Brain Abscess in the Current Decade (2010–2019) in India—A Review

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Abstract

Brain abscess outcomes have improved in recent years due to advancements in cranial imaging, microbiological techniques, minimally invasive neurosurgical procedures, and effective antibiotic treatments. However, the incidence of brain abscess remains unchanged in developing countries. We searched PubMed and Google Scholar for references using the key words "brain abscess" and "India" and reviewed both retrospective and prospective studies published in peer-reviewed journals in the current decade to understand the present status. The review shows that the patients' ages, the predominance of male patients, the symptoms and locations of brain abscesses, and the types of bacteria associated with them have remained unchanged over the past decade. The most common predisposing condition in recent years has been chronic suppurative otitis media with a mortality rate of 7 to 10%. Middle ear infection is often neglected and not treated aggressively in Asian countries. It requires multidisciplinary treatment strategies to address the primary source of infection and better health awareness to prevent the development of brain abscess.

Keywords
- brain abscess
- chronic suppurative otitis media (CSOM)
- prevention

Introduction

Brain abscess is a focal collection of pus in the brain parenchyma surrounded by a well-vascularized collagenous capsule.[1] It is life-threatening condition with long-term neurological sequelae in 9 to 36% of patients.[2] With the advancements in imaging and microbiological techniques, neurosurgical procedures, and effective antibiotic treatments, brain abscess mortality has decreased in recent years.[3] However, the incidence of brain abscess remains unchanged in developing countries, particularly among populations of lower socioeconomic status due to chronic suppurative otitis media (CSOM) and immunosuppression.[4,5] We searched PubMed and Google Scholar for references using the key words "brain abscess" and "India" and reviewed both retrospective and prospective studies published in peer-reviewed journals in this decade to understand the current status. There were eight brain abscess (►**Table 1**) and six otogenic brain abscess (►**Table 2**) journal articles. The number of years of study from various institutions in ►**Table 1** ranges from 1.5 to 28 years and the number of patients in these studies ranges from 8 to 89 per year with an average of 24 brain abscess cases per year. Lakshmi et al reported the average number of brain abscess specimens received for microbiological analysis was 21 per year.[6]

Common Symptoms

As shown in ►**Table 1**, the majority of brain abscess patients in India was males, which is in line with findings of studies across the globe.[20-22] The average age of the patients was 20 to 30 years, which is similar or a decade lower compared with

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Table 1 Publications on brain abscess in India in the current decade (2010–2019)

Reference and place of study	Duration and (y)	No. of patients	Age range (average)	Gender (%)		No. of culture positive (%) and organisms	Predisposing factors (%)	Location (%)	No. of died patients (%)
				Male	Fe-male				
Tomar et al, 2011[7] Chhatrapati Sahuji Maharaj Medical University, Lucknow, Uttar Pradesh	Aug 2009–Dec 2010 (1.5)	30	9–47 (25)	24 (69)	11 (31)	22 (73). Pyogenic: 18 (82) *Streptococci*: 10 (33) *Staphylococci*: 1 (3) *Bacteroides sp.*: 2 (6) Nocardia: 1(3); Fungal:1 (3) Mycobacteria: 3 (10) Mixed infection 4: (13)	CSOM: 15 (50) CHD: 3 (10) Postoperative/traumatic: 2(6) Pulmonary tuberculosis: 2 (6)	Temporal: 10 (33) Cerebellar: 9 (30) Frontal: 3 (10) Parietal: 4 (13) Temporoparietal: 4 (13)	
Lakshmi et al, 2011[6] Nizam's Institute of Medical Sciences, Hyderabad, Telangana	1987–2010 (24)	352	2–80 (28)			247 (70); Pyogenic: 232 (94) *Staphylococcus aureus:* 68 (28) *Streptococcus*: 35(14) *Enterococcus*: 34 (14) GNB:62(25) parasitic 2(0.5) Anaerobes: 39 (16) Mixed infections: 30 (12) Fungal: 5 (1) Nocardia: 3(0.8) Mycobacteria: 9 (5)	CSOM: 135 (38) CHD: 32 (9) Post-traumatic/operative: 42(12) Pulmonary: 9 (3) Sepsis: 33 (9) Sinusitis: 8 (2)	Temporal: 81 (23) Cerebellar: 26 (7) Frontal: 81 (23) Parietal: 102 (29) Occipital: 12 (3) Others: 11 (3) Multiple: 39 (11)	
Muzumdar et al, 2011[8] Seth GS Medical College & King Edward Memorial Hospital, Mumbai, Maharashtra	1999–2006 (7)	289	1.5–62 (32)	204 (71)	86 (29)	76 (26) *Streptococcus*:19 (25) *Staphylococcus*: 18 (24) *Klebsiella*: 17 (22) *Prevotella aeruginosa:*16(21)	CSOM: 120 (42) Pulmonary/CHD: 17 (6) Post-traumatic/operative: 12 (4) Sinusitis: 15 (5)	Temporal: 111 (38) Cerebellar: 74 (25) Frontal: 61 (21) Parietal: 19 (7) Occipital: 7 (2) Multiple: 17 (6)	8 (3)
Sarmast et al., 2012[9] Sher I Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir (SKIMS)	Oct 2001–2011 (10)	114	0.5–70 (31)	83 (73)	31 (27)	93 (82) *S. pneumoniae:* 22(24) *Staphylococcus:*29(31) *Streptococcus*: 16(17) *P. aeruginosa:*11(12) Enterobacter 4: (4) *Klebsiella pneumoniae*: 3 (3) *Haemophilus influenzae:* 6 (6) *Bacteroides fragilis:* 1 (1) Peptostreptococcus: 1 (1) Mixed infection: 4 (3)	CSOM: 57 (50) CHD: 4 (4) Post-traumatic/operative: 21(18) Pulmonary: 8 (7) Sinusitis: 6 (5) Adjacent local infection: 3(2)	Temporal: 33 (29) Cerebellar: 16(14) Frontal: 17 (15) Parietal: 12 (10) Occipital: 6 (5) Temporoparietal: 28(24) Parieto-occipital: 9 (7)	8 (7)

