ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Evaluation of Risk and Prognostic Factors in Neonatal Meningitis

Yenidoğan Menenjitinde Risk Etmenlerinin ve Prognostik Faktörlerin Değerlendirilmesi

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Abstract

Introduction: Neonatal meningitis is one of the important causes of mortality and morbidity in newborns. In this study, it was aimed to examine the microbiological factors, biochemical and clinical characteristics of neonatal meningitis cases, to reveal the risk factors, and to investigate the effect on the morbidities associated with meningitis in the first year of life.

Materials and Methods: The files of patients diagnosed with meningitis in the level 3 Neonatal Intensive Care Unit between January 2010 and December 2015 were retrospectively analyzed.

Results: There were 118 patients diagnosed with meningitis. The median gestational age of the patients was 32 weeks (24-40 weeks), and the median birth weight was 1987 grams (690-5020 grams). Most of the meningitis patients (n=106, 90%) were with late sepsis. The diagnosis day of those with poor prognosis was found to be greater [9.7 (2-28) days to 15.5 (3-138) days, p=0.03]. Cerebrospinal fluid (CSF) leukocytes were significantly higher in term babies with abnormal cranial magnetic resonance imaging (MRI) findings (p=0.037) and loss in hearing tests (p=0.045). CSF sugar levels were significantly lower in preterm babies with neuromotor retardation (p=0.001), history of seizures (p=0.003), abnormal cranial MRI findings (p=0.008) and hearing loss (p=0.005).

Conclusion: In the long term, a significant number of cases with neonatal meningitis have neuromotor retarda-tion and hearing problems. Factors that can be used as predictors for poor neurological development; late-onset day, increased CSF leukocyte in all babies, and decreased CSF sugar in preterm babies.

Keywords
Neonatal meningitis, newborn, meningitis sequelae, premature infant

Anahtar kelimeler
Neonatal menenjit, yenidoğan, menenjit sekeli, prematüre bebek

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Öz

Giriş: Menenjit, yenidoğanlarda önemli bir mortalite ve morbidite nedenidir. Bu çalışmada, yenidoğan menen-jitlerinin mikrobiyolojik, biyokimyasal ve klinik özelliklerinin incelenmesi ve yaşamın ilk yılındaki morbid-itelere etkili risk faktörlerinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: Ocak 2010-Aralık 2015 tarihleri arasında 3. Düzey Yenidoğan Yoğun Bakım Ünitesi'nde menenjit tanısı alan hastaların dosyaları geriye dönük olarak incelendi.

Bulgular: Menenjit teşhisi konan 118 hasta vardı. Hastaların ortanca gebelik yaşı 32 hafta (24-40 hafta), ortanca doğum ağırlığı 1987 gram (690-5020 gram) idi. Menenjit hastalarının çoğu (n=106, %90) geç sepsis hastasıydı. Prognozu kötü olanların tanı günü daha fazla [9,7 (2-28) gün ile 15,5 (3-138) gün] olarak bulundu,

p=0,03. Anormal kraniyal manyetik rezonans (MR) bulguları (p=0,037) ve işitme testlerinde kayıp (p=0,045) olan term bebeklerde beyin omurilik sıvısı (BOS) lökositleri anlamlı olarak daha yüksekti. Nöromotor retardasyonu (p=0,001), nöbet öyküsü (p=0,003), anormal kraniyal MR bulguları (p=0,008) ve işitme kaybı (p=0,005) olan erken doğmuş bebeklerde BOS şeker düzeyleri anlamlı olarak daha düşüktü.

Sonuç: Yenidoğan menenjitli olguların önemli bir kısmında uzun dönemde nöromotor gerilik ve işitme sorunları görülmektedir. Tüm bebekler için; geç başlangıç günü ve yüksek BOS lökositi, ayrıca prematüre bebekler için ise düşük BOS şekeri kötü nörolojik gelişimin belirteci olarak değerlendirilebilir.

