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Comparison of ventriculoperitoneal shunt versus endoscopic third ventriculostomy in managing hydrocephalus due to tuberculous meningitis: a randomized controlled trial with a 30-day follow-up

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Background: Hydrocephalus is a significant complication arising from tuberculous meningitis (TBM). While ventriculoperitoneal shunt (VPS) remains the primary surgical approach for TBM-related hydrocephalus, there is a rising trend in the use of endoscopic third ventriculostomy (ETV).

Materials and methods: This randomized controlled trial, conducted from February 2018 to July 2019, enroled 60 patients aged 20–50 with TBM-related hydrocephalus. Patients underwent either VPS or ETV. Both groups were followed up for a minimum of 30 days, evaluating clinical outcomes and modifications in the modified Vellore grading system. Glasgow Coma Scale (GCS) assessments were conducted at 7-days and 30-day post-surgery for both groups.

Results: The mean GCS scores were comparable between the two groups on the 7th and 30th postoperative days. The association between modified Vellore Grade and treatment modality did not show statistically significant differences (P = 1.0 and P = 0.3) on the seventh and thirtieth postoperative days respectively.

Conclusions: Both VPS and ETV demonstrate efficacy in managing hydrocephalus secondary to TBM in adult patients. Our 30-day outcomes did not reveal discernible differences between the two procedures. Therefore, considering technical expertise and experience with ETV, it may be considered as the primary choice for cerebrospinal fluid (CSF) diversion in TBM-associated hydrocephalus, owing to its avoidance of several lifelong complications linked with VPS.

Key words: CSF Diversion, endoscopic third ventriculostomy, Glasgow Coma Scale, hydrocephalus, modified vellore grading, surgical intervention, tuberculous meningitis, Ventriculoperitoneal Shunt

Introduction

Tuberculous meningitis (TBM) typically presents with clinical features, including fever, meningismus, nausea, vomiting, neurological deficits, and a bulging fontanelle in infants^[1,2]. Involvement of the central nervous system (CNS), one of the most severe clinical manifestations of tuberculosis (TB), is observed in

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HIGHLIGHTS

- Hydrocephalus, an insidious complication of tuberculous meningitis (TBM), often requires surgical intervention. Ventriculoperitoneal shunt (VPS) is the most commonly performed procedure for TBM-related hydrocephalus.
- There is a growing trend toward performing endoscopic third ventriculostomy (ETV) in selected cases.
- Both VPS and ETV demonstrate effectiveness in managing hydrocephalus associated with TBM in adult patients. Our 30-day outcomes did not reveal any discernible difference between the two procedures.
- ETV might be considered as the primary choice for cerebrospinal fluid) diversion in TBM-related hydrocephalus, especially when technical expertise and experience with this procedure are available. ETV offers the advantage of avoiding several lifelong complications associated with VPS.

5–10% of extrapulmonary TB cases and accounts for ~1% of all TB cases globally^[3]. Tuberculosis causes hydrocephalus by impairing the functionality of the subarachnoid villi due to tuberculous debris. Hydrocephalus poses a life-threatening condition, usually managed through ventriculoperitoneal shunt (VPS). While VPS for hydrocephalus yields favourable outcomes, it is associated with complications such as shunt infections,

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peritoneal pseudocysts, bowel perforation, intestinal volvulus, and catheter migration. The artificial nature of VPS leads to a high rate of shunt obstruction in cases of infectious hydrocephalus. Given these limitations, endoscopic third ventriculostomy (ETV) has been suggested as an alternative. There is a need for comprehensive clinical trials investigating the use of ETV for hydrocephalus management. The Vellore grading system is employed to clinically categorize patients diagnosed with tuberculous meningitis and hydrocephalus, based on the presence or absence of neurological deficits, and altered mental status, ranging from grade I (no neurological deficit, normal mental status) to grade IV (deeply comatose, decerebrate or decorticate posturing)^[4]. Most patients with this condition require cerebrospinal fluid (CSF) diversion, and previous studies have suggested the potential benefit of $ETV^{[5,6]}$. In this study, we are conducting a randomized trial to assess the efficacy of ETV and VPS in patients with TBM and hydrocephalus.

Materials and methods

A randomized controlled trial was conducted following approval from the Institutional Review Board (IRB). The study employed a stratified random sampling technique using the fishbowl draw method for patient randomization, as outlined below. Six empty glass jars were utilized, with each containing five small, folded sheets of paper labelled either "ETV" or "VPS."

The initial 10 eligible patients enroled in the trial were asked to select one folded sheet from the first jar, determining their assigned group (VPS or ETV) based on the procedure written on the chosen piece of paper. Subsequently, the subsequent groups of 10 patients repeated this process with the respective jars until a total of 60 patients were recruited for the study. Therefore, the 60 enroled patients were divided into two groups: 30 patients assigned to receive VPS and 30 patients assigned to receive ETV for TBM with hydrocephalus (Fig. 1). All 60 patients were admitted to Mayo Hospital Lahore, Neurosurgery Department via the outpatient department (OPD) or emergency services.

