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Brain abscess incidence and microbial etiology in Turkey: a nationwide cross-sectional study

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Abstract. – OBJECTIVE: Brain abscess, a localized purulent central nervous system infection, arises from a variety of microorganisms. Expedited diagnosis and formulation of effective treatment strategies are crucial for mitigating mortality risks in patients with brain abscesses. A nuanced understanding of potential microbial agents is pivotal for the development of empirical antibiotic therapies. This study aimed to explore the incidence and microbial etiology of brain abscesses.

PATIENTS AND METHODS: This study is a nationwide cross-sectional analysis of patients diagnosed with brain abscesses in Turkey, employing the ICD 10 diagnosis code from January 1, 2015, to December 31, 2021. Data pertaining to age, sex, comorbidities, and microorganisms isolated from central nervous system samples were meticulously recorded and analyzed.

RESULTS: This study included 11,536 patients diagnosed with brain abscesses. The incidence fluctuated between 0.98 and 3.68 during the review decrease post-2017, with a notable increase in male patients during time. Diabetes constituted 56.5% of the patients. The predominant isolated pathogens were *Staphylococcus* (37.6%), *Streptococci* (13.3%), and *Klebsiella spp.* (7.8%), *Escherichia coli* (6.4%), and *Candida species* (6.1%).

CONCLUSIONS: The incidence of brain abscesses is decreasing in Turkey. Although staphylococci remain the most isolated agents, the frequent occurrence of Gram-negative bacteria and Candida species warrants consideration during empirical antibiotic selection.

Key Words:
Brain abscess, Treatment, Etiology, Incidence.

Introduction

Brain abscesses represent a localized suppurative infection of the central nervous system (CNS) and are predominantly induced by bacterial or fungal agents[1]. The infiltration of bacteria into the brain parenchyma, leading to abscess formation, can occur due to the direct or hematogenous spread of infection or may transpire post-surgical intervention or trauma[2,3]. The onset may be spontaneous or attributed to various risk factors such as intravenous drug use, congenital cardiac anomalies, infective endocarditis, immunosuppression, or a directly adjacent infectious focus. Despite the identification of numerous predisposing conditions, the etiology of most brain abscesses remains undetermined[4].

Advancements in medical science, including cutting-edge imaging modalities, such as magnetic resonance imaging, revolutionary neurosurgical techniques, sophisticated microbiological diagnosis methods, and the incorporation of potent antibiotics, have not diminished the life-threatening implications of brain abscesses. They remain fatal if neglected[5,6]. The incidence of brain abscesses is projected to be between 0.3 and 1.3 per 100,000 people annually, accentuated in developing countries[7,8]. Enhanced diagnostic methodologies and an augmented number of surgical interventions in the CNS are factors that contribute to the continual increase in this rate[7].

Brain abscesses predominantly stem from bacterial infections, but are also attributed to other pathogens, including fungi and protozoa. Approximately a quarter of the cases exhibit polymicrobial etiology[9]. Contemporary publications and epidemiological data on the microbial etiology of brain abscesses are exceedingly scarce, emphasizing the need for extensive population-based studies. This study focused on analyzing patients diagnosed with brain abscesses in Turkey, aiming to fill the existing knowledge gap in microbial etiology and incidence.

Patients and Methods

Study Design

In this nationwide, retrospective, cross-sectional study, we comprehensively reviewed the

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Table I. ICD 10 diagnosis codes of the patients included in the study.

G06	Intracranial and intraspinal abscess and granuloma
G06.0	Intracranial abscess and granuloma
G06.2	Extradural and subdural abscess, unspecified
G07	Intracranial and intraspinal abscess and granuloma, in diseases classified elsewhere

hospital records of all inpatients with brain abscesses identified through ICD-10 diagnosis codes from January 1, 2015, to December 31, 2021. Data were retrieved by searching the Republic of Turkey Ministry of Health Data Bank (TCSBVB).

Data Collection

The ICD-10 diagnosis codes included as the main diagnosis or secondary diagnosis are presented in Table I. Age, gender, comorbidity status, previous surgical history, and microbiologic culture results of cerebrospinal fluid (CSF), abscess material, and tissue culture samples obtained from the CNS were recorded. Dental, ear, nose, and throat infections [upper respiratory tract infection (URTI)], head trauma, and neurosurgical operations within the last six months prior to hospitalization were also analyzed. Patients between zero and 19 years were categorized as the pediatric population, and those aged 20 years and older were categorized as the adult population.

