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Association of Cerebrospinal Fluid Leukocyte and Lactate Dehydrogenase Levels with Length of Hospital Stay in Pediatric Patients with Ventriculitis Receiving Intrathecal Antibiotic Therapy at Adam Malik Hospital, Medan, Indonesia, 2024–2025

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ABSTRACT

Introduction: Pediatric ventriculitis is a serious central nervous system infection frequently associated with invasive neurosurgical procedures. Intraventricular inflammation leads to alterations in cerebrospinal fluid (CSF) parameters, including elevated leukocyte count and lactate dehydrogenase (LDH) levels. However, the relationship between these biomarkers and length of hospital stay remains unclear. To analyze the association between CSF leukocyte and LDH levels with length of hospital stay in pediatric patients with ventriculitis receiving intrathecal antibiotic therapy.
Methods: This study was an observational analytic study with a cross-sectional design involving pediatric patients diagnosed with ventriculitis. Bivariate analysis was performed using Spearman's correlation test to assess the relationships between variables.
Results: The majority of subjects were infants (85%) with a median age of 3.5 months. All patients demonstrated elevated CSF LDH levels, while 45% had increased CSF leukocyte counts. The median length of hospital stay was 30 days. A strong positive correlation was found between CSF leukocyte and LDH levels ($r = 0.720$; $p < 0.001$). However, no significant association was observed between CSF leukocyte levels and length of hospital stay ($r = 0.000$; $p = 0.999$), nor between CSF LDH levels and length of hospital stay ($r = 0.187$; $p = 0.430$).
Conclusion: CSF leukocyte and LDH levels are strongly correlated as indicators of intraventricular inflammation; however, neither parameter is significantly associated with length of hospital stay in pediatric ventriculitis patients.

Keyword: Ventriculitis, Cerebrospinal fluid, Leukocyte, Lactate dehydrogenase, Length of stay, Intrathecal antibiotics, Pediatric

1. Introduction

Ventriculitis is a serious inflammatory condition of the cerebral ventricular system that frequently occurs as a complication of nosocomial infections or post-neurosurgical procedures, such as shunt placement or external ventricular drain (EVD) insertion. In the pediatric population, ventriculitis presents unique challenges due to an immature immune system and subtle or atypical clinical manifestations. The occurrence of ventriculitis in children can lead to increased neurological morbidity, the need for repeated interventions, and prolonged hospital stays [1]. Categorized as healthcare-associated ventriculitis and meningitis (VM), its incidence varies depending on the procedure type and diagnostic criteria used. The incidence of EVD-related VM reaches up to 11.4 per 1,000 catheter-days, whereas for permanent shunts, it ranges from 4.1% to 20.5% [2].

Ventriculitis is characterized by inflammation of the ventricular system of the brain, accompanied by alterations in cerebrospinal fluid (CSF) biochemical parameters, such as elevated leukocyte counts, protein levels, and lactate dehydrogenase (LDH) enzyme activity [3]. Management of ventriculitis in children includes systemic antibiotics; however, in certain cases, adjunctive therapy using intrathecal or intraventricular antibiotics is required to achieve high local drug concentrations at the site of infection. Multiple retrospective studies have demonstrated the efficacy of this therapy in reducing mortality rates and accelerating ventricular fluid sterilization, particularly in infections caused by resistant Gram-negative bacteria such as *Acinetobacter baumannii* [4][5].

Length of stay (LOS) is a crucial indicator in clinical management, healthcare efficiency, and the assessment of therapeutic success. Analyzing the relationship between CSF leukocyte and LDH levels and the length of stay in pediatric ventriculitis patients receiving intrathecal antibiotics could offer new insights into understanding therapeutic response and potentially predicting hospital stay duration early on. However, limited research has specifically evaluated the association between CSF leukocyte and LDH levels and the length of stay among pediatric patients with ventriculitis undergoing intrathecal antibiotic therapy.

