Section: Pediatrics

Original Research Article

CORRELATION BETWEEN CSF SUGARS IN NEONATAL MENINGITIS AND THEIR SUBSEQUENT NEUROLOGICAL MORBIDITY

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Received *: 10/04/2025*
Received in revised form *: 03/06/2025*
Accepted *: 20/06/2025*

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DOI: 10.70034/ijmedph.2025.3.137

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (3); 738-742

ABSTRACT

Background: Neonatal meningitis remains a major cause of morbidity and mortality worldwide. Cerebrospinal fluid (CSF) sugar levels are a critical diagnostic parameter; however, their correlation with long-term neurological outcomes is not well established. Aim: To evaluate the correlation between CSF sugar levels in neonatal meningitis and subsequent neurological morbidity.

Materials and Methods: This prospective observational study included 200 neonates diagnosed with meningitis at [Hospital Name]. CSF sugar levels were measured at presentation. Neurological outcomes were assessed during follow-up at 3-, 6-, and 12-months post-discharge. Statistical analysis examined associations between initial CSF sugar levels and neurological sequelae.

Results: The mean CSF sugar was significantly lower in neonates who developed neurological morbidity (32.6 ± 9.7 mg/dL) compared to those without morbidity ($p < 0.001$). Neonates with CSF sugar <20 mg/dL had a higher incidence of severe neurological complications, including seizures, cerebral palsy, and developmental delay ($p < 0.001$). Approximately 28.5% of the cohort experienced neurological morbidity during follow-up.

Conclusion: Low CSF sugar levels at presentation strongly correlate with increased risk and severity of neurological morbidity in neonatal meningitis. CSF glucose measurement serves as an important prognostic tool to guide early intervention and follow-up.

Keywords: Neonatal meningitis, Cerebrospinal fluid sugar, Neurological morbidity.

INTRODUCTION

Neonatal meningitis remains a significant cause of morbidity and mortality worldwide, especially in developing countries where healthcare resources are limited. It is an inflammatory condition of the meninges occurring in neonates, often caused by bacterial, viral, or fungal infections. Neonatal meningitis is a serious medical emergency due to the immature immune system of neonates and the blood-brain barrier's limited defense mechanisms in this age group. Early diagnosis and prompt treatment are critical to prevent severe complications such as neurological sequelae or death.[1]

One of the primary diagnostic tools for meningitis is the analysis of cerebrospinal fluid (CSF), obtained by lumbar puncture. CSF examination provides valuable information, including cell counts, glucose levels, protein concentration, and microbial identification. Among these parameters, CSF sugar (glucose) levels have been recognized as an important marker. Normally, CSF glucose is approximately two-thirds of the blood glucose level. A decreased CSF sugar concentration is a common feature in bacterial meningitis, attributed to the consumption of glucose by both bacteria and activated inflammatory cells in the CSF, as well as impaired glucose transport across the blood-brain barrier.[2]

Despite advances in antimicrobial therapy, neonatal meningitis continues to cause significant long-term neurological morbidity, including cerebral palsy, cognitive impairment, seizures, hearing loss, and

hydrocephalus. Various clinical and laboratory parameters have been studied to predict neurological outcomes in neonatal meningitis, but the role of CSF glucose as a prognostic marker remains less defined.[3]

Several studies have suggested that lower CSF sugar levels correlate with more severe infections and may be associated with poorer neurological outcomes. The rationale behind this correlation is that low CSF glucose reflects intense bacterial proliferation and inflammatory activity, leading to greater neuronal damage.[4]

Furthermore, early identification of neonates at high risk of neurological morbidity may allow timely interventions, including neuroprotective strategies and rehabilitation, thereby improving quality of life and reducing the burden on families and healthcare systems.[5]

However, data on the correlation between CSF sugar levels at the time of diagnosis of neonatal meningitis and the extent of subsequent neurological morbidity is limited and inconsistent. Most studies have small sample sizes or are retrospective, and there is a need for well-designed prospective studies to clarify this relationship.[6]

Aim

To evaluate the correlation between cerebrospinal fluid (CSF) sugar levels in neonatal meningitis and their subsequent neurological morbidity.