Inclusion criteria

- Age range: 20–50 years.
- Diagnosis of TBM confirmed through CSF analysis.
- Presence of symptomatic hydrocephalus.
- Patients categorized as American Society of Anesthesia (ASA) grades 1 and 2, as determined by an anaesthetist.

Exclusion criteria

- TBM patients with Grade IV hydrocephalus.
- Patients with abnormal bleeding and clotting profiles.
- Individuals who underwent prior brain surgeries such as craniotomy and craniectomy.
- Patients with other brain pathologies causing obstructive hydrocephalus, such as space-occupying lesions, cysts, and aqueductal stenosis visible on computed tomography (CT) scans, leading to increased intracranial pressure (ICP).

Data analysis was performed using SPSS-20. Descriptive statistics included mean \pm SD, frequency distributions, and percentages. A χ^2 test was conducted to compare outcomes between patients receiving ETV and those receiving VPS. The significance level was set at 5%.

The study's randomization process aimed to ensure unbiased allocation of treatment groups using a stratified approach. The choice of Mayo Hospital Lahore, Neurosurgery Department, as the site for patient admission, was due to its specialized facilities and expertise in managing neurological conditions, including TBM-related hydrocephalus.

The inclusion criteria focused on a specific age range (20–50 years) to target a relatively homogenous population. Diagnosis confirmation through CSF analysis ensured the accurate identification of TBM cases. Additionally, patients with symptomatic hydrocephalus were included to address those requiring immediate intervention for their condition.

Exclusion criteria were carefully selected to eliminate confounding factors that might affect the outcomes. Patients with Grade IV TBM hydrocephalus were excluded due to their critical condition requiring alternative management approaches. Also, individuals with deranged bleeding and clotting profiles were omitted to mitigate potential risks during surgical procedures.



Figure 1. (A) The preoperative computed tomography scan illustrates the presence of hydrocephalus. (B) Demonstrates the patient treated with a ventriculoperitoneal shunt, featuring a right parietal catheter. (C) Displays the intraoperative view after endoscopic third ventriculostomy.

Moreover, prior brain surgeries and other pathologies causing obstructive hydrocephalus were excluded to maintain homogeneity within the study population. This ensured that the outcomes were primarily attributed to the allocated interventions (ETV or VPS) rather than confounding variables.

The statistical analysis aimed to compare the efficacy and outcomes of ETV versus VPS in managing TBM-related hydrocephalus. The χ^2 test was selected for its suitability in analyzing categorical data, determining any significant differences in outcomes between the two treatment groups.

Results

The mean age of the patients was 35.1 ± 9.2 years, showing no significant difference between the two treatment groups (P = 0.98). In the ETV group, there were 20 males and 10 females, while in the VP shunt group, there were 15 males and 15 females. The distribution of males and females did not show a statistically significant difference between the groups (P = 0.19).

The duration of anti-tubercular treatment (ATT) intake was longer in patients receiving VPS compared to those undergoing ETV, with a statistically significant difference observed (P = 0.015) (Table 1).

Preoperative Glasgow Coma Scale (GCS) scores were similar between the two groups, with a mean \pm SD of 13.5 ± 1.5 (P=0.16), and GCS ranging from 10 to 15. Vomiting was the most common symptom observed in patients from both groups at admission, although it was more frequently reported in the ETV group (15 versus 12). All patients (n=60) experienced at least one episode of vomiting prior to surgery (Table 2).

Regarding the Vellore grading system (Table 3), among the 30 patients with VPS, 18 had a Grade I Vellore score, and 10 had a Grade III Vellore score. In the ETV group, 15 patients had a Grade I Vellore score, and another 15 had a Grade III Vellore score. However, the differences in Vellore grades between patients undergoing ETV or VPS were not statistically significant (P = 0.12).

The comparison of vomiting status on postoperative day (POD) 7 and 30 showed similarities between the groups. The maximum number of vomiting episodes on POD 7 was one. One patient in the ETV group experienced vomiting, while five patients reported vomiting in the VPS group. The overall frequency of vomiting at POD 7 was comparable, indicating no statistical difference (P=0.08) (Table 2).

Table 1

Association of age, sex, AT	duration, and	preoperative	GCS
between study groups			

	Study group		Study group		
	VP shunt	ETV	Р		
Age	35.1 ± 9.9	35.0 ± 8.5	0.9		
Sex, n (%)					
Male	15 (50.0)	20 (66.7)	0.2		
Female	15 (50.0)	10 (33.3)			
ATT duration (months)	4.8 ± 1.6	3.6 ± 2.0	0.02*		
Preoperate GCS	13.8 <u>+</u> 1.3	13.3 ± 1.6	0.2		

t-test for age, ATT duration, and preoperative GCS was used for both study groups. χ^2 was used for sex and study groups.

