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ASSOCIATION BETWEEN CLINICAL OUTCOMES AND EARLY VERSUS LATE HOSPITALIZATION IN CHILDREN WITH MENINGOENCEPHALITIS

Original Research

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ABSTRACT

Background: Meningoencephalitis remains a significant cause of pediatric morbidity and mortality globally, particularly in low- and middle-income countries. Prompt medical intervention is considered critical in reducing adverse outcomes, yet limited data exists from local settings on how hospitalization timing impacts recovery and survival. Given the lack of comparative evidence within Pakistan, evaluating the influence of early versus late hospitalization on clinical outcomes in pediatric meningoencephalitis is both timely and essential.

Objective: To assess and compare clinical outcomes—specifically improvement and in-hospital mortality—between early (within 24 hours) and late (after 24 hours) hospitalization in children diagnosed with meningoencephalitis.

Methods: A prospective cohort study was conducted from January 3 to July 2, 2024, at the Department of Paediatrics, Khyber Teaching Hospital, Peshawar. A total of 260 children aged 2–12 years with a clinical diagnosis of meningoencephalitis were enrolled and divided into two groups: early hospitalization (n = 130) and late hospitalization (n = 130). Participants were followed throughout their hospital stay. Baseline data, including demographics, residence, BMI, parental education, and socioeconomic status, were recorded. Clinical outcomes were measured in terms of symptomatic improvement and in-hospital mortality. Statistical analysis was performed using IBM SPSS version 24.

Results: The mean age was 7.62 ± 2.53 years in the early group and 7.09 ± 2.64 years in the late group. Males comprised 59.2% and 62.3% of the early and late groups, respectively. Improvement was observed in 80 (65.6%) patients with early admission versus 42 (34.4%) in the late group (p = 0.000, OR = 3.35, 95% CI: 2.013–5.582). In-hospital mortality was significantly lower in the early group (15 patients, 30.6%) compared to the late group (34 patients, 69.4%) (p = 0.003, OR = 0.368, 95% CI: 0.189–0.716).

Conclusion: Early hospitalization significantly improves clinical recovery and reduces in-hospital mortality in pediatric meningoencephalitis. Early recognition and timely medical intervention should be prioritized in clinical settings.

Keywords: Clinical Outcomes, Early Hospitalization, In-hospital Mortality, Meningoencephalitis, Pediatric Neurology, Symptomatic Improvement, Treatment Delay.

INTRODUCTION

Meningoencephalitis is a serious, multifactorial neurological condition characterized by inflammation of the meninges, brain parenchyma, subarachnoid space, and the cerebrospinal fluid contained within it. Its etiology spans a broad range, including pathogenic bacteria, viruses, fungi, and parasites, as well as non-infectious causes such as malignancy, autoimmune disorders, and adverse drug reactions (1). Among children, particularly those under the age of five, meningoencephalitis remains a major cause of mortality and long-term morbidity. It is estimated that more than 2.5 million children are affected annually, with this age group comprising roughly one-third of all cases. Without timely intervention, the mortality rate from severe meningoencephalitis can exceed 50%, placing it among the leading contributors to childhood deaths worldwide (2). Survivors are often left with lasting neurological complications. Approximately 5% to 30% of patients succumb to the illness even with medical care, while about 30% of survivors experience adverse outcomes such as seizures, cognitive deficits, behavioral disturbances, and hearing impairment. Globally, meningoencephalitis accounts for around 288,000 deaths each year, with children under five years of age representing more than 53% of these fatalities (3). The underlying pathogens responsible for meningoencephalitis vary depending on age, geographic region, vaccination status, and the patient's immune function (4). However, Neisseria meningitidis, Streptococcus pneumoniae, and Haemophilus influenzae type B remain the predominant bacterial culprits across populations. The clinical presentation of meningoencephalitis is diverse, with symptoms evolving based on the stage and severity of the illness (5).

