Journal of Infection 90 (2025) 106394

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Infectious Disease Practice

Clinical features and outcome of brain abscess after introduction of CT and MRI: A meta-analysis

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A R T I C L E I N F O

Article history:
Accepted 22 December 2024
Available online 27 December 2024

Keywords:
Brain abscess
Cerebral abscess
Clinical features
Outcome
Prognosis
Meta-analysis
Systematic review

S U M M A R Y

Objective: To describe the clinical features and outcome of brain abscess since introduction of computerised tomography and magnetic resonance imaging.
Methods: MEDLINE and Embase were searched using "brain abscess" or "cerebral abscess" from 1970 through 2023 and analyses restricted to study populations hospitalised after 1980. Single-variable meta-analyses were done using a random-effects model.
Results: A total of 21,840 patients from 209 studies were included. The mean age was 34 years (95% confidence interval [CI] 30–38) and 11,817/17,406 (66%, 95% CI 64–67) were male. The aetiologies were consistent across time and continents with *Streptococcus spp.* 2064/6393 (32%, 95% CI 28–36), *Staphylococcus* spp. 1061/6393 (14%, 95% CI 12–16), and Gram-negative enteric bacteria 696/6393 (9%, 95% CI 7–11) as the most common. Predisposing conditions included otitis media/mastoiditis 1909/6433 (27%, 95% CI 22–33), immunocompromise 1022/4652 (19%, 95% CI 14–24), sinusitis 565/3725 (16%, 95% CI 12–20), and neurosurgery 745/4927 (16%, 95% CI 12–20). The case-fatality was 2444/18,991 (12%, 95% CI 11–14) and good recovery was found in 3419/5409 (63%, 95% CI 58–68).
Conclusions and relevance: Brain abscess remains a disease predominantly occurring in men and is caused by contiguous or distant infections. Case fatality and outcome have not improved during recent decades.

Introduction

Brain abscess is defined as a collection of pus surrounded by a collagenous capsule within the brain parenchyma.[1,2] It is most often caused by bacteria, but opportunistic pathogens like fungi and parasites are also important in some settings and in severely immune-compromised patients.[3,4] Recent population-based data suggest that the incidence has increased from 0.4 to 0.9–1.3 per 100,000 person-years during the last decades.[5,6] This may be partly attributable to improved detection by increased availability of computed tomography (CT) since the 1970s and magnetic resonance imaging (MRI) since the 1980s. Moreover, demographic shifts have occurred with more elderly individuals at risk as well as an expanding arsenal of immune-modulating treatments rendering patients more susceptible to severe infections including brain abscess.[5,7] Significant advances in the management of brain abscess have also been made with stereotactic neurosurgery and newer antimicrobial drugs with improved bioavailability and penetration into the central nervous system.[1]

All these factors combined may be associated with changes in the clinical characteristics and prognosis of patients with brain abscess. A previous systematic review and meta-analysis of published studies on brain abscess included study populations from 1935 until 2012, including studies performed before antimicrobials and brain imaging were available in clinical care.[8] This study provides an updated systematic review and meta-analysis of the clinical features and outcome of patients with brain abscess after the introduction of modern brain imaging and treatment.

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https://doi.org/10.1016/j.jinf.2024.106394

Methods

Study identification and inclusion

The database of a previous systematic review and meta-analysis of studies on brain abscess from 1970 until 2013 was accessed and updated with studies published since then.[8] In brief, the MEDLINE and Embase databases were searched for all studies on brain abscess from January 1, 2013 until December 13, 2023, using "brain abscess" or "cerebral abscess" as Medical Subject Heading (MeSH) terms or text. Studies were screened by title and abstract by the last author (JB) using Rayyan software.[9] Reference lists of included studies were manually reviewed for additional relevant publications. Studies were excluded if they reported on < 10 individuals or if intracranial empyema comprised > 50% of the study population unless data could be extracted specifically for patients with brain abscess. Other exclusion criteria were duplicate study populations and reports of brain abscess due to a single specific pathogen. The updated search excluded non-English language publications. After merging of the two databases, studies were excluded if the study populations comprised patients hospitalised before 1980 as an indicator for the availability of CT at most hospitals. Studies without a specified observation period (n=12) were omitted if published before year 2000 (n=3).

