of CSF (white blood cell count, glucose, and protein), result of CSF culture, polymerase chain reaction (PCR) amplification for enterovirus, date of cranial MRI examination and the discharge diagnosis. The patients were divided into preterm group (N = 18, gestational age at birth was<37 wk) and term group (N = 47, gestational age at birth was ≥37 wk and <42 wk).

Clinical characteristics of meningitis included fever, neck stiffness, vomiting, seizure, irritability, altered consciousness and so on. Because these features were nonspecific manifestations, the date when positive CSF was certified from lumbar puncture was designated as the onset date of meningitis.

Diagnosis of acute meningitis was based on the clinical findings and CSF examination. Referring to previously published studies [15–17], neonatal meningitis was diagnosed if any one of the following criteria was met: 1) positive CSF culture for the bacterial pathogen and negative PCR amplification for enterovirus; 2) more than 10 white blood cells/ml in CSF with positive blood culture for the bacterial pathogen on day 3 of admission; 3) negative for both CSF culture and PCR amplification, but showing pleocytosis (more than 100 white blood cells/mL in preterm infants while more than 32 white blood cells/mL in term infants) with CSF glucose less than 1.66 mmol/L; 4) more than 1000 white blood cells/ml of CSF with 75% polymorphonuclear cells.

Criteria for excluding the newborn from study enrollment were: 1) clinical evidence of the congenital malformation or syndrome; 2) congenital TORCH infection; 3) hypoxic ischemic encephalopathy (HIE).

The cranial MR images were reviewed if the newborn met one of the following criteria: 1) be a preterm infant, the onset time of meningitis was ≤40 corrected gestational weeks; 2) be a term infant, the onset time of meningitis was ≤28 day after birth.

Table 1 listed the infants'ages, times of meningitis onset and MRI examination performed in preterm and term newborns in this study.

### 2.2. MRI parameters

All MRI examinations were performed using a 1.5-T scanner (Magnetom, Siemens, Avanto, Germany). The MR imaging protocol included axial fast spin-echo T2-weighted imaging with the parameters included TR/TE 5000/78 or 82 ms, FOV 119 × 200 ~ 168 × 220, matrix, 246 × 512 ~ 284 × 640; axial spin-echo T1-weighted imaging with the parameters included TR/TE 500/12 ms, FOV 141 × 200 ~ 168 × 220, matrix 135 × 256 ~ 179 × 320; axial FLASH T1-weighted imaging with the parameters included TR/TE 195/4.8 ms, FOV 173 × 230, matrix 384 × 512; sagittal spin-echo T1-weighted imaging with the parameters included TR/TE 500/12 ms, FOV 131 × 200–141 × 220, matrix 123 × 256–135 × 256; axial turbo inversion recovery magnitude (Tirm) dark-fluid T2-weighted imaging with the parameters included TR/TE 5800 or 7800/89 ms, TI 1983.4 or 2340 ms, FOV 119 × 200 ~ 168 × 220, matrix 274 × 512; axial DWI with the parameters included TR/TE 2900/99 ms, FOV 200 × 200–210 × 210, matrix 128 × 128 or 192 × 192 and axial contrast-enhanced spin-echo T1-weighted imaging with the parameters included TR/TE 552/17 ms, FOV 210 × 168, matrix 320 × 154, slice thickness 4 mm and an interslice gap of 0.32 mm. DWI was performed using the single-shot EPI