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Frequency of Hydrocephalus in Patients with Tuberculous Meningitis: A Prospective Observational Study at the Neurology Department of BMC Hospital

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ABSTRACT

Background: Tuberculous meningitis (TBM) is a severe neurological infection with hydrocephalus as a frequent and debilitating complication. This study aimed to determine the frequency, predictors, and outcomes of hydrocephalus in TBM patients admitted to a tertiary care center in Balochistan, Pakistan. **Methods:** This prospective observational cohort study analyzed 86 TBM patients at BMC Hospital's Neurology Department over six months. Inclusion required TBM diagnosis by modified Marais criteria, with exclusion of non-TBM meningitis or pre-existing hydrocephalus. Statistical analysis included descriptive statistics, chi-square/Fisher's exact tests, and multivariate logistic regression to identify predictors, adjusted for confounders. **Results:** The cohort comprised 86 TBM patients, predominantly male (60.5%) and urban residents (62.8%), with low socioeconomic status (54.7%). Headache (95.3), fever (88.4), and altered sensorium (57.0) were common. Hydrocephalus was identified in 58 patients (67.4; 95% CI: 56.8–76.5), with communicating type predominating (72.4) and moderate severity being most common (44.8). Management included VP shunts (55.2), with 62.1 showing post-intervention improvement. In-hospital mortality was 10.5%, and 38.4% had significant disability (MRS 3–5) at discharge. Independent predictors of hydrocephalus were altered sensorium (OR 8.2; p<0.001), CSF protein >200 mg/dL (OR 8.6; p<0.001), and basal exudates on MRI (OR 5.2; p=0.001). HIV coinfection was rare (2.3) and not a significant predictor (p=0.55). **Conclusion:** Hydrocephalus is highly frequent in TBM patients in this setting. Altered sensorium, elevated CSF protein, and basal exudates on MRI are crucial predictors. These findings emphasize the importance of early detection and aggressive management to improve outcomes in TBM-endemic regions like Balochistan, where the disease poses a significant public health burden.

INTRODUCTION

Tuberculous meningitis (TBM) is the most severe form of extrapulmonary tuberculosis, a major global health issue that is caused by Mycobacterium tuberculosis[1-3]. Despite progress in antitubercular therapies, tuberculous meningitis (TBM) continues to be a catastrophic brain infection linked to significant morbidity and mortality, especially in areas with a high prevalence of tuberculosis and constrained healthcare resources[4-6]. The insidious onset and nonspecific initial signs frequently postpone diagnosis, resulting in severe disease stages marked by significant neurological impairments.

A significant and common complication of TBM is hydrocephalus, a condition marked by the abnormal accumulation of cerebrospinal fluid (CSF) in the brain's ventricles[7, 8]. Hydrocephalus in tuberculous meningitis may result from multiple pathophysiological processes, such as inflammation and exudate accumulation at the brain's base, causing obstruction of cerebrospinal fluid pathways or poor reabsorption of cerebrospinal fluid over the cerebral convexity[9-11]. Hydrocephalus exacerbates neurological damage by increasing intracranial pressure, causing brain herniation, and resulting in severe long-term disability or death[12-14]. Prompt identification and therapy of hydrocephalus are essential for enhancing patient outcomes[15]. Nonetheless, differentiating the kind and severity of hydrocephalus and forecasting its onset continues to pose therapeutic challenges, particularly in resource-constrained environments where advanced neuroimaging and specialised neurosurgery procedures may be less accessible.

Despite the well-established link between TBM and hydrocephalus, there is a scarcity of comprehensive, prospective observational studies that specifically investigate the frequency, precise clinical and radiological predictors, and spectrum of outcomes of hydrocephalus in

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TBM patients within specific regional contexts. Comprehending the local epidemiology and discovering easily identifiable predictors of hydrocephalus should substantially improve early diagnosis, facilitate timely therapeutic measures, and eventually boost the prognosis for people afflicted by TBM. Additionally, recognising populations with an elevated risk of hydrocephalus might inform focused surveillance methods and resource distribution.

