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Original Article

Low peripheral oxygen saturation as a risk factor for brain abscess in children with cyanotic CHD

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Abstract

Background Brain abscess is a severe infection of brain parenchyma, which occurs in 25-46% of cases of uncorrected cyanotic (CHD). Low arterial oxygen saturation is the main risk factor for brain abscess in children with cyanotic CHD, however, the arterial oxygen saturation test is invasive and not routinely done in our setting.

Objective To evaluate low peripheral oxygen saturation as a risk factor for brain abscess in children with cyanotic CHD.

Methods We conducted a matched, case-control study at Sardjito Hospital, Yogyakarta, for children aged less than 18 years with cyanotic CHD, from 2010-2016. Case subjects were children with brain abscess complications. The control group had only cyanotic CHD, and were matched for age and sex to the case group. During hospitalization due to the brain abscess complication in the case group, data regarding peripheral oxygen saturation, polycythemia, pneumonia, sepsis, dental caries and restricted pulmonary blood flow were collected and compared between both groups.

Results During the study period, 18 children with cyanotic CHD had brain abscesses. This group was compared to the control group of 36 children. Bivariate analysis revealed that the lowest level of peripheral oxygen saturation (OR 0.92; 95%CI 0.85 to 0.98; P=0.02) and dental caries (OR 3.3; 95%CI 1.01 to 11.18; P=0.04) were significant risk factors for brain abscess. However, in the multivariate analysis, the only statistically significant risk factor associated with brain abscess was the lowest level of peripheral oxygen saturation (OR 0.92; 95%CI 0.86 to 0.99; P=0.04).

Conclusion Low peripheral oxygen saturation is a significant risk factor for brain abscess development in children with cyanotic CHD. A decrease of 1% peripheral oxygen saturation may increase the risk of brain abscess by 8%. **[Paediatr Indones. 2018;58:252-6; doi: http://dx.doi.org/10.14238/pi58.5.2018.252-6]**.

Keywords: *brain abscess; cyanotic heart disease; peripheral oxygen saturationrisk factors*

Brain abscess is a severe infection of brain tissue that can be caused by bacteria, fungi, protozoa, and parasites.[1-3] The mortality rate caused by brain abscess is about 10%.[1]

Cyanotic congenital heart disease (CHD) with right-to-left shunt is one of the most frequent predisposing factors to brain abscess in children.[1,4] Of children with cyanotic CHD, 5-18% develop brain abscess complications.[1] Past studies from 1974 at Boston Children's Hospital and 1992 at the Neurological Institute and Heart Institute of Japan showed that the level of arterial oxygen saturation (SaO_2) in the abscess group was significantly lower than in the control group, in children with cyanotic CHD.[5,6]

Indonesia has an estimated 50,000 babies born with CHD every year. Like other developing countries, most patients with CHD seek medical treatment at later ages to have corrective cardiac surgery, which increases the risk of brain abscess complication. The oxygen saturation (SaO_2) level can be detected by

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arterial blood gas analysis, however, this examination is not done routinely in our setting, because it is invasive and expensive. Oxygen saturation can also be estimated by peripheral oxygen saturation level (SpO_2), as detected by pulse oximetry. The SpO_2 level considered to be a risk factor for brain abscess is still unclear. Hence, we aimed to evaluate low peripheral oxygen saturation as a risk factor for brain abscess in children with cyanotic CHD.

Methods

A matched, retrospective, case-control study was conducted in Dr Sardjito Hospital, Yogyakarta, from 2010 until 2016. Data were collected from medical records. Inclusion criteria for the case group were age between 1 month-18 years with diagnoses of brain abscess and cyanotic CHD, while the control group had only cyanotic CHD patients. The control group was matched for age and sex with the case group, at a ratio of 2:1. The exclusion criteria were incomplete medical records or cases of cyanotic CHD who had undergone corrective heart surgery.

