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ASSOCIATION BETWEEN DELAY IN ANTIBIOTIC ADMINISTRATION AND OUTCOME IN CHILDREN WITH SUSPECTED BACTERIAL MENINGITIS

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Abstract

Background: *Bacterial meningitis is a serious pediatric emergency associated with high morbidity and mortality.*

Objective: *To determine the association between delay in antibiotic administration and clinical outcomes in children with suspected bacterial meningitis.*

Methodology: *This cross-sectional analytical study was conducted in the department of Paediatrics, University of Child Health Sciences, The Children's Hospital Lahore, from January 2025 to June 2025. A total of 185 children aged 1 month to 12 years with suspected bacterial meningitis were included using non-probability consecutive sampling.*

Results: *Out of 185 patients, 102 (55.1%) received antibiotics within 1 hour, while 83 (44.9%) had delayed antibiotic administration. Delayed antibiotics were significantly associated with poor outcome (41.0% vs. 18.6%, p=0.001), PICU admission (42.2% vs. 21.6%, p=0.003), neurological complications (32.5% vs. 14.7%, p=0.004), and mortality (16.9% vs. 6.9%, p=0.031).*

Conclusion: *Delayed antibiotic administration was significantly associated with poor clinical outcomes in children with suspected bacterial meningitis. Early empirical antibiotic therapy within the first hour is essential to reduce complications and mortality.*

Introduction

Although there have been significant advances in antimicrobial therapy and critical care management, bacterial meningitis still is one of the most severe infectious diseases affecting children worldwide and is still linked with a high morbidity and mortality rate. The disease consists of a sudden onset of inflammation of the meninges, usually due to bacterial organisms, such as Streptococcus pneumoniae, Neisseria meningitidis and Haemophilus influenzae type b. Children are particularly vulnerable because their immune system is immature and they are more likely to become infected by invasive bacteria [1, 2]. Bacterial meningitis is responsible for an important fraction of the mortality and morbidity in children with infectious diseases worldwide. The incidence of meningitis caused by vaccine preventable pathogens has significantly declined since the introduction of the conjugate vaccines however meningitis continues to be a significant public health problem in LMICs due to its late diagnosis, limited access to health services and the lack of effective treatment resources [3,4]. Survivors often suffer from significant problems such as hearing loss, epilepsy, cognitive dysfunction, motor dysfunction, hydrocephalus, and learning disabilities that can impact their daily functioning and quality of life and may be

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permanent [5]. The early diagnosis and prompt institution of proper antibiotic treatment are generally accepted as the keystones to successful treatment of bacterial meningitis. The inflammatory response to bacterial invasion of the central nervous system can rapidly develop, causing cerebral edema, raised ICP, cerebral ischemia and irreversible neuronal damage. Therefore, delaying effective antimicrobial therapy by an hour or more could help to aggravate clinical situations and increase the risk of a poorer outcome [6,7]. Based on current international guidelines, empirical intravenous antibiotics should be started as soon as bacterial meningitis is suspected and not be deferred to a time when the child may need neuroimaging evaluation, lumbar puncture or laboratory confirmation in the critically ill child [8]. Several studies have shown that a delayed administration of antibiotic drugs is correlated with higher mortality rate, longer hospital stay, higher intensive care unit admission rate and higher risk of neurological sequelae. A delay of treatment >1-3 hours from presentation onset has been proposed to significantly increase the risk of adverse outcomes [9,10]. Despite the known significance of prompt antibiotic treatment, however, the delay in taking antibiotics is prevalent in many health care environments. Risk factors for late presentation are atypical presentation, diagnostic uncertainty, lack of referral, overcrowding of ED, lack of diagnostic service and prolonged decision making. These issues might be even greater and more difficult in low-resource environments, and children affected by the issues might experience worse outcomes [11]. While there are several international studies that have assessed the association between treatment delay and clinical outcomes of bacterial meningitis, there is limited local evidence, especially in children, from developing countries.