Data collection

Studies identified by the updated search were divided evenly between authors (EME, MDN, TM, LSD) and data was extracted independently by each co-author in accordance with the pre-defined template used in the previous meta-analysis (Excel spreadsheet, variables available in supplementary Table 1).[8] This included information on study design, inclusion criteria, baseline demographics, predisposing conditions, symptoms and signs of brain abscess at admission, neuroanatomic distribution of brain abscesses, causative pathogens, treatment, and outcome as reported in each study. Study variables were also expanded to include duration of antibiotic treatment, use of oral consolidation therapy, and risks of rupture, hydrocephalus, epilepsy, and recurrence or relapse whenever available in both the original and updated systematic review. Data were checked for consistency and outliers by one co-author (EME) and discussed with the senior author (JB) in cases of doubt. Authors of published studies were not contacted for additional information.

Since this was a systematic review and meta-analyses of descriptive studies on brain abscess, risk of bias assessment was restricted to general epidemiological features of external validity (single-centre or multi-centre, and retrospective or prospective study designs). Correspondingly, tests of heterogeneity were not carried out.

Statistical analyses

The accuracy and detail of the studies varied considerably. Thus, the results of the meta-analysis are presented as number of reported observations of a given characteristic out of the total number of cases specifically assessed for this parameter. For data on mean duration of symptoms of brain abscess, three studies were censored *post-hoc* due to perceived unrealistic reports of duration > 1 year.[10–12] Data on adults and children were combined in most studies and are reported as such in the current meta-analysis unless specifically described as paediatric studies.

Meta-analyses were done using a random-effects model and data are presented as proportions or means with 95% confidence intervals (95% CI) as appropriate. For meta-analyses of proportions, the Freeman-Tukey double-arcsine transformation was applied with back-transformation using the inverse of the variance of the overall effect sizes.[13,14] Due to unclear reporting at the patient level in many studies, analyses of aetiology were carried out using the total number of identified pathogens as the denominator. Analyses of the neuroanatomic distribution was restricted studies reporting more than one brain abscess localisation. Moreover, the number of frontal abscesses (n=23) was re-categorised to align with the total number of patients (n=20) in one study to allow convergence of the model.[15]

Stata MP 18.0 (StataCorp, College Station, TX, USA) was used for all statistical analyses.

Standard protocol approvals, registrations, and patient consents

This was a systematic review and meta-analysis of already published studies, and approvals or consent was not required. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) standards for reporting were followed whenever appropriate for this meta-analysis of single proportions or continuous variables. The study protocol was based on the previously published systematic review and meta-analysis and was not registered at PROSPERO.[8]

Data availability statement

The data can be shared with qualified researchers upon request.

Results

This systematic review and meta-analysis included 209 studies with a total of 21,840 patients hospitalised between 1980 and 2022 (Supplementary Figure 1). Of these studies, 40/209 (19%) were restricted to children and 29/209 (14%) to patients treated with aspiration or excision for their brain abscess. The median observation period of each study was 10 years (IQR 6–14, range 1–38), and the median number of included patients was 44 (IQR 24–82; range 10–6027). The study designs comprised exclusively observational cohorts of which 186/202 (92%) were retrospective and 16/202 (8%) were prospective. The patients were from single centres in 188/209 (90%) and several centres in 21/209 (10%) of studies. The geographic location of the study populations was from Asia in 118/209 (56%), Europe in 57/212 (27%), North America in 16/209 (8%), Africa in 11/209 (5%), South America in 3/209 (1%), Australia in 3/209 (1%), and from multiple continents in 1/209 (0.5%).

Aetiology

Results of bacterial cultures of brain abscess material were available for 7342/21,840 (34%) patients and were positive in 4946/7342 (71%, 95% CI 66–76) yielding a total of 6393 pathogens (Table 1, Supplementary Table 2). Polymicrobial brain abscess was detected in 1265/4243 (22%, 95% CI 18–27) of reported patients.