(*Continued*)

Table 1 (*Continued*)

Reference and place of study	Duration and (y)	No. of patients	Age range (average)	Gender (%)		No. of culture positive (%) and organisms	Predisposing factors (%)	Location (%)	No. of died patients (%)
				Male	Fe-male				
Bajpai et al, 2014[10] Sanjay Gandhi Post Graduate Institute of Medical Sciences& King George Medical University Lucknow, Uttar Pradesh		90	(24)	67 (74)	23 (26)	64 (71) *S. aureus:*13 (20) *S. intermedius:*8 (12) *Enterococcus sp.:*4 (7) *Escherichia coli:*7 (11) *P. aeruginosa:* 4 (7) *P. mirabilis:*2 (3) *B. fragilis:*8 (12) *Fusobacterium sp.:* 6 (10) *Peptostreptococcus sp.:*5 (9) Mixed infection: 7(8)	CSOM: 34 (49) CHD: 3 (4) Head trauma: 8(11) Dental infection: 5(7) Sinusitis: 6(6) Pulmonary tuberculosis: 4 (5) HIV: 2 (2) Diabetes: 1(1)	Temporal: 11 (12) Cerebellar: 12 (13) Frontal: 23 (25) Parietal: 21 (23) Occipital: 3(3) Temporoparietal: 6 (6) Frontoparietal: 5 (5) Temporo-occipital: 1 (1)	
Kothari et al, 2015[11] King Edward Memorial Hospital & Seth Gordhandas Sunderdas Medical College, Mumbai, Maharashtra	1998–2006 (8)	715				Tuberculosis: 426 (60) Pyogenic: 280 (39) Fungal: 9 (1)	CSOM: 189 (67) CHD: 50 (18) Post-traumatic: 14 (5) Miscellaneous: 27(10)	Temporal: 111(39) Cerebellar: 72 (26) Frontal: 54(19) Parietal: 19 (7) Occipital: 7 (2) Multiple: 17 (6)	39 (5)
Naik et al 2015[12] Osmania Hospital, Hyderabad, Telangana	June 2009–2012 (3)	24	2–70	20 83	4 17	11 (46) *Staphylococcus*: 4 (17) *Streptococcus*: 3 (13) *Klebsiella*: 2 (9) Mixed infection: 2 (9)	CSOM:10 (42) CHD: 5 (20) Post-traumatic/ operative: 5 (20)	Temporal: 3 (13) Cerebellar: 7(29) Parietal: 6 (25) Frontal: 3(13) Occipital: 1 (4) Temporoparietal: 2 (8) Multiple: 2 (8)	
Sudhaharan et al, 2016[13] Nizam's Institute of Medical Sciences, Hyderabad, Telangana	1987–2014 (28)	430		35 (73)	13 (27)	116:(27); anaerobes: 48 (41) Peptostreptococcus: 26(54) Bacteroides: 18 (37) Peptococcus: 5 (10) *Veillonella*: 3 (6) *P. melaninogenicus*: 1(2) Mixed 14: (3)	CSOM: 36(75) CHD: 5 (10) Trauma: 4 (8) Pulmonary:1 (2)	Temporal: 13(27) Cerebellar: 10(21) Frontal: 12 (25) Parietal: 4 (8) Occipital: 2(4) Frontoparietal: 6 (12)	1 (2)

Abbreviations: CSOM, chronic suppurative otitis media; CHD, congenital heart disease; GNB, gram negative bacteria; No., number.

