Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2023 Jan 02; 11(B):141-144.
https://doi.org/10.3889/oamjms.2023.11243
eISSN: 1857-9655
Category: *B - Clinical Sciences*
Section: *Pediatrics*

Factors Associated with Mortality in Children with Congenital Heart Disease and Cerebral Abscess

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Edited by: Eli Djulejic
Citation: Rahayuningsih SE, Budi R, Rayani P, Adrizain R, Lesmanawati DAS, Murni IK, Nopita I. Factors associated with mortality in children with congenital heart disease and cerebral abscess. Open Access Maced J Med Sci. 2023 Jan 02; 11(B):141-144. https://doi.org/10.3889/oamjms.2023.11243
Keywords: Cerebral abcess; Congenital heart disease; Mortality
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Received: 09-Nov-2022
Revised: 25-Nov-2022
Accepted: 15-Dec-2022

Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist

Abstract

BACKGROUND: In children, a cerebral abscess is a rare yet life-threatening condition. Children account for about 25% of all cerebral abscess cases in the general population. One of the most common predisposing factors for developing a cerebral abscess with increased mortality risk is congenital heart disease (CHD).

AIM: This study aims to determine the prevalence of death and factors associated with death in children with CHD and cerebral abscesses.

METHODS: This study is a cross-sectional design which collects retrospective data. Secondary data of CHD patients with cerebral abscesses were retrieved from patients' medical records.

RESULTS: From January 1, 2012, to December 31, 2021, a total of 107 children with a history of CHD were diagnosed with cerebral abscesses during this study. Thus, mortality rates in cases with cerebral abscess were 38.3% in children with a history of CHD. Patients with a focal infection in the ear, nose, and throat (ENT) area have a 3.6 times higher risk of dying than those with a focal infection elsewhere (odds ratio [OR] = 3.6 [95% confidence interval [CI], 1.57–8.32, p = 0.004). Patients who did not have neurosurgery had a 2.5- fold increased risk of death than those who did (OR = 2.5, 95% CI, 1.11–5.96, p < 0.05). Nutritional status, anemia status, and culture results, which were anticipated to be linked with death in CHD children with cerebral abscess, were not statistically significant.

CONCLUSION: We conclude that this study provides an overview of the prevalence of mortality and variables related to death in incidents of cerebral abscess in children with CHD in Indonesia.

Introduction

In children, a cerebral abscess is a rare yet life-threatening condition. Children account for about 25% of all cerebral abscess cases in the general population, primarily affecting those aged 4–7 years old [1]. The incidence is more common in boys than girls, with varied ratios ranging from 2:1 to 3:1 [2]. Despite the advancements in managing the etiology of cerebral abscess, late-treated patients, especially in low-resource countries, are still common, leaving a high burden of mortality and morbidity. One of the most common predisposing factors for developing a cerebral abscess with increased mortality risk is congenital heart disease (CHD). In recent decades, the incidence of cerebral abscess in patients with cyanotic CHD (CCHD) has reduced. According to Boston research, from 1981–2000 to 1945–1980, the ratio fell from 50% to 25% [3]. The decline in the number of patients happened most often in the age group >10 years, although the number of occurrences in children and newborns did not change. This reduction occurs in affluent countries when CHD can be diagnosed, treated with antibiotics, and corrected early. In comparison, this is still a big issue in developing countries. In developing countries, cerebral abscess accounts for roughly 8% of intracranial mass cases, while it accounts for only 1%–2% in developed countries. In developing nations, around half of all occurrences of brain abscess occur in children aged 0–20. A lack of proper infrastructure, nutritional circumstances that might accelerate infection, and a lack of resources to treat brain abscess conditions are all variables that influence this [4]. Brain abscess is a serious infection with poor outcome if diagnosed late. Delayed surgical drainage has high morbidity and mortality [5].

Cerebral abscess is common in children with uncorrected or partially corrected CCHD, and individuals who are between corrective procedures (>1 corrective surgery) are especially vulnerable [6]. A cardiogenic cerebral abscess usually occurs in the first decade of life, with an average age of 7.19 years. With a frequency of 5%–18%, heart disease is the second most common cause of secondary cerebral abscess in children. Because of the hematogenous spread of germs, brain abscesses in individuals with CCHD usually take the appearance of numerous lesions. Spot with several lesions in children under five is associated with a bad prognosis [7]. Children aged 6 months or above

with cerebral abscesses who manifested neurologic impairments had a worse prognosis. According to the previous study, the following conditions indicate a poor prognosis in CCHD patients with cerebral abscess: Decreased consciousness when admitted to the hospital; the presence of meningitis; antibiotic therapy was not started immediately after diagnosis; the lesion is located near the ventricle and is significant; aspiration surgery is not performed [7]. The mortality rate of cerebral abscess among children with a history of CHD varied greatly from 3.7% to 24%, depending on individual and environmental situations [3].