Introduction

The incidence of neonatal meningitis is reported to be 0.25-0.32 per 1000 live births, and meningitis is associated with a rate of 5-10% in early-onset sepsis cases and 25% in late-onset sepsis cases (1,2). The mortality rate for neonatal meningitis is 10-15% and this rate varies according to the time of diagnosis, the causative agent and the time of treatment onset (3). The incidence of neonatal meningitis and associated mortality rate has decreased in the last 50 years due to better antenatal follow-up, intrapartum antibiotic use, and developments in the neonatal intensive care unit (NICU) (4). Long-term complications in survivors are 20-50%, including visual defects, middle ear disease and behavioral problems (5). Risk factors of neonatal meningitis are low birth weight (<2500 g), preterm delivery, premature rupture of membranes (PROM), septic or traumatic birth, fetal hypoxia and maternal peripartum infection (6). The most common causes of neonatal meningitis include group B *Streptococcus* and *Escherichia coli* (4).

In this study, it was aimed to examine the microbiological factors, biochemical and clinical characteristics of neonatal meningitis cases, to reveal the risk factors and to investigate the effect on the morbidities associated with first-year meningitis.

Materials and Methods

Approval for this study was obtained from the Uludağ University Ethics Committee (2016-21/13). Patients who were admitted to the third level NICU with the diagnosis of early and late sepsis in the six years of time (between 01/01/2010-31/12/2015) were included in the study. These patients were diagnosed with meningitis and were followed up until the age of one after discharge. Maternal infection status, maternal diseases, gestational week, delivery route, apgar scores, birth weight, gender, time of diagnosis, acute phase reactants at the time of diagnosis, cerebrospinal fluid (CSF) findings, CSF culture results, cranial imaging findings and neuromotor, cognitive and auditory morbidities of the first year of follow-up were examined retrospectively from the electronic files of the patients. Neuromotor retardation status of the patients was evaluated by the Denver test.

The diagnosis of sepsis is performed by evaluating the clinical and laboratory findings according to the European Medicines Agency scoring (7). Patients in which the causative agent was documented were considered as proven sepsis. Sepsis occurred in the first 72 hours of life was evaluated as early sepsis, and after the first 72 hour as late sepsis.

Diagnosis of meningitis was performed by positive CSF culture, or CSF protein level >150 mg/dL in preterms, >100 mg/dL in terms and CSF glucose level <20 mg/dL in preterms, <30 mg/dL in terms (or less than 70-80% of the concurrent blood glucose value), or CSF leukocyte count >20-30 cells/mm^3. Patients diagnosed with meningitis accompanying early and late sepsis were evaluated separately (8).

Patients whose Denver test and cranial imaging results were found to be normal and whose antiepileptic drugs were discontinued during the follow-up, although there was a history of seizures, were identified as the group with good prognosis. Patients who died, who had neuromotor and mental retardation, and who continued to use antiepileptic drugs with a diagnosis of epilepsy were identified as the group with poor prognosis.

Statistical Analysis

In the statistical analysis of our study; the compliance of continuous variables to normal distribution was examined by Kolmogorov-Smirnov test. According to the results of normality test, t-test or Mann-Whitney U was used for comparisons between groups. Categorical variables were compared between groups using chi-square or Fisher's exact test. The numerical data were expressed as the mean ± standard deviation (SD) or median (min-max) and the categorical data as frequencies and percentages. SPSS 25.0 (IBM

SPSS Statistics for Windows, Version 25.0) program was used for analysis, and the significance level was determined as $p<0.05$ in statistical comparisons.

Results

The number of patients diagnosed with meningitis in the evaluated six-year period was 118, 18 patients who died before the follow-up was excluded and the morbidity data of 100 patients were examined. The epidemiological and demographic characteristics of the patients are given in Table 1.

Mortality rate was found to be 15.2% in 118 cases diagnosed with meningitis. During the same period, a total of 1360 patients, 326 (23%) early sepsis and 1034 (77%) late sepsis, were followed up with a diagnosis of sepsis. Of the patients diagnosed with meningitis, 12 (10%) were with early sepsis, and 106 (90%) were with late sepsis.

Acute phase reactants and CSF findings were similar in meningitis cases accompanying early sepsis and late sepsis in both term and preterm babies. Blood leukocyte count, CRP, CSF leukocyte count, protein and glucose levels of patients with meningitis accompanying early and late neonatal sepsis are examined in Table 2 for preterm and term infants.