Nutritional status was determined with WHO growth chart (normal: weight for age and weight for height between 2SD and -2SD, undernourished: weight for age or weight for height < -2SD, severe malnutrition: weight for age or weight for height < -3SD, and stunted: height for age <-2SD). Developmental status was determined using Denver II developmental screening test and was assesed in 4 major milestones aspect of which were, personal social, fine motor, language and gross motor aspect (normal: no developmental delay, delayed: delay in no more than 1 aspect, global developmental delay: delay in 2 or more aspect); and immunization status was classified as completed or not based on *National Immunization Programme* of Indonesia based on the age of subject.[8]

The SpO_2 levels recorded were the highest and lowest during hospitalization for every subject. The mean was calculated based on adding the highest and lowest SpO_2 values and dividing by two.

Data were collected and analyzed with *STATA 12.0.* Bivariate analysis using paired sample T-test or Wilcoxon signed rank test for numerical data, and P values <0.05 were considered to be statistically significant. Bivariate odds ratio (OR) for numerical data (SpO_2) was obtained by logistic regression with only SpO_2 as the predictor variable. Multivariate analysis using conditional logistic regression was done for the significant variables from the bivariate analysis. Results are reported as OR with 95% confidence interval (CI).

The study was approved by the Medical and Health Research Ethics Committee (MHREC), Universitas Gadjah Mada Medical School/Dr. Sardjito General Hospital, Yogyakarta.

Results

A total of 18 cases of brain abscess in children with cyanotic CHD were found in the 7-year study period. This case group was compared to the control group who had been matched for sex and age, at a 2:1 ratio (36 controls). The baseline characteristics of subjects are described in **Table 1**. Overall, the subjects' mean age was 7 years, and most subjects were male (83.3%). Stunting was frequently found in the case group (66.6%) and in the control group (50%).

The outcomes of the case group are described in **Table 2**. Abscess drainage was done only in 5 cases (27.7%). The abscess fluid culture results in subjects with abscess drainage were *Pasteurella pneumotropica*, *Eschericia coli*, and *Staphylococcus warneri*, while in 2 cases there were no growth. Antibiotics were given based on sensitivity and resistance results.

Bivariate analysis revealed that the mean lowest SpO_2 in the case group was significantly lower than that of the control group (P=0.02) (**Table 3**).

Bivariate and multivariate analyses were done to identify the confounding factors possibly contributing to the brain abscess incidence. Sepsis, pneumonia, and restricted pulmonary blood flow (PBF) could not be further analyzed because these variables each had a total of subjects below 5 in the case or control group.

Bivariate analyses revealed that lowest SpO_2 level during hospitalization was inversely associated with the occurrence of brain abscess (OR 0.93; 95%CI 0.86 to 0.99; P=0.023). Another significant variable for risk of brain abscess was dental caries (OR 3.3; 95%CI 1.01 to 11.18; P=0.04). Polycythemia had no significant correlation to brain abscess (OR 1.18;

Table 1. Baseline characteristics of subjects

Characteristics	With brain abscess (n=18)	Without brain abscess (n=36)
Mean age (SD), years	7.8 (4.4)	7.8 (4.4)
Sex		
Male, n (%)	15	30
Nutritional status, n		
Normal	6	14
Undernourished	6	15
Malnutrition	6	7
Stunted	12	18
Developmental status, n		
Normal	12	30
Delayed	3	2
GDD	3	4
Immunization status, n		
Complete based on NIP	11	35
Incomplete	7	1
Mean age at diagnosis of cyanotic CHD (SD), months	14.8 (22.4)	28.5 (41.5)
Type of cyanotic CHD, n		
TF	9	19
TGA	3	7
DORV	4	8
Pulmonal atresia	2	2
History of catheterization, n	6	27
History of spells, n	6	18
Heart failure, n	7	8

SD= standard deviation, GDD= global development delay, NIP=*National Immunization Programme,* TF=Tetralogy of Fallot, TGA=transposition of great arteries, DORV=double outlet of right ventricle

Table 2. Outcomes of cyanotic CHD subjects with brain abscess

Outcomes	With brain abscess (n=18)
Main symptoms, n	
Fever	14
Seizure	8
Vomiting	8
Headache	10
Neurological deficits	3
Decreased consciousness	1
Mean length of stay (SD), days	47.6 (24)
Brain abscess characteristics	
Location, n*	
Cerebellum	1
Thalamus	1
Brainstem	1
Fronto-parietal lobe	3
Parieto-occipital lobe	2
Parieto-temporal lobe	4
Occipital lobe	1
Parietal lobe	6
Number of abscesses, n	
Single	7
Multiple	11
Other main findings in head CT-scan, n	
Brain edema	8
Ventriculomegaly	8
Intracranial bleeding	4
Midline shift	4
Management, n	
Adequate antibiotics	7
Inadequate antibiotics	6
Abscess drainage	5
Outcomes, n	
Died	3
Lived with neurological sequelae	8
Lived without neurological sequelae	7
Neurological sequelae, n	
Seizure	1
Paresis	6
Seizure and paresis	1

