RESEARCH ARTICLE

Microbiological spectrum of organisms in patients undergoing external ventricular drain insertion at a tertiary care hospital

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Abstract

Objective: To assess the incidence, causative pathogens, and impact of external ventricular drain-related infection on disease prognosis.

Method: The observational, cross-sectional study was conducted from September 2022 to March 2023 after obtaining approval from the ethics review board of Shifa International Hospital, Islamabad, Pakistan, and comprised patients having no prior cerebrospinal fluid infection. The patients underwent external ventricular drain administration as part of their treatment. Unneeded antibiotics or cerebrospinal fluid sampling before removing the drain were avoided. External ventricular drain-related infection was defined as pathogenic growth on one or more cerebrospinal fluid culture/sensitivity test post-insertion of the drain. Data was analysed using SPSS 26.

Results: Of the 74 patients, 42(56.8%) were males and 32(43.2%) were females. Overall, 25(33.8%) patients were aged 20-50 years. A total of 86 external ventricular drain were inserted for a mean period of 10.77+/-7.42 days (range: 1-40), with a total of 797 catheter days. Hydrocephalus 21(28.4%) and tumours 20(27%) were the most common aetiologies for external ventricular drain, but no significant aetiological risk factors for external ventricular drain-related infection were identified (p>0.05). Overall, 39(52.7%) patients recovered with external ventricular drain removal, and 12(16.2%) needed a shunt. External ventricular drain-related infection developed in 12(16.2%) patients (95% confidence interval: 4.15-4.75), having external ventricular drain for a mean period of 14.92+/-10.5 days (range 5-40) and 179 total catheter days. Coagulase-negative staphylococcus epidermidis was found in 4(33.3%) and it was sensitive to vancomycin, followed by Klebsiella pneumoniae and Pseudomonas aeruginosa 2(16.7%) each, and they were sensitive to amikacin and colistin, respectively. External ventricular drain-related infection was associated with poor outcomes (p=0.04), a longer intensive care unit stay (p<0.05), a longer hospital stay (p<0.05), and a longer external ventricular drain in-situ (p=0.05).

Conclusion: Aseptic external ventricular drain placement and its early removal could avoid external ventricular drain-related infections.

Key Words: Extra-ventricular drainage, EVD, EVD-related infection, ERI, Ventriculitis, Hydrocephalus, HCP.
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Introduction

Extra ventricular drain (EVD), also known as ventriculostomy catheter, is an emergency procedure done to relieve raised intracranial pressure (ICP) by placing a small flexible catheter in the ventricular system of brain under sterile conditions in an operating room (OR).[1] EVD origin traces back to 1744, when Clauds-Nicholas Le Cat introduced it for the management of hydrocephalus (HCP).[1]

Being an invasive procedure, patients with EVD can develop complications, like multiloculated HCP[2], blockage or haemorrhage of the ventricular system, dislodged or misplaced EVD, and, most significantly, EVD-related infection (ERI).[1,3] It can, in turn, be further complicated into subdural empyema, ventriculitis, brain abscesses and meningitis.[3] Factors such as systemic infection, subarachnoid haemorrhage (SAH), repeated catheter manipulation, prolonged EVD duration, and cerebrospinal fluid (CSF) leakage around the catheter insertion site significantly increase the risk of ERIs.[3,4]

ERI has been defined by the Centre of Disease Control and Prevention (CDC) criteria[5] as having a positive CSF culture or a combination of positive cultures, clinical symptoms, and laboratory findings showing elevated cell counts and/or decreased glucose levels.

The reported incidence of ERIs ranges 0-45%[1,3,6-8] with almost 4% reported in the largest study[8] and 0.6% in children aged <3 years.[9] A 35-study meta-analysis reported its incidence as 11.4 per 1,000 catheter days (95% CI 9.3-13.5).[10]

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Due to nonspecific clinical signs and laboratory parameters of CSF, the diagnosis of such an infection is often delayed, leading to prolonged length of hospital stay (LOS), increased treatment costs and an overall poor prognosis.[3] ERI is mostly caused by gram-negative pathogens,[3,6] and, hence, antibiotics with appropriate coverage should be considered for empirical treatment and then adjusted as per culture and sensitivity (C/S) findings.

To the best of our knowledge, no study has reported data regarding ERIs in the local population. The current study was planned to fill the gap by establishing the incidence, underlying risk factors, and prognosis of ERI cases in a Pakistani setting.