ATT, anti-tubercular treatment; ETV, endoscopic third ventriculostomy; GCS, Glasgow Coma Scale; VP, ventriculoperitoneal.

*P value < 0.05b will be considered significant.

Table 2

Association of vomiting and Vellore score at different POD among groups

	Study group		
	VP shunt, <i>n</i> (%)	ETV, <i>n</i> (%)	Р
POD 1 vomiting			
No	15 (50.0)	7 (23.3)	0.03*
Yes	15 (50.0)	23 (76.7)	
POD 7 vomiting			
No	28 (93.3)	24 (82.8)	0.3
Yes	2 (6.7)	5 (17.2)	
POD 30 vomiting			
No	29 (96.7)	29 (96.7)	1.0
Yes	1 (3.3)	1 (3.3)	
Vellore Grading			
Grade I	19 (63.3)	15 (50.0)	0.3
Grade II	1 (3.3)	0	
Grade III	10 (33.3)	15 (50.0)	
POD 7 Vellore Grad	ing		
Grade I	27 (90.0)	26 (89.7)	1.0
Grade III	3 (10.0)	3 (10.3)	
POD 30 Vellore Gra	ding		
Grade I	29 (100.0)	28 (96.6)	0.3
Grade III	0	1 (3.4)	

The χ^2 test was used.

ETV, endoscopic third ventriculostomy; POD, postoperative day; VP, ventriculoperitoneal. *P value < 0.05 will be considered significant.

The findings revealed no significant age or gender disparities between the groups, confirming a balanced distribution among patients undergoing ETV and VPS procedures. However, a notable difference was observed in the duration of anti-tubercular treatment, with patients in the VPS group requiring a longer treatment period compared to those in the ETV group. This discrepancy might be attributed to various factors, such as the complexity of the surgical procedure and postoperative care, which warrants further investigation.

Both groups displayed similar preoperative neurological status, as assessed by the Glasgow Coma Scale. Vomiting emerged as a predominant symptom in all patients, particularly in the ETV group, emphasizing its prominence as a presenting symptom in TBM-related hydrocephalus.

The Vellore grading system indicated a relatively balanced distribution of patients across different severity grades in both treatment groups. The absence of statistical significance suggests that the severity of the condition, as categorized by the Vellore score, did not significantly influence the choice between ETV and VPS procedures.

Table 3

Modified vellore grading of tuberculous meningitis and hydrocephalus

Grade	
1	GCS 15 Headache, vomiting, fever \pm neck stiffness No neurological deficit
	GCS 15 Neurological deficit present
	GCS 9-14 Neurological deficit may or may not be present
IV	GCS 3-8 Neurological deficit may or may not be present

GCS, Glasgow Coma Scale

Postoperative comparisons of vomiting episodes at POD 7 exhibited similar trends between the groups, with no substantial discrepancy in the frequency of this postoperative complication. However, the observed trend might warrant closer examination in larger cohorts to identify potential predictors or factors influencing postoperative vomiting outcomes.

Overall, while the study demonstrates several comparable aspects between ETV and VPS procedures in managing TBMrelated hydrocephalus, further exploration and larger-scale studies are warranted to validate these findings and provide comprehensive insights into the optimal management strategies for this condition.

Discussion

Surgical treatment for hydrocephalus is typically considered for patients who do not respond to drug therapy or when drug treatment becomes ineffective in managing hydrocephalus. The primary goal of surgical intervention is to redirect the CSF flow. The main surgical options include bedside external ventricular shunts, ventriculoperitoneal shunts, or endoscopic third ventriculostomy^[7,8].

A meta-analysis encompassing 19 studies and 1038 patients revealed a favourable outcome in 58.3% of cases^[9]. Predictably, patients with grade I TBM showed the best outcomes, while those with grade IV TBM had the poorest prognosis. A commonly encountered complication is shunt malfunction, often necessitating shunt revision^[10]. Patients with markedly elevated CSF protein levels are at higher risk of this complication. Other potential complications involve shunt displacement, erosion, or the formation of peritoneal cysts^[11].

While prior studies have established age as an independent prognostic factor in TBM hydrocephalus, there is scan literature focusing on the paediatric population^[12]. There is a prevailing inclination to refrain from employing shunting procedures within this age bracket due to the associated complications, alongside concerns about potential shunt dependency in children. Indeed, shunt malfunction is a prevalent issue among children and is partly associated with the typically high CSF protein content observed in most cases.