By analyzing the comparison of CSF leukocyte and LDH levels in pediatric ventriculitis patients treated with intrathecal antibiotics, this study is expected to contribute to the formulation of monitoring protocols and optimize the efficient use of intrathecal antibiotics in pediatric patients, particularly at Adam Malik General Hospital Medan.

2. Method

2.1. Study design and setting

This observational, quantitative analytical study employed a retrospective cohort design to evaluate the relationship between cerebrospinal fluid (CSF) leukocyte and lactate dehydrogenase

(LDH) levels and the length of hospital stay (LOS) in pediatric patients diagnosed with ventriculitis who received intrathecal antibiotic therapy. The study was conducted at Adam Malik General Hospital in Medan, Indonesia. Data collection and medical record reviews were carried out over a 3-month period from July to September 2025, encompassing eligible pediatric cases treated at the facility between 2024 and 2025.

2.2. Participants

The study population comprised all pediatric patients (aged 0–18 years) diagnosed with ventriculitis who received intrathecal antibiotic therapy at Adam Malik General Hospital, Medan, between 2024 and 2025. Eligibility Criteria:

1. Inclusion Criteria:
   a. Pediatric patients (aged 0–18 years) with a confirmed diagnosis of ventriculitis based on clinical findings and CSF analysis.
   b. Receipt of intrathecal antibiotic therapy during hospitalization.
   c. Complete laboratory data for CSF leukocyte counts and LDH levels.
   d. Complete medical records regarding the length of stay (LOS).

2. Exclusion Criteria:
   a. Presence of severe underlying comorbidities (e.g., malignancies, severe immunodeficiency) that could independently prolong hospital stay.
   b. Incomplete medical records or laboratory data.
   c. Diagnosis of meningitis or other central nervous system (CNS) infections without ventriculitis.

2.3. Sample size

The minimum sample size was calculated using the sample size estimation formula for correlation tests:

$$n = \left(\frac{Z_{1-\alpha} + Z_{1-\beta}}{0.5 \text{ In } \left(\frac{1+r}{1-r}\right)} \right)^2 + 3$$

The calculation incorporated a two-sided significance level (α) of 0.05 ($Z_{1-\alpha/2}$ = 1.96), statistical power of 80% ($Z_{1-\beta}$ = 0.84), and an expected minimum correlation coefficient (r) of 0.60, which reflects a strong correlation chosen considering the limited pediatric ventriculitis case volume receiving intrathecal therapy at a single tertiary center. The calculation yielded a minimum required sample size of 19 patients. A total sampling method was employed, enrolling all eligible pediatric patients who met the inclusion and exclusion criteria during the two-year observation period (2024–2025).

2.4. Variables and Operational Definitions

The primary independent variables were cerebrospinal fluid (CSF) leukocyte counts (cells/mm^3) and LDH activity (U/L), measured both before (pre-treatment) and after (post-treatment) intrathecal antibiotic administration. CSF leukocyte levels were categorized as normal (≤ 5 cells/mm^3) or elevated (> 5 cells/mm^3). CSF LDH levels were categorized as normal (< 40 U/L) or elevated (≥ 40 U/L).

The dependent variable was the length of hospital stay (LOS), measured as a continuous numerical variable (total days from admission to discharge) and dichotomized into short (≤ 14 days) and prolonged (> 14 days) stay.

Covariates and demographic variables included age (infants: 0–12 months; toddlers: 12–60 months; children: > 60 months), sex, causative pathogens (Gram-positive, Gram-negative, fungal, or negative culture), concurrent neurosurgical procedures (external ventricular drain [EVD], permanent shunt, or combined EVD and shunt), and the specific type of intrathecal antibiotic administered (vancomycin or amikacin).

2.5. Data Collection and Workflow

Data collection was conducted systematically following institutional ethical approval. Eligible patient records were identified through the hospital's medical record installation. Relevant demographic characteristics, clinical parameters, neurosurgical procedure details, and intrathecal antibiotic regimens were extracted. Pre- and post-intrathecal treatment laboratory values for CSF leukocyte counts and LDH levels were documented alongside the total duration of hospital stay. All retrieved data were verified for completeness before statistical processing.