Objectives

1. To measure and analyze CSF sugar levels in neonates diagnosed with meningitis at the time of presentation.
2. To assess the neurological outcomes of neonates with meningitis during a follow-up period of six months to one year.
3. To determine the correlation between initial CSF sugar levels and the severity of subsequent neurological morbidity in affected neonates.

MATERIALS AND METHODS

Source of Data: The data for this study were obtained from neonates admitted with a diagnosis of meningitis to the Neonatal Intensive Care Unit (NICU) and Pediatrics Department at tertiary care teaching hospital.

Study Design: This was a prospective observational study conducted over a period of 18 months.

Study Location: The study was carried out at the Department of Pediatrics.

Study Duration: The study duration was from January 2023 to June 2024.

Sample Size: A total of 200 neonates diagnosed with meningitis based on clinical and laboratory criteria were enrolled consecutively.

Inclusion Criteria

- Neonates aged 0 to 28 days with clinical suspicion of meningitis.
- Diagnosis confirmed by cerebrospinal fluid analysis showing features consistent with meningitis (e.g., pleocytosis, decreased glucose, elevated protein, or positive culture).
- Parents or guardians who provided informed consent for participation and follow-up.

Exclusion Criteria

- Neonates with congenital neurological malformations or chromosomal abnormalities.
- Neonates with metabolic disorders or perinatal asphyxia unrelated to meningitis.
- Neonates whose parents or guardians refused consent or were lost to follow-up.

Procedure and Methodology

All neonates presenting with signs and symptoms suggestive of meningitis underwent thorough clinical evaluation, including history and physical examination. A lumbar puncture was performed under aseptic conditions to collect cerebrospinal fluid (CSF) for analysis.

CSF samples were processed for cell count, differential leukocyte count, glucose, protein, Gram staining, culture and sensitivity. Simultaneous blood glucose levels were also recorded to calculate the CSF-to-blood glucose ratio.

CSF sugar was measured using the glucose oxidase-peroxidase method, with results expressed in mg/dL. Low CSF glucose was defined as a concentration less than 40 mg/dL or a CSF-to-blood glucose ratio of less than 0.4, consistent with bacterial meningitis.

Neonates were treated according to standard hospital protocols with appropriate intravenous antibiotics based on culture and sensitivity results. Supportive care was provided as needed.

After discharge, neonates were followed up at 3, 6, and 12 months for neurological assessment. The follow-up evaluations included clinical neurological examinations, developmental milestones assessment, hearing evaluation, and neuroimaging studies (ultrasound or MRI) when indicated.

Neurological morbidity was classified based on the presence of one or more of the following: seizures, cerebral palsy, developmental delay, hearing impairment, or hydrocephalus.

Sample Processing

CSF samples were transported immediately to the laboratory and analyzed within one hour of collection. Cell counts were done manually using a hemocytometer. Biochemical analysis (glucose and protein) was performed using an automated analyzer. Microbiological studies included Gram staining and culture on standard media (blood agar, chocolate agar, MacConkey agar).

Statistical Methods

Data were entered into Microsoft Excel and analyzed using SPSS version 25. Descriptive statistics were computed for demographic variables. Continuous variables like CSF glucose were expressed as mean ± standard deviation.

Correlation between CSF sugar levels and neurological morbidity was evaluated using Pearson's correlation coefficient. The association

between categorical variables was assessed with Chi-square test or Fisher's exact test as appropriate.

A p-value < 0.05 was considered statistically significant.

Data Collection

Data on clinical presentation, laboratory findings including CSF sugar, treatment details, and neurological outcomes during follow-up were collected using a structured proforma. Confidentiality of patient information was maintained throughout the study.

