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Incidence, clinical profile and short term outcome of cerebral abscess in cyanotic congenital heart diseases

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ABSTRACT

Background: Brain abscess is a serious infection of brain parenchyma in patients with cyanotic congenital heart disease (CCHD) and around 25–46 % of unrepaired CCHD patients develop brain abscess. Aim of this study was to determine the incidence, clinical features, microbiology and factors associated with early and short term outcome of cerebral abscess in CCHD.

Method: ology: This is a retrospective study, conducted at Pediatric cardiology department, National Institute of Cardiovascular Diseases (NICVD) Karachi. The data was collected from January 2019 to December 2021. All CCHD patients between 1 and 25 years of age were included. Data of patients with cerebral abscess was reviewed.

Results: Among the 544 pediatric patients hospitalized in the last two years, brain abscesses were identified in 51 (9.3 %). Polycythemia (31.4 %) was the most significant contributing factor, especially in patients aged above 10 years. The most frequently seen CCHD was tetralogy of fallot (TOF) 60.8 %. Majority of the patients (84.3 %) had a single abscess while 15.7 % had multiple abscesses. E coli (9.7 %) was the most common isolated pathogen. Immediate complication identified was cerebral edema in 22 (43.1 %). Four patients (7.8 %) died, 47 (92.2 %) patients completed treatment course. 45.1 % had complete recovery however, 17 (33.3 %) had neurological deficits, 8 (15.7 %) had seizures and 2 (3.9 %) patients had residual abscess. Prolonged hospitalization was observed in patients of age group <10 years.

Conclusion: In patients with underlying CCHD,early referrals and intervention are key to mitigating the severe consequences of cerebral abscesses and can drastically improve patient outcomes.

1. Introduction

Brain abscess is a serious infection of brain parenchyma in congenital heart disease caused by various microorganisms, poses significant morbidity and mortality risks [1]. In developing countries the incidence of brain abscesses is approximately 8 % however, 1 %–2 % in western countries [2]. The common predisposing factors of a brain abscess are chronic suppurative otitis media (CSOM), congenital cyanotic heart disease (CCHD), paranasal sinusitis [3]. Around 20 % of the cases present with no underlying illness or

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source of infection. CCHD is the most common predisposing factor and about 12.8–69.4 % patients with CCHD develop brain abscess [4,5], while 25–46 % of un-corrected CCHD patients develop brain abscess [6,7]. Brain abscesses in CCHD patients often result from persistent hypoxia, leading to polycythemia, hyperviscosity, and sluggish blood flow in cerebral microcirculation. This promotes the formation of micro thrombi and focal infarcts which serve as entry points for microorganisms, causing brain abscesses [8]. Clinical manifestations of brain abscesses vary depending on the site of abscess involved. Patients typically present with focal neurological deficits such as paralysis, visual impairment, cranial nerve palsies, cerebellar signs and papilledema [9]. It is important to note that brain abscesses are commonly caused by bacteria, including Gram-positive cocci and Gram-negative bacilli, as well as fungal infections. The mortality rate associated with brain abscess is around 10 % [11,12]. Predictors of poor prognosis are multiple brain abscesses, cerebral edema, delayed presentation, low GCS, intraventricular rupture of brain abscess (IVROBA), immunocompromised host, and inappropriate treatment. It is crucial to detect brain abscesses early in order to prevent these complications. Therefore, any child presenting with neurological deficits, altered sensorium, headache, and seizures should be evaluated promptly, especially if they have predisposing factors such as sinusitis, otitis media, congenital heart disease, or an immunocompromised state [13,14] (see Fig. 4)

The aim of this retrospective study is to evaluate the incidence, factors associated with early and short term outcome of cerebral abscess in CCHD. Although we have huge burden of un repaired CCHD with complications, the brain abscess is frequently seen in our setting. These patients are either missed or inappropriately treated before presenting to tertiary care hospital. Evaluating predisposing

Table 1
Demographics and Characteristics of CCHD patients with Brain Abscess.