2.6. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 31.0. Categorical variables were presented as frequencies and percentages (n, %). Continuous variables were tested for normality using the Shapiro–Wilk test ($n < 50$). Normally distributed data were expressed as mean ± standard deviation (SD), whereas non-normally distributed data were presented as median and interquartile range (IQR).

Bivariate analysis was conducted to evaluate the relationship between CSF leukocyte and LDH levels and the length of hospital stay. Correlation analysis was performed using Pearson's correlation coefficient for normally distributed data or Spearman's rank correlation coefficient for non-normally distributed data. Differences in hospital length of stay across clinical categories were analyzed using the independent t-test for normally distributed variables or the Mann–Whitney U test for non-normally distributed variables. A two-tailed p-value < 0.05 was considered statistically significant.

2.7. Ethical considerations

The study protocol received ethical clearance from the Health Research Ethics Committee at the Faculty of Medicine, Universitas Sumatera Utara. Written informed consent was obtained from all participants prior to enrollment, following a comprehensive explanation of the study objectives, procedures, and potential risks. Participation was strictly voluntary, with subjects retaining the right to withdraw at any time without compromising their standard clinical care. All collected data were anonymized using unique identification codes, with access to personal information restricted *exclusively* to the research team.

3. Results and Discussion

3.1. Subject characteristics

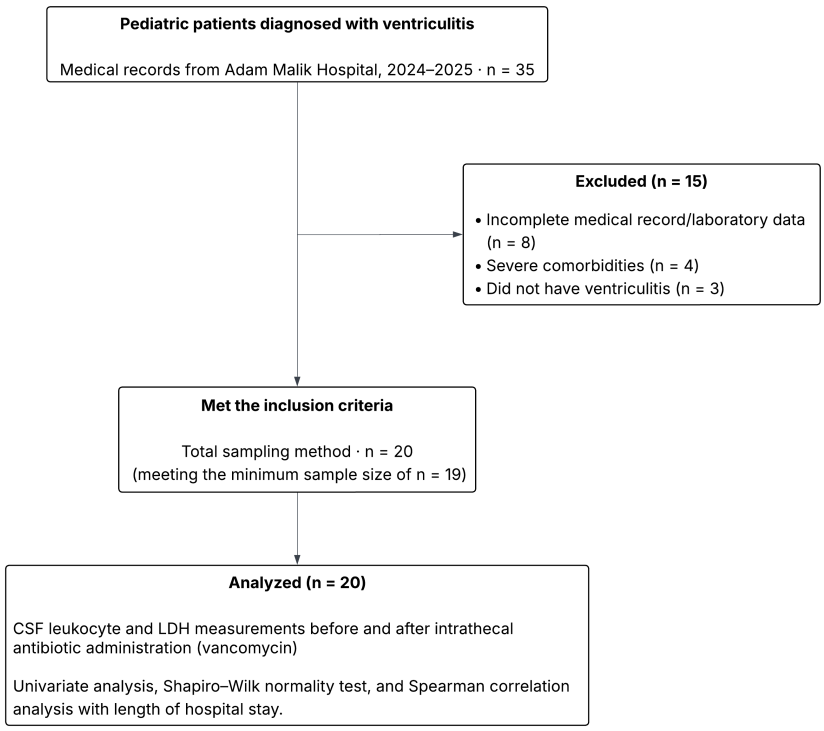


Figure 1 CONSORT Flowchart of Subject Selection

A total of 35 pediatric patients with ventriculitis were initially identified from the medical records of Adam Malik General Hospital between 2024 and 2025. Following eligibility screening, 15 patients were excluded due to incomplete medical or laboratory records (n = 8), severe comorbidities (n = 4), or alternative diagnoses (n = 3). Consequently, 20 patients met all inclusion criteria and were included in the final analysis using total sampling.