Using the total number of identified pathogens as the denominator, the most frequent aetiology was *Streptococcus* species totalling 2064/6393 (32%, 95% CI 28–36), most commonly the viridans group in 977/6393 (13%, 95% CI 10–17). *Staphylococcus* spp. was identified in 1061/6393 (14%, 95% CI 12–16) of pathogens among which *S. aureus* was the most frequent 779/6393 (10%, 95% CI 8–12). Gram-negative enteric bacteria were the third most common group of pathogens and comprised 696/6393 (9%, 95% CI 7–11). Other pathogens included actinomycetales in 341/6393 (5%, 95% CI 4–6), fungi in 165/6393 (3%, 95% CI 2–4), and *Pseudomonas aeroginosa* in 147/6393 (2%, 95% CI 2–3). Comparable distributions of pathogens were observed when restricting the analyses to studies reporting specifically on children, except that Gram-negative enteric bacteria were more frequent in this age group (17% vs. 9%). Of note, neonatal brain abscess may occur following meningitis due to *Proteus mirabilis* and *Escherichia coli*.[16–18]

Table 1
Culture results and major groups of causative microorganisms.[a]

	All patients		Children		Studies restricted to neurosurgically treated patients	
Brain abscess culture results	**n/N (115 studies)**	**% (95% CI)**	**n/N (20 studies)**	**% (95% CI)**	**n/N (23 studies)**	**% (95% CI)**
Positive culture, overall	4946/7342	71 (66–76)	699/1057	65 (56–73)	783/1199	68 (55–79)
Monomicrobial versus polymicrobial	**n/N (82 studies)**	**% (95% CI)**	**n/N (6 studies)**	**% (95% CI)**	**n/N (19 studies)**	**% (95% CI)**
Monomicrobial	2983/4243	78 (73–82)	160/211	79 (67–89)	520/637	83 (78–88)
Polymicrobial	1265/4243	22 (18–27)	51/211	21 (11–33)	117/632	17 (12–22)
Cultured microorganisms	**n, N=6393 (124 studies)**	**% (95% CI)**	**n, N=641 (21 studies)**	**% (95% CI)**	**n, N=1055 (24 studies)**	**% (95% CI)**
Streptococcus spp	2064	32 (28–36)	232	35 (26–43)	400	39 (30–49)
Viridans streptococci	977	13 (10–17)	88	14 (8–22)	200	15 (8–24)
S. pneumoniae	128	2 (1–3)	25	4 (2–6)	17	2 (1–3)
Enterococci	86	1 (1–2)	11	2 (1–4)	17	-[b]
Other/not specified	829	9 (7–12)	93	6 (2–12)	154	14 (7–22)
Staphylococcus spp	1061	14 (12–16)	112	19 (13–26)	149	11 (7–16)
S. aureus	779	10 (8–12)	79	12 (7–18)	133	8 (5–13)
S. epidermidis	118	1 (1–2)	8	2 (1–3)	3	1 (0.3–1)
Other/not specified	164	2 (2–3)	25	4 (2–7)	13	1 (0.4–3)
Gram-negative enteric	696	9 (7–11)	103	17 (12–23)	100	6 (3–10)
Proteus spp	219	3 (2–3)	35	5 (3–9)	14	1 (1–2)
K. pneumoniae	147	2 (2–3)	15	-[b]	34	2 (1–4)
E. coli	136	2 (2–3)	26	5 (2–7)	26	2 (1–3)
Enterobacteriae	106	1 (1–2)	13	2 (1–3)	14	1 (1–2)
P. aeroginosa	147	2 (2–3)	17	3 (1–5)	27	3 (2–4)
Actinomycetales	341	5 (4–6)	13	2 (1–4)	40	4 (2–6)
Nocardia spp.	106	2 (1–2)	1	1 (0.2–2)	13	1 (1–3)
Actinomyces spp.	139	2 (1–2)	1	1 (0.2–2)	8	1 (0.5–2)
M. tuberculosis	66	1 (1–2)	7	1 (0.6–2)	9	1 (0.4–2)
Haemophilus spp	95	2 (1–2)	17	-[b]	20	2 (1–3)
Peptostreptococcus spp	155	2 (2–3)	24	3 (2–6)	26	2 (1–5)
Bacteroides spp	190	3 (2–3)	14	2 (1–4)	25	2 (1–4)
Fusobacterium spp	182	3 (2–3)	17	3 (2–4)	42	4 (2–6)
Parasites	42	1 (0.6–1)	1	1 (0.2–1)	6	1 (0.5–2)
Fungi	165	3 (2–4)	25	4 (2–6)	24	3 (1–5)
Other	975	12 (10–15)	61	8 (5–11)	174	16 (9–24)

[a] List of all pathogen species is given in table e-1.
[b] Convergence of the model could not be achieved (tau2 estimation).

The aetiology of brain abscess remained unchanged during the study period and across continents except for Africa and the Americas (North and South), where *S. aureus* was as common as *Streptococcus* spp. (Fig. 1).