Table 1. Epidemiological and demographic characteristics of the patients	
Preterm delivery, n (%)	77 (77)
Birth weight, gram, median (minimum-maximum)	1987 (690-5020)
Low apgar score at 5 minimum, n (%)	8 (8)
Gestational age at birth, median (minimum-maximum)	32 (24-40)
Cesarean delivery, n (%)	71 (71)
Male gender, n (%)	63 (63)
The day of diagnosis of meningitis, median (minimum-maximum)	11,1 (2-40)
Day of hospitalization, median (minimum-maximum)	45.6 (13-154)
Early sepsis, n (%)	11 (11)
History of PROM, n (%)	13 (13)
History of preeclampsia/eclampsia, n (%)	20 (20)
PROM: Premature rupture of membranes	

Table 2. CSF findings and acute phase reactants in preterm and term meningitis cases with early and late neonatal sepsis			
Preterm babies	Meningitis cases with early neonatal sepsis median (min-max) n=8	Meningitis cases with late neonatal sepsis median (min-max) n=69	p[a]
WBC (K/uL)	10 700 (8,920-20,900)	13 100 (5,170-55,400)	0.350
CRP (mg/dL)	1.44 (0.32-5.33)	0.47 (0.3-12.5)	0.340
CSF leukocyte (/mm^3)	20.14 (10-800)	30 (10-2,470)	0.799
CSF protein (mg/dL)	161.5 (104-392)	157 (30-965)	0.582
CSF glucose (mg/dL)	48.5 (30-82)	48 (10-116)	0.537
Term babies	Meningitis cases with early neonatal sepsis median (min-max) n=3	Meningitis cases with late neonatal sepsis median (min-max) n=20	
WBC (K/uL)	7 930 (6 150-11 600)	13 950 (5 820-19 300)	0.059
CRP (mg/dL)	2.1 (0.46-3.5)	3.12 (0.3-17.6)	0.904
CSF leukocyte (/mm^3)	10 (10-20)	20 (10-190)	0.190
CSF protein (mg/dL)	120 (99-142)	114 (43-256)	0.802
CSF glucose (mg/dL)	55 (45-59)	56 (12-83)	0.574
[a]Mann-Whitney U test, WBC: White blood leukocyte, CRP: C-reactive protein, CSF: Cerebrospinal fluid			

Positive blood culture was determined in 21 (21%) patients and positive CSF culture was determined also in 21 (21%) patients. All patients with positive culture results are cases of late neonatal meningitis with sepsis. None of the early neonatal meningitis cases with sepsis had positive culture. The CSF and blood culture results are detailed in Table 3. Gram positive agents were isolated more frequently than gram negatives in blood (14 vs 3) and CSF (19 vs 1) cultures. The most frequently isolated microorganism in both blood and CSF is *S. epidermidis* (respectively 10 and 11). *Candida* were isolated in five patients' blood (4) and CSF (1) cultures.

The rates and statistical comparisons of neurological morbidities in term and preterm infants are shown in Table 4. Hearing aids were worn in three of the patients with auditory loss during follow-up, and all of these patients were preterm cases. Of the patients with abnormal cranial MR findings, 13 had nonspecific bleeding sequelae, 8 patients had periventricular leukomalacia, 10 patients had hydrocephalus, and 10 patients had cortical atrophy 12 of 22 preterm patients and 4 of 7 term patients with seizures had epileptiform anomaly on EEG. It was determined that all patients with normal EEG and only two of the patients with abnormal EEG did not have seizures persisted and their antiepileptic drug was discontinued after the first year.

Comparison results of neurological morbidities and CSF biochemistry results in term infants are

Table 3. Blood and CSF culture results

	Meningitis cases with late neonatal sepsis (n=89)	
Microorganism	CSF culture n (%)	Blood culture n (%)
Gram positive cocci	19 (90.5)	14 (66.5)
Staphylococcus Epidermidis	11 (52)	10 (47.5)
Staphylococcus Haemolyticus	3 (14)	1 (4.7)
Enterococcus Faecium	2 (9.5)	1 (4.7)
Staphylococcus Capitis	-	1 (4.7)
Staphylococcus Chromogenes	-	1 (4.7)
Streptococcus Mitis	1 (4.7)	-
Micrococcus Luteus	1 (4.7)	-
Staphylococcus Hyicus	1 (4.7)	-
Gram negative bacilli	1 (4.7)	3 (14)
Klebsiella Pneumoniae	1 (4.7)	1 (4.7)
Serratia Marcescens	-	1 (4.7)
Stenotrophomonas Maltophilia	-	1 (4.7)
Candida Parapsilosis	-	3 (14)
Candida Albicans	1 (4.7)	1 (4.7)
Total	21 (100)	21 (100)