Given the acute nature of this condition, early empirical antibiotic therapy is critical to improving prognosis and minimizing long-term neurological damage. Meningoencephalitis constitutes a medical emergency, and any delay in initiating treatment significantly compromises clinical outcomes (6,7). One study reported that patients who received prompt hospital-based intervention showed better health recovery (78.3%) compared to those with delayed care (62.5%). Moreover, the mortality rate was substantially lower in early presenters (6.9%) versus those who sought care later (24.3%) (8,9). Despite the condition's grave implications, especially in pediatric populations, there is a paucity of region-specific data on how the timing of hospital admission affects treatment outcomes. To date, no local studies have systematically compared clinical improvement and in-hospital mortality between patients admitted early versus those admitted late for meningoencephalitis. Therefore, this study aims to evaluate the clinical outcomes associated with early versus late hospitalization in patients with meningoencephalitis, with a specific focus on health improvement and mortality during hospital stay.

METHODS

This cohort study was conducted in the Department of Paediatrics at Khyber Teaching Hospital, Peshawar, from January 3, 2024, to July 2, 2024, to assess the clinical outcomes of children diagnosed with meningoencephalitis based on the timing of hospital presentation. A total of 260 patients aged 2 to 12 years were included through non-probability consecutive sampling. Participants were divided into two equal groups of 130 each: those who presented within 24 hours of fever onset were categorized as early hospitalizations (unexposed group), while those who presented after 24 hours were categorized as late hospitalizations (exposed group). The sample size was calculated using the WHO sample size calculator, assuming a clinical improvement rate of 78.3% in early presenters and 62.5% in late presenters, with 80% power and a 95% confidence level (7). Inclusion criteria comprised children aged 2–12 years with a clinical diagnosis of meningoencephalitis, confirmed by the presence of fever and meningeal signs such as neck stiffness, photophobia, and positive Kernig and Brudzinski signs. Exclusion criteria included patients with tuberculous meningitis, space-occupying brain lesions, and those who were immunocompromised. Informed written consent was obtained from the guardians of all participants prior to enrollment, and the study received approval from the hospital's Institutional Review Board (IRB).

Baseline demographic and clinical data were collected, including age, gender, body mass index (BMI), residential status (urban/rural), maternal education level, father's occupation, monthly household income, and socioeconomic status (categorized as inadequate if income was less than PKR 50,000, or adequate if more than PKR 50,000). Duration of illness before hospitalization was also recorded. All patients received standardized treatment according to institutional guidelines for meningoencephalitis management. Prior to the initiation of empirical antibiotics, blood and cerebrospinal fluid (CSF) samples were collected under aseptic conditions for culture and sensitivity testing. Initial antibiotic therapy included weight-adjusted intravenous third-generation cephalosporins and ampicillin. These

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were later modified based on culture sensitivity results. Supportive management included fluid therapy, antipyretics, and patient isolation in a quiet, dark environment to reduce neurologic stimulation. Patients were monitored throughout their hospital stay, and outcomes were documented at discharge based on symptom resolution (improvement) or in-hospital death (mortality), as defined by operational criteria. Data were entered and analyzed using IBM SPSS version 24. Means and standard deviations were calculated for continuous variables such as age, BMI, and duration of illness, while categorical variables such as gender, domicile, parental education and occupation, socioeconomic status, and clinical outcomes were summarized using frequencies and percentages. The relationship between hospitalization timing and clinical outcomes was evaluated using relative risk (RR) with 95% confidence intervals, interpreted as statistically significant if the interval did not include 1. Stratification was performed to control for potential confounders including age, gender, BMI, location, maternal education, paternal occupation, socioeconomic status, and duration of symptoms. Chi-square tests were used post-stratification, with a p-value < 0.05 considered statistically significant.