Clinical characteristics

The mean age of patients with brain abscess was 34 years (95% CI 30–38) and 11,817/17,406 (66%, 95% CI 64–67) were male. Predisposing conditions comprised otitis media or mastoiditis in 1909/6433 (27%, 95% CI 22–33), immuno-compromise in 1022/4652 (19%, 95% CI 14–24), sinusitis in 565/3725 (16%, 95% CI 12–20), postoperative after neurosurgery in 745/4927 (16%, 95% CI 12–20), head trauma in 1517/12,083 (11%, 95% CI 9–13), congenital cyanotic heart disease or endocarditis in 946/8073 (18%, 95% CI 13–23), other hematogenous seeding in 914/8450 (14%, 95% CI 10–17), odontogenic in 598/6069 (11%, 95% CI 9–14), meningitis in 803/9904 (11%, 95% CI 8–15), pulmonary disease in 716/10,281 (10%, 95% CI 7–12), and were unknown in 1335/5902 (24%, 95% CI 19–29).

Regarding symptoms and findings at admission, headache was reported in 3989/5893 (64%, 95% CI 59–69), fever in 3142/5907 (53%, 95% CI 48–58), and neurological deficits in 2466/5284 (42%, 95% CI 37–48). The mean duration of symptoms was 14 days (95% CI 10–19). Blood leucocytosis was observed in 905/1646 (57%, 95% CI 48–65) and 494/880 (62%, 95% CI 54–70) had an elevated C-reactive protein. Blood cultures were positive in 250/1117 (25%, 95% CI 17–34). Analyses of cerebrospinal fluid (CSF) obtained by lumbar puncture were reported for 507 individuals among whom an elevated leukocyte count was observed in 355/446 (77%, 95% CI 64–87). CSF cultures were positive in 192/850 (23%, 95% CI 16–31). Clinical deterioration due to lumbar puncture was described in 70/372 (25%, 95% CI 0–67) of patients.

Brain abscess distribution on imaging was specified in 6627 patients (Table 3). The abscesses were located in the frontal lobe in 2213/6627 (32%, 95% CI 28–36), the temporal lobe in 1406/6627 (21%, 95% CI 19–24), the parietal lobe in 1557/6627 (20%, 95% CI 18–24), the occipital lobe in 570/6627 (8%, 95% CI 7–10), the cerebellum or brainstem in 689/6627 (9%, 95% CI 7–11), and the basal ganglia in 175/6627 (3%, 95% CI 2–4). The proportion of patients with a single brain abscess was 5266/6529 (80%, 95% CI 77–83) and 1263/6529 (20%, 95% CI 17–23) had multiple abscesses.

Treatment and outcome

Neurosurgical procedures for diagnosis and treatment of brain abscess were carried out in 10,780/13,040 (91%, 95% CI 89–93) of patients. Aspiration was used in 4468/5876 (76%, 95% CI 70–81) and excision in 1453/5133 (33%, 95% CI 26–39), whereas a combination of aspiration and excision was described in 126/1559 (9%, 95% CI 5–13) of patients. Reoperation was carried out in 1048/3861 (21%, 95% CI 17–26). Corticosteroids were reported to have been used in 1134/2341 (51%, 95% CI 40–63) of patients.

The overall reported case-fatality rate among patients with brain abscess was 2444/18,991 (12%, 95% CI 11–14) and declined from

Table 2
Clinical characteristics and laboratory examinations in patients with brain abscess.