Characteristics	Total	Age		*P*-value
		1–10 years	>10 years	
Total (N)	51	30 (58.8 %)	21 (41.2 %)	–
Gender				
Male	29 (56.9 %)	19 (63.3 %)	10 (47.6 %)	0.265
Female	22 (43.1 %)	11 (36.7 %)	11 (52.4 %)	
Age (years)	10.73 ± 6.6	6.4 ± 2.96	16.9 ± 5.29	<0.001*
1–10 years	58.8 % (30)	100 % (30)	0 % (0)	–
>10 years	41.2 % (21)	0 % (0)	100 % (21)	
GCS				
<5	2 % (1)	3.3 % (1)	0 % (0)	0.842
5–10	9.8 % (5)	10 % (3)	9.5 % (2)	
10–14	25.5 % (13)	26.7 % (8)	23.8 % (5)	
15+	62.7 % (32)	60 % (18)	66.7 % (14)	
Sodium				
<135	13.7 % (7)	10 % (3)	19 % (4)	0.355
136–145	86.3 % (44)	90 % (27)	81 % (17)	
Location of abscess				
frontal lobe	21.6 % (11)	6.7 % (2)	42.9 % [9]	0.002*
temporal lobe	17.6 % (9)	20 % (6)	14.3 % [3]	0.598
parietal lobe	62.7 % (32)	63.3 % (19)	61.9 % [13]	0.917
occipital lobe	21.6 % (11)	23.3 % (7)	19 % [4]	0.714
basal ganglia (thalamus)	9.8 % (5)	13.3 % (4)	4.8 % [1]	0.311
Number of abscessrowhead				
Single	84.3 % (43)	90 % (27)	76.2 % [16]	0.182
Multiple	15.7 % (8)	10 % (3)	23.8 % [5]	
Duration of hospital stayrowhead				
1–2 weeks	19.6 % (10)	20 % (6)	19 % [4]	0.875
2–4 weeks	7.8 % (4)	6.7 % (2)	9.5 % [2]	
4–6 weeks	39.2 % (20)	43.3 % (13)	33.3 % [7]	
>6 weeks	33.3 % (17)	30 % (9)	38.1 % [8]	
Surgical drainage	54.9 % (28)	60 % (18)	47.6 % [10]	0.382
****Number of drainage**				
1	92.9 % (26)	100 % (18)	80 % [8]	0.119
2	7.1 % (2)	0 % (0)	20 % [2]	
Pus culture	60.8 % (31)	63.3 % (19)	57.1 % [12]	0.656
Microbial isolates of pus culture				
No growth	74.2 % (23)	63.2 % (12)	91.7 % [11]	0.319
Streptococcus milleri	6.5 % (2)	10.5 % (2)	0 % (0)	
Staph aureus	6.5 % (2)	5.3 % (1)	8.3 % [1]	
Coagulase negative staph	3.2 % (1)	5.3 % (1)	0 % (0)	
E coli	9.7 % (3)	15.8 % (3)	0 % (0)	
Microbial isolates of blood C/S				
No growth	82.4 % (42)	80 % (24)	85.7 % [18]	0.622
Staph Aureus	2 % (1)	0 % (0)	4.8 % [1]	
Gram negative streptococci	2 % (1)	3.3 % (1)	0 % (0)	
Burkholdaria cepacia	3.9 % (2)	3.3 % (1)	4.8 % [1]	
Candida glabarata	3.9 % (2)	3.3 % (1)	4.8 % [1]	
streptpcocus specie	3.9 % (2)	6.7 % (2)	0 % (0)	
E coli	2 % (1)	3.3 % (1)	0 % (0)	

factors leading to this catastrophic complication would alert clinicians to refer patients at early stage of disease for proper management. This will help in improving the outcome and reducing morbidity and mortality. Moreover this study comprises incidence, microbiology and outcome in CCHD which was not been previously done in our region.