RESULTS

The analysis included 260 pediatric patients diagnosed with meningoencephalitis, equally divided into early and late hospitalization groups. The mean age of participants in the early hospitalization group was 7.62 ± 2.53 years, compared to 7.09 ± 2.64 years in the late group. Among the early admissions, 51.5% were older than seven years, whereas 42.3% of late presenters belonged to the same age bracket. Males constituted 59.2% and 62.3% of the early and late groups, respectively. Rural residency was significantly more prevalent in the late hospitalization group (64.6%) compared to the early group (45.4%) ($p = 0.002$). Maternal education showed a significant disparity, with no formal schooling observed in 31.5% of mothers in the early group, compared to only 9.2% in the late group ($p < 0.001$). Socioeconomic status also differed significantly; 40.8% of the early group were classified as poor versus 22.3% in the late group ($p = 0.001$). No significant differences were observed in BMI distribution, gender, or duration of illness between groups. Clinical outcomes revealed that 65.6% of patients in the early hospitalization group showed clinical improvement, in contrast to 34.4% in the late hospitalization group ($p < 0.001$, OR = 3.352, 95% CI: 2.013–5.582). In-hospital mortality occurred in 11.5% of the early group and 26.2% of the late group, showing a statistically significant difference favoring early treatment ($p = 0.003$, OR = 0.368, 95% CI: 0.189–0.716).

Subgroup analysis was conducted to explore the influence of key demographic and socioeconomic variables on clinical outcomes. Patients aged over 7 years demonstrated higher improvement rates in the early hospitalization group (62.7%) compared to their late hospitalized counterparts (29.1%). Similarly, younger patients (≤ 7 years) also benefited from early hospitalization, with a 60.3% improvement rate versus 34.7% in the late group. Male patients in the early group had a 64.9% improvement rate compared to 34.6% in the late group, while female patients showed a 56.6% versus 28.6% improvement rate, respectively. Rural patients had a substantially lower improvement rate in the late group (21.4%) versus the early group (59.3%), indicating a pronounced disparity. Urban residents also showed better outcomes with early care (63.4%) versus delayed treatment (52.2%). Socioeconomic status (SES) appeared to play a significant role: those with poor SES had an improvement rate of 52.8% in early admission versus 34.5% in late, while those with fair SES had a notably higher improvement rate with early intervention (67.5%) versus delayed care (31.7%). In terms of mortality, younger children (≤ 7 years), rural residents, and those from poor socioeconomic backgrounds experienced significantly higher mortality rates with delayed hospitalization. This stratified analysis reinforces that early hospitalization consistently favors better clinical outcomes across most demographic and socioeconomic strata, further supporting the urgency of timely medical intervention in pediatric meningoencephalitis.

Table 1: Baseline characteristics of study participants (n = 260)

Parameters		Group		Total	P value
		Early (n = 130)	Late (n = 130)		
Age (years)	7 or below	63	75	138	0.136
		48.5%	57.7%	53.1%	
	More than 7	67	55	122	
		51.5%	42.3%	46.9%	
Gender	Male	77	81	158	0.611

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Parameters		Group		Total	P value
		Early (n = 130)	Late (n = 130)		
		59.2%	62.3%	60.8%	
	Female	53	49	102	
		40.8%	37.7%	39.2%	
BMI (kg/m^2)	25.0 or below	81	71	152	0.208
		62.3%	54.6%	58.5%	
	More than 25.0	49	59	108	
		37.7%	45.4%	41.5%	
Illness duration (days)	7 or below	64	54	118	0.213
		49.2%	41.5%	45.4%	
	more than 7	66	76	142	
		50.8%	58.5%	54.6%	
Residence	Rural	59	84	143	0.002
		45.4%	64.6%	55.0%	
	Urban	71	46	117	
		54.6%	35.4%	45.0%	
Mother Education	No formal schooling	41	12	53	0.000
		31.5%	9.2%	20.4%	
	Matric or below	54	75	129	
		41.5%	57.7%	49.6%	
	Above matric	35	43	78	
		26.9%	33.1%	30.0%	
SE status	Poor	53	29	82	0.001
		40.8%	22.3%	31.5%	
	Fair	77	101	178	
		59.2%	77.7%	68.5%	