*one subject had abcesses in both the parieto-occipital lobe and thalamus, hence counted as 2 subjects

Table 3. Peripheral oxygen saturation level as a risk factor of brain abscess in patient with cyanotic CHD

Risk factors	With brain abscess (n=18)	Without brain abscess (n=36)	P value *
Median of SpO_2 (IQ range)	73.5 (66-76)	75.5 (72-81)	0.27
Median highest SpO_2 (IQ range)	81.5 (78-87)	83.5 (78-88)	0.98
Mean lowest SpO_2 (SD)	63.0 (10.1)	70.3(7.6)	0.02

SpO_2=peripheral oxygen saturation, SD=standard deviation, IQ=interquartile, *=paired sample T-test/Wilcoxon signed rank

Table 4. Risk factor of brain abscess in children with cyanotic CHD

Risk factors	With brain abscess (n=18)	Without brain abscess (n=36)	Bivariate analysis		Multivariate analysis	
			OR (95%CI)	P value	aOR (95%CI)	P value
Mean lowest SpO2 level (SD)	63.0 (10.1)	70.3 (7.6)	0.92 (0.85 to 0.98)	0.02	0.92 (0.86 to 0.99)	0.04
Polycythemia, n	6	13	1.18 (0.37 to 3.75)	0.77	-	-
Sepsis, n	8	1	-	-	-	-
Pneumonia, n	2	0	-	-	-	-
Dental caries, n	10	9	3.3 (1.01 to 11.1)	0.04	2.7 (0.75 to 10.21)	0.12
Restricted PBF, n	16	36	-	-	-	-

SpO_2=peripheral oxygen saturation, SD=standard deviation, OR=odds ratio, aOR=adjusted odds ratio, CI=confidence interval, PBF=pulmonary blood flow

95%CI 0.37 to 3.75; P=0.77). Multivariate analysis on the significant variables in the bivariate analysis revealed that the only significant risk factor for brain abscess was the lowest SpO_2 level (OR 0.92; 95%CI 0.86 to 0.99; P=0.04) (**Table 4**).

Discussion

In a 7-year period, there were 18 subjects with brain abscess and cyanotic congenital heart disease. Subjects' mean age was 7 years and the youngest subject was 2 years of age. These data support the previous evidence which concluded that the brain abscess formation rarely happen on infants (<1 year old).[7] Bacteremia episodes in infants are extremely rare. Also, den-tation has been theorized as the most frequent source of intermittent bacteremia, so younger children with incomplete tooth growth may be less prone.[8]

The outcomes of our serial 18 brain abcess cases were as follows: 3/18 subjects died, 8/18 subjects lived with neurological sequelae and 7/18 subjects lived without neurological deficits. Similarly, a previous study in 2006 reported that 16% of subjects died, 53% lived with neurological sequelae, and 30% lived without neurological sequelae.[1]

Our study demonstrated that the main risk factor for brain abscess in children with cyanotic congenital heart disease was the low level of peripheral oxygen saturation recorded. Peripheral oxygen saturation measurement is non-invasive, and therefore, frequently used as an estimate of arterial oxygen saturation. Previous study concluded that the main risk factor was the low level of arterial oxygen saturation, however, there has been limited study on peripheral oxygen saturation as a risk factor of brain abscess. Fischbein *et al.* reported that the level of arterial oxygen saturation was a significant risk factor (P<0.01).[5] In addition, Takeshita et al. showed that the mean level of SaO_2 in 21 subjects with cyanotic congenital heart disease and brain abscess [67.2 (SD 12.5)%] was significantly lower than the control group [79.7 (SD 10.3)%], with P<0.01.[6] We also found that the lowest mean SpO_2 level in the abscess group [63