Prevalence and Antibiotic Resistance Profile of Cerebrospinal Fluid Pathogens from Neurosurgical Patients from Level 1 Trauma Center in India

Abstract

Introduction: The purpose of this study was to investigate the prevalence of Postoperative central nervous system infections (PCNSIs) and antibiotic resistance profiles of causative organisms in trauma patients following neuroinvasive procedures. **Materials and Methods:** This was a retrospective study conducted over a period of 4 years (2013–2017). All in-patients admitted under a neurotrauma unit meeting the inclusion criteria of PCNSIs were included in the study. Surgical site infections (SSIs) were defined according to the Centers for Disease Control and Prevention 2018 (CDC) criteria. We retrospectively examined the demographic characteristics, type of neurosurgery performed, laboratory data, causative organisms, and antimicrobial susceptibility testing results of patients who had positive cerebrospinal fluid cultures following craniotomy between January 2013 and December 2017. **Results:** Of total 2500 patients operated during the study, 961 patients were screened for PCNSIs. The estimated prevalence (95% confidence interval) of PCNSIs which is a type of organ/space SSI was 7.2% (6.3–8.3). Males were predominantly affected (85.0%). The mean age (standard deviation) of patients was 31.9 (16.5) years. Of all the cultures sent for microbiological examination, 18.6% were positive. The proportion of Gram-negative bacteria causing PCNSIs was 91.6%. Multidrug-resistant (MDR) *Acinetobacter baumannii* (41%) was the most common organism isolated. Among Gram-positive bacteria, the most common organism was *Staphylococcus aureus* (5.5%). All the Gram-positive isolates were susceptible to vancomycin, teicoplanin, and linezolid. **Conclusion:** There is a high burden of PCNSI caused by MDR *Acinetobacter baumannii* can pose a major clinical challenge with only few antimicrobials left in the pipeline.

Keywords: *Craniotomy, multidrug-resistant Acinetobacter baumannii, neuroinvasive procedures, postoperative central nervous system infections, trauma patients*

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Introduction

Postoperative central nervous system infection (PCNSI) in patients undergoing neurosurgical procedures represents a significant threat following neurosurgery, which requires immediate attention. The most common presentations of PCNSI include meningitis, subdural empyema, epidural abscess, and brain abscess.[1] The risk factors for postoperative infections after neurosurgical procedures include cerebrospinal fluid (CSF) leak, postoperative monitoring of intracranial pressure, placement of foreign body, ventricular drains, shunt infection, longer duration of procedures, repeat or additional neurosurgical procedures, and emergency procedures.[2] A recent study involving 16,200 craniotomies showed that CSF leakage and male sex as independent risk factors for the development of PCNSI.[3] Several studies have identified the role of antibiotic prophylaxis after neurosurgical procedures in relation to PCNSI, demonstrating the decline in the incidence of PCNSI with antibiotic prophylaxis.[1,4]

Recent studies have reported that the incidence of PCNSI after neurosurgical procedures varies from 0.7%–8.9%.[3] The incidence of PCNSI varies between different regions with developed countries having lower incidence than developing countries. Studies have shown the most common causative agent of PCNSIs being *Staphylococcus aureus,* Coagulase-negative staphylococci followed by the Gram-negative organisms.[5] The present study was conducted to establish the prevalence and causative organisms

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Access this article online
Website: www.asianjns.org
DOI: 10.4103/ajns.AJNS_268_18
Quick Response Code:

How to cite this article: Govindaswamy A, Bajpai V, Singh P, Lohiya A, Ayyanar M, Gupta DK, *et al.* Prevalence and antibiotic resistance profile of cerebrospinal fluid pathogens from neurosurgical patients from level 1 trauma center in India. Asian J Neurosurg 2019;14:834-8.

of PCNSIs and the antibiotic resistance profiles of CSF pathogens in trauma patients following neuroinvasive procedures.