The categorical demographic and clinical characteristics of the study cohort are summarized in Table 1. Males accounted for the majority of subjects (n = 11, 55%). Categorized by age, most patients were infants aged 0–12 months (n = 17, 85%), followed by toddlers (n = 2, 10%) and older children (n = 1, 5%).

Prior to intrathecal antibiotic administration, baseline cerebrospinal fluid (CSF) leukocyte counts were within the normal range (≤ 5 cells/mm^3) in 11 subjects (55%) and elevated (> 5cells/mm^3) in 9 subjects (45%). Following intrathecal antibiotic therapy, CSF leukocyte levels normalized in all subjects (n = 20, 100%). Baseline CSF lactate dehydrogenase (LDH) activity was elevated (≥ 40 U/L) in all subjects (n = 20, 100%). Post-treatment CSF LDH activity normalized in 3 subjects (15%), while 17 subjects (85%) maintained elevated levels.

Regarding hospital length of stay (LOS), 19 subjects (95%) experienced a prolonged stay (> 14 days), whereas only 1 subject (5%) had a short stay (≤ 14 days). Gram-negative bacteria were the predominant causative pathogens (n = 12, 60%), followed by Gram-positive organisms (n = 6, 30%), and culture-negative cases (n = 2, 10%). All patients (n = 20, 100%) received intrathecal vancomycin monotherapy during hospitalization. Neurosurgical management consisted of combined external ventricular drain (EVD) and shunt procedures in 15 subjects (75%) and EVD insertion alone in 5 subjects (25%).

Table 1 Baseline Categorical Characteristics of Study Subjects

Variable	n	%
Sex		
Male	11	55
Female	9	45
Age Category		
Infant (0–12 months)	17	85
Toddler (12–60 months)	2	10
Child (> 60 months)	1	5
Pre-Treatment CSF Leukocyte Category		
Normal (≤ 5 cells/mm^3)	11	55
Elevated (> 5cells/mm^3)	9	45
Post-Treatment CSF Leukocyte Category		
Normal (≤ 5 cells/mm^3)	20	100
Elevated (> 5cells/mm^3)	0	0
Pre-Treatment CSF LDH Category		
Normal (< 40 U/L)	0	0
Elevated (≥ 40 U/L)	20	100
Post-Treatment CSF LDH Category		
Normal (< 40 U/L)	3	15
Elevated (≥ 40 U/L)	17	85
Length of Stay Category		
Short (≤ 14 days)	1	5
Prolonged (> 14 days)	19	95
Causative Pathogen		
Gram-negative	12	60
Gram-positive	6	30
No growth	2	10
Intrathecal Antibiotic Therapy		

Vancomycin	20	100
Neurosurgical Intervention		
Combined (EVD + Shunt)	15	75
EVD alone	5	25

The detailed microbiological distribution of causative pathogens is presented in Table 2. *Escherichia coli* was the most frequently isolated microorganism (n = 7, 35%), followed by *Staphylococcus aureus* (n = 4, 20%) and *Klebsiella pneumoniae* (n = 3, 15%). Other identified species included *Enterobacter hormaechei*, *Serratia marcescens*, *Staphylococcus capitis*, and *Staphylococcus saprophyticus* (n = 1, 5% each).

Table 2 Distribution of Isolated Pathogens in Ventriculitis

Microorganism	n	%
Escherichia coli	7	35
Staphylococcus aureus	4	20
Klebsiella pneumoniae	3	15
No growth identified	2	10
Enterobacter hormaechei	1	5
Serratia marcescens	1	5
Staphylococcus capitis	1	5
Staphylococcus saprophyticus	1	5
Total	20	100

3.2. Distribution of Continuous Variables and Normality Testing

Descriptive statistics for continuous variables are shown in Table 3. The median patient age was 3.50 months (range: 1–96 months; IQR: 10). Median pre-treatment CSF leukocyte count was 0.3055 cells/mm^3 (range: 0.016–57,735.000; IQR: 292.402), which decreased to 0.0420 cells/mm^3 (range: 0.001–154.000; IQR: 0.230) post-treatment. Baseline CSF LDH activity demonstrated a median of 415.50 U/L (range: 52–3,436; IQR: 1,036), decreasing to 173.50 U/L (range: 27–1,554; IQR: 438) following therapy. The median overall hospital length of stay was 30.00 days (range: 4–90 days; IQR: 38).