Characteristics	n/N or mean	% (95% CI)	No. of studies
Age, mean (y)[a]	34	(30–38)	79
Sex, male	11,817/17,406	66 (64–67)	140
Predisposing conditions[b]			
Otitis/mastoiditis	1909/6433	27 (22–33)	98
Sinusitis	565/3725	16 (12–20)	74
Unspecified ENT infections	270/1280	30 (11–54)	13
Congenital heart disease or endocarditis	946/8073	18 (13–23)	96
Head trauma	1517/12,083	11 (9–13)	61
Hematogenous	914/8450	14 (10–17)	40
Pulmonary disease	716/10,281	10 (7–12)	54
Postoperative (neurosurgery)	745/4927	16 (12–20)	69
Odontogenic	598/6069	11 (9–14)	61
Immunocompromise[c]	1022/4652	19 (14–24)	52
Meningitis	803/9904	11 (8–15)	43
Other	319/2770	12 (8–16)	38
Unknown	1335/5902	24 (19–29)	71
Symptoms and signs			
Headache	3989/5893	64 (59–69)	76
Nausea/vomiting	1572/3634	45 (38–53)	54
Fever	3142/5907	53 (48–58)	81
Altered consciousness	1976/5578	36 (32–41)	76
Neurologic deficits	2466/5284	42 (37–48)	66
Seizures	1406/5673	25 (22–29)	75
Nuchal rigidity	871/2985	20 (14–25)	32
Papilledema	10/122	7 (0–26)	4
Mean duration of symptoms (d)[d]	14	(10–19)	12
Blood investigation			
Leucocytosis	905/1646	57 (48–65)	29
Elevated CRP	494/880	62 (54–70)	20
Elevated ESR	85/143	70 (15–100)	3
Positive blood culture	250/1117	25 (17–34)	21
CSF investigation			
LP	507/518	98 (96–100)	15
Normal CSF	77/359	22 (12–34)	10
Pleocytosis	355/446	77 (64–87)	12
Elevated CSF protein	72/106	69 (53–84)	6
Culture positive	192/850	23 (16–31)	28
Clinical deterioration attributed to LP	70/372	25 (0–67)	7

[a] Based on reported mean age and standard errors (sometimes after conversion from standard deviations) of 11,518 patients. If studies restricted to children were excluded, the mean age was 42 years (95% CI 40–45) based on 61 studies with 10,823 patients.
[b] Numbers do not add up to 100% because multiple predisposing conditions could be present in 1 patient.
[c] Immunocompromise as reported in each study and also included intravenous drug use and cancer.
[d] Based on reported mean symptom duration and standard errors (sometimes after conversion from standard deviations) of 1383 patients.

approximately 22% in studies from the 1980s to appr. 10% in study populations from year 2000 and onwards (Table 3, Fig. 2). Correspondingly, the proportion of patients reported to have good recovery was 3419/5409 (63%, 95% CI 58–68) without any major changes during the study period. Acute complications of brain abscess such as rupture was reported in 469/4502 (7%, 95% CI 5–10) and hydrocephalus in 522/3924 (11%, 95% CI 8–14). Longer-term complications included epilepsy in 338/2611 (14%, 95% CI 10–17) and recurrence or relapse in 390/3119 (11%, 95% CI 8–14).

Discussion

This updated systematic review and meta-analyses showed that brain abscess remains a condition that occurs most commonly in male patients with predisposing conditions. The aetiology is heterogeneous but constant over time and across continents despite an increasing proportion of brain abscesses attributable to preceding neurosurgical procedures, immuno-compromising conditions, and dental infections. Aspiration is still the preferred neurosurgical treatment for brain abscess, especially when guided by stereotactic navigation. Nonetheless, the case fatality and risk of poor recovery remain high and largely unchanged during the last two decades.

The broad range of potential pathogens poses a great challenge for empiric treatment strategies of patients with brain abscess in terms of appropriate antimicrobial coverage while being mindful towards principles of antimicrobial stewardship and risks of toxicity.[1] The current meta-analysis showed that a multitude of *Streptococcus* spp, often residing e.g. in the oral cavity and the gastrointestinal tract, are the most frequent causes of brain abscess globally. In particular, *S. intermedius* and other streptococci belonging to the viridans group were also predominant in other recent studies.[19–23] Molecular-based diagnostics have been used in several studies to consistently show that almost all brain abscesses due to *Streptococcus* spp. are polymicrobial and contain many other bacteria that are usually found in the oral cavity such as *Fusobacterium spp.*, *Actinomyces spp*., and *Aggregatibacter spp*.[21,24–26] *S. aureus* was the second most frequent pathogen and was typically caused by open head trauma or preceding neurosurgery. Of note, *S. aureus* was just as common as *Streptococcal spp*. in Africa. However, this observation was heavily influenced by one large South African study of 973 patients with brain abscess from 1983–2002 among which 33% were traumatic.[27] A larger relative proportion of *S. aureus* was also observed in North America, which may be biased by reports from selected sites with highly specialised neurosurgical care that may involve deep-brain stimulators and similar hardware in the central nervous system.[28] In contrast, *P. aeruginosa* and opportunistic pathogens like fungi, nocardiosis, and parasites were relatively rare. They should be considered in certain patient populations, e.g. post-neurosurgical brain abscess or chronic cholesteatoma for *P. aeruginosa* and severely immuno-compromised patients for fungi, nocardiosis, and parasites.[1,4]