Patients and Methods

The single-centre, observational, cross-sectional study was conducted from September 2022 to March 2023 after obtaining approval from the ethics review board of Shifa International Hospital, Islamabad, Pakistan. The sample was raised using consecutive sampling technique. Those included were patients of either gender regardless of who underwent EVD placement after presenting either via emergency department (ED) or neurosurgical outpatient department (OPD) with clinical signs of raised ICP confirmed on computed tomography (CT) scan. Patients with open skull fractures, base of skull fracture with CSF leaks, sepsis, and pre-diagnosed central nervous system (CNS) infections were excluded. The sample size was calculated using openepi online free portal[11] using proportion from similar study for which the sample size was calculated to be 74 patients.

After taking informed consent, clinical data was recorded for age, gender, underlying aetiology, EVD, causative organism, duration, and outcome. At least one positive CSF culture post-EVD insertion in a previously non-CNS infection patient was documented as positive ERI. Patients were followed until discharge, and no follow-up information was recorded.

Gram-positive or gram-negative pathogens with isolated organism growth from CSF culture and/or drain tips were also recorded. The need for EVD revision, the total number of EVD revisions done, and the total timeframe of EVD in-situ were noted in days. All EVDs were challenged at day 14 of EVD insertion, and the outcome was observed as in-hospital mortality, ventriculoperitoneal (VP) shunt placement, or EVD removal.

All catheters (INTEGRA Hermetic TM Ventricular Catheter Set - USA) were inserted via the right or left frontal approach in OR under sterile conditions. A tunnelled procedure technique was adopted. Fixed catheter replacement or routine CSF sampling were avoided. 2g of ceftriaxone and 1g of vancomycin were given to all patients, including 1 dose given pre-operatively in the OR and a minimum of 3 doses post-operatively. Neurological degradation, fever, a rise in serum C-reactive protein (CRP) level and total white blood cell (WBC) count were signs that called for CSF sampling due to suspicion of ERI. Once growth was confirmed on gram stains, empiric antibiotics were started, and later adjusted as per CSF C/S. Intrathecal antibiotics were administered, and clamping the drain for 30 minutes was done, if necessary.

The decision regarding EVD re-insertion was made based on the clinical deterioration of the patients or bacterial colonisation of the tract. The patients were discharged once EVD was removed after the underlying aetiology was resolved or CSF cultures became negative during the post-operative course.

Data was analysed by two researchers independently, using SPSS 26. Data was expressed as frequencies and percentages or as means +/- standard deviation along with min-max range, as appropriate. Data was compared using t-test, Fisher's test, or chi-square test as appropriate. ERI incidence was expressed with 95% CI which was determined using the Kaplan-Maier method. Cox regression was used to calculate incidence density, predictors of ERI and cumulative incidence CIs. $P< 0.05$ was considered significant.

Results

Of the 74 patients, 42(56.8%) were males and 32(43.2%) were females. Overall, 25(33.8%) patients were aged 20-50 years. Age and gender had no significant association with ERIs ($p>0.05$). Patients with ERI had a longer EVD

Table-1: Demographics, risk factors and outcomes

	Total (n=74)	ERI (n=12)	p Value
Gender, n (%)			0.552
Male	42 (56.8%)	7 (58.3%)	
Female	32 (43.2%)	5 (41.7%)	
Ages			0.934
0-1 month	1	-	
1 months – 2 years	13	3 (25%)	
2 - 10 years	7	-	
10-20 years	11	3 (25%)	
20-50 years	25	3 (25%)	
>50 years	17	3 (25%)	
Aetiology			0.764
ICB + IVE	13(17.6%)	4 (33.3%)	
aSAH	9 (12.2%)	1 (8.3%)	

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Traumatic SAH	10 (13.5%)	2 (16.7%)	
Tumours	20 (26.9%)	2 (16.7%)	
HCP	21 (28.4%)	3 (25%)	
Dermoid cyst	1 (1.4%)	-	
In hospital deaths	2 (2.7%)	2 (16.7%)	0.004
Total duration (days)	797 (1-40)	179 (1-40)	<0.05
Mean duration (days)	10.77	14.92	0.05
Mean LOS – hospital (days)	15.67	23.5	<0.05
Mean LOS – ICU (days)	1.5	3.88 +/- 4.04	<0.05

ERI: External ventricular drain-related infection, ICB: Intracranial bleed, IVE: Intraventricular extension, aSAH: Aneurysmal subarachnoid haemorrhage, SAH: Subarachnoid haemorrhage, HCP: Hydrocephalus, LOS: Length of hospital Stay, ICU: Intensive care unit.