Therefore, this study aims to contribute to the current understanding of TBM-associated hydrocephalus by prospectively analyzing a cohort of TBM patients admitted to a tertiary care neurology department in a high-burden setting. The findings of this study conducted at BMC Hospital in Quetta, Balochistan, hold significant relevance. Situated within a region marked by distinctive geographical and socioeconomic characteristics, Balochistan encounters unique healthcare challenges, including disparities in access to specialized medical services and notable variations in disease prevalence. By focusing on this context, our findings promise to offer a granular understanding of TBM and its complications that is directly applicable to similar underserved populations globally, thereby informing more effective public health strategies and clinical guidelines. The primary objectives of this study are to determine the frequency of hydrocephalus among patients with tuberculous meningitis.

METHODOLOGY

This study was conceived as a prospective observational cohort study with the primary objective of systematically determining the frequency of hydrocephalus, identifying significant clinical predictors that contribute to its development, and evaluating the associated neurological and functional outcomes among patients diagnosed with tuberculous meningitis or TBM. The study was meticulously conducted within the Neurology Department of BMC Hospital, Quetta. Data collection spanned a continuous six-month period, commencing on November 1, 2024, and concluding on April 30, 2025. Before any data collection activities, comprehensive ethical approval for the study protocol was secured from the institutional review boards of both the College of Physicians and Surgeons Pakistan (CPSP) (Reference: CPSP/REU/NEU-2023-001-805).

The study population comprised patients admitted to the Neurology Department who met specific inclusion and exclusion criteria. Patients of all ages, both adult and pediatric, admitted to the Neurology Department were included if they had a confirmed or suspected diagnosis of TBM based on the modified Marais criteria (Definite, Probable, or Possible TBM, as per Marais et al., 2010), and if voluntary written informed consent was obtained from the patient or their legally authorized guardian[16]. Patients were excluded if they had other forms of meningitis (bacterial, viral, fungal), pre-existing hydrocephalus attributable to non-TBM etiologies (congenital malformations, intracranial tumors), or incomplete clinical documentation or neuroimaging records that precluded comprehensive assessment.

To ensure adequate statistical power, the minimum required sample size was meticulously calculated using the formula $n=d2Z2\cdot p\cdot(1-p)$, where Z=1.96 (for a 95-confidence level), p=0.65 (representing an estimated expected frequency of hydrocephalus in TBM patients based on existing literature), and d=0.1 (a 10 margin of error). This calculation determined a minimum sample size of 86 patients, which also accounted for a potential 10% attrition rate. A consecutive non-probability sampling method was employed, allowing for the prospective enrollment of all eligible patients diagnosed with TBM admitted during the stipulated six-month study period.

Data collection

Data Collection was systematically executed by trained research personnel. TBM confirmation relied on a comprehensive diagnostic approach, encompassing cerebrospinal fluid (CSF) analysis (acid-fast bacilli smear, GeneXpert MTB/RIF for *Mycobacterium tuberculosis* and rifampicin resistance, and conventional mycobacterial culture), characteristic neuroimaging findings (computed tomography [CT] or magnetic resonance imaging [MRI] of the brain), and a thorough clinical assessment aligned with modified Marais criteria. Hydrocephalus assessment was primarily based on neuroimaging, with CT or MRI scans performed at admission and repeated if clinical neurological deterioration was observed. Hydrocephalus was objectively defined as an Evan's Index >0.3 on axial neuroimaging, corroborated by supporting clinical signs such as papilledema or a reduction in Glasgow Coma Scale (GCS) score. A standardized, structured proforma was utilized for systematic data capture across various domains, including demographics, TBM diagnostic parameters, hydrocephalus features (type, severity, management), comorbidities, and clinical outcomes, with all variables operationally defined following WHO and NIH guidelines. Patients were meticulously monitored daily throughout hospitalization, and key clinical outcomes, including functional status (assessed using the Modified Rankin Scale) and mortality, were rigorously evaluated at hospital discharge.

Operational definitions were precisely established for TBM classification (Definite, Probable, Possible based on Marais et al., 2010), hydrocephalus severity (Mild: Evan's Index 0.31–0.35; Moderate: 0.36–0.40; Severe: >0.40), and functional outcome using the Modified Rankin Scale (Good outcome: MRS 0–2; Poor outcome: MRS 3–5).