2. Methodology

This study is a retrospective analysis conducted in the Pediatric Cardiology Department of the National Institute of Cardiovascular Diseases (NICVD) in Karachi, following the approval from its ethical review board. We systematically collected data from hospital records obtained from January 2019 to December 2021. Sampling was non probability consecutive. The study included patients aged 1–25 years who were diagnosed with CCHD confirmed by 2D echocardiography. Exceptions were patients older than 25 years, those with acquired heart disease, and cases lacking relevant information, who were excluded from our study. The selection criteria were strictly adhered to prevent any bias. The data of all the patients was obtained on a preformed questionnaire. The records of CCHD patients clinically diagnosed with brain abscess were examined. Details such as demographics, clinical presentation, predisposing factors, imaging results, microbiological findings, treatment methods, and both immediate and short-term outcomes were thoroughly analyzed. Brain abscess diagnosis was confirmed via contrast computed tomography (CT) of the brain. Standard investigations such as CBC, ESR, CRP, serum sodium, and blood culture were conducted. The prescribed treatment regimen consisted of antipyretic and triple regime (ceftriaxone, vancomycin, and metronidazole) for four weeks followed by two weeks oral antibiotics while observing neuroprotective measures. Antibiotics were reviewed after culture and sensitivity (C/S) reports, furthermore mannitol and antiepileptic drugs were used according to patients symptoms. Our study also involved a neurosurgery consultation for each patient. In cases of brain abscess larger than 2 cm, procedures like Burr hole aspiration and craniotomy were performed, and pus cultures were obtained. The analyzed patient details encompassed aspects like abscess locations, causative agents, treatment methods, prognostic data, and respective outcomes.

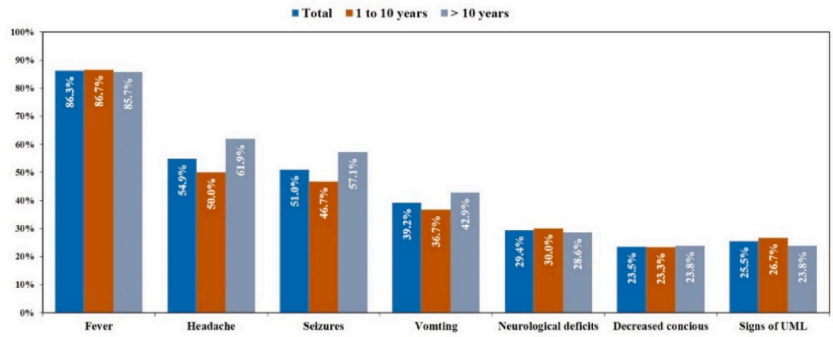
3. Results

Among the 544 pediatric patients hospitalized for CCHD between January 2019 and December 2021, brain abscesses were identified in 51 (9.3 %). The patient demographic consisted of a slight male preponderance with a distribution of 29 (56.9 %) male and 22 (43.1 %) female patients. Age-wise, a larger proportion was between 1 and 10 years, while the remaining were above 10 years of age (Table 1).

Patients' symptoms ranged from 1 to 42 days duration, the most common being fever (86.3 %), followed by headaches (54.9 %), seizures (51 %), and vomiting (39.2 %). A correlation was seen between the presenting symptoms and neurological deficits such as motor deficits (29.4 %) and consciousness level (23.5 %) illustrated in (Bar Chart 1). Many patients exhibited motor deficit (29.4 %), signs of upper motor neuron lesions (25.5 %), cranial nerve involvement (21.6 %) and meningitis (19.6 %). Furthermore, hemi paresis was observed in just under half of the cases (47.1 %), with only one case (2 %) of vision loss (Table 1).

In regard to the predisposing factor for brain abscess development, polycythemia (31.4 %) was the most significant contributing factor, especially in patients aged above 10 years. BT shunt (7.8 %) and septicemia (9.8 %) were common factors, however, chronic ear discharge (7.8 %) and thromboembolic events (2 %) were less commonly found in younger patients (Table 2). The most frequently seen CCHD was tetralogy of fallot (TOF) 60.8 %, followed by other CCHDs including transposition of great arteries (TGA) with ventricular septal defect (VSD) and pulmonary stenosis (PS) 15.7 % (Bar chart 2) (see Fig. 3).