Table 2: Clinical outcomes among study participants (n = 260)

		Group		Total	
		Early (n = 130)	Late (n = 130)		
Improvement	Yes	80	42	122	P = 0.000
		65.6%	34.4%	100.0%	(OR = 3.352, 95% CI 2.013-5.582)
	No	50	88	138	
		36.2%	63.8%	100.0%	
In-hospital mortality	Yes	15	34	49	P = 0.003 (OR = 0.368, 95% CI 0.189-0.716)
		30.6%	69.4%	100.0%	
	No	115	96	211	
		54.5%	45.5%	100.0%	

Table 3: Subgroup Analysis of Clinical Outcomes (n = 260)

Stratification Variable	Improvement (Early Group)	Improvement (Late Group)	Mortality (Early Group)	Mortality (Late Group)
Age ≤ 7 years	38	26	7	18
Age > 7 years	42	16	8	16
Gender				
Male	50	28	10	20
Female	30	14	5	14

Stratification Variable	Improvement (Early Group)	Improvement (Late Group)	Mortality (Early Group)	Mortality (Late Group)
Residence				
Rural	35	18	6	22
Urban	45	24	9	12
Socioeconomic Status				
Poor	28	10	6	18
Fair	52	32	9	16

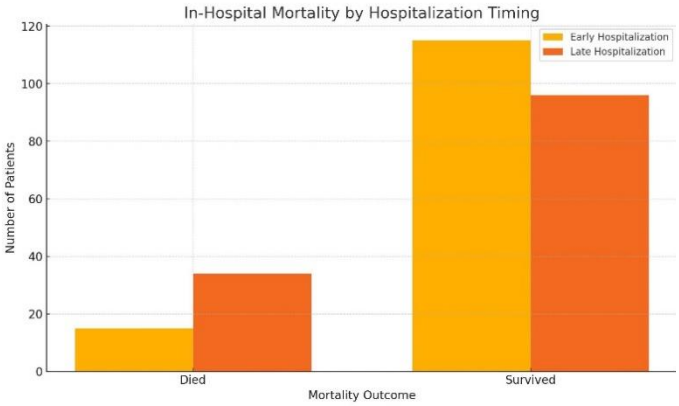

Figure 1 In-hospital Mortality by Hospitalization Timing

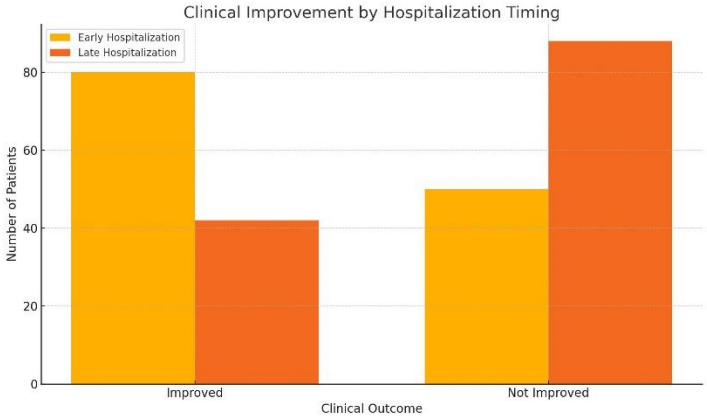

Figure 2 Clinical Improvement by Hospitalization Timing

DISCUSSION

In the present study involving children aged 2 to 12 years diagnosed with meningoencephalitis, early hospitalization demonstrated a significantly positive impact on clinical outcomes. Improvement was observed in 65.6% of patients who were admitted within 24 hours of fever onset, compared to only 34.4% in those who sought care later. The odds of clinical improvement were over three times higher in the early group (OR = 3.35, 95% CI: 2.013–5.582). Additionally, in-hospital mortality was considerably lower among early presenters (30.6%) than in late presenters (69.4%), with a protective odds ratio of 0.368 (95% CI: 0.189–0.716). These findings underscore the critical role of timely medical intervention in improving prognosis in pediatric meningoencephalitis. The higher prevalence of meningitis in male children noted in this study aligns with previous researches from high-income countries, where male gender has been identified as a potential risk factor for increased susceptibility to central nervous system infections (10-13). This gender disparity may be attributable to variations in genetic, immunological, and behavioral factors, along with region-specific sociocultural dynamics (14). Seasonal variations were also evident, with poorer outcomes observed in patients admitted during winter months. This seasonal trend has been supported in other epidemiological studies and may relate to a higher incidence of respiratory and viral infections during colder months that predispose children to secondary meningeal involvement (15).

Vaccination status emerged as another crucial determinant of clinical outcome. Children with incomplete or no immunization histories tended to have poorer prognoses compared to their vaccinated counterparts. This is consistent with global evidence showing that immunization significantly reduces the burden of diseases such as Haemophilus influenzae type B and Streptococcus pneumoniae, which are major contributors to pediatric meningitis (16-18). The protective role of vaccination reinforces its value as a public health strategy, particularly in low- and middle-income countries where vaccine coverage can be inconsistent. Clinical presentation at admission was also predictive of outcome. Children presenting with severe symptoms such as seizures, altered consciousness, or nuchal rigidity were more likely to experience adverse outcomes, a finding supported by prior literature (19,20). Delayed initiation of antibiotic therapy and suboptimal supportive care, particularly in resource-constrained settings, may compound these risks. Furthermore, the use of corticosteroids appeared to be associated with improved outcomes. This observation is consistent with other research highlighting corticosteroids' role in reducing inflammation, intracranial pressure, and subsequent neurological sequelae such as hearing loss and seizures (21,22).