Statistical analysis

For statistical analysis, all collected data were entered and analyzed using SPSS statistical software, version 28.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics summarized categorical variables as frequencies and percentages, and continuous variables as mean ± standard deviation (SD). The primary outcome, frequency of hydrocephalus, was calculated as a percentage with its corresponding 95% confidence interval (CI). Associations between categorical variables were assessed using the Chi-square test or Fisher's exact test. Binary logistic regression analysis was performed to identify independent clinical predictors of hydrocephalus development, with results reported as adjusted Odds Ratios (OR) and their 95% Confidence Intervals (CI). To account for potential

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confounding effects, multivariate logistic regression models were adjusted for age, baseline TBM severity, and HIV status. A two-tailed p-value of <0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Profile

The demographic assessment of the study cohort revealed a distinct male predominance, with 52 males (60.5%) compared to 34 females. The mean age of the patients was 36.4±14.8 years, indicating a broad age distribution; however, the most affected age group was individuals between 18 and 40 years, accounting for 44.2% of the total cohort (Table 1). Geographical analysis showed that the majority of patients (62.8%) resided in urban areas, which might reflect referral patterns or higher incidence rates in densely populated regions. A significant proportion of the study population, 54.7%, was categorized as belonging to low socioeconomic strata, a factor consistently associated with increased vulnerability to tuberculosis.

The diagnostic classification of TBM was performed meticulously using the modified Marais criteria. This rigorous approach classified 55.8% of cases as probable TBM and 25.6% as definite TBM, underscoring the diagnostic challenges inherent in this disease. Microbiological confirmation, a critical aspect of TBM diagnosis, was achieved in 46.5% of cases, primarily through CSF GeneXpert or culture methods (Table 2). Clinical presentation was remarkably consistent across the cohort; headache was almost universally reported (95.3%), followed closely by fever (88.4%). Altered sensorium, a hallmark of severe neurological involvement, was present in over half of the patients (57.0%). Cerebrospinal fluid (CSF) analysis provided crucial biochemical indicators: elevated protein levels (exceeding 200 mg/dL) were observed in 67.4 of patients, indicative of significant meningeal inflammation, and a reduced CSF: blood glucose ratio (<0.3) was recorded in 77.9 of cases, consistent with bacterial consumption of glucose in the CSF (Table 2).

Frequency and Characteristics of Hydrocephalus

A pivotal finding of this study was the high frequency of hydrocephalus, identified in 58 patients, constituting 67.4 (95% CI: 56.8–76.5) of the TBM cohort (Table 3). This highlights hydrocephalus as a very common and severe complication of TBM. Further characterization of hydrocephalus revealed that communicating hydrocephalus was significantly more prevalent (72.4%) than obstructive hydrocephalus (27.6%). The severity of hydrocephalus, objectively assessed using Evan's Index on neuroimaging, showed a distribution of moderate in 44.8% of cases, mild in 31.0%, and severe in 24.1%, suggesting a wide spectrum of ventricular dilation.

Management strategies for hydrocephalus vary according to its type and severity. Ventriculoperitoneal (VP) shunts were the most frequently employed neurosurgical intervention, utilized in 55.2% of cases. Endoscopic third ventriculostomy (ETV) was performed in 17.2% of patients, offering an alternative surgical approach. Conservative medical therapy was pursued in 27.6% of patients, typically for milder forms or those unsuitable for surgical intervention. Post-intervention outcomes were largely encouraging, with 62.1% of patients demonstrating clinical improvement. However, a notable 13.8% experienced worsening conditions despite therapeutic efforts, underscoring the challenges in managing this complex complication (Table 3).

Comorbidities and Risk Factors

The assessment of comorbidities revealed insights into factors that might influence disease progression. HIV coinfection was found to be relatively uncommon in this specific cohort, identified in only 2 patients (2.3%, Table 4). Of these two, one patient presented with a severely compromised immune status, evidenced by a CD4 count less than 200 cells/mm^3. Other significant comorbidities included malnutrition, affecting a substantial 47.7% of patients, which can further compromise immune function and recovery. A history of previous tuberculosis was reported by 27.9% of patients, suggesting potential reactivation or re-infection dynamics. Additionally, diabetes mellitus was identified in 14.0% of the cohort. BCG vaccination coverage, documented in 60.5% of the patients, provides a demographic context for population-level immunity against tuberculosis (Table 4).