Table 3 Distribution of Continuous Numerical Variables

Variable	Median	Minimum–Maximum	IQR
Age (months)	3.50	1–96	10
Pre-treatment CSF Leukocytes (cells/mm^3)	0.3055	0.016–57,735.000	292.402
Post-treatment CSF Leukocytes (cells/mm^3)	0.0420	0.001–154.000	0.230
Pre-treatment CSF LDH (U/L)	415.50	52–3,436	1,036
Post-treatment CSF LDH (U/L)	173.50	27–1,554	438
Length of Stay (days)	30.00	4–90	38

Table 4 Shapiro–Wilk Normality Test Results

Variable	Shapiro–Wilk Statistic	p-value	Distribution
Age (months)	0.514	< 0.001	Non-normal
Pre-treatment CSF Leukocytes	0.283	< 0.001	Non-normal
Post-treatment CSF Leukocytes	0.242	< 0.001	Non-normal
Pre-treatment CSF LDH	0.715	< 0.001	Non-normal
Post-treatment CSF LDH	0.750	< 0.001	Non-normal
Length of Stay (days)	0.848	0.005	Non-normal

The Shapiro–Wilk test was utilized to evaluate data normality given the sample size ($n < 50$). As detailed in Table 4, all continuous variables exhibited a non-normal distribution ($p < 0.05$). Consequently, non-parametric Spearman's rank correlation analysis was selected for bivariate hypotheses testing.

3.3. Association Between CSF Leukocyte Counts and Length of Stay

Spearman's rank correlation revealed no statistically significant correlation between pre-treatment CSF leukocyte counts and length of hospital stay ($r_s = 0.000$, $p = 0.999$; Table 5).

Table 5 Association Between Pre-Treatment CSF Leukocyte Counts and Hospital Length of Stay

Variable Pair	Spearman Correlation Coefficient (rs)	p-value
Pre-treatment CSF Leukocytes vs. Length of Stay	0.000	0.999

Evaluated using Spearman's rank correlation; statistical significance set at $p < 0.05$.

3.4. Association Between CSF LDH Levels and Length of Stay

Spearman's correlation analysis demonstrated a very weak, positive correlation between pre-treatment CSF LDH activity and length of stay; however, this relationship was not statistically significant ($r_s = 0.112$, $p = 0.637$; Table 6).

Table 6 Association Between Pre-Treatment CSF LDH Levels and Hospital Length of Stay

Variable Pair	Spearman Correlation Coefficient (rs)	p-value
Pre-treatment CSF LDH vs. Length of Stay	0.112	0.637

Evaluated using Spearman's rank correlation; statistical significance set at $p < 0.05$.

3.5. Discussion

The male predominance (55%) observed in this study aligns with the broader epidemiological profile of pediatric ventriculitis as an infectious complication associated with invasive neurosurgical procedures, such as external ventricular drain (EVD) placement and shunt insertions, for which no consistent sex-dependent risk disparities have been established in the literature [2]. The vast majority of subjects were infants (85%) with a median age of 3.50 months,

consistent with the characteristic presentation of neonatal bacterial ventriculitis and meningitis, which frequently complicates enteric Gram-negative bacterial infections due to immune system immaturity and hyperpermeability of the blood-brain barrier in this age group [6][7]. These findings reinforce reports indicating that neonates and infants represent the highest-risk demographic for Gram-negative central nervous system infections, carrying significantly worse neurological outcomes compared to older pediatric cohorts [8]. Furthermore, 75% of patients underwent combined surgical interventions involving both EVD and shunt placement, underscoring a substantial burden of invasive management. Repeated intraventricular manipulations and serial device revisions consistently elevate the risk of ventriculitis while prolonging hospital stays due to the necessity for ongoing clinical monitoring and serial cerebrospinal fluid (CSF) evaluations [2][9].