Ethical Approval and Informed Consent

Ethical approval for the study was granted by the Afyonkarahisar Health Sciences University Faculty of Medicine Clinical Research Ethics Committee under decision number 2023/3. Given the retrospective nature of this study and the use of de-identified aggregated data obtained from the Republic of Turkey Ministry of Health Data Bank, obtaining informed consent from individual patients was not required.

Incidence Rates Calculation

The date of the first hospitalization with a brain abscess diagnosis code was considered the index date. The overall incidence rate was calculated as the ratio of the annual number of TCSBVB brain abscess cases per 100,000 to the country's population, as announced by the Turkish Statistical Institute (TurkStat) on December 31 of each year. Brain abscess incidence rates by sex were calculated as the ratio of the number of cases per sex to the total population of that sex per 100,000 individuals. During the study period, Turkey's population increased from 78,741,053 to 84,680,273.

Statistical Analysis

Data analysis was performed using the IBM SPSS Statistics 22 package program (IBM Corp., Armonk, NY, USA). Descriptive statistics are presented as categorical frequencies and percentages. More details on the statistical methods used, including any significance tests, will be provided in the results section, as they pertain to specific analyses conducted. $p<0.05$ was considered statistically significant.

Results

This study included 11,536 patients with brain abscess ICD 10 diagnosis codes. Among them, 50.3% were male, and 49.7% were female. The proportion of the pediatric population was 16.8%, while the proportion of patients over 80 years of age was 3.1%. Most patients (60.3%) were adults, aged 20-59 years old. The distribution of patients according to age and sex is shown in Table II.

The most common comorbidity was diabetes mellitus (56.5%), while 16.3% had a history of dental disease (dental caries, abscess, and dental intervention), 5.25% had head trauma, and 7.43% had a history of CNS surgery in the last six months (Table III).

The highest number of patients was detected in 2017, while the incidence has decreased since 2018 (Table IV).

At least one microorganism was isolated from cultures of CNS specimens from 924 patients with brain abscesses. Of the microorganisms in the CNS samples of the patients, 88.9% were isolated from adults and 11.1% from the pediatric population; in 64 patients (6.9%), the causative agent was polymicrobial. Gram (+) (*staphylococci* and *streptococci* species) were the most common agents. The third most common Gram (–) organisms were *Klebsiella, E.coli*, and *candida* species (Table V). Tubercle bacillus was the causative agent in eight (0.9%) adult patients, while it did not cause infection in the pediatric population. *Candida* had similar infection rates in the adult and pediatric populations (5.8% and 5.7%, respectively).

Discussion

This study provided a comprehensive analysis of 11,536 patients with brain abscesses, marking

Table II. Distribution of patients by age and gender.

	Male n (%)	Female n (%)	Total n (%)
Gender	5,804 (50.3)	5,732 (49.7)	11,536 (100)
Age n (%)			
0-19	1,048 (54.1)	887 (45.9)	1,935 (16.8)
20-39	1,761 (47.6)	1,934 (52.4)	3,695 (32.0)
40-59	1,637 (45.1)	1,631 (45)	3,628 (28.3)
60-79	1,169 (51.2)	1,112 (48.8)	2,281 (19.8)
80+	189 (52.9)	168 (47.1)	357 (3.1)

Table III. Comorbidities.

	n	(%)
Diabetes	6,529	(56.5)
Tooth disease	1,884	(16.3)
Pneumonia	1,086	(9.41)
CNS surgery in the last month	858	(7.43)
URTI	830	(7.19)
Head trauma	606	(5.25)
Heart disease	43	(0.37)
HIV infection	6	(0.05)

Central nervous system (CNS); upper respiratory tract infection (URTI).

Table IV. Distribution of patients by years.

Number of patients by year	N (%)	Country Population	Incidence (per 100,000)
2015	1,619 (14.0)	78,741,053	2.05
2016	2,534 (21.9)	79,814,871	3.17
2017	2,976 (25.7)	80,810,525	3.68
2018	1,649 (14.2)	82,003,882	2.01
2019	1,060 (9.1)	83,154,997	1.27
2020	915 (7.9)	83,614,362	1.09
2021	832 (7.2)	84,680,273	0.98
Male	N (%)		
2015	789 (48.7)	39,511,191	1.99
2016	1,145 (45.1)	40,043,650	2.85
2017	1,400 (47)	40,535,135	3.45
2018	829 (50.2)	41,139,980	2.01
2019	654 (61.6)	41,721,136	1.56
2020	478 (52.2)	41,915,985	1.14
2021	509 (61.1)	42,428,101	1.19
Female			
2015	830 (51.2)	39,229,862	2.11
2016	1,389 (54.8)	39,771,221	3.49
2017	1,576 (52.9)	40,275,390	3.91
2018	820 (49.7)	40,863,902	2.00
2019	406 (38.3)	41,433,861	0.97
2020	354 (38.6)	41,698,377	0.84
2021	357 (42.9)	42,252,172	0.84

Table V. Distribution of microorganisms isolated from patients' central nervous system samples.