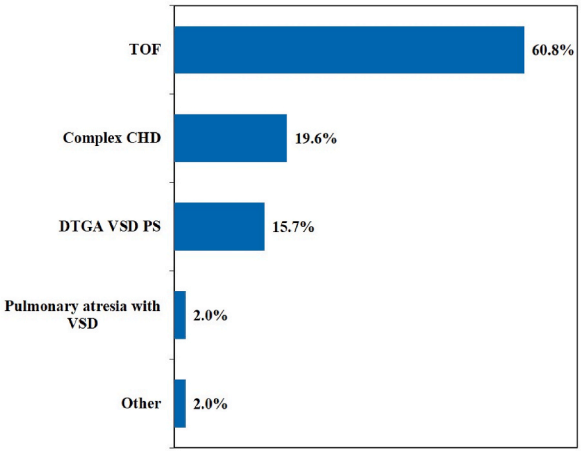
The parietal lobe was the most frequently affected brain region (62.7 %), with other areas such as the occipital lobe and frontal lobe also involved. Less common were temporal lobe (17.6 %) and Basal ganglia and thalamus (9.8 %). Cerebral infarct and hemorrhage were seen in (15.7 %), and (2 %) cases respectively. The majority of patients (84.3 %) had a single abscess, with just above 15 % presenting with multiple abscesses. About half of the patients had to undergo surgical procedures like bur hole aspirations and nearly 75 % of patients had sterile pus cultures. E coli (9.7 %) was the most frequently isolated pathogen. Blood cultures were positive in 9 (17.6 %) cases, however, isolation of pathogens like streptococcus specie, Burkholdaria cepacia and Candida glabarata specie were



Bar Chart 1. Presenting complaints.

Table 2
Predisposing Factors , Treatment and Outcome of CCHD Patients with Brain Abscess.

Characteristics	Total	Age		*P*-value
		1–10 years	>10 years	
Predisposing factors				
Polycythemia	31.4 % [16]	23.3 % [7]	42.8 % [9]	0.309
Meningitis	19.6 % [10]	26.7 % [8]	9.5 % [2]	0.129
Septicemia	9.8 % [5]	10 % [3]	9.5 % [2]	0.955
Ear discharge	7.8 % [4]	13.3 % [4]	0 % (0)	0.081
BT shunt	7.8 % [4]	6.7 % [2]	9.5 % [2]	0.709
Thromboembolic event	2 % [1]	3.3 % [1]	0 % (0)	0.398
Treatment				
Antibiotics	100 % (51)	100 % (30)	100 % (21)	–
Mannitol	62.7 % (32)	73.3 % (22)	47.6 % [10]	0.062
Anticonvulsants	54.9 % (28)	50 % [15]	61.9 % [13]	0.400
Duration of antibiotics				
1–2 weeks	3.9 % [2]	3.3 % [1]	4.8 % [1]	0.520
4–6weeks	70.6 % (36)	76.7 % (23)	61.9 % [13]	
>6 weeks	25.5 % [13]	20 % [6]	33.3 % [7]	
Short-term outcome				
cranial nerve palsy	21.6 % [11]	30 % [9]	9.5 % [2]	0.080
hemiparesis	47.1 % (24)	46.7 % [14]	47.6 % [10]	0.947
vision loss	2 % [1]	3.3 % [1]	0 % (0)	0.398
Life threatening complications				
cerebral edema	43.1 % (22)	50 % [15]	33.3 % [7]	0.237
massive bleeding into abscess	7.8 % [4]	3.3 % [1]	14.3 % [3]	0.152
IVROBA	2 % [1]	3.3 % [1]	0 % (0)	0.398
SIADH	3.9 % [2]	3.3 % [1]	4.8 % [1]	0.796
tentorial herniation	2 % [1]	3.3 % [1]	0 % (0)	0.398
Mid-term outcome				
Improved/complete recovery	45.1 % (23)	40 % [12]	52.4 % [11]	0.382
Death	7.8 % [4]	6.7 % [2]	9.5 % [2]	0.709
residual abscess	3.9 % [2]	0 % (0)	9.5 % [2]	0.085
residual neurological deficits	33.3 % [17]	40 % [12]	23.8 % [5]	0.227
seizure disorder	15.7 % [8]	20 % [6]	9.5 % [2]	0.311