Table-2: Organisms identified with external ventricular drain-related infection (ERI) and outcomes.

Organisms		**N**
Gram-positive		5
	Staphylococcus epidermidis	4
	Mycobacterium tuberculosis	1
Gram-negative		7
	Acinobacter	1
	e. coli	1
	Enterobacter	1
	Klebsiella pneumoniae XDR	2
	Pseudomonas aeruginosa XDR	2

VP shunt	1 (8.3%)	Mycobacterium tuberculosis
Expiry	2 (16.7%)	Klebsiella pneumoniae XDR, acinobacter
Removal	4 (33.3%)	Staphylococcus epidermidis (2), pseudomonas aeruginosa XDR (2)
Referred to other facility	1 (8.3%)	Enterobacter
Re-do EVD	4 (33.3%)	E. coli, Klebsiella pneumoniae XDR, staphylococcus epidermidis (2)

VP: Ventriculoperitoneal, EVD: External ventricular drain, XDR: Extensively drug-resistant,

Table-3: Culture and sensitivity of external ventricular drain-related infection (ERI) organisms to antibiotics.

Antibiotic sensitivity	**Gram-positive**	**Gram-negative**				
	Staphylococcus epidermidis (n=4)	**E. Coli XDR (n=1)**	**Pseudomonas XDR (n=2)**	**Klebsiella pneumoniae (n=2)**	**Actinobacterer (n=1)**	**Enterococcus (n=1)**
Vancomycin	S	R	R	R	R	R
Linezolid	S	R	R	R	R	R
Amikacin	S	R	I	S	S	S
Colistin	S	R	I	I	I	S
Chloramphenicol	S	S	R	R	R	R

XDR: Extensively drug-resistant, S: Sensitive, I: Intermediate, R: Resistant.

duration in-situ and longer LOS compared to those without (p<0.05). A total of 86 EVDs were inserted for a mean period of 10.77+/-7.42 days (range: 1-40), with a total of 797 catheter days. Overall, 39(52.7%) patients recovered with EVD removal, and 12(16.2%) needed a VP shunt. ERI developed in 12(16.2%) patients (95% CI: 4.15-4.75), having EVD for a mean period of 14.92+/-10.5 days (range 5-40) and 179 total catheter days (p<0.05) (Table 1).

The second EVD was placed in 8(10.8%) patients for 122 days, with a mean value of 15.25+/-12.97 days (range 7-35). The third EVD was placed in 4(5.4%) patients for 40 days with a mean of 11.67 +/-4.93 days (range 4-14). HCP 21(28.4%) and tumours 20(27%) were the most common aetiologies for EVD, but no significant aetiological risk factors for ERI were identified (p>0.05) (Table 1).

In the 12(16.2%) cases, there were 5(41.7%) gram-positive and 7(58.3%) gram-negative organisms. The pathogen most isolated was Staphylococcus (S.) epidermidis 4(33.2%), followed by Klebsiella (K.) pneumoniae and Pseudomonas (P.) aeruginosa 2(16.7%) each (Table 2). Within the ERI subset, re-do EVD was done in 8(66.6%) patients, with the first EVD infected in 1(12.5%) patient, the second EVD in 4(50%) patients, 1(12.5%) patient had ERI in both the second and third EVDs, while 1(12.5%) patient died.

Coagulase-negative staphylococcus (S.) epidermidis was found in 4(33.3%) and it was sensitive to vancomycin, followed by Klebsiella (K.) pneumoniae and Pseudomonas (P.) aeruginosa 2(16.7%) each, and they were sensitive to amikacin and colistin, respectively (Tables 2-3). The organisms isolated from the 2(2.7%) patients who died were acinobacter and K. pneumoniae.

ERI was associated with poor outcomes (p=0.04), a longer ICU stay (p<0.05), a longer LOS (p<0.05), and a longer EVD in-situ (p=0.05).