Materials and Methods

This was a retrospective study which included patients admitted under a neurotrauma unit who underwent craniotomy between January 2013 and December 2017. These patients were investigated for possible PCNSIs based on clinical signs and symptoms. The patients who met the clinical diagnostic criteria of central nervous system infection were included in the study.[6] Patients who underwent cranial operation previously, both by elective and emergency procedures were also included in the study. The patients with clinical, radiological, or microbiological examination suggestive of tubercular/viral/fungal meningitis were excluded from the study. The data of patients with positive culture isolates were collected from medical records. The data included demographic characteristics, types of neurosurgery performed, laboratory data, causative organisms, and antimicrobial susceptibility testing. The main outcome of interest is PCNSIs which is a type of organ/space Surgical site infection (SSI) according to Centers for Disease Control and Prevention 2018 (CDC) criteria used to define SSIs.[7] The isolation of the same organism within 7 days from the same patient was regarded as the same isolate and not counted multiple times. All patients received (dose) 2 g of cefoperazone-sulbactam and 300 mg netilmicin as prophylactic therapy 1 h before incision, followed by a 24-h postoperative course.

CSF samples were collected on suspicion of infection as per standard procedures. One of the specimens was used for Gram staining and bacterial culture the other was used for cytology, protein, and sugar estimations. All CSF-positive culture isolates were identified up to the species level by VITEK 2 GN card (version 7.02, BioMérieux, Inc., Durham, USA). Antimicrobial susceptibility testing was performed by Kirby-Bauer disc diffusion method on Mueller Hinton agar and by Vitek 2 (BioMérieux) system. The results of antibiotic susceptibility were interpreted based on the Clinical and Laboratory Standards Institution guidelines.[8] SSIs had to meet the CDC and Prevention 2018 (CDC) criteria.[7]

Statistical analysis was done using IBM SPSS (Statistical Package for Social Sciences) Statistics version 22.0 (IBM, Armonk, NY, United States of America). Results were presented with 95% confidence intervals (CIs) in case of categorical variables and as mean or median in case of continuous variables. Chi-square test was used to compare proportions. Student *t*-test and Mann–Whitney test were used to compare means and medians, respectively.

Results

From 2013–2017, a total of 2500 in-hospital patients were operated on in the department of neurosurgery. We obtained 3591 CSF culture samples from 961 patients admitted under a neurotrauma unit. Of these, 338 CSF samples had a positive growth in culture. The patient's medical records were reviewed. Following review, 180 CSF-positive cultures which met the inclusion cultures were included in the study. The remaining 158 CSF samples were excluded from the study due to multiple CSF samples obtained from the same patient and failure to retrieve patient's medical records. The prevalence (95% CI) of PCNSIs among trauma patients following neuroinvasive procedure was 7.2% (6.3–8.3). Out of 961 patients sampled, 180 (18.7%) patients had a positive CSF culture.

The mean age of the patients with PCNSIs was 31.9 (16.5) years. A majority of patients were males (85.0%). A total of 91 (50.6%) out of 180 patients with PCNSIs did not survive. The proportion of patients who underwent craniotomy, shunt placement, decompressive craniectomy, duraplasty, and Ommaya placement were 33.9%, 51.1%, 61.7%, 26.1%, and 28.9%, respectively. CSF analysis indicated that the patients had low-CSF glucose and high protein levels postoperatively. Male patients ($P = 0.001$) and decompressive-craniotomy patients ($P = 0.02$) had higher chances of mortality among PCNSI patients [Table 1].

Table 1: Comparison of demographic and clinical parameters of dead and alive patients with postneurosurgical bacterial meningitis (*n*=180)

	Dead (*n*=91)	Alive (*n*=89)	*P*
Demographic characteristics			
Mean (SD) age (years)	31.6 (16.6)	26.0 (15.0)	0.02
n (%) of males (*n*=153)	85 (55.6)	68 (44.4)	0.001
Clinical parameters			
Median (IQR) interval between infection and initial neurosurgery (days)	20 (9, 43)	18.5 (8, 38)	0.45
Median (IQR) days in hospital	55 (24, 91)	50 (26, 89)	0.93
Craniotomy (*n*=61)	32 (52.5)	29 (47.5)	0.72
Shunt placement (*n*=92)	46 (50.0)	46 (50.0)	0.88
Decompressive craniectomy (*n*=111)	64 (57.7)	47 (42.3)	0.02
Duraplasty (*n*=47)	28 (59.6)	19 (40.4)	0.15
Ommaya placement (*n*=52)	28 (53.8)	24 (46.2)	0.57