Predisposing conditions for brain abscess are important for understanding the underlying pathogenesis and ensuring adequate treatment including source control in the brain and elsewhere. Compared with the previous meta-analysis, the proportions with postoperative brain abscess and immuno-compromising conditions have increased from 9% to 16% and from 9% to 19%, respectively.[8] This is likely a reflection of a lowered threshold and increased availability of both highly specialised neurosurgery and immuno-modulating treatments.[5] Although immunocompromise was found to be associated with increased mortality in a nationwide Danish cohort study,[3] the mortality and proportion with good recovery remained similar over time in this meta-analyses. This may be explained by improved diagnostics and treatment modalities.[5] The proportion of patients with brain abscess involving an odontogenic focus has also increased from 5% to 11% compared with the previous meta-analysis.[8] This may be due to an increased awareness of this potential association by clinicians and routine dental evaluations during diagnostic work-up in many settings although the exact pathophysiological mechanism remains unclear.[19,20,29,30]

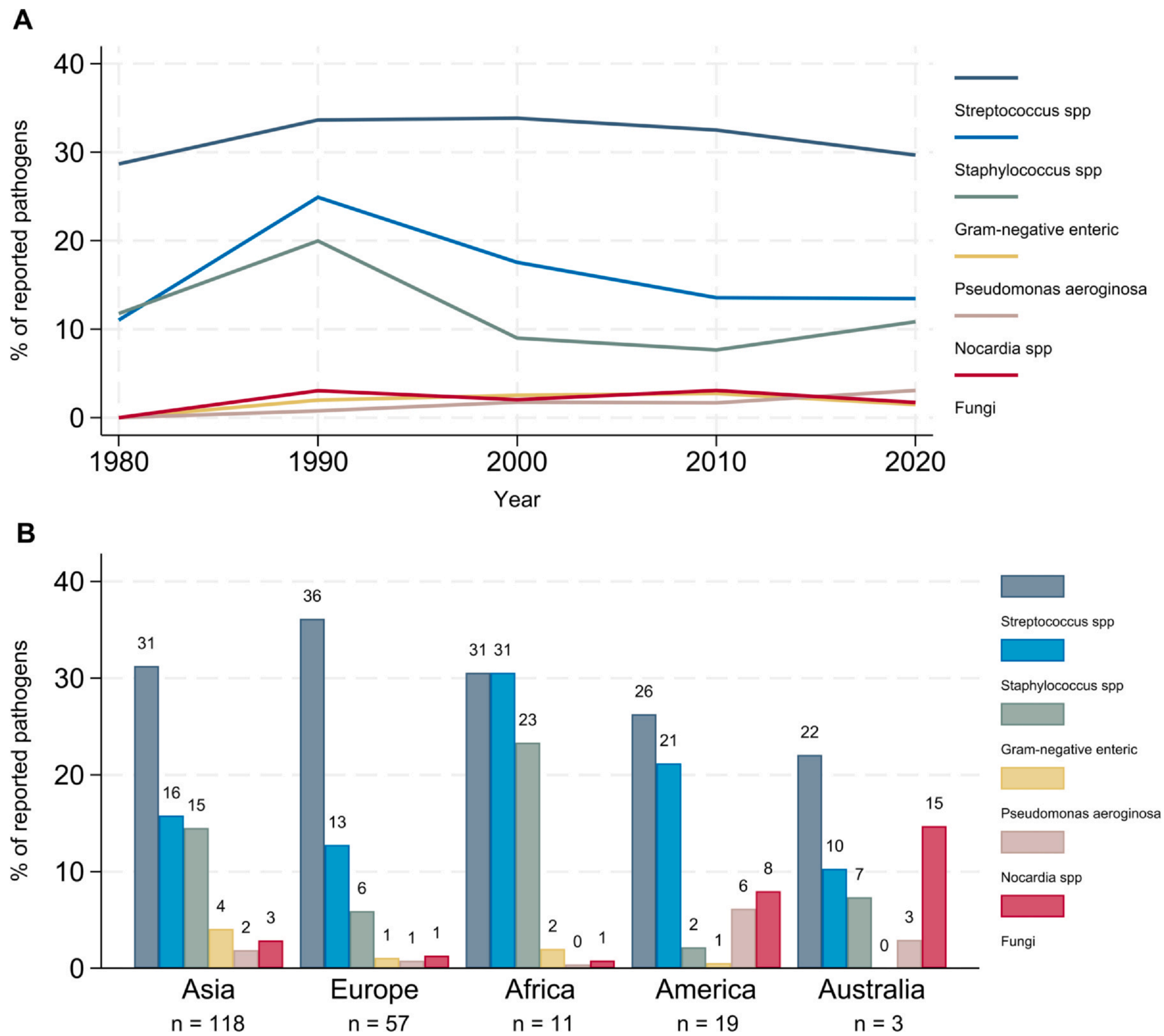

Fig. 1. Distribution of causative pathogens through time (A) and per continent (B). (A)Relative proportion of selected pathogens over time for the middle year of the study period. For nine studies published after year 2000 without a defined study period, the year of publication was used. (B)Relative proportion of selected pathogens according to continents. One study spanned several continents and was excluded from this analysis.[47].

Aspiration was still the most frequently used neurosurgical procedure for brain abscess and was applied in 76% of patients, often assisted by stereotactic navigation (75% of aspirated cases). However, the optimal neurosurgical treatment of brain abscess remains unresolved and mortality and neurological outcome appears to be comparable between patients treated with either aspiration or excision for brain abscesses amenable to both procedures.[1,31,32] Although aspiration is associated with increased risk of reoperation, it is less invasive and associated with a lower risk of bleeding compared with excision. Of note, risks of recurrence/relapse in this meta-analysis should be interpreted with caution due to lacking or unclear definitions in the included studies and estimates likely overlap considerably with risks of reoperation during the acute stage of disease. Recurrence of brain abscess, defined as formation of a new brain abscess after previous documented cure, has been shown to be exceedingly rare in other studies and usually occurs in patients with vascular right-to-left shunts or permanent neuroanatomic defects.[3,19,30,33–35]