Objective

To determine the association between delay in antibiotic administration and clinical outcomes in children with suspected bacterial meningitis.

Methodology

This was a cross-sectional analytical study conducted in the department of Paediatrics, University of Child Health Sciences, The Children's Hospital Lahore, from January 2025 to June 2025. A total of 185 children with suspected bacterial meningitis were included in the study. Non-probability consecutive sampling technique was used.

Inclusion Criteria

- Children aged 1 month to 12 years.
- Children presenting with clinical suspicion of bacterial meningitis, including fever, neck stiffness, altered consciousness, irritability, seizures, bulging fontanelle, photophobia, or other meningeal signs.
- Children admitted through the emergency department or pediatric wards.
- Patients whose parents or guardians provided informed consent.

Exclusion Criteria

- Children who had received intravenous antibiotic therapy for more than 24 hours before presentation.
- Children with confirmed viral, tuberculous, or fungal meningitis.
- Children with known immunodeficiency disorders or malignancies.
- Patients with incomplete medical records or missing data regarding timing of antibiotic administration.
- Children whose parents or guardians refused participation.

Data Collection

Following IRB approval, 185 children who met the inclusion criteria were consecutively enrolled. Parental/legal guardian informed consent was obtained. Data was collected on a structured proforma, regarding the demographic details such as age, gender, weight, vaccination status, duration of symptoms prior to presentation and referral status. A clinical evaluation was conducted by the pediatric team in attendance. All pertinent laboratory tests – complete blood count, blood cultures, CSF analysis, CSF cultures, serum electrolytes, and inflammatory markers – were performed, following hospital protocol. Presumed bacterial meningitis was confirmed by clinical presentation along with laboratory data. Time of hospital presentation and time of the first dose of intravenous antibiotic given were recorded. The time for antibiotic administration was defined as the

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time between the patient's arrival at the hospital and the first dose of antibiotic. Patients were divided into two groups: early antibiotic administration (less than 1 hour from presentation) and delayed antibiotic administration (more than 1 hour after presentation). Patients were followed up during hospital stay. In-hospital outcome measures included in-hospital mortality, neurological complications, requirement of pediatric intensive care unit, hospital stay, seizure, hearing impairment, hydrocephalus and overall clinical outcome at discharge.

Data Analysis

The data were entered and analyzed by SPSS Version 29. Means and standard deviations or medians and interquartile ranges were used to describe quantitative variables like age, time to antibiotic use, duration of symptoms and length of hospitalisation, depending on the distribution of these variables. The Shapiro-Wilk test was used for assessing normality. Frequencies and percentages were used with qualitative variables such as gender, vaccine status, frequency of seizures, hospital admission to intensive care unit, neurological complications, mortality and clinical outcome. The relationship between the delay of antibiotic use and patient outcomes were evaluated using the chi-square test or Fisher's exact test as appropriate. A p value of <0.05 was deemed to be statistically significant.

Results

Data were collected from 185 patients, mean age of children was 4.82 ± 3.41 years. Most patients were aged 1–5 years, 81 (43.8%), followed by 6–12 years, 66 (35.7%), and <1 year, 38 (20.5%). Males were more common, 108 (58.4%), while females were 77 (41.6%). The mean duration of symptoms was 3.1 ± 1.6 days. Complete vaccination was noted in 104 (56.2%) children, while 81 (43.8%) had incomplete or unknown vaccination status. Seizures at presentation were present in 62 (33.5%) children.

Table I. Baseline Demographic and Clinical Characteristics of Children with Suspected Bacterial Meningitis (N = 185)

Variable	Category	n (%) / Mean ± SD
Age (years)	Mean ± SD	4.82 ± 3.41
Age group	<1 year	38 (20.5%)
	1–5 years	81 (43.8%)
	6–12 years	66 (35.7%)
Gender	Male	108 (58.4%)
	Female	77 (41.6%)
Duration of symptoms (days)	Mean ± SD	3.1 ± 1.6
Vaccination status	Complete	104 (56.2%)
	Incomplete/unknown	81 (43.8%)
Seizures at presentation	Yes	62 (33.5%)
	No	123 (66.5%)

Table II shows that 102 (55.1%) children received antibiotics within 1 hour of presentation, while 83 (44.9%) received antibiotics after 1 hour. The mean time to antibiotic administration was 1.46 ± 0.88 hours. Delayed presentation with symptoms for more than 48 hours was observed in 79 (42.7%) children, while 106 (57.3%) presented within 48 hours.