SD – Standard deviation; IQR – Interquartile range

The most common organisms causing PCNSIs were Gram-negative bacteria (92.1%). The predominant Gram-negative organism was *Acinetobacter baumannii* (41.0%) followed by *Klebsiella pneumoniae* (14.0%), *Escherichia coli* (11.7%), *Pseudomonas aeruginosa* (7.8%), *Serratia marcescens* (7.3%), and *Enterobacter cloacae* (4.4%). The predominant Gram-positive isolate was *Staphylococcus aureus* (5.6%) followed by *Enterococcus faecium* (1.1%) and coagulase-negative staphylococci (1.1%) [Table 2].

All the *Staphylococcus aureus* isolates were sensitive to linezolid, teicoplanin, vancomycin, and netilmicin. The two *Enterococcus faecium* isolates were all sensitive to linezolid, rifampicin, teicoplanin, and vancomycin. The two coagulase-negative staphylococcus isolates were sensitive to linezolid, rifampicin, teicoplanin, and vancomycin [Table 3]. Of the Gram-negative isolates, there were 73 *Acinetobacter baumannii*, 25 *Klebsiella pneumoniae*, 21 *Escherichia coli*, and 14 *Pseudomonas aeruginosa* isolates available for analysis. The susceptibility testing of the Gram-negative isolates showed that colistin was the most active agent (100%) [Table 4].

Table 2: Bacteria isolated from cerebrospinal fluid (*n*=180)

Organism	*n* (%)
Gram-negative bacteria	
Acinetobacter baumannii	73 (41.0)
Klebsiella pneumonia	25 (14.0)
Escherichia coli	21 (11.7)
Pseudomonas aeruginosa	14 (7.8)
Serratia marcescens	13 (7.3)
Enterobacter cloacae	8 (4.4)
Others#	12 (6.7)
Gram-positive bacteria	
Staphylococcus aureus	10 (5.6)
Enterococcus faecium	2 (1.1)
Coagulase-negative staphylococci	2 (1.1)

#Others: *Acinetobacter lwoffii* (*n*=1), *Pseudomonas putida* (*n*=1), *Pseudomonas* spp. (*n*=1), *Pseudomonas stutzeri* (*n*=1), *Providencia stuartii* (*n*=1), *Morganella morganii* (*n*=1), *Elizabethkingia meningoseptica* (*n*=1), *Stenotrophomonas maltophilia* (*n*=1), *Sphingomonas paucimobilis* (*n*=1), *Aeromonas salmonicida* (*n*=1), *Chrysobacterium indologenes* (*n*=1). Coagulase-negative staphylococci - *Staphylococcus epidermidis* (*n*=1), *Staphylococcus haemolyticus* (*n*=1)

Discussion

PCNSI is one of the most dreadful complications following cranial operations. They are associated with increased costs of treatment, increased length of hospital stay, psychological trauma, and delay in postoperative adjuvant therapies.[9] Before the advent of antibiotics for surgical prophylaxis and sterile surgical techniques, the rates of PCNSI were quite high.[10-12] The overall rate of PCNSIs varies between 0.72% and > 12% according to various size limited studies.[13-15] The PCNSI patients included in the study were diagnosed by CSF culture, the prevalence of PCNSI in our center was found to be 7.2% which was similar to few previously conducted studies.[16,17] However, there are other studies in which the rates were high ranging from 6.5%–12%.[18,19]

The culture positive rate of PCNSI in our study was found to be 18.6%, which is low compared to previous studies which showed culture-positive rate of infection approximately 50%.[15,18,19] The possible reasons could be similar isolates obtained from the same patient within 7 days were considered as a single isolate. Another reason could be the use of cefoperazone-sulbactam and netilmicin as prophylactic antibiotics followed by the used of therapeutic antibiotics once the infection was diagnosed. The mortality rate of PCNSI in our study was found to be 50.6% which is higher than reported by other studies.[20,21]

The predominant organism was Gram-negative bacteria which accounted for 92.1% of the total isolates. *Acinetobacter baumannii* was the most common causative Gram-negative agent, accounting for 41% of the total isolates. Among the Gram-positive bacteria, *Staphylococcus aureus* (5.6%) was the most common organism followed by Coagulase-negative staphylococci (1.1%) and *Enterococcus faecium* (1.1%). The microbiological findings in this study were consistent with previously published studies.[10,15,22]