The overall outcome of brain abscess has remained largely unchanged since year 2000 with a case fatality rate of 10% and a good outcome in 60% of survivors as reported by the included studies. Although the functional outcome of survivors does seem to improve during the first year after diagnosis,[3,36] patients with brain abscess have an increased long-term risk of death, cancer, epilepsy, anxiety disorders, and disability pension compared with population controls matched by age, sex, and geographic location.[37–42] Importantly, risk of epilepsy is likely underestimated in the current meta-analysis due to potential selection bias and incomplete follow up. Other population-based cohort studies with extended and complete follow-up have shown that long-term risk of epilepsy is about 30–32% among survivors of brain abscess.[37,43]

Rupture of brain abscess after admission may be a key modifiable parameter to improve the prognosis of patients with brain abscess. In the current meta-analyses, rupture was diagnosed in 7% of patients which is lower than previous estimates of 10–35%.[44–46] Reasons for this discrepancy are unclear. A recent large population-based cohort study of 485 adults with brain abscess observed that rupture occurred in 16% and was independently associated with a substantially increased risk of death and unfavourable outcome.[3] Proximity to brain surfaces has been suggested as a prognostic

Table 3
Brain abscess location, treatment, and outcome.

Characteristics	n/N or mean	% (95% CI)	No. of studies
Abscess localisations[a]	N=6627		91
Frontal	2213	32 (28–36)	
Temporal	1406	21 (19–24)	
Parietal	1557	20 (18–24)	
Occipital	570	8 (7–10)	
Basal ganglia and Thalamus	175	3 (2–4)	
Cerebellum and brainstem	689	9 (7–11)	
Single abscess	5266/6529	80 (77–83)	87
Multiple abscesses	1263/6529	20 (17–23)	87
Treatment			
Operation	10,780/13,040	91 (89–93)	176
Operation (excl. studies with surgery as incl. criterion)	9130/11,379	89 (86–92)	150
Aspiration	4468/5876	76 (70–81)	94
Stereotactic aspiration	1262/2709	75 (60–87)	38
Excision	1453/5133	33 (26–39)	76
Aspiration and excision	126/1559	9 (5–13)	29
Reoperation	1048/3861	21 (17–26)	48
Medical treatment alone	722/4595	12 (8–16)	69
Duration of antibiotic treatment (d)[b]	57	(46–68)	18
Oral consolidation therapy[c]	1642/2317	69 (48–87)	21
Steroids	1134/2341	51 (40–63)	29
Complications and outcome			
Mortality	2444/18,991	12 (11–14)	170
Asia	1470/12,082	11 (9–14)	96
Europe	614/4159	12 (10–14)	45
Africa	201/1468	14 (10–19)	10
North America	111/1030	18 (3–40)	13
South America	16/88	19 (3–41)	2
Australia	32/145	20 (11–31)	3
Rupture of brain abscess	469/4502	7 (5–10)	43
Hydrocephalus	522/3924	11 (8–14)	38
Epilepsy	338/2611	14 (10–17)	39
Recurrence/relapse[d]	390/3119	11 (8–14)	58
Good outcome	3419/5409	63 (58–68)	68