Clinical Outcomes

The clinical outcomes during hospitalization provided critical insights into the prognosis of TBM with hydrocephalus. In-hospital mortality occurred in 9 patients, accounting for 10.5% of the total cohort. Functional status at the time of hospital discharge, rigorously assessed using the Modified Rankin Scale (MRS), indicated that 51.2% of patients achieved good outcomes (MRS 0–2), signifying independence or minimal disability in daily activities. Conversely, a substantial proportion, 38.4%, experienced significant disability (MRS 3–5), ranging from moderate disability requiring some help to severe disability necessitating being bedbound or incontinent (Table 5). This highlights the profound and often debilitating neurological sequelae associated with TBM. Furthermore, the complexity of TBM management and recovery was reflected in the prolonged hospital stays, with admissions exceeding 14 days occurring in a significant 73.3% of cases (Table 5).

Predictors of Hydrocephalus

Multivariate logistic regression analysis was conducted to identify independent clinical and radiological predictors for the development of hydrocephalus in TBM patients. The analysis revealed three statistically significant predictors (Table 6). Altered sensorium at presentation emerged as a very strong independent predictor, demonstrating an Odds Ratio (OR) of 8.2 (95% Confidence Interval [CI]: 3.1–21.9; p<0.001). This suggests that a compromised state of consciousness upon admission is highly indicative of impending or existing hydrocephalus. Similarly, elevated CSF protein levels greater than 200 mg/dL were identified as a robust predictor (OR 8.6; 95% CI: 3.3–22.6; p<0.001), indicating that more severe meningeal inflammation and exudate formation strongly predispose to hydrocephalus. The presence of basal exudates on MRI was also found to be a strong independent predictor (OR 5.2; 95% CI: 1.9–14.5; p=0.001),

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emphasizing the critical role of specific radiological findings in predicting this complication. Notably, HIV status, despite its known association with severe TBM, showed no statistically significant association with hydrocephalus in this particular cohort (p=0.55), a finding likely attributable to its relatively low prevalence within this study population (Table 6).

Table 1

Demographic Characteristics (n=86)

Variable	Category	Frequency	Percentage
Age (years)	<18	16	18.6%
	18–40	38	44.2%
	41–60	24	27.9%
	>60	8	9.3%
Sex	Male	52	60.5%
	Female	34	39.5%
Residence	Urban	54	62.8%
	Rural	32	37.2%
SES	Low	47	54.7%
	Medium	28	32.6%
	High	11	12.8%

Table 2

TBM Diagnostic Profile (n=86)

Variable	Category	Frequency	Percentage
TBM Category	Definite	22	25.6%
	Probable	48	55.8%
	Possible	16	18.6%
Microbiological Confirmation	GeneXpert (+)	34	39.5%
	Culture (+)	18	20.9%
Clinical Features	Fever	76	88.4%
	Headache	82	95.3%
	Altered Sensorium	49	57.0%
CSF Protein (mg/dL)	>200	58	67.4%
CSF Glucose Ratio	<0.3	67	77.9%

Table 3

Hydrocephalus Frequency & Characteristics Overall Frequency (n=86)

Hydrocephalus	Frequency	Percentage
Present	58	67.4%
Absent	28	32.6%

Subgroup Analysis (n=58 with Hydrocephalus)

Variable	Category	Frequency	Percentage
Type	Communicating	42	72.4%
	Obstructive	16	27.6%
Severity	Mild	18	31.0%
	Moderate	26	44.8%
	Severe	14	24.1%
Management	VP Shunt	32	55.2%
	ETV	10	17.2%
	Conservative	16	27.6%
Outcome	Improved	36	62.1%
	Stable	14	24.1%
	Worsened	8	13.8%

Table 4

Comorbidities & Risk Factors (n=86)

Variable	Category	Frequency	Percentage
HIV (+)	Yes	2	2.3%
CD4 Count (cells/mm^3)	<200	1/2	50.0%
Previous TB	Yes	24	27.9%
BCG Vaccination	Yes	52	60.5%
Malnutrition	Yes	41	47.7%
Diabetes Mellitus	Yes	12	14.0%

All HIV-negative patients were confirmed via ELISA/PCR. No unknown statuses.