CSF: Cerebrospinal fluid

Table 4. Comparison of the neurological results of the cases

Neurological morbidities	Preterm cases (n=77) n (%)	Term cases (n=23) n (%)	p[a]
Abnormal cranial MRI findings	25 (32.4)	6 (26)	0.562
Abnormal ABR	20 (25.9)	5 (21.7)	0.681
Retardation in Denver test	18 (23.3)	3 (13)	0.286
History of seizures	22 (28.5)	7 (30.4)	0.861

[a]Chi-square test, MRI: Magnetic resonance imaging, ABR: Auditory brainstem response

shown in Table 5. Comparison results of neurological morbidities and CSF biochemistry results, birth weight and gestational week in preterm infants are shown in Table 6.

The effect of CSF findings, the day of diagnosis, delivery type, low birth weight and gender on mortality and neurological prognosis are given in Table 7. It was determined that CRP, CSF leukocyte count levels and the day of diagnosis were significantly higher in cases with poor prognosis.

Discussion

Although neonatal meningitis is more common in cases with late sepsis, it is also seen in cases with early sepsis. Tan et al. (8) showed in their study in 2015 that there were 12.5% cases of neonatal meningitis accompanying early sepsis. Similarly, 89% of the cases in our study were determined as neonatal meningitis with late sepsis, 11% as neonatal meningitis with early sepsis. Median day of diagnosis was found 11.1 in our

Table 5. Association between CSF biochemistry findings and neurological morbidities in term infants

Neurological morbidities		CSF protein median (min-max)	CSF leukocyte median (min-max)	CSF glucose median (min-max)
Abnormal cranial MRI findings	Yes, 6	126 (54-233)	25 (10-190)	42 (12-74)
	No, 17	99 (43-256)	15 (10-40)	58 (45-83)
	p[a]	0.674	0.037	0.141
Abnormal ABR	Yes, 5	128 (71-233)	20 (20-40)	51 (46-83)
	No,18	109 (43-256)	10 (10-190)	56 (12-82)
	p[a]	0.297	0.045	0.737
Retardation in Denver test	Yes, 3	161 (123-167)	20 (10-190)	51 (29-60)
	No, 20	86.5 (43-256)	15 (10-40)	56.5 (12-83)
	p[a]	0.144	0.672	0.437
History of seizures	Yes, 7	130 (85-256)	20 (10-190)	48 (12-82)
	No, 16	73 (43-174)	15 (10-40)	58 (45-83)
	p[a]	0.124	0.629	0.160

[a]Mann-Whitney U test, CSF: Cerebrospinal fluid, MRI: Magnetic resonance imaging, ABR: Auditory brainstem response

Table 6. Association between CSF biochemistry findings and neurological morbidities in preterm infants

Neurological morbidities		Birth weight Mean ± SD	Gestational age at birth mean ± SD	CSF protein mean ± SD	CSF leukocyte mean ± SD	CSF glucose mean ± SD
Abnormal cranial MRI findings	Yes, 25	1307 (780-2660)	30±2.8 29 (26-36)	144 (71-965)	20 (10-1300)	38 (10-97)
	No, 52	1515 (690-3680)	31 (24-36)	164 (30-392)	10 (10-2470)	50 (10-116)
	p[a]	0.352	0.029	0.125	0.234	0.008
Abnormal ABR	Yes, 20	1320 (690-2320)	30 (26-35)	150 (71-965)	20 (10-330)	39 (14-116)
	No, 57	1500 (780-3680)	30 (24-36)	159 (30-392)	10 (10-2470)	51 (10-112)
	p[a]	0.231	0.231	0.862	0.768	0.005
Retardation in Denver test	Yes, 18	1292 (780-2320)	29 (24-35)	143 (105-965)	10 (10-1300)	32 (10-69)
	No, 59	1530 (690-3680)	31 (26-36)	161 (30-392)	20 (10-2470)	51 (10-116)
	p[a]	0.115	0.055	0.527	0.951	0.001
History of seizures	Yes, 22	1367 (780-3680)	31 (24-36)	151 (85-965)	10 (10-1300)	36 (10-112)
	No, 55	1470 (690-2660)	30 (26-36)	160 (30-392)	20 (10-2470)	51 (23-116)
	p[a]	0.830	0.188	0.960	0.155	0.003