[a] Only includes studies reporting abscess distributions in more than one location.
[b] Based on reported overall mean duration of treatment and standard errors (sometimes converted from standard deviations) of 873 patients.
[c] After completion of a full course of intravenous antibiotic treatment (if specified ≥4 weeks).
[d] Occurrence of relapse and recurrence is summarised as reported and may include both treatment failure requiring e.g. re-aspiration and also recurrence of brain abscess after completion of treatment.

factors for rupture of brain abscess in crude analyses in a few small single-centre cohort studies and certainly makes sense from a mechanistic point of view.[44–46]

This systematic review and meta-analysis has several limitations. First, the meta-analysis was based on observational studies with inherent risks of information and selection bias that may affect the results in an unpredictable manner. These biases may become accentuated when compiled into a meta-analysis. Furthermore, opportunistic pathogens such as cerebral toxoplasmosis, aspergillosis, nocardiosis are often reported separately and may thereby be underestimated in the current study. Retrospective cohort studies may have missing values for some parameters and the data are therefore consistently presented as number of observations per number of individuals with this information available. Finally, publication bias cannot be excluded in terms of the unexpected comparable case fatality and proportions with a poor outcome between low- and high-resource settings.

In conclusion, this systematic review and meta-analysis found that brain abscess occurs about twice as often in males as in females. *Streptococcus spp*. and other oral cavity bacteria were the predominant pathogens and remained constant across time and continents. Important predisposing conditions for brain abscess were previous neurosurgery, immune-compromising conditions, and dental infections. Although stereotactic aspiration is more frequently used, the case fatality and proportion of patients with a poor outcome remain high during the last two decades. The results of this study may inform future trials on management of brain abscess and help identify barriers for timely diagnosis and treatment in different healthcare settings.

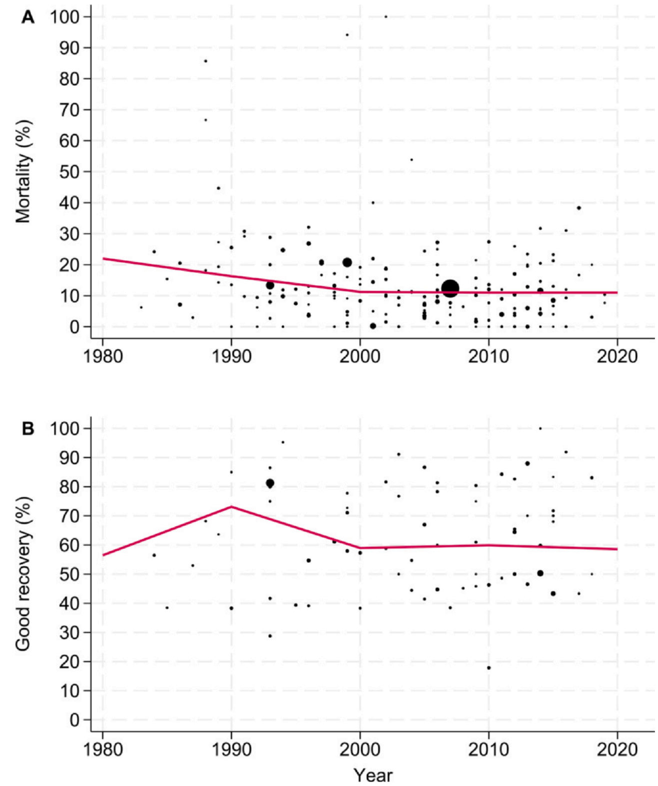

Fig. 2. Case-fatality (A) and complete recovery (B) of patients with brain abscess through time. Case fatality and proportions with good recovery over time for the middle year of the study period. For nine studies published after year 2000 without a defined study period, the year of publication was used.

Funding

None.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

None.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jinf.2024.106394.

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