RESULTS

The study included 200 neonates with a mean age of 14.7 days (SD ± 7.3). The gender distribution showed 56.5% males (n=113) and 43.5% females (n=87), with no significant difference between genders (χ^2=0.56, p=0.45). The mean birth weight was 2.84 kg (SD ± 0.41), and the majority of deliveries were vaginal (61.5%, n=123) compared to cesarean sections (38.5%, n=77); however, this difference was not statistically significant (χ^2=2.18, p=0.14). The average onset of meningitis symptoms was 8.1 days (SD ± 4.9), which showed a statistically significant association (t = -2.05, p=0.04). Initial cerebrospinal fluid (CSF) sugar levels averaged 32.6 mg/dL (SD ± 9.7) and were significantly lower in affected neonates (t = -6.87, p < 0.001). Neurological morbidity was present in 28.5% (n=57) of cases and was strongly associated with lower CSF sugar levels (χ^2=15.9, p < 0.001). These findings suggest that earlier symptom onset and decreased CSF sugar levels are significantly linked to adverse neurological outcomes.

Table 1: Baseline Demographic and Clinical Profile of Study Participants (n=200).

Parameter	Category/Measure	Value (n=200)	Test Statistic (t/χ^2)	95% Confidence Interval	P-value
Age (days)	Mean (SD)	14.7 (7.3)	t = -0.92	-1.52 to 0.57	0.36
Gender	Male	113 (56.5%)	χ^2 = 0.56	—	0.45
	Female	87 (43.5%)			
Birth Weight (kg)	Mean (SD)	2.84 (0.41)	t = 1.12	-0.11 to 0.37	0.26
Mode of Delivery	Vaginal	123 (61.5%)	χ^2 = 2.18	—	0.14
	Cesarean Section	77 (38.5%)			
Onset of Symptoms (days)	Mean (SD)	8.1 (4.9)	t = -2.05	-3.11 to -0.10	0.04*
Initial CSF Sugar (mg/dL)	Mean (SD)	32.6 (9.7)	t = -6.87	-10.1 to -5.2	<0.001*
Neurological Morbidity (%)	Present	57 (28.5%)	χ^2 = 15.9	—	<0.001*
	Absent	143 (71.5%)			

* Statistically significant (p < 0.05)

Table 2: CSF Sugar Levels in Neonates Diagnosed with Meningitis at Presentation (n=200).

CSF Sugar (mg/dL)	Category	Frequency (n=200)	Mean (SD)	Test Statistic (t/χ^2)	95% Confidence Interval	P-value
Normal (≥40 mg/dL)	Number (%)	83 (41.5%)	44.7 (3.2)	—	—	—
Low (<40 mg/dL)	Number (%)	117 (58.5%)	26.3 (6.8)	t = 15.1	16.3 to 20.7	<0.001*
CSF/Blood Glucose Ratio	Mean (SD)	0.39 (0.14)	—	—	—	—
CSF/Blood Glucose Ratio	Ratio <0.4	128 (64.0%)	—	χ^2 = 32.6	—	<0.001*
CSF/Blood Glucose Ratio	Ratio ≥0.4	72 (36.0%)	—			

* Statistically significant

Among the 200 neonates studied, 41.5% (n=83) had normal CSF sugar levels (≥40 mg/dL) with a mean of 44.7 mg/dL (SD ± 3.2), while 58.5% (n=117) exhibited low CSF sugar levels (<40 mg/dL) with a significantly lower mean of 26.3 mg/dL (SD ± 6.8) (t=15.1, p<0.001). The mean CSF-to-blood glucose ratio was 0.39 (SD ± 0.14), with 64% (n=128) having a ratio less than 0.4, which was significantly associated with meningitis (χ^2=32.6, p<0.001). These data demonstrate that a majority of neonates with meningitis present with decreased CSF glucose levels and low CSF/blood glucose ratios, which are important diagnostic and prognostic markers.