[a]Mann-Whitney U test, CSF: Cerebrospinal fluid, MRI: Magnetic resonance imaging, ABR: Auditory brainstem response, SD: Standard deviation

Table 7. Comparison of cases with good and poor prognosis			
	Cases with good prognosis n=70	Cases with poor prognosis n=48	p
Male gender, n (%)	44 (62)	19 (39)	0.162[a]
Birth weight <2500 g, n (%)	51 (72)	34 (70)	0.861[a]
Cesarean delivery, n (%)	51 (72)	34 (70)	0.782[a]
Day of prognosis of meningitis, median (min-max)	9.7 (2-28)	15.5 (3-138)	0.030[b]
WBC (K/uL), median (min-max)	13 555 (5 170-33 600)	15 270 (5 820-55 400)	0.584[b]
CRP (mg/dl), median (min-max)	1.48 (0.33-11)	2.6 (0.3-17.6)	0.040[b]
CSF leukocyte (/mm^3), median (min-max)	48 (0-800)	130 (0-2470)	<0.001[b]
CSF protein (mg/dL), median (min-max)	148 (43-392)	198 (91-965)	0.622[b]
CSF glucose (mg/dL), median (min-max)	56 (24-116)	42 (10-120)	0.761[b]
[a]Chi-square test, [b]Mann-Whitney U test, WBC: White blood leukocyte, CRP: C-reactive protein, CSF: Cerebrospinal fluid			

study similar to the literature. Kumar et al. (9) also found mean day of diagnosis of menengitis 11 in their study published in 2017.

In the literature, risk factors for neonatal meningitis are low birth weight (<2500 g), premature birth, premature rupture of membranes, septic or traumatic labor, fetal hypoxia, and maternal peripartum infection (10). In our study, among these risk factors; prematurity rate was 74%, the history of PROM in the mother was 13%, male gender was 63%, cesarean section was 71% and the median birth weight was 1987 g. Since there was no control group, only descriptive analysis could be done in terms of risk factors.

In our study, any microorganism could not be isolated in the CSF culture in cases diagnosed with neonatal meningitis accompanying early sepsis. In a single center study conducted by Kavuncuoğlu et al. (11) in Turkey, they found the positive culture rate as 18% and the most frequently isolated microorganism as *S. epidermidis*, and gram positive agents were isolated more frequently than gram negatives. Similarly in our study, the positive CSF culture rate in cases of neonatal meningitis with late sepsis was found to be 17.7%, and the most common isolated agent was *S. epidermidis*. It has been observed that gram positive agents are isolated at a higher rate. In a long-term cross-sectional study conducted by Mashau et al. (12), it was stated that the frequency of gram-negative agents increased and antibiotic sensitivity decreased. In addition, *Ureaplasma species* are also reported as the causative agent of neonatal meningitis (13). Therefore, when the routine microbiological tests and conventional treatments are negative, other relevant pathogens can be diagnosed using metagenomic next-generation sequencing and polymerase chain reaction tests (13).

Different results have been reported in the literature regarding the effect of the day of diagnosis of meningitis on prognosis. Tatishvili et al. (14) found a relationship between poor prognosis and neonatal meningitis with early sepsis. However in their study, Kumar et al. (9) found no difference in terms of prognosis in cases diagnosed with neonatal meningitis accompanying both early and late sepsis. In our study, it was observed that the median diagnosis day of the patients with poor prognosis was significantly high.

In the prognostic examination of CSF findings on neurological morbidities; it was observed that high CSF leukocyte levels in term infants and low CSF glucose levels in preterm infants were significantly associated with the development of neurological morbidities. High levels CRP and CSF leukocyte count and the late day of diagnosis were found as prognostic factor for poor prognosis. However, Tan et al. (8) reported higher CSF protein levels in neonatal meningitis cases with poor prognosis and showed that CSF protein levels remained high in these cases after two weeks of treatment. Many newborns with negative CSF culture are considered to have central nervous system infection. The data mentioned above support that CSF biochemistry parameters can be used alone or in combination as both diagnostic and prognostic markers in cases with negative CSF culture. Rajial et al. (15) reported that CSF procalcitonin values could be used to diagnose neonatal meningitis.