Of the Gram-positive isolates, approximately 60% (6 isolates) of *Staphylococcus aureus* isolates were methicillin-resistant *Staphylococcus aureus* (MRSA), and these isolates were susceptible to vancomycin, linezolid, teicoplanin, and netilmicin. The incidence of MRSA in our study was higher in comparison to other studies.[23,24] The two coagulase-negative staphylococci isolates were methicillin-resistant coagulase-negative

Table 3: Proportion percentage of Gram-positive bacteria sensitive to antibiotics

Organism	AMC	AMP	FOX	CIP	CLI	SXT	ERY	GEN	LVX	LNZ	NET	OXA	PEN	RIF	TEC	TCY	TGC	VAN
Staphylococcus aureus (*n*=10)	38	0	40	33	63	72	26	40	37	100	100	43	0	50	100	67	-	100
Coagulase-negative Staphylococci (*n*=2)	0	0	0	50	50	50	0	0	50	100	100	0	0	100	100	-	-	100
Enterococcus faecium (*n*=2)	0	0	-	0	-	-	-	-	0	100	-	-	0	100	100	50	-	100

AMC – Amoxicillin-clavulanate; AMP – Ampicillin; FOX – Cefoxitin; CIP – Ciprofloxacin; CLI – Clindamycin; SXT – Sulfamethoxazole-trimethoprim; ERY – Erythromycin; GEN – Gentamycin; LVX – Levofloxacin; LNZ – Linezolid; NET – Netilmicin; OXA – Oxacillin; PEN – Penicillin; RIF – Rifampicin, TEC – Teicoplanin; TCY – Tetracycline, TGC – Tigecycline, VAN – Vancomycin

Table 4: Proportion percentage of Gram-negative bacteria sensitive to antibiotics

Organism	AMK	FEP	CPT	CSL	CTX	CAZ	CRO	CHL	CIP	COL	GEN	IPM	LVX	MEM	NET	PIP	TZP	TIC	TGC	SXT
Acinetobacter baumannii (*n*=73)	9	4	8	19	0	0	0	-	0	100	5	15	6	17	11	0	3	3	88	-
Klebsiella pneumonia (*n*=25)	16	14	25	0	0	0	0	48	0	100	0	43	0	38	12	0	6	0	94	12
Escherichia coli (*n*=21)	67	0	33	17	0	0	0	57	0	100	36	71	0	57	77	0	50	0	79	14
Pseudomonas aeruginosa (*n*=14)	47	60	62	27	-	28	-	-	28	100	20	47	48	51	50	47	55	47	-	-

AMK – Amikacin; FEP – Cefepime; CPT – Cefepime tazobactam; CSL – Cefoperazone-sulbactam; CTX – Cefotaxime, CAZ – Ceftazidime, CRO – Ceftriaxone; CHL – Chloramphenicol, CIP – Ciprofloxacin, COL colistin, GEN – Gentamycin; IPM – Imipenem; LVX – Levofloxacin; MEM – Meropenem; NET – Netilmicin, PIP – Piperacillin; TZP – Piperacillin-tazobactam; TIC – Ticarcillin clavulanate; TGC – Tigecycline; SXT – Sulfamethoxazole-trimethoprim

staphylococci (MRCoNS) and were also susceptible to vancomycin, teicoplanin, linezolid rifampicin, and netilmicin. The two *Enterococcus faecium* isolates were susceptible to linezolid, vancomycin, teicoplanin, and rifampicin. The results of Gram-positive antibiotic sensitivity rates indicate that most effective antibiotics against MRSA, MRCoNS, *Enterococcus faecium* were vancomycin, teicoplanin, and linezolid. Vancomycin is considered to be the last resort and drug of choice for the treatment of CNS infections caused by the Gram-positive bacteria. However, in the study conducted by Chang *et al*. had PCNSI caused by vancomycin-resistant Enterococcus faecalis isolates.[9] Thus, the emergence of vancomycin resistance could be serious threat for PCNSIs caused by the Gram-positive organisms.