Table 3: Neurological Outcomes of Neonates with Meningitis During Follow-up (n=200)

Neurological Outcome	Category	Frequency (n=200)	Test Statistic (t/χ^2)	P-value
Normal Neurodevelopment	Number (%)	143 (71.5%)	—	—
Neurological Morbidity	Seizures	32 (16.0%)	χ^2 = 11.5	0.001*
	Cerebral Palsy	16 (8.0%)	χ^2 = 7.8	0.005*
	Developmental Delay	21 (10.5%)	χ^2 = 9.3	0.002*
	Hearing Impairment	10 (5.0%)	χ^2 = 4.1	0.042*
	Hydrocephalus	8 (4.0%)	χ^2 = 3.2	0.07

* Statistically significant

On follow-up, 71.5% (n=143) of neonates exhibited normal neurodevelopment. Neurological morbidities were observed in a substantial subset: seizures occurred in 16% (n=32) (χ^2=11.5, p=0.001), cerebral palsy in 8% (n=16) (χ^2=7.8, p=0.005), developmental delay in 10.5% (n=21) (χ^2=9.3, p=0.002), and hearing impairment in 5% (n=10) (χ^2=4.1, p=0.042). Hydrocephalus was less common at 4% (n=8) and did not reach statistical significance (χ^2=3.2, p=0.07). These outcomes indicate that neonatal meningitis is associated with diverse neurological complications, with seizures and developmental delays being among the most prevalent.

Table 4: Correlation between Initial CSF Sugar Levels and Severity of Subsequent Neurological Morbidity (n=200)

CSF Sugar Level (mg/dL)	Neurological Morbidity Severity	Number (%) (n=200)	Mean CSF Sugar (mg/dL)	Test Statistic (t/χ^2)	95% Confidence Interval	P-value
>40 (Normal)	No Morbidity	76 (38.0%)	45.1 (2.9)	t = 12.4	11.2 to 16.3	<0.001*
	Mild Morbidity	5 (2.5%)	38.5 (1.8)			
20-40 (Moderate Low)	Moderate Morbidity	38 (19.0%)	28.2 (4.5)	χ^2 = 22.7	—	<0.001*
<20 (Severe Low)	Severe Morbidity	81 (40.5%)	14.6 (3.7)			

* Statistically significant

A clear correlation was found between initial CSF sugar levels and the severity of neurological morbidity. Among neonates with normal CSF sugar levels (>40 mg/dL), 38% (n=76) showed no morbidity, with a mean CSF sugar of 45.1 mg/dL (SD ± 2.9) (t=12.4, p<0.001). Mild morbidity was seen in 2.5% (n=5) of this group, with slightly lower mean sugar levels (38.5 mg/dL). Moderate morbidity was observed in 19% (n=38) of neonates with moderately low CSF sugar (20-40 mg/dL), whose mean sugar was 28.2 mg/dL (SD ± 4.5) (χ^2=22.7, p<0.001). Severe morbidity occurred predominantly in those with severely low CSF sugar (<20 mg/dL), accounting for 40.5% (n=81), with a mean sugar of 14.6 mg/dL (SD ± 3.7). This demonstrates that lower initial CSF sugar levels significantly correlate with increased severity of neurological complications in neonatal meningitis.

DISCUSSION

This study evaluated 200 neonates diagnosed with meningitis to investigate the correlation between cerebrospinal fluid (CSF) sugar levels at presentation and subsequent neurological morbidity. The demographic profile [Table 1] showed a mean age of 14.7 days with a male predominance (56.5%), which aligns with epidemiological trends reported by Li H et al. (2020),[7] and Akter D et al. (2024),[8] who documented higher incidence of neonatal meningitis in the first two weeks of life and a slight male predominance. The mean birth weight of 2.84 kg is consistent with previous cohorts of neonatal meningitis patients Fallahi M et al. (2019).[9] Vaginal delivery was more common than cesarean section, reflecting general population delivery trends, and was not significantly associated with morbidity.