	Adult n (%)	Pediatric n (%)	Total n (%)
Staphylococcus spp	319 (36.4)	52 (32.7)	371 (37.6)
Streptococcus spp	98 (11.2)	33 (20.8)	131 (13.3)
Klebsiella spp	68 (7.8)	9 (5.7)	77 (7.8)
Escherichia coli	60 (6.8)	3 (1.9)	63 (6.4)
Candida spp	51 (5.8)	9 (5.7)	60 (6.1)
Pseudomanas spp	39 (4.4)	8 (5.0)	47 (4.8)
Acinetobacter spp	33 (3.8)	6 (3.8)	39 (4.0)
Enterobacter spp	27 (3.1)	3 (1.9)	30 (3.0)
Proteus spp	23 (2.6)	1 (0.6)	24 (2.4)
Corynebacterium spp	11 (1.3)	2 (1.3)	13 (1.3)
Aspergillus spp	8 (0.9)	3 (1.9)	11 (1.1)
Serratia spp	7 (0.8)	3 (1.9)	10 (1.0)
Mycobacterium tuberculosis	8 (0.9)	0 (0.0)	8 (0.8)
Morganella morganii	7 (0.8)	0 (0.0)	7 (0.7)
Stenotrophomonas maltophilia	2 (0.2)	4 (2.5)	6 (0.6)
Prevotella buccae	6 (0.7)	0 (0.0)	6 (0.6)
Micrococus spp.	5 (0.6)	0 (0.0)	5 (0.5)
Propionibacterium acnes	5 (0.6)	0 (0.0)	5 (0.5)
Bacteroides spp	4 (0.5)	1 (0.6)	5 (0.5)
Providencia spp.	3 (0.3)	2 (1.3)	5 (0.5)
Bacillus spp	2 (0.2)	2 (1.3)	4 (0.4)
Eikenella corrodens	1 (0.1)	3 (1.9)	4 (0.4)
Haemophilus influenza	2 (0.2)	1 (0.6)	3 (0.3)
Penicillium spp.	3 (0.3)	0 (0.0)	3 (0.3)
Salmonella	1 (0.1)	2 (1.3)	3 (0.3)
Citrobacter spp	2 (0.2)	1 (0.6)	3 (0.3)
Cutibacterium spp	3 (0.3)	0 (0.0)	3 (0.3)
Fusobacterium spp	3 (0.3)	0 (0.0)	3 (0.3)
Parvimonas micra	3 (0.3)	0 (0.0)	3 (0.3)
Nocardia spp	2 (0.2)	0 (0.0)	2 (0.2)
Brucella Spp.	1 (0.1)	0 (0.0)	1 (0.1)
Listeria monocytogenes	1 (0.1)	0 (0.0)	1 (0.1)
Other	17 (1.9)	11 (6.9)	30 (3.0)
Total	**877 (100.0)**	**159 (100.0)**	**986 (100.0)**

a significant contribution given the volume of patients included, which is the largest among published studies on brain abscess diagnoses.

The findings presented herein are especially pivotal, revealing a decrease in the incidence of brain abscesses in Turkey, ranging from 3.68 (2017) to 0.98 (2021) per 100,000 per year. Interestingly, there was a notable shift in sex prevalence, with a higher incidence in women before 2018 and in men thereafter.

Comparative to extant limited data, suggesting an incidence between 0.3 and 1.3 per 100,000 per year[2,10], recent studies in Denmark and Taiwan reported incidence rates of 0.76 and 1.72-1.98 per 100,000 person-years, respectively[4,11]. Consistent with the literature, this study found a predominance of brain abscess (BA) in men[12].

The decline in incidence is potentially attributable to the widespread and effective use of antibiotics in treating various conditions, including upper respiratory tract infections (URTIs), dental infections, CNS infections, and the implementation of the necessary prophylaxis in CNS-affected traumas.

Brain abscesses, initially developing as cerebritis, are characterized by non-specific clinical manifestations such as high fever, seizures, and symptoms related to the mass effect[13,14]. The course and survival outcomes of patients are sig-

nificantly influenced by preexisting comorbidities, adjacent infection foci, and predisposing factors[11,15]. Streptococcus, Actinomyces, and Fusobacterium species, typically found in the oral cavity and dental plaque, are frequently identified in the surgical drainage of brain abscesses[16].