Table 2 Publications on otogenic brain abscess in India in the current decade (2010–2019)

Reference and place of study	Duration (y)	No. of patients/samples	Age range in years (average)	Gender (%)		Symptoms and predisposing factors	No. of culture positive and isolated organisms (%)	Location (%)		No. of died patients (%)
				Male	Female			Temporal	Cerebellar	
Borade et al, 2011[14] Dr. Vaishampayan Memorial Govt. Medical College, Solapur, Maharashtra	Jan 1997–Dec 2010 (4)	72	6–54 (16 y)	40 (55)	32 (45)	Cholesteatoma: 62 (86) Granulations: 10 (14)	(20) *Escherichia coli, Pseudomonas Proteus spp. Staphylococcus Streptococcus*	12(17)	60 (83)	5 (7)
Suligavi et al, 2015[15] SN Medical College, Agra, Uttar Pradesh	2008–2013 (6)	8	8–51 (21 y)	5 (63)	3 (37)	Headache: (100) Vomiting: (63) Seizures: (38)	*Pseudomonas sp.*: 1 *Bacteroides fragilis*:1	6 (75)	2 (25)	0
Borgohain et al, 2015[16] Gauhati Medical College & Hospital, Guwahati, Assam	July 2013–Dec 2014 (1.5)	17	5–20 (14 y)	12 (75)	4 (25)	Headache, nausea, and vomiting: (100)	12 (71) *Klebsiella*: 5 (38) *Pseudomonas*: 7 (54)	1 (6)	16 (94)	NA
Bhattacharjee et al, 2016.[17] Silchar Medical College, Silchar, Assam	Sept 2014–2015 (1)	33	9–65 (21 y)	18 (54)	15 (46)	Headache: (90) Fever: 25 (76) Seizures: 55 Cholesteatoma: (76)	*Proteus mirabilis and Enterococcus*: 17 (52) *P. aeruginosa:* 16 (48)	25 (76)	8 (24)	0
Mukherjee et al, 2016[18] KPC Medical College & Hospital, Kolkata, West Bengal	May 2009–April 2014 (5)	22	8–58 (26 y)	17 (77)	5 (23)	Headache: (100) Fever: 13 (59) Altered sensorium: 9 (41)	NA	7 (32)	15 (68)	0
Melkundi and Melkundi, 2017[19] MR Medical College and Gulbarga Institute of Medical Sciences, Gulbarga, Karnataka	2006–2015 (10)	20	4–32 (18 y)	16 (80)	4 (20)	NA	NA	6 (30) T-P 5 (25)	8 (40)	2 (10)

Abbreviations: NA, not available; No., number; T-P, temporoparietal.

studies in other countries.[2,5,23] Headache was found to be the most common symptom. Other symptoms include fever, focal neurologic deficit, seizure, nausea, and vomiting.[8-11] Studies in other countries have reported similar symptoms.[24] The classic triad of fever, headache, and focal neurologic deficit was observed in half of the patients, and the mean duration of the symptoms before diagnosis was approximately 8 days.[25-27]

Neuropathology

Brain abscess begin as localized areas of cerebritis in the brain parenchyma in response to an infection. The computed tomography (CT) or magnetic resonance imaging (MRI) studies show that the brain abscess development can be divided into four stages: early cerebritis (Days 1–3), late cerebritis (Days 4–9), early capsule formation (Days 10–13), and late capsule formation (after Day 14). A well-developed abscess consists of five distinct histological zones: a necrotic center, a peripheral zone of inflammatory cells, a dense collagenous capsule, a layer of neovascularization, and cerebral edema external to the capsule.[27]