Table II. Timing of Antibiotic Administration (N = 185)

Variable	Category	n (%) / Mean ± SD
Antibiotic administration	Within 1 hour	102 (55.1%)
	>1 hour	83 (44.9%)
Time to antibiotic administration (hours)	Mean ± SD	1.46 ± 0.88
Delayed presentation	>48 hours symptoms	79 (42.7%)

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	≤48 hours symptoms	106 (57.3%)

Table III demonstrates that favorable clinical outcome was observed in 132 (71.4%) children, while poor outcome occurred in 53 (28.6%). PICU admission was required in 57 (30.8%) patients. Neurological complications developed in 42 (22.7%) children, hearing impairment in 18 (9.7%), and hydrocephalus in 14 (7.6%). Mortality was reported in 21 (11.4%) patients. The mean hospital stay was 8.9 ± 4.3 days.

Table III. Clinical Outcomes of Children with Suspected Bacterial Meningitis (N = 185)

Outcome	Category	n (%) / Mean ± SD
Clinical outcome	Favorable	132 (71.4%)
	Poor	53 (28.6%)
PICU admission	Yes	57 (30.8%)
	No	128 (69.2%)
Neurological complications	Yes	42 (22.7%)
	No	143 (77.3%)
Hearing impairment	Yes	18 (9.7%)
	No	167 (90.3%)
Hydrocephalus	Yes	14 (7.6%)
	No	171 (92.4%)
Mortality	Yes	21 (11.4%)
	No	164 (88.6%)
Hospital stay (days)	Mean ± SD	8.9 ± 4.3

Favorable outcome was higher among children who received antibiotics within 1 hour compared with those who received antibiotics after 1 hour, 83 (81.4%) versus 49 (59.0%) (p=0.001). Poor outcome was more frequent in the delayed antibiotic group, 34 (41.0%), compared with the early antibiotic group, 19 (18.6%).

Table IV. Association Between Delay in Antibiotic Administration and Clinical Outcomes

Outcome	Early antibiotics ≤1 hour (n=102)	Delayed antibiotics >1 hour (n=83)	p-value
Favorable outcome	83 (81.4%)	49 (59.0%)	0.001
Poor outcome	19 (18.6%)	34 (41.0%)	
PICU admission	22 (21.6%)	35 (42.2%)	0.003
Neurological complications	15 (14.7%)	27 (32.5%)	0.004
Hearing impairment	6 (5.9%)	12 (14.5%)	0.047
Hydrocephalus	4 (3.9%)	10 (12.0%)	0.035
Mortality	7 (6.9%)	14 (16.9%)	0.031

Table VI shows that children with delayed antibiotic administration had significantly longer hospital stay compared with those receiving antibiotics within 1 hour, 10.8 ± 4.8 days versus 7.4 ± 3.2 days (p<0.001). Time to clinical improvement was also longer in the delayed antibiotic group, 5.2 ± 2.1 days, compared with 3.6 ± 1.4 days in the early antibiotic group (p<0.001).