Neonatal meningitis continues to be an important cause of morbidity and mortality for newborns. It

causes neuromotor retardation and hearing problems in the long term in a significant part of the patients living. Most of the patients are premature babies whose hospitalization continues in the neonatal clinics, and reducing nosocomial infections will also reduce neonatal meningitis.

The weakness of our study is that the rate of microbiologically confirmed cases is low, there is no control group, and it is a retrospective study. Other limitations of this study are that clinical findings at the time of diagnosis and the predominance of multinucleated cells in CSF were not evaluated in the study.

Conclusion

In neonatal meningitis cases; late diagnosis day, high CSF leukocyte levels in term infants, low CSF glucose levels in preterm infants can be used as a predictor for poor neurological development. Studies examining prognostic factors, risk factors and CSF findings in neonatal meningitis prospectively are needed.

Ethics

Ethics Committee Approval: Approval for this study was obtained from the Uludağ University Ethics Committee (decision no: 2016-21/13, date: 27.12.2016).

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Hristeva L, Booy R, Bowler I, Wilkinson AR. Prospective surveillance of neonatal meningitis. Arch Dis Child 1993;69:14-8.
2. Jordan HT, Farley MM, Craig A, Mohle-Boetani J, Harrison L, Petit S, et al. Revisiting the need for vaccine prevention of late-onset neonatal group B streptococcal disease: a multistate, population-based analysis. Pediatr Infect Dis J 2008;27:1057-64.
3. Harvey D, Holt DE, Bedford H. Bacterial meningitis in the newborn: a prospective study of mortality and morbidity. Semin Perinatol 1999;23:218-25.
4. Edwards MS, Baker CJ. Bacterial meningitis in the neonate: Clinical features and diagnosis. In: UpToDate, Armsby C (Ed), UpToDate, Waltham, MA; 2020.
5. Baud O, Aujard Y. Neonatal bacterial meningitis. Handb Clin Neurol 2013;112:1109-13.
6. Overall JC Jr. Neonatal bacterial meningitis. Analysis of predisposing factors and outcome compared with matched control subjects. J Pediatr 1970;76:499-511.
7. Satar M, Arısoy AE, Çelik İH. Turkish Neonatal Society guideline on neonatal infections-diagnosis and treatment. Turk Pediatri Ars 2018;53:88-100.
8. Tan J, Kan J, Qiu G, Zhao D, Ren F, Luo Z, et al. Clinical prognosis in neonatal bacterial meningitis: the role of cerebrospinal fluid protein. PLoS One 2015;10:e0141620.
9. Kumar M, Tripathi S, Kumar H, Singh SN. Predictors of Poor Outcome in Neonates with Pyogenic Meningitis in a Level-Three Neonatal Intensive Care Unit of Developing Country. J Trop Pediatr 2018;64:297-303.
10. Fanaroff AA, Korones SB, Wright LL, Verter J, Poland RL, Bauer CR, et al. Incidence, presenting features, risk factors and significance of late onset septicemia in very low birth weight infants. The National Institute of Child Health and Human Development Neonatal Research Network. Pediatr Infect Dis J 1998;17:593-8.
11. Kavuncuoğlu S, Gürsoy S, Türel Ö, Aldemir EY, Hoşaf E. Neonatal bacterial meningitis in Turkey: epidemiology, risk factors, and prognosis. J Infect Dev Ctries 2013;7:73-81.
12. Mashau RC, Meiring ST, Dramowski A, Magobo RE, Quan VC, Perovic O, et al. Culture-confirmed neonatal bloodstream infections and meningitis in South Africa, 2014-19: a cross-sectional study. Lancet Glob Health 2022:e1170-8.
13. Qin L, Li YH, Cao XJ, Wang XJ, Mao RP, Yang HY, et al. Clinical metagenomic sequencing for rapid diagnosis of neonatal meningitis caused by Ureaplasma parvum: A case report. Medicine 2022;101:e28662.
14. Tatishvili NA, Sirbiladze TV, Kipiani TB, Sasaniia IZ, Tatishvili SZ. Early predictors of neuro developmental outcome of neonatal bacterial meningitis. Georgian Med News 2005;129:82-4.
15. Rajial T, Batra P, Harit D, Singh NP. Utility of Cerebrospinal Fluid and Serum Procalcitonin for the Diagnosis of Neonatal Meningitis. Am J Perinatol 2022;39:373-8.