Regarding inflammatory biomarker kinetics, 45% of subjects exhibited elevated baseline CSF leukocyte counts prior to therapy, whereas complete normalization (100%) was achieved following intrathecal antibiotic administration, accompanied by a sharp decline in median cell counts from 0.3055 to 0.0420 cells/mm³. This rapid clearance accords with evidence demonstrating a swift reduction in CSF leukocyte counts typically within the first seven days following adequate antimicrobial initiation, particularly in patients receiving combined intravenous and intraventricular antibiotic therapy under strict monitoring protocols [10]. Nevertheless, Infectious Diseases Society of America (IDSA) guidelines emphasize that CSF leukocyte counts should not serve as a sole surrogate marker for infection eradication, as both normal and abnormal cell counts can yield misleading interpretations in patients with indwelling intraventricular devices [1]. Consequently, serial CSF leukocyte monitoring must be interpreted alongside clinical and microbiological parameters rather than as an isolated determinant of therapeutic resolution [11].

In contrast to leukocyte kinetics, all subjects (100%) demonstrated elevated baseline CSF lactate dehydrogenase (LDH) activity, reflecting widespread cellular damage and cytolysis secondary to intraventricular inflammation [2]. Following intrathecal therapy, median CSF LDH levels decreased from 415.50 to 173.50 U/L; however, 85% of subjects maintained persistent LDH elevation at the final assessment. This pattern is consistent with the pathophysiological characteristic of LDH as a biomarker of structural neuronal and glial injury, which resolves at a markedly slower rate than cellular inflammatory infiltrates, as structural recovery lags behind active infectious control [12]. Previous literature has established that CSF LDH levels are consistently higher in bacterial meningitis and ventriculitis compared to non-bacterial inflammatory conditions, offering complementary diagnostic and prognostic value alongside other CSF markers such as creatine kinase and gamma-glutamyl transpeptidase [13]. Thus, CSF LDH in this setting is best conceptualized as a marker of ongoing structural tissue recovery rather than a binary indicator of acute infectious clearance at a single time point.

Microbiologically, *Escherichia coli* was the most frequently isolated organism (35%), followed by other Gram-negative bacilli including *Klebsiella pneumoniae*, *Enterobacter hormaechei*, and *Serratia marcescens*, bringing the overall Gram-negative pathogen burden to 60%. This distribution reflects an epidemiological shift in device-associated pediatric ventriculitis toward multidrug-resistant Gram-negative organisms, departing from the classic dominance of coagulase-negative staphylococci typically reported in adult populations [14]. The high prevalence of *E. coli* among infants in this cohort aligns with established evidence identifying this organism as a leading cause of neonatal Gram-negative meningitis and ventriculitis, which carries significantly higher morbidity compared to Gram-positive etiologies [8]. Notably, all subjects in this cohort received intrathecal vancomycin monotherapy. While intrathecal or intraventricular vancomycin has been demonstrated to be safe and effective in achieving high local CSF bactericidal concentrations for staphylococcal device-related infections [15], its systemic blood-brain barrier penetration remains poor reported at approximately 7% of serum levels despite high-dose administration [10]. Given that 60% of isolated pathogens were Gram-negative bacilli against which vancomycin lacks pharmacological activity, these findings highlight a potential mismatch between empirical intrathecal therapy selection and local microbiological profiles. Both IDSA guidelines and recent systematic reviews on intraventricular therapy stress the necessity of tailoring antimicrobial regimens to culture results and local susceptibility patterns, advocating for adjunctive Gram-negative active agents such as aminoglycosides or colistin when resistant Gram-negative bacilli are confirmed or strongly suspected [1]; [4].