More than 90% of the brain abscesses reported in ►**Tables 1** and **2** were single and were located in the frontal and temporal lobes and the cerebellum, and occasionally in the parietal and occipital lobes. The most common predisposing condition was middle ear infection (8–75%), as shown in ►**Table 1**. Other common predisposing conditions were congenital heart disease (CHD; 4–20%), post-traumatic, and neurosurgical procedures (4–20%). Other studies have reported CSOM as the main predisposing factor, followed by post-traumatic and CHD.[5,24,28] Middle ear infections are associated with abscess formation in the temporal or cerebellar lobes (►**Table 2**). In addition, intraventricular rupture of brain abscess has been reported, resulting in acute deterioration and death.[29,30] Other factors that contribute to intracranial complications are the virulence of organisms and the host's immunity status.[15] Whole genome sequencing of *Streptococcus intermedius* TYG1620 isolated from a human brain abscess showed the presence of the type VII secretion system, which might be associated with strain-specific pathogenicity, including abscess formation.[31] The host inflammatory response, which increases with bacterial cell lysis following the administration of antibiotics, can cause damage to the surrounding normal brain parenchyma, which exceeds the brain area occupied by the infecting organism.[32] It has been shown that several inflammatory cytokine (tumor necrosis factor-α [TNF-α], interferon-γ, interleukin-1β [IL-1β], IL-10, IL-17, IL-23) levels are significantly higher in a brain abscess than in blood, and their expression in the abscess is influenced by the bacterial pathogen and the duration of symptoms.[10]

Etiology

This review found that 26 to 82% of the brain abscess samples were culture-positive (►**Table 1**). The most frequently identified bacteria were *Streptococci* (12–42%), *Staphylococci* (3–31%), *Enterococci* (7–14%), and gram-negative bacteria (9–23%), including *Escherichia coli*, *Klebsiella*, *Enterobacter*, *Citrobacter*, *Proteus*, and *Pseudomonas*. Anaerobic bacteria (2–41%) such as *Peptostreptococcus*, *Bacteroides*, *Peptococcus*, *Fusobacterium*, and *Veillonella* were also isolated in some studies. Nocardia and fungi were seen in 1 to 3% of samples. *Mycobacterium tuberculosis* was isolated from 5% (9 cases) and 10% (3 cases) of brain abscess samples in two studies.[6,7] Only one study showed 60% tubercular abscess outnumbering pyogenic abscesses probably due to endemicity of tuberculosis in India.[11] Mixed infections were observed in 3 to 13% of samples. A retrospective analysis of 317 brain abscess samples collected over a 3-year period (January 2012 to December 2014) at the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, found rare pathogens in 19 samples (12%), including *Cryptococcus neoformans*, *Aspergillus flavus*, *Mucor*, *Salmonella*, and *Pantoea*.[33] Molecular characterization of methicillin-resistant *S. aureus* (MRSA) showed community-acquired (CA-MRSA), hospital-acquired (HA-MRSA), and livestock-associated (LA-MRSA) strains in brain abscess samples.[34] CSOM was mostly caused by gram-negative bacteria, including *E. coli*, *Klebsiella*, *Pseudomonas*, and *Proteus* (►**Table 2**). The distribution of bacterial pathogens identified in brain abscesses has been shown to be relatively similar in different continents and to have remained stable over the past 60 years.[2]

Diagnosis

Imaging techniques such as cranial CT and MRI were used in most studies to confirm the clinical diagnosis and for follow ups. In some cases, imaging techniques enabled safe and successful medical treatment without surgical intervention.[8,9] MRI, when combined with diffusion-weighted images (DWI) and apparent diffusion coefficients (ADC) images, differentiates pyogenic brain abscess from non-pyogenic abscesses, neoplasm, cystic, or necrotic tumors.[7,8] Magnetic resonance spectroscopy (MRS) analysis differentiated between brain abscesses and tumors, as well as between anaerobes and aerobes.[35]

Comprehensive microbiological investigations of brain abscesses were conducted in most studies, including wet mounts, Gram's staining, Ziehl–Neelsen staining, and conventional aerobic and anaerobic cultures. BACTEC aerobic and anaerobic media were used in some studies to isolate bacterial pathogens.[7,10] In other studies, anaerobic incubation was performed in jars using commercial GasPak systems.[6,13]The isolates were identified by standard biochemical tests. Smears and cultures were also performed for mycobacteria, nocardia, and fungi when requested. This review shows that the incidence of negative cultures was 18 to 73% (►**Tables 1** and **2**), which is similar to other reports.[21,36] Polymerase chain reaction(PCR) was not performed routinely, but PCR amplification and sequencing of 16S ribosomal RNA (rRNA) in one study showed the presence of bacterial DNA in 37% of the culture-negative samples.[35] Other reports demonstrated the usefulness of 16S rRNA PCR sequencing in bacterial identification in culture-negative samples and samples containing fastidious bacteria.[37,38] Multiple sequencing by metagenomics

increases the number of identified bacteria in brain abscess samples, and next-generation sequencing (NGS) identifies infectious agents with higher confidence where microbiology fails to detect the presence of microbes.[39,40]