Table 5

Clinical Outcomes (n=86)

Outcome	Category	Frequency	Percentage
Mortality	In-hospital death	9	10.5%
Functional Status (MRS)	0–2 (Good outcome)	44	51.2%
	3–5 (Poor outcome)	33	38.4%
	6 (Death)	9	10.5%
Hospital Stay	>14 days	63	73.3%

Table 6

Key Associations with Hydrocephalus

Risk Factor	Hydrocephalus (+)	Hydrocephalus (-)	p-value	OR (95% CI)
Altered Sensorium	42/58 (72.4%)	7/28 (25.0%)	<0.001	8.2 (3.1–21.9)
CSF Protein >200 mg/dL	48/58 (82.8%)	10/28 (35.7%)	<0.001	8.6 (3.3–22.6)
Basal Exudates on MRI	34/58 (58.6%)	6/28 (21.4%)	0.001	5.2 (1.9–14.5)
HIV (+)	1/58 (1.7%)	1/28 (3.6%)	0.55	0.47 (0.03–7.5)

Figure 1

Demographic Characteristics of TBM Cohort

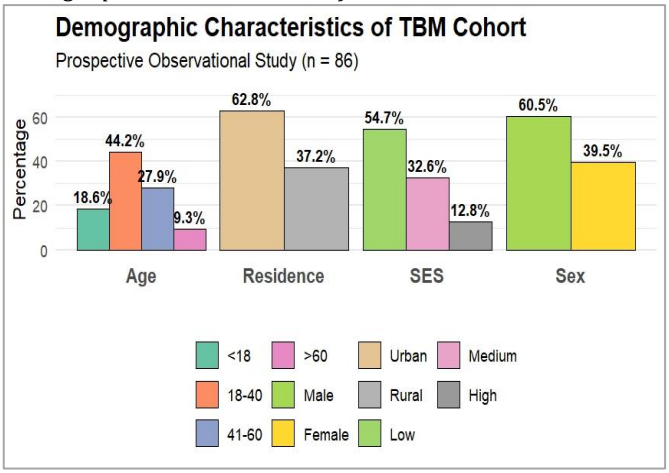

Figure 2

Clinical and Diagnostic Features

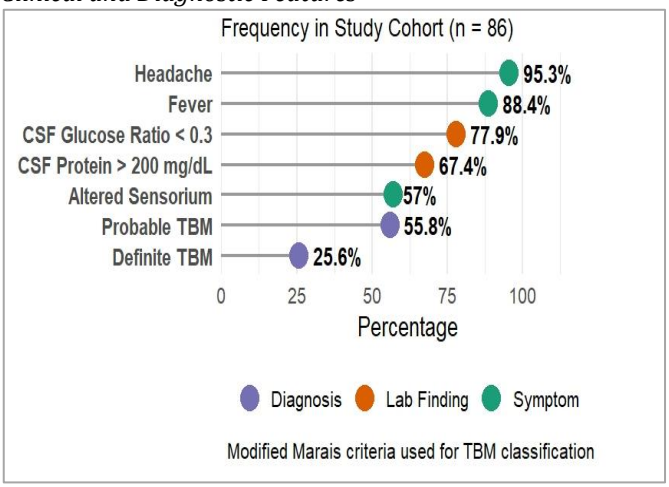

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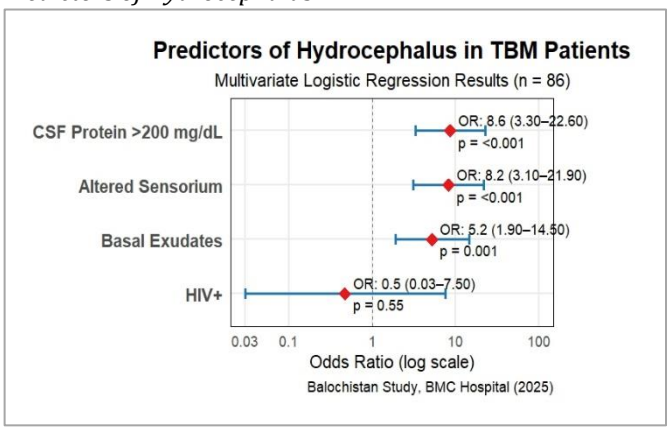
Figure 3
Predictors of Hydrocephalus



DISCUSSION

This prospective observational study, conducted at BMC Hospital in Quetta, Balochistan, aimed to delineate the frequency, predictors, and outcomes of hydrocephalus in patients with tuberculous meningitis (TBM). Our findings underscore the significant burden of hydrocephalus as a complication of TBM and identify crucial clinical and radiological markers that can predict its development, offering valuable insights for improving patient management in high-burden settings.