In pediatric patients with CHD, cases of cerebral abscess continue to be a significant health concern in Indonesia. They are suspected of causing a high number of child mortality. However, few studies have investigated the burden of disease of cerebral abscesses and CHD in developing countries, including Indonesia. This study aims to determine the prevalence of death and factors associated with death in children with CHD and cerebral abscesses.

Materials and Methods

This study is a cross-sectional design which collects retrospective data. Secondary data of CHD patients with cerebral abscesses were retrieved from patients' medical records. From January 1, 2012, to December 31, 2021, medical records were collected from Hasan Sadikin Central Hospital in Bandung, Indonesia. The study included that all pediatric patients aged 0–18 years old who had a history of CHD and were diagnosed with a cerebral abscess. Radiologists and neuropediatricians at Hasan Sadikin Hospital performed standard clinical criteria and a thorough computed tomography (CT)-scan examination to diagnose a cerebral abscess. Samples with incomplete medical records will be excluded. During the data collection process, all patients will be recruited consecutively.

Multiple variables, including dependent, independent, and other variables, were measured from the study population. The primary dependent variable, death status, is directly determined from medical records. Nutritional status, anemia status, type of focal infection, bacterial culture results, and whether the patients have neurosurgery were the independent variables that would become the essential measurements. This study separated certain infections that developed in the ear, nose, and throat (ENT) from conditions outside the ENT. Age, gender, anthropometric measurements, length of hospitalisation, type of CHD, and CHD complications are the other characteristics calculated in this study. Researchers collected data straight from electronic medical records at the study site. Paper-based CRF prepared previously is used to retrieve data from source documents. Ethical considerations were already approved from Hasan Sadikin hospital – Padjadjaran University Faculty of Medicine with number LB.02.01/X.6.5/236/2022.

The analysis will be done either descriptively or statistically. The prevalence of mortality will be presented as a frequency and a proportion in descriptive analysis. A variety of demographic and clinical characteristics will also be described using tables and narratives. Chi-square analysis with effect size Odds Ratio (OR) was performed to answer the hypothesis about what factors influence death in children with a history of CHD with a cerebral abscess. The Independent *t*-test will be used to analyze numerical data. The Mann–Whitney test is employed as an alternative for numerical variables that determine the mean difference between death cases and survival cases if data is not normally distributed. The Kolmogorov–Smirnov method is used to determine the distribution of numerical data. All data will be analyzed with $p < 0.05$ significance level and a 95% confidence interval (CI). IBM SPSS Statistics for Windows, version 26, will be used for analyzing (IBM Corp., Armonk, NY, USA).

Results

A total of 107 children with a history of CHD were diagnosed with cerebral abscesses during this study. Thus, mortality rates in cases with cerebral abscess were 38.3% in children with a history of CHD. The study sample's demographic and clinical characteristics are shown in Table 1.

Table 1: Demographic and clinical characteristics of samples (n = 107)

Characteristics	Mean+SD N(%)
Age (months), mean ± SD	68.9 ± 40.8
Sex, n (%)	
Males	45 (42.1)
Females	62 (57.9)
Weight (kg), mean ± SD	14.6 ± 6.7
Height (cm), mean ± SD	99.6 ± 24.3
Length of hospitalisation (days), mean ± SD	33.6 ± 14.8
Type of CHD, n (%)	
Ventricle septal defect	16 (15.0)
Patent ductus arteriosus	11 (10.3)
Complete atrioventricular septal defects	10 (9.3)
Pulmonary stenosis	13 (12.1)
Transposition of great arteries	9 (8.4)
Pulmonary atresia	12 (11.2)
Tetralogy fallot	28 (26.2)
Double outlet right ventricle	8 (7.5)
Complications of CHD, n (%)	
Heart failure	26 (24.3)
Cyanotic attack	12 (11.2)
Pulmonary hypertension	21 (19.6)
No complication	48 (44.9)

SD: Standard deviation, CHD: Congenital heart disease.

Table 1 shows that the mean age of the patients involved in this study was 68.9 months (approximately 5.7 years). Girls were the majority of the study sample, accounting for 62 persons (57.9%). Anthropometric measurements included weight and height, with an average of 14.6 kg and 99.6 cm, respectively. The average length of stay in the hospital was calculated

as long as 33.6 days. The three most common type of CHD found was the Tetralogy of Fallot with 28 (26.2%), ventricular septal defect 16 (15.0%), and pulmonary stenosis 13 (12.1%). Less prevalent diagnoses of CHD were pulmonary atresia, patent ductus arteriosus, complete atrioventricular septal defects, transposition of great arteries, and double outlet right ventricle. More than half (55.1%) of patients had complications, with the highest proportion being complications of heart failure (24.3%), pulmonary hypertension (19.6%), and cyanotic attack (11.2%).

Meanwhile, as indicated in Table 2, some factors are significantly associated with fatality in CHD children with cerebral abscess. Table 2 shows two statistically significant factors related to child death: Focal infection and neurosurgery intervention.