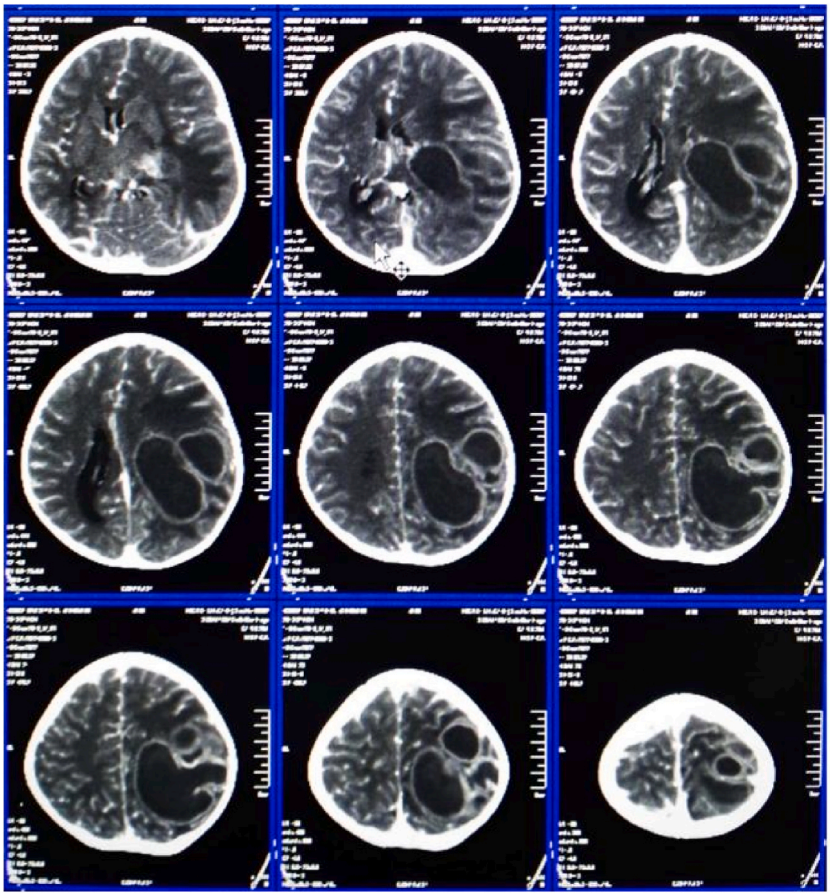


Bar Chart 2. Types of predisposing cyanotic congenital heart disease.

observed in 2 (3.9 %) of patients each. Staphylococcus Aureus was grown in 1 (2 %), Gram negative streptococci 1 (2 %) and E coli in 1 (2 %) (Table 1).

Immediate complications identified were cerebral edema in 22 (43.1 %), massive bleeding into the abscess cavity in 4 (7.8 %) syndrome of inappropriate secretion of antidiuretic hormone in 2 (3.9 %), tentorial herniation and intraventricular rupture of brain abscess (IVROBA) was found in 1 (2 %) each (Table 2).

Four patients (7.8 %) died within 1st week of admission. 47 (92.2 %) patients completed treatment course and were discharged. 23 (45.1 %) patients had complete recovery at the time of discharge, while 17 (33.3 %) had neurological deficits, 8 (15.7 %) had seizure disorder and 2 (3.9) patients had residual abscess (Table 2). Duration of hospital stay ranges from 14 to 56 days. Hospitalization was prolonged in patients of age group <10 years.