Table VI. Hospital Stay and Clinical Improvement According to Timing of Antibiotics

Variable	Early antibiotics ≤1 hour	Delayed antibiotics >1 hour	p-value

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Hospital stay (days), mean ± SD	7.4 ± 3.2	10.8 ± 4.8	<0.001
Time to clinical improvement (days), mean ± SD	3.6 ± 1.4	5.2 ± 2.1	<0.001

Discussion

Bacterial meningitis is one of the most severe paediatric infectious emergencies in which prompt diagnosis and early administration of antimicrobial treatment should be undertaken to minimise death and neurological sequalae. The present study aimed to assess the correlation of the delay in antibiotic treatment and clinical outcomes in children with suspected bacterial meningitis. Results showed that there was a significant association between delayed antibiotic administration and poor clinical outcome, neurologic complications, development of hydrocephalus, hearing impairment, admission to the PICU, extended hospital stay, and death. In this study, the mean age of the children was 4.82 ± 3.41 years and most of the children were in the age group of 1-5 years [12]. The males accounted for 58.4% of the study population. The age distribution of the patients in this study was similar to that seen in prior studies where younger children were found to have a higher risk of bacterial meningitis, due to their less mature immune system and greater susceptibility to invasive bacterial infections. Similar to the present study, a slight male predominance among children with meningitis has been observed in previous studies [13].

Of children presented to the hospital, a large proportion received antibiotic therapy within one hour (55.1%) and 44.9% did not get it administered on time. This discovery illustrates that treatment is still being delayed despite the recommendations for early empirical antibiotic treatment for suspected bacterial meningitis. Treatment delays due to diagnostic uncertainty, delayed recognition of the severity of the disease, emergency department overcrowding and limited resources of health services have also been reported in previous studies [14]. The present study showed that antibiotic treatment within 1 hour led to favorable outcomes in 81.4% of children while delayed antibiotic treatment led to favorable outcomes in 59.0% of children. On the contrary, children who did not receive antibiotics in time had a much higher rate of adverse outcomes. These findings corroborate previous research showing that early treatment with antimicrobial drugs is one of the most critical factors in bacterial meningitis treatment and is associated with better outcomes. Early eradication of bacteria limits inflammatory response within the CNS and thus prevents further neuronal damage and the development of the severe disease [15].

Children who received delayed antibiotic treatment had a higher rate of neurological complications (32.5%) than those who received early antibiotic treatment (14.7%). Like this, 14.5% of the patients who received delayed treatment experienced hearing impairment, whereas 5.9% of those who received early treatment experienced impairment. Vast literature exists that has consistently demonstrated a correlation between the time of treatment and neurologic sequelae from the continued proliferation of bacteria and inflammation of the meninges and brain parenchyma. One of the most prevalent sequelae of bacterial meningitis in children is hearing loss and this has been closely associated with delayed treatment initiation [16]. Children who had delayed administration of antibiotics had a significantly longer stay in the hospital. Patients who were treated delayed were in the hospital for 10.8 ± 4.8 days, whereas promptly treated patients were in the hospital for 7.4 ± 3.2 days. The time to clinical improvement was also increased. Similar results have also been reported in previous studies, which indicate that delayed treatment is associated with poorer clinical results, higher health care utilization, longer hospitalization, and higher economic costs of health care systems and families [17].

Limitations

There were some limitations to this study. First, it was done in one center, so the results might not be applicable in other health care centers. First, the cross-sectional analytical design provided the opportunity to assess association, but not necessarily a causative link between delayed initiation of antibiotic therapy and poor outcomes. Third, recall may have been

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influenced by the timing of the onset of symptoms before presentation to the hospital by parent/guardians. Fourth, there was no pathogen-specific analysis so results could not be compared based on the causative organism. Fifth, no evaluation was performed on the long-term neurological outcome after discharge. Additional multicenter prospective studies with longer follow-up are suggested to better assess the long-term outcomes of pediatric meningitis after antibiotic delay.

Conclusion

Delayed antibiotic administration was significantly associated with poor outcomes in children with suspected bacterial meningitis. Children who received antibiotics after one hour had higher rates of PICU admission, neurological complications, hearing impairment, hydrocephalus, mortality, and prolonged hospital stay. Early recognition and prompt empirical antibiotic therapy within the first hour of presentation are essential to improve clinical outcomes and reduce preventable complications in pediatric bacterial meningitis.

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