Discussion

In the current study, the cumulative ERI was 16.2%, which is comparable to studies in the past.[1,3,6-8] The average collective rate of positive CSF cultures has been reported to be 8-10%.[12] According to a meta-analysis of 35 studies, the cumulative occurrence of ERI was 11.4 per 1,000 catheter days (95% CI: 9.3-13.5).[10]

The current study showed that coagulase-negative S. epidermidis was the most isolated organism in patients with ERI, which is in line with literature, as coagulase-negative staphylococcus is 62% responsible for ERI, followed by Enterococcus (E.) species, S. aureus, Citibecterium (C.) acnes, and Citrobacter kerosi.[3,7] This pattern coincides with that of the usual skin flora and hospital environment.[3] Organisms that commonly cause systemic infections along with ERI include E. species, Enterobacter species and S. aureus.[13]

In the literature, the most common underlying risk factor for ERI is tumour (55%), followed by HCP (40%).[6] Adjunct EVD placement before or during tumour resection led to more frequent post-operative CNS infections compared to stand-alone craniotomies (30.4% vs. 1.5%) in a study.[14] For non-haemorrhagic pathologies, the literature reported a significantly higher incidence of ERI in patients with subarachnoid and/or intraventricular haemorrhage,[3] but the current study could not confirm this to be an independent risk factor.

Multiple studies reviewed the correlation between ERI and existing system infections, showing that synchronous system infections, basilar skull fracture and prior surgery had a correlation.[3,7,12] All these conditions were excluded from the current study. Also, repeated catheter manipulation, CSF leakage around the EVD catheter insertion site, repeated CSF sampling, insufficient tunnelling of the EVD catheter, or insufficient hair clipping, and tract haemorrhage have been identified as risk factors for ERI.[3,7,12] However, none of the current patients had any such condition.

In our study, patients with ERI had a longer median total external drainage duration (10.77 vs 14.92 days, $p = 0.05$), had a significantly longer ICU stay (1.5 versus 3.88 days, $p < 0.05$) and longer hospital stay (15.67 versus 23.5 days, $p < 0.05$). Prolonged duration of EVD in-situ was a risk factor seen in the current study as well as in the literature,[3,7] accentuating the fact that the lengthening of total drainage time in patients with ERI is an aftermath of ERI and not vice versa. Long-term catheterisation has been linked to ERI in multiple studies and was seen in the current study as well. However, because some researchers used daily infection rates and others used cumulative infection rates, analysing these studies may be difficult.

The best possibility to avoid ERI is to insert EVD under aseptic techniques. The prevailing theory is that microbes introduced during EVD installation or post-operative EVD contamination induce ERI.[3,15]

If a patient develops ERI, it should be treated with empirical vancomycin[16] and then intrathecal antibiotics as per C/S. A recent systemic analysis, stated that the use of aminoglycosides through the intrathecal route proved to be effective in treating gram-negative rod ERI.[12] In the current study, all patients with ERI received intrathecal antibiotics empirically with intravenous (IV) vancomycin and ceftriaxone until results of CSF cultures were available. Antibiotics were then adjusted as per CSF culture and sensitivity reports. In most patients, S. epidermidis was sensitive to vancomycin; hence, the patients were continued therapeutically on intrathecal vancomycin. Gram-negative rods were a challenge to treat as they were differently sensitive to aminoglycosides, and they were shifted to therapeutic intrathecal amikacin and colistin.

Antimicrobial-coated EVD catheters reduce ERI in adults [17,18] as well as in paediatric patients.[19] Ideally, it should be attempted to insert EVD under sterile condition with aseptic techniques to avoid ERI. ERI prevention methods have been considered and implemented in many centres, including antibacterial catheters and antibiotics before EVD insertion.[12] The current study administered preventative pre-operative systemic antibiotics in all the patients despite limited scientific evidence. Several studies found that injecting antibiotics directly into the ventricles (for example: amikacin) and collecting CSF samples before removing the EVD reduced ERI rates.[10] CSF sampling can be done daily or as needed.[12] Due to its controversy, the current study did not use this approach.

EVD insertion and management strategies have reduced EVD infections at some facilities. This strategy involves limiting EVD manipulation, avoiding CSF fluid collection, and cleaning the insertion site with alcoholic chlorhexidine while the EVD is in-situ. In cases where CSF infection is suspected, the distal component of the system is replaced, CSF drainage is improved, and, if required, the entire system is removed.[12]

The current study has limitations as it was a single-centre small-duration study. Multi-centre, long-duration studies are needed to validate the findings and to know the cumulative incidence rate of ERI in the region.

Conclusion

ERI, a life-threatening but treatable complication of one of the most common neurosurgical procedures, could be avoided by ensuring EVD insertion under aseptic conditions. Early diagnosis is challenging and critical but is critical to plan an intervention. ERI patients should be treated with empirical intrathecal vancomycin until CSF cultures are pending. and then intrathecal antibiotics should be started as per sensitivity.

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Authors' Contribution:
MA: Principle investigator.
SVH, MN: Supervision.
AI: Data collection, writing and corrections.
TR: Data collection and analysis.
SN: Writing.