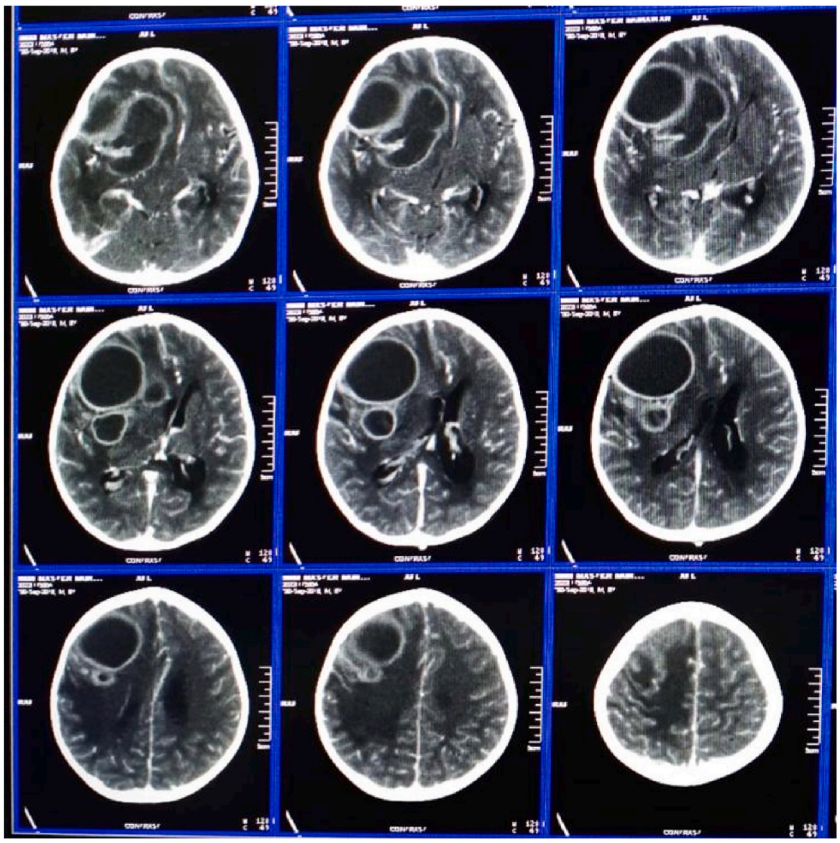
Patient:1. CT brain contrast of 7 years old male known case of TOF presented with complain of headache. He was polycythemic at the time of scan. Two large abscesses involving left parieto-occipital area. Surgically drained and treated with antibiotics.

4. Discussion

In a two-year study period, brain abscesses were found in 51 patients (9.3 %) among 544 patients admitted with CCHD. Males were more affected than females, with the most common age group being 1–10 years. Similar findings were reported in a study conducted by Prasad et al.[12], although Atique et al.[14] reported an equal distribution between genders. Polycythemia was identified as the primary predisposing factor, with over 31 % of patients displaying elevated haematocrit levels, however, a study by Ziaullah et al. noted a much higher prevalence of polycythemia in their patients.[6] Meningitis was the second most relevant factor, affecting 21.5 % of cases, consistent with other reports.[14] Given our hospital's status as a tertiary care and major referral center for complicated cardiac cases, 49 % of patients arrived within 1st week. However, 51 % arrived late. Despite 54.9 % of patients undergoing surgical drainage, 74 % showed no growth in culture, which may be attributed to prior antibiotic use. E coli was the most commonly isolated organism in our setting noted in 9.7 % of patients. Comparatively, Atique et al. and Ziaullah et al. reported Streptococcus milleri and Staphylococcus as the most common organisms [6,14].

All patients were administered a six-week course of broad-spectrum antibiotics. The administration of antifungals was only required in patients (3.9 %) diagnosed with fungal abscess. They were treated with intravenous amphotericin B and voriconazole (after the C/S report) for four weeks followed by two weeks of oral regimen. Few patients (21.4 %) who had non drainable abscess, developed complications and needed prolonged treatment. Symptoms mirrored those discussed in the literature, with 60–70 % presenting with headache, fever, and vomiting, and only 30 % with the classic triad of fever, headache, and focal deficits. The most common presenting symptom in our patient population was fever, experienced by 83.6 % of patients. The clinical presentation of brain abscess in our study aligns with findings from previous research other studies [12,15–17].