Management

Patients were managed with combined medical (e.g., antibiotic, steroid, and anticonvulsant) and surgical (aspiration and excision) treatments and monitored with weekly CT or MRI scans until the abscess completely disappeared. Empirical intravenous broad-spectrum antibiotic treatments were immediately initiated upon diagnosis and were further modified according to microbiological isolation and antibiotic sensitivity. Antibiotics that are active against both aerobes and anaerobes such as a third-generation cephalosporin, metronidazole and vancomycin to cover streptococci, staphylococci, strict anaerobes, and Enterobacteriaceae were used. Aminoglycosides were used for *Pseudomonas* infection. Long-term therapy with cotrimoxazole or sulfadiazine was used for nocardia abscesses and antituberculosis drugs were used for treating tuberculous abscesses. Flucytosine, amphotericin B, and voriconazole were used for fungal infections.[8] Antibiotic therapy was continued for 6 weeks or longer, depending on the therapeutic response and the neuroimaging findings.[8,9,11] Abscesses in the cerebritis stage measuring less than 2 cm in diameter and multiple deep-seated abscesses were treated with medical regimens alone.[9] Surgery was performed for large abscesses and in patients with a poor response to medical treatment. Most patients underwent abscess aspiration through a single burrhole.[11] If the size of the abscess shown in CT or MR images after the first aspiration increased or was not reduced despite antibiotic therapy, the aspiration was repeated. Patients with a poor response to repeated aspirations and post-traumatic abscesses underwent complete abscess excision through craniotomy.[1,8] Stereotactic aspiration is associated with few complications compared with excision that involves hemorrhage, cerebrospinal fluid (CSF) leakage, seizure, and stroke.[41] When the efficacies of aspiration and excision were compared for the management of pyogenic brain abscesses, excision was found to be better with respect to duration of antibiotic use, length of hospital stay, and overall cost of treatment.[42] However, excision is said to have a poor outcome when the abscess is deep-seated and in the cerebritis stage.[41] In CSOM cases, patients underwent craniotomy for abscess removal followed by radical mastoidectomy under single anesthesia in the same session or mastoidectomy was done after the patient's general and neurological conditions were stabilized.[17,19] High-dose corticosteroid treatment was administered to patients with life-threatening cerebral edema or cerebral herniation and tapered over a period of 4 weeks.[8] Anticonvulsants were administered as prophylactics, and the duration of therapy was individualized and guided by electroencephalographic (EEG) reports.[9,11] The mortality rate in brain abscess patients was 2 to 7%, and up to 10% in patients with middle ear infection (►**Tables 1** and **2**).

Prevention

Eradication of potential sources of infection before the abscess fully develops is a reasonable preventive strategy. Middle ear infection, which is often neglected and not treated aggressively, remains the most frequent predisposing condition in India (►**Tables 1** and **2**) and other Asian countries.[43-46] Multidisciplinary treatment strategies to address the primary source have helped to improve outcomes in otogenic brain abscesses.[19] Congenital cyanotic heart disease (CCHD) in the majority of children in Asia remains either uncorrected or only partially palliated. Uncured CCHD is a high-risk factor for the occurrence, persistence, and recurrence of a brain abscess.[47,48] Prompt diagnosis of CCHD and corrective surgery might help to reduce the development of brain abscesses in children.[49] Head trauma has become an important predisposing factor with the increasing incidence of traffic accidents, which requires safety measures.[23] Tooth extraction and treatment for sinusitis may also help to remove the focus of infection and prevent further spread of bacteria.[50] The duration of hospitalization increases the risk of nosocomial infections concomitant with higher mortality.[36] Infection control strategies in intensive care units (ICUs) may help to improve brain abscess outcomes.[20] Health awareness in terms of ear and oral hygiene may help to reduce the overall incidence of brain abscess.[51,52]

Conclusion

The incidence of brain abscess continues to be high in India due to CSOM, particularly among socioeconomically vulnerable populations with poor health consciousness (►**Tables 1** and **2**). New developments include hyperbaric oxygen therapy, which improves brain abscess outcomes.[53] Gene therapy is another prospect, as there is an association between single nucleotide polymorphisms in TNF-α, IL-1β, Intercellular Adhesion Molecule 1 (ICAM-1), and monocyte chemoattractant protein-1 (MCP-1) genes and increased risk of brain abscess development.[54,55] Identifying pathogens associated with brain abscess using NGS might contribute to early detection and appropriate treatment.

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Conflict of Interest

None declared.

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