Table 2: Factors associated with mortality rate (n = 107)

Risk factors	Death (n = 41), *n* (%)	Survive (n = 66), *n* (%)	OR (95% CI)	p*-value
Nutrition status				
Adequate	26 (63.4)	40 (60.6)	1.1 (0.50−2.51)	0.771
Less adequate	15 (36.6)	26 (39.4)		
Status of anemia				
Yes	22 (53.7)	35 (53.0)	1.0 (0.47−2.24)	0.950
No	19 (46.3)	31 (47.0)		
Focal infection				
ENT	22 (53.7)	16 (24.2)	3.6 (1.57−8.32)	0.004
Others than ENT	19 (46.3)	50 (75.8)		
Cultures				
Positive	36 (87.8)	54 (81.8)	1.6 (0.52−4.93)	0.935
Negative	5 (12.2)	12 (18.2)		
Neurosurgery				
Not done	30 (73.2)	34 (51.5)	2.5 (1.11−5.96)	0.044
Done	11 (26.8)	32 (48.5)		

*Chi-square (continuity correction). OR: Odds ratio, 95% CI: Convidence interval, ENT: Ear nose throat.

Patients with a focal infection in the ENT area have a 3.6 times higher risk of dying than those with a focal infection elsewhere (OR = 3.6 (95% CI, 1.57–8.32, p = 0.004). Aside from focal infection, whether or not the patients had neurosurgery during their illnesses was also associated with the incidence of mortality. Patients who did not have neurosurgery had a 2.5-fold increased risk of death than those who did (OR = 2.5, 95% CI, 1.11–5.96, p < 0.05). Nutritional status, anemia status, and culture results, which were anticipated to be linked with death in CHD children with cerebral abscess, were not statistically significant.

Discussion

The incidence of cerebral abscess is around 8% of the total intracranial mass incidence in developing countries, while the incidence in developed countries is only 1%–2%. Most cases in developing countries occur in the group of 0–20 years old [8], [9]. In this study, we found that the mortality rate of cerebral abscess patients with a history of CHD is 38.3%. This finding is superior to the prior study in China which the overall mortality was 21.6%, with 50.0% of deaths happening in the 1st week after diagnosis [10]. Another study in Pakistan also shows that the mortality rate is lower than ours, with only 7.5% of prevalence[11].

The high mortality rate in this study may be due to several reasons. The first reason is the disease severity of the patients recruited in this study. Although it was not described in detail in this study, it can be seen that more than 50% of patients in this study have other complications, which will increase the severity of the disease. Moreover, other reasons may contribute to the high mortality rate. In the several previous studies stated that the poor prognosis in CCHD patients with cerebral abscess could be seen from the following conditions: (a) Decreased consciousness on admission to the hospital, (b) the presence of meningitis, (c) therapy antibiotics were not started immediately after diagnosis, (d) the lesion was located near the ventricle or was large, and (e) surgical aspiration was not performed [12]. A retrospective study stated that the time between diagnosis and antimicrobial therapy was 2 days on average [12]. Treatment of cerebral abscess in CCHD is controversial. Usually, large abscesses (more than 2 cm) are considered for aspiration or excision based on the surgical skills of the operator. The approach for multiple abscesses includes a long course (4–8 weeks) of high-dose antibiotics with or without aspirations, based on weekly CT scanning. The basic condition of heart in CCHD could make intervention much difficult and complex. The use of third-generation cephalosporins and metronidazole is currently the best recommendation [12], [13]. Vancomycin may be added if the cerebral abscess is suspected to be of staphylococcal origin [12].

This study also found that focal ENT infections carried a high mortality risk. There is no evidence that ENT infection is associated with a higher mortality rate in children with cerebral abscesses. According to a study by Gilard *et al*. [14], ENT infection was directly associated with a higher incidence of cerebral abscess in older children, whose prognosis was also poorer. Consequently, ENT factors may be linked to more severe infections. In addition to ENT infections, there are neurosurgical procedures for which patients who do not undergo surgery have an increased risk of death. This results from the drainage procedures associated with preventing critical conditions in children with cerebral abscesses. Delay in surgical procedure was associated with higher morbidity and mortality.

One of the strengths of this study is that it takes place in a tertiary hospital, with Hasan Sadikin Hospital providing the main referral hospital in West Java Province, Indonesia's most populous province. Therefore, the findings may demonstrate a robust regional-scale condition. This study's design and the use of a single site as a study setting are its weaknesses. It was a single-center study that may have affected demographic patient characteristics. Identifying risk factors using a cross-sectional design is not the optimal method, especially when combined with retrospective data and the possibility of missing data

and measurements for included variables. However, this study provides an overview of the prevalence of mortality and variables related to death in incidents of cerebral abscess in children with CHD in Indonesia. This study may provide better insight into undertaking the same topic research with a better study design.

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