A central finding of our study is the high frequency of hydrocephalus, observed in 67.4 (n=58) of TBM patients. This prevalence is at the higher end of the spectrum reported in global literature, which typically ranges from 30 to 80 [17-19]. This elevated frequency in our cohort from Balochistan might reflect factors such as delayed presentation to tertiary care centers, higher disease severity at admission, or specific regional virulence of *Mycobacterium tuberculosis* strains. The predominance of communicating hydrocephalus (72.4) over obstructive forms is consistent with the pathophysiology of TBM, where basal meningeal inflammation and exudate impair CSF absorption over the convexities more commonly than causing direct ventricular outflow obstruction. The observed spectrum of severity (moderate > mild > severe) highlights the variable impact of CSF pathway derangement. The high rate of surgical intervention, particularly VP shunting (55.2), reflects the necessity of aggressive management for TBM-associated hydrocephalus to prevent irreversible neurological damage. While a majority showed improvement post-intervention, the non-trivial proportion (13.8) experiencing worsening conditions underscores the inherent challenges in managing this complex complication.

Our multivariate analysis identified three independent and robust predictors of hydrocephalus: altered sensorium at presentation, elevated CSF protein levels (>200 mg/dL), and the presence of basal exudates on MRI. These findings align well with established pathophysiological understanding and previous research. Altered sensorium is often a direct consequence of increased intracranial pressure due to hydrocephalus and/or diffuse brain inflammation, serving as a critical early clinical warning sign [9, 20, 21]. Elevated CSF protein indicates intense meningeal inflammation, and high protein content in CSF can impede arachnoid villi function, leading to impaired CSF reabsorption and communicating hydrocephalus. The presence of basal exudates on MRI is a hallmark radiological feature of TBM and represents organized inflammatory material at the base of the brain, directly contributing to CSF pathway obstruction and subsequent hydrocephalus[22-24]. The strong odds ratios associated with these predictors (OR 8.2 for altered sensorium, OR 8.6 for CSF protein >200 mg/dL, OR 5.2 for basal exudates) emphasize their clinical utility in risk stratification upon patient admission.

Interestingly, HIV coinfection showed no statistically significant association with hydrocephalus in our cohort (p=0.55), likely due to its remarkably low prevalence (2.3). This contrasts with studies from regions with high HIV prevalence, where HIV-positive TBM patients often exhibit a higher propensity for hydrocephalus and more severe disease, possibly due to altered immune responses and delayed inflammatory resolution [25-27]. Our low HIV prevalence is atypical for TBM cohorts globally and might be specific to our regional demographic, warranting further investigation. Other comorbidities like malnutrition and previous TB history were common, reflecting the broader socioeconomic and public health challenges associated with tuberculosis in the region.

The clinical outcomes observed in our study reflect the severe nature of TBM and its complications. The in-hospital mortality rate of 10.5 is comparable to, or slightly lower than, figures reported from other resource-limited settings (15–25), which could be partly attributed to aggressive hydrocephalus management in our center [28-30]. However, the high proportion of patients experiencing significant disability (38.4% with MRS 3–5) at discharge highlights the persistent neurological sequelae, underscoring the need for robust rehabilitation programs. The prolonged hospital stays (73.3 for >14 days) further emphasize the protracted and complex course of TBM, demanding substantial healthcare resources.

However, certain **limitations** must be acknowledged. As a single-center study, the generalizability of findings to other regions with different demographic profiles, healthcare systems, or TBM strains may be limited. The relatively small sample size for subgroup analyses, particularly for less common comorbidities like HIV, might have affected the power to detect weaker associations. The reliance on discharge outcomes also means that long-term functional and neurological sequelae were not assessed. Future multi-center studies with larger cohorts and extended follow-up periods are warranted to validate these findings and explore additional prognostic factors and long-term quality of life. Investigation into genetic susceptibility and specific *M. tuberculosis* genotypes prevalent in the region could also offer further insights into disease pathogenesis and hydrocephalus development.

CONCLUSION

This study from BMC Hospital in Balochistan confirms that hydrocephalus is a highly common and severe complication of tuberculous meningitis (TBM). We identified altered sensorium, elevated CSF protein, and basal exudates on MRI as crucial predictors, highlighting

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the need for early detection. Despite aggressive treatment, TBM-associated hydrocephalus often leads to significant disability and mortality. Our findings underscore the importance of prompt diagnosis and intervention to improve patient outcomes in TBM-endemic regions. This research provides vital local epidemiological data, contributing to a better understanding of TBM complexities in underserved populations. Ultimately, these insights can guide targeted public health strategies and resource allocation to alleviate the substantial burden of this disease.

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