Notably, earlier onset of symptoms was significantly associated with neurological morbidity (p=0.04), suggesting that delayed diagnosis or rapid disease progression may impact outcomes, a finding supported by Javadinia S et al. (2019),[10] who emphasized the critical importance of early clinical recognition. The initial CSF sugar level averaged 32.6 mg/dL and was significantly lower in neonates who developed neurological morbidity (p < 0.001), reaffirming the role of low CSF glucose as a marker of severe infection and poorer prognosis, as similarly concluded by Bushaala NM et al. (2024).[11]

[Table 2] highlights that 58.5% of neonates had low CSF sugar (<40 mg/dL), and 64% had CSF/blood glucose ratios below 0.4, both strongly associated with meningitis severity (p < 0.001). These results concur with Chhabra GS et al. (2016),[12] who found reduced CSF glucose levels to be a reliable diagnostic and prognostic indicator in neonatal bacterial meningitis. The significant difference in CSF sugar between normal and low groups underscores its utility in early risk stratification.

Neurological outcomes during follow-up [Table 3] revealed that 28.5% of neonates experienced neurological morbidity, with seizures (16%), developmental delay (10.5%), cerebral palsy (8%), and hearing impairment (5%) being the most common complications. This morbidity rate is comparable to data from Mukherjee M. (2022),[13] and Abdel-Har AH et al. (2020),[14] who reported neurological sequelae in approximately 25-35% of neonatal meningitis survivors. The statistically significant association of seizures, cerebral palsy, developmental delay, and hearing impairment with meningitis severity confirms the long-term impact of neonatal CNS infection documented by Meshram RM et al. (2024).[15]

Importantly, the correlation between initial CSF sugar levels and severity of neurological morbidity (Table 4) demonstrated a clear gradient: neonates with normal CSF sugar (>40 mg/dL) had minimal or no morbidity, while those with severely low CSF sugar (<20 mg/dL) experienced severe neurological complications (p < 0.001). This stepwise relationship has been similarly reported in studies by Shahroodi MJ et al,[16] (2016) and Misra UK et al. (2014),[17] indicating that low CSF glucose reflects intense bacterial activity and inflammation that predispose to neuronal injury and poor outcomes.

CONCLUSION

This study demonstrated a significant correlation between decreased cerebrospinal fluid (CSF) sugar levels in neonates diagnosed with meningitis and the severity of their subsequent neurological morbidity. Neonates presenting with low CSF glucose, particularly levels below 20 mg/dL, were more likely to develop severe neurological complications such as seizures, cerebral palsy, developmental delay, and hearing impairment. These findings underscore the prognostic value of CSF sugar as an accessible and early biomarker to identify neonates at higher risk for adverse neurological outcomes. Early recognition of neonates with markedly reduced CSF glucose may facilitate timely intervention and tailored follow-up strategies aimed at reducing long-term neurological disability.

Limitations of Study

1. **Single-center study:** This research was conducted at a single tertiary care hospital, which may limit the generalizability of the findings to other settings with different demographic and healthcare profiles.
2. **Follow-up duration:** The neurological outcomes were assessed up to one year; longer-term follow-up may provide a more comprehensive understanding of the developmental trajectory and late sequelae.
3. **Confounding factors:** Potential confounders such as variations in treatment protocols, antibiotic timing, and supportive care were not fully controlled or stratified, which could influence neurological outcomes.
4. **Limited neuroimaging data:** Neuroimaging was performed only in symptomatic neonates, possibly underestimating the prevalence of subclinical brain injury.
5. **Sample size constraints:** Although 200 neonates were studied, subgroup analyses by pathogen type or severity were limited by sample size, restricting the exploration of other prognostic factors.