Of the Gram-negative isolates, the most predominant organism was *Acinetobacter baumannii* (41%) followed by *Klebsiella pneumoniae* (14%), *Escherichia coli* (11.7%), and *Pseudomonas aeruginosa* (7.8%). The rate of carbapenem-resistant *Acinetobacter baumannii* was 79.4%. The emergence of multidrug-resistant (MDR) *Acinetobacter baumannii* known as one of the ESKAPE pathogens has become a serious medical problem globally.[25] The rise in incidence of MDR *Acinetobacter baumannii* infections is of great concern due to the lack of treatment options for such pathogens. The most effective antibiotics for the treatment of Gram-negative infections were tigecycline and colistin. The finding was similar to previously published studies.[9,26,27]

Early diagnosis and appropriate use of antibiotics is necessary for the management of PCNSIs. There are only few studies available from India with regard to the causative organisms and drug sensitivities of PCNSIs.[2,3,28] The present study demonstrated that the distribution of pathogens from our region was similar to the trend observed globally, thus helping the clinicians to choose the appropriate empirical antibiotic treatment for PCNSIs. The limitations of the study were that data with regard to clinical variables were not studied, the isolates included in the study may not be a representative for the whole of India, and the isolates were not characterized to molecular level to depict the resistance characteristics.

Conclusion

PCNSIs represent as serious threat, leading to higher mortality rate. This study also highlights the prevalence and causative organisms of PCNSIs from a tertiary care center located in North India. Our study shows an increasing prevalence of Gram-negative organisms in CSF cultures from PCNSIs after neurosurgery. The management of MDR *Acinetobacter baumannii* remains a major clinical challenge with only few antibiotics options left for the treatment of PCNSIs.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. McClelland S 3rd, Hall WA. Postoperative central nervous system infection: Incidence and associated factors in 2111 neurosurgical procedures. Clin Infect Dis 2007;45:55-9.
2. Chidambaram S, Vasudevan MC, Nair MN, Joyce C, Germanwala AV. Impact of operating room environment on postoperative central nervous system infection in a resource-limited neurosurgical center in South Asia. World Neurosurg 2018;110:e239-44.
3. Srinivas D, Veena Kumari HB, Somanna S, Bhagavatula I, Anandappa CB. The incidence of postoperative meningitis in neurosurgery: An institutional experience. Neurol India 2011;59:195-8.
4. Mollman HD, Haines SJ. Risk factors for postoperative neurosurgical wound infection. A case-control study. J Neurosurg 1986;64:902-6.
5. Ma YF, Wen L, Zhu Y. Prospective study evaluating post-operative central nervous system infections following cranial surgery. Br J Neurosurg 2018. Doi: 10.1080/02688697.2018.1519112.
6. Tunkel AR, Hasbun R, Bhimraj A, Byers K, Kaplan SL, Michael Scheld W, *et al.* 2017 Infectious Diseases Society of America's Clinical Practice Guidelines for healthcare-associated ventriculitis and meningitis. Clin Infect Dis 2017. Doi: 10.1093/cid/ciw861.
7. Clinical and Laboratory Standards Institute: CLSI Guidelines. Clinical and Laboratory Standards Institute. Available from: https://www.clsi.org/. [Last accessed on 2018 Oct 25].
8. Centers for Disease Control and Prevention. National Healthcare Safety Network (NHSN) Overview. Centers for Disease Control and Prevention; 2018. Available from: http://www.cdc.gov/nhsn/pdfs/pscmanual/pcsmanual_current.pdf. [Last accessed on 2018 Dec 12].
9. Chang JB, Wu H, Wang H, Ma BT, Wang RZ, Wei JJ, *et al.* Prevalence and antibiotic resistance of bacteria isolated from the cerebrospinal fluid of neurosurgical patients at Peking Union medical college hospital. Antimicrob Resist Infect Control 2018;7:41.