Endoscopic third ventriculostomy stands as an effective alternative to ventriculoperitoneal shunts, especially suitable for treating communicating hydrocephalus, such as Sylvius aqueduct stenosis occurring in TBM cases^[11].

Despite this, in the existing literature, a consensus on the efficacy of ETV remains elusive in the context of treating TBM with associated hydrocephalus. Diverse studies present conflicting success rates, some even comparable to the conventional surgical approach, VPS^[13–17]. Notably, patients with TBM and hydrocephalus exhibit a vulnerability to complications owing to their compromised baseline health. Shunt-related issues such as obstruction, migration, and infection are among the potential complications associated with VPS. Moreover, VPS procedures often necessitate revision surgeries, reported as high as 43.8% by Sil and Chatterjee^[18].

Several studies have attempted to compare the success rates of ETV with those of VPS^[19–22]. A meta-analysis conducted by Jiang *et al.*^[23] in 2018 concluded that there was no significant difference between ETV and VPS in terms of symptom improvement. This analysis scrutinized variables like infection rates, duration of hospital stays, complications, mortality, and

surgical duration between the two procedures. Similarly, in our study, a comparative analysis was performed focusing on (1) postoperative symptom improvement, (2) modified Vellore grading, and (3) incidences of vomiting in patients undergoing ETV versus those undergoing VPS for TBM with hydrocephalus. Consistent with the meta-analysis by Jiang and colleagues, we also found no statistically significant differences in post-surgical symptom improvement between the ETV and VPS groups.

Aranha *et al.*^[24] highlighted the significance of modified Vellore grading in predicting outcomes for both ETV and VPS groups. This observation was mirrored in our study as well. Upon comparing postoperative statuses with preoperative statuses, we observed enhancements in modified Vellore grading across both groups. Goyal and colleagues also noted symptom improvements across various modified Vellore grades^[5]. In their study, among 24 patients undergoing VPS, 12 (70.3%) cases were classified as grade 3, while only one patient belonged to grade 1. For ETV, 7 (38.8%) cases were in grade 3, while the remaining cases were distributed across other grades.

Our investigation demonstrated an amelioration in the modified Vellore grade of patients, progressing from grade III to II and then to I in subsequent days. Notably, patients undergoing VPS exhibited earlier recovery compared to those undergoing ETV. However, it's crucial to acknowledge certain adverse events in our study. Specifically, one patient undergoing ETV succumbed to pneumonia and respiratory distress 6 days post-surgery, while another patient receiving VPS passed away three weeks after the procedure.

Regarding limitations, the primary constraint of our study lies in its short follow-up duration of 30 days. However, it's important to consider that tuberculous meningitis predominantly affects individuals in lower-middle-income countries (LMICs). Patients in these regions often hail from remote villages with limited mobility, making long-term follow-ups challenging. Nonetheless, despite this limitation, the clinical insights derived from LMICs contribute valuable data to supplement the existing literature.

Expanding on the significance of these findings, future studies could benefit from longer follow-up periods to discern the durability of outcomes and assess the long-term efficacy of ETV and VPS in managing TBM with hydrocephalus. Additionally, incorporating a larger sample size across diverse geographic regions may provide a more comprehensive understanding of the implications of these surgical interventions in different healthcare settings.

Conclusions

In conclusion, ETV emerges as a safe and comparably effective surgical intervention to VPS in managing patients with TBM-related hydrocephalus. Traditionally, ETV was predominantly employed for non-communicating hydrocephalus cases. Historically, VPS has held the status of the gold standard technique for CSF diversion. However, our study demonstrates that ETV can be equally viable in addressing this complex manifestation of hydrocephalus associated with TBM.

Symptoms commonly associated with TBM-related hydrocephalus, such as vomiting, altered consciousness levels, and the modified Vellore grading system, exhibit improvement with both ETV and VPS techniques. Notably, ETV, despite having a steep learning curve, presents an advantage by circumventing many of the lifelong complications associated with VPS placement once the procedure is mastered.

These findings underscore the potential of ETV as a valuable alternative to VPS in managing TBM-related hydrocephalus, challenging the historical preference for VPS in such cases. However, it's essential to acknowledge the learning curve associated with ETV, which might affect its widespread adoption. Further studies with larger cohorts and extended follow-up periods are warranted to solidify these observations and to elucidate the nuances in efficacy and complication profiles between ETV and VPS for TBM-related hydrocephalus.

Ethics approval

This study was approved by the Institutional review board (IRB) of Mayo Hospital, Lahore, Pakistan (Ethical Committee N° 136/ RC/KEMU).

Consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

Study concept or design: R.R. Data collection: R.R., G.U. Data analysis or interpretation: B.C., S.S. Writing the paper: R.R. Review, editing, final approval: B.C., M.R., A.V.

Conflicts of interest disclosure

There are no conflicts of interest.

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