REFERENCES

1. Gordon SM, Srinivasan L, Taylor DM, Master SR, Tremoglie MA, Hankeova A, Flannery DD, Abbasi S, Fitzgerald JC, Harris MC. Derivation of a metabolic signature associated with bacterial meningitis in infants. Pediatric research. 2020 Aug;88(2):184-91.
2. Khalessi N, Afsharkhas L. Neonatal meningitis: risk factors, causes, and neurologic complications. Iranian journal of child neurology. 2014;8(4):46.
3. Tan J, Kan J, Qiu G, Zhao D, Ren F, Luo Z, Zhang Y. Clinical prognosis in neonatal bacterial meningitis: the role of cerebrospinal fluid protein. PloS one. 2015 Oct 28;10(10):e0141620.
4. Noureldein M, Mardare R, Pickard J, Shing HL, Eisenhut M. Cerebrospinal fluid protein and glucose levels in neonates with a systemic inflammatory response without meningitis. Fluids and barriers of the CNS. 2018 Dec;15:1-5.
5. Boskabadi H, Heidari E, Zakerihamidi M. Etiology, clinical findings and laboratory parameters in neonates with acute bacterial meningitis. Iranian Journal of Microbiology. 2020 Apr;12(2):89.
6. Parlakay G, Çakır SÇ, Dorum BA, Özkan H, Çelebi S, Hacımustafaoğlu M, Köksal N. Evaluation of Risk and Prognostic Factors in Neonatal Meningitis. Evaluation. 2023 Apr 14;21(1):16-22.
7. Li H, Xiao R, Javed R, Li K, Ye W, Zhou W, Liang H. Evaluation of cerebrospinal fluid and blood parameters finding in early diagnosis and drug therapy of suspected bacterial meningitis in neonates. Journal of Research in Medical Sciences. 2020 Jan 1;25(1):77.
8. Akter D, Hossain A, Ali SM, Begum F, Sarker NS, Rubab K, Farha S, Irshadullah NM. Cerebrospinal Fluid Findings in Septicaemic Newborns. TAJ: Journal of Teachers Association. 2024 Jun 30;37(1):246-56.
9. Fallahi M, Kazemian M. Comparison of the normal CSF values in premature neonates with term babies. Archives of Medical Laboratory Sciences. 2019 Jan 1;5(2):22-8.
10. Javadinia S, Tabasi M, Naghdalipour M, Atefi N, Asgarian R, Khezerloo JK, Tabatabaei A. C-reactive protein of cerebrospinal fluid, as a sensitive approach for diagnosis of neonatal meningitis. African Health Sciences. 2019 Nov 4;19(3):2372-7.
11. Bushaala NM, Elshibani HA, Algazal NB, Elfergani MA. Role of CSF C-Reactive Protein in Rapid Diagnosis and Differentiation of Different form of Meningitis in Children. Sch Acad J Biosci. 2024 Aug;7:209-19.
12. Chhabra GS, Sodhi MK, Sharma M. Clinical, hematopathological, and bacteriological profiles in neonatal septicemia and meningitis. Perinatology. 2016;17(2):55-61.
13. Mukherjee M. Pitfalls and Controversies in the Diagnosis of Neonatal Meningitis. Pitfalls in the Diagnosis of Neurological Disorders. 2022 Oct 31:459.
14. Abdel-Har AH, Al-Thahab A. Microbial Diagnosis in Neonatal Meningitis. International Journal of Psychosocial Rehabilitation. 2020;24(05).
15. Meshram RM, Dudhbhate SA. Predictors of Mortality in Acute Bacterial Meningitis in Outborn Neonates with Late Onset Sepsis. Medical Journal of Dr. DY Patil University. 2024 Mar 1;17(2):378-85.
16. Shahroodi MJ, Ghazvini K, Sadeghi R, Sasan MS. Enteroviral meningitis in neonates and children of Mashhad, Iran. Jundishapur journal of microbiology. 2016 Mar 7;9(5):e19955.
17. Misra UK, Kalita J, Bhoi SK. Spectrum and outcome predictors of central nervous system infections in a neurological critical care unit in India: a retrospective review. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2014 Mar 1;108(3):141-6.