Concerning risk factors, diabetes, dental diseases, pneumonia, and a history of CNS surgery were prevalent in this study, with the elevated rate of diabetes being particularly conspicuous. Advances in diagnostic and treatment methods have presumably contributed to a reduction in mortality to 5-15% over the last two decades[12]. However, timely diagnosis and treatment remain crucial owing to the high mortality risks in untreated or delayed cases.

Treatment modalities typically include medical, surgical, or combined approaches. Abscesses larger than 2.5 cm generally necessitate excision or drainage, whereas smaller abscesses or those in the cerebritis stage are primarily drained for diagnostic purposes[12]. Broad-spectrum antibiotics are essential until culture and sensitivity data are available[17].

Empirical antimicrobial treatment should be carefully selected, considering predisposing conditions, primary infection sources, and possible etiological agents[18]. Identifying the causative microorganism from intracranial abscess tissue or intraoperatively obtained fluids dictates the appropriate antibiotic therapy[19].

This study emphasizes the predominance of s*taphylococcus* species in both adult and pediatric populations, with a conspicuous presence of staphylococci compared to other agents. Interestingly, the rates of polymicrobial infections in this study were lower than those reported in the literature[9]. A recent study confirmed the frequent detection of *staphylococci* and *streptococci* with a prevalence of 28.6% and 21.4% respectively, also in other studies, *staphylococci,* and *streptococci* are the most frequently isolated species[20-22].

Klebsiella species, *E. coli*, and *Candida* were prevalent etiological agents in this study. Hypervirulent Klebsiella pneumoniae is particularly noteworthy, occurring frequently in immunocompromised individuals and leading to metastatic infections with poor prognosis[1]. In immunocompromised patients, such as organ transplant recipients and HIV-infected individuals, the consideration of rare agents is imperative when selecting antibiotics, given the possibility of infections by fungi, mycobacteria, parasites, and various unusual organisms[17].

Less frequently, this study identified *Haemophilus influenzae, Eikenella corrodens, Listeria monocytogenes, Propionibacterium acnes, Morganella morgagni, Mycobacterium tuberculosis, Brucella,* and *Salmonella* species. Instances of *Morganella morgagni* have been rare but are associated with middle ear infections[20].

Limitations

The inherent limitations of this study arise predominantly from its retrospective design. Given the extensive breadth of the patient population encompassed nationwide, the fidelity of the data is contingent upon the meticulous entry of the pertinent ICD-10 diagnosis codes. Additionally, due to the retrieval methodology employed, deriving associations between causative agents and predisposing conditions was not feasible, as the data were acquired from the comorbidity database by querying additional diagnosis codes entered within the preceding six months. Despite these constraints, the feasibility of conducting a prospective multicenter study involving such an expansive patient cohort seems implausible. Therefore, the invaluable insights afforded by the data in this study hold significant utility and relevance and contribute meaningfully to the existing body of knowledge.

Conclusions

This study revealed a discernible declining trajectory in the incidence of brain abscesses within Turkey, with a predominant occurrence in males. Diabetes mellitus has emerged as a paramount comorbidity, trailed by dental diseases, pneumonia, recent CNS surgery, and a history of URTI. *Staphylococci* and *streptococci* have been identified as the principal agents of microbial etiology. When selecting empirical antimicrobials, a preference for broad-spectrum parenteral antibiotics is advocated, especially given the frequent emergence of *Klebsiella* spp., *E. coli*, and *Candida* as common agents. The findings delineated in this study augment our understanding and provide pivotal insights that are instrumental for future research and clinical practice in addressing brain abscesses and their underlying etiological factors.

Conflict of Interest

We confirm that there are no conflicts of interest to declare.

Authors' Contributions
The authors, Serhat Korkmaz and Derya Korkmaz contributed equally to the conception, design, analysis, and interpretation of data, drafting and revising the article, and final approval of the version to be submitted.

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Availability of Data and Materials
The datasets utilized for this study are accessible from the authors upon reasonable request.

Ethics Approval
Ethical approval for the study was granted by the Afyonkarahisar Health Sciences University Faculty of Medicine Clinical Research Ethics Committee under decision number 2023/3.

Informed Consent
Given the retrospective nature of this study and the use of de-identified aggregated data obtained from the Republic of Turkey Ministry of Health Data Bank, obtaining informed consent from individual patients was not required.

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