Hypothesis testing revealed no statistically significant correlation between baseline CSF leukocyte counts and hospital length of stay (r_s = 0.000, p = 0.999). This finding demonstrates that initial CSF pleocytosis severity cannot function as an independent predictor of hospitalization duration in pediatric ventriculitis, mirroring IDSA assertions regarding the unreliability of single-point CSF cellular abnormalities in device-related CNS infections [1]. Overall length of stay in pediatric ventriculitis is heavily influenced by overall management complexity including the requirement for serial neurosurgical revisions, the appropriateness and timeliness of targeted antimicrobial coverage, and device-related complications rather than any single baseline laboratory value [2][16]. Furthermore, prior antibiotic administration before CSF sampling can alter biochemical profiles without reliably shifting cell counts, diminishing the predictive capacity of baseline leukocyte levels [16]. Additionally, the highly homogeneous distribution of length of stay in this cohort, where 95% of patients required hospitalization exceeding 14 days, mathematically constrained correlation analysis from detecting subtle statistical associations, a phenomenon similarly observed in other healthcare-associated CNS infection cohorts [5][17].

Similarly, baseline CSF LDH activity demonstrated a very weak, non-significant positive correlation with length of stay (r_s= 0.112, p = 0.637). This indicates that while baseline LDH elevation universally highlights intraventricular tissue destruction across all subjects, the magnitude of initial enzyme elevation does not directly dictate hospitalization duration, as clinical

recovery kinetics depend far more on sustained therapeutic response and pathogen eradication [12][2]. Hospital length of stay in pediatric ventriculitis remains a multifactorial clinical outcome driven by neurological complication severity, the necessity for drainage system revisions, and pathogen resistance profiles, rather than biomarker concentrations measured at a single diagnostic time point [7][11]. Consequently, while CSF leukocytes and LDH serve as essential diagnostic and therapeutic monitoring markers, neither acts as an independent predictor of hospital length of stay in pediatric ventriculitis patients receiving intrathecal antibiotic therapy.

4. Conclusion and Future Research

In conclusion, pediatric patients with ventriculitis receiving intrathecal antibiotic therapy in this study were predominantly male infants, with *Escherichia coli* identified as the most prevalent causative pathogen and vancomycin monotherapy as the uniform intrathecal regimen. Following intrathecal treatment, cerebrospinal fluid (CSF) leukocyte counts demonstrated rapid clearance, normalizing in all subjects (100%), whereas CSF lactate dehydrogenase (LDH) activity exhibited a slower resolution, with median levels decreasing from 415.50 to 173.50 U/L but remaining elevated in 85% of patients at the final assessment, indicating that tissue repair lags behind cellular infection clearance. Furthermore, neither baseline CSF leukocyte counts (r_s = 0.000, p = 0.999) nor baseline LDH activity (r_s = 0.112, p = 0.637) showed a statistically significant association with hospital length of stay. Ultimately, CSF leukocyte and LDH levels serve as key diagnostic tools and markers for tracking therapeutic response to intrathecal antibiotics, but neither parameter acts as an independent predictor of hospitalization duration in pediatric ventriculitis.

Clinically, serial monitoring of CSF leukocyte counts and LDH activity throughout therapy, rather than relying on a single baseline measurement, is recommended to evaluate treatment response, given their distinct clearance kinetics [10][12]. From an antimicrobial stewardship perspective, the high proportion of Gram negative isolates (60%) highlights the need for continuous evaluation of empirical vancomycin monotherapy against local microbiological profiles, with early consideration of adjunctive Gram negative active intraventricular agents per IDSA recommendations [1]. Finally, future prospective, multicenter studies with larger sample sizes are required to evaluate serial biomarker dynamics and explore other potential determinants of length of stay, such as specific pathogen species, therapeutic appropriateness, and neurosurgical complications.

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Conflict of Interest

The authors declare that they have no conflict of interest. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

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