10. Patir R, Mahapatra AK, Banerji AK. Risk factors in postoperative neurosurgical infection. A prospective study. Acta Neurochir (Wien) 1992;119:80-4.
11. Woodhall B, Neill RG, Dratz HM. Ultraviolet radiation as an adjunct in the control of postoperative neurosurgical infection: II clinical experience 1938-1948. Ann Surg 1949;129:820-4.
12. Young RF, Lawner PM. Perioperative antibiotic prophylaxis for prevention of postoperative neurosurgical infections. A randomized clinical trial. J Neurosurg 1987;66:701-5.
13. Valentini LG, Casali C, Chatenoud L, Chiaffarino F, Uberti-Foppa C, Broggi G, *et al.* Surgical site infections after elective neurosurgery: A survey of 1747 patients. Neurosurgery 2008;62:88-95.
14. Reichert MC, Medeiros EA, Ferraz FA. Hospital-acquired meningitis in patients undergoing craniotomy: Incidence, evolution, and risk factors. Am J Infect Control 2002;30:158-64.
15. Korinek AM, Baugnon T, Golmard JL, van Effenterre R, Coriat P, Puybasset L, *et al.* Risk factors for adult nosocomial meningitis after craniotomy: Role of antibiotic prophylaxis. Neurosurgery 2008;62 Suppl 2:532-9.
16. Dashti SR, Baharvahdat H, Spetzler RF, Sauvageau E, Chang SW, Stiefel MF, *et al.* Operative intracranial infection following craniotomy. Neurosurg Focus 2008;24:E10.
17. Cassir N, De La Rosa S, Melot A, Touta A, Troude L, Loundou A, *et al.* Risk factors for surgical site infections after neurosurgery: A focus on the postoperative period. Am J Infect Control 2015;43:1288-91.
18. Shi ZH, Xu M, Wang YZ, Luo XY, Chen GQ, Wang X, *et al.* Post-craniotomy intracranial infection in patients with brain tumors: A retrospective analysis of 5723 consecutive patients. Br J Neurosurg 2017;31:5-9.
19. Zhan R, Zhu Y, Shen Y, Shen J, Tong Y, Yu H, *et al.* Post-operative central nervous system infections after cranial surgery in China: Incidence, causative agents, and risk factors in 1,470 patients. Eur J Clin Microbiol Infect Dis 2014;33:861-6.
20. Tängdén T, Enblad P, Ullberg M, Sjölin J. Neurosurgical gram-negative bacillary ventriculitis and meningitis: A retrospective study evaluating the efficacy of intraventricular gentamicin therapy in 31 consecutive cases. Clin Infect Dis 2011;52:1310-6.
21. Wang KW, Chang WN, Huang CR, Tsai NW, Tsui HW, Wang HC, *et al.* Post-neurosurgical nosocomial bacterial meningitis in adults: Microbiology, clinical features, and outcomes. J Clin Neurosci 2005;12:647-50.
22. Erman T, Demirhindi H, Göçer AI, Tuna M, Ildan F, Boyar B, *et al.* Risk factors for surgical site infections in neurosurgery patients with antibiotic prophylaxis. Surg Neurol 2005;63:107-12.
23. Sipahi OR. Economics of antibiotic resistance. Expert Rev Anti Infect Ther 2008;6:523-39.
24. Rolston KV, Nesher L, Tarrand JT. Current microbiology of surgical site infections in patients with cancer: A retrospective review. Infect Dis Ther 2014;3:245-56.
25. Talbot GH, Bradley J, Edwards JE Jr., Gilbert D, Scheld M, Bartlett JG, *et al.* Bad bugs need drugs: An update on the development pipeline from the Antimicrobial Availability Task Force of the Infectious Diseases Society of America. Clin Infect Dis 2006;42:657-68.
26. Shrestha S, Tada T, Miyoshi-Akiyama T, Ohara H, Shimada K, Satou K, *et al.* Molecular epidemiology of multidrug-resistant acinetobacter baumannii isolates in a university hospital in Nepal reveals the emergence of a novel epidemic clonal lineage. Int J Antimicrob Agents 2015;46:526-31.
27. Stienen MN, Moser N, Krauss P, Regli L, Sarnthein J. Incidence, depth, and severity of surgical site infections after neurosurgical interventions. Acta Neurochir (Wien) 2019;161:17-24.
28. Vengamma B, Rajguru M, Prasad BC, Ramesh Chandra V. Central nervous system infections in the intensive care unit. J Clin Sci Res 2014;3:106.