Predominantly, brain abscesses occurred in children with TOF (60.8 % of our patient population) [8,14,18]. Majority of our patients had single abscess located in parietal and frontal lobes, 62.7 % and 21.6 % respectively. Similar preponderance of parietal and frontal lobe involvement has been seen in previous studies [15–17]. Presence of multiple abscesses was less frequent in our findings, in contrast to previous study [6]. Outcomes were primarily influenced by the early diagnosis and appropriate treatment of brain abscess. Factors such as low GCS, cerebral edema, focal neurologic deficit, and the abscess's critical location were associated with poor outcomes, paralleling findings by Ziaullah et al. [6].



Patient:2. CT brain contrast of 10 years old male known case of DTGA VSD PS presented with fever headache vomiting. He was polycythemic at the time of scan. One abscess involving right forntal region compressing ventricles and another small involving fronto-parietal region. Successfully drained and treated with antibiotics.

In our study, the mortality rate was 7.8 %, substantiating prior research findings The fatal two had abscesses at critical locations such as the basal ganglia, rendering drainage infeasible; or they presented with complications such as intraventricular rupture of the brain abscess (IVROBA) and cerebral herniation. Other two patient subset had a low Glasgow Coma Scale score upon arrival: one such case had been complicated by multiple abscess-induced cerebral edema, and another presented with significant bleeding in the abscess. The aforementioned mortalities align with incidences reported in other studies [17,19]. The most common complication was focal neurological deficit (33.3 %), which was higher in our series than other studies, possibly due to the fact that our patients survived acute complications and had lower mortality. The second most prevalent complication was seizure disorder, observed in 15.7 % patients (Table 2).

5. Conclusion

This study highlights the importance of early diagnosis and treatment of brain abscess in children CCHD. Moreover, clinicians need to maintain a high level of suspicion when dealing with CCHD patients. Timely referrals and intervention are key to mitigating the severe consequences of cerebral abscesses and can drastically improve patient outcomes.

6. Recommendation

Early evaluation for brain abscess is crucial in patients with cyanotic congenital heart disease, particularly those experiencing polycythemia, febrile illness, and headaches. Detecting and preventing complications promptly are essential to reduce mortality and morbidity. Patients eligible for corrective surgery should undergo timely repair to prevent life-threatening complications. For patients who are not suitable candidates for corrective surgery, appropriate management of predisposing factors and administration of infective endocarditis prophylaxis are necessary to prevent severe infections.

7. Limitation of study

Due to late presentation of patients at our hospital and their prior use of antibiotics, it was challenging to isolate the responsible

organism in most cases. Additionally, due to the delayed arrival of patients, we were unable to record the earliest signs and symptoms.

Further research is needed to overcome the limitations of this study, such as implementing strategies to encourage earlier presentations of patients and minimizing use of antibiotics prior to arrival.

Ethics approval and consent to participate

This study was reviewed and approved by the ethical review committee of the National Institute of Cardiovascular Diseases (NICVD), Karachi (ERC-64/2021). Verbal informed consent was obtained from all the patients regarding their participation in the study and publication of data while maintaining confidentiality and anonymity. Due to observational nature of the study verbal consent was approved by the ERC.

Consent for publication

Not applicable.

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Data availability statement

Data included in article/supp. Material/referenced in article.

The datasets generated and/or analyzed during the current study are not publicly available due to restrictions by the data sharing policy of the institution but are available from the corresponding author on reasonable request.

CRediT authorship contribution statement

Rumana Sangi: Conceptualization, Project administration, Writing – review & editing. **Aliya Kemal Ahsan:** Data curation, Investigation, Writing – original draft. **Abdul Sattar Shaikh:** Project administration, Conceptualization, Funding acquisition. **Ali Raza:** Methodology. **Hussain Bux Korejo:** Investigation. **Veena Kumari:** Formal analysis, Visualization. **Musarat Nazir Sandano:** Data curation, Software. **Ume Rubab Sandano:** Data curation, Software.

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.

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