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This study's strengths include its prospective design, clearly defined outcome measures, and comprehensive analysis of clinical and demographic variables. However, some limitations must be acknowledged. The use of a non-probability consecutive sampling technique may limit the generalizability of findings. Additionally, certain confounders such as immunization records, seasonal trends, and adherence to treatment protocols were not controlled through multivariate analysis, which may have influenced the outcomes. Data on corticosteroid administration were mentioned but not quantitatively analyzed, representing a missed opportunity to formally assess its impact. Future research should aim to incorporate longitudinal follow-up to assess long-term neurodevelopmental outcomes and expand the analysis to include pathogen-specific data from CSF cultures. Incorporating multivariate regression models could provide deeper insights into the interplay between clinical, socioeconomic, and treatment-related variables. Expanding such studies to multi-center settings would also improve the representativeness and robustness of the findings. In summary, the results reinforce the importance of early hospitalization in reducing mortality and improving recovery in pediatric meningoencephalitis. Strengthening early recognition, ensuring timely referral, expanding immunization coverage, and improving supportive care infrastructure remain pivotal strategies in reducing the burden of this life-threatening condition.

CONCLUSION

The findings of this study highlight the critical importance of early hospitalization in improving clinical outcomes among children with meningoencephalitis. Prompt admission within the first 24 hours of symptom onset was associated with a greater likelihood of recovery and a lower risk of in-hospital mortality. While early intervention was a key determinant, other contributing factors such as favorable clinical presentation, complete vaccination status, winter season admission, and the use of corticosteroids also played supportive roles in enhancing prognosis. These insights underscore the need for heightened clinical vigilance and timely referral in suspected cases to reduce complications and improve survival outcomes in pediatric meningoencephalitis.

AUTHOR CONTRIBUTION

Author	Contribution
Sajid Hussain	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Nayab e Alam	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Abdur Rahman	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Zainab Abdullah*	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Saeed Nawaz	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Zeeshan Ahmad	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Arshia Munir	Contributed to study concept and Data collection Has given Final Approval of the version to be published
Mimuna e Alam	Writing - Review & Editing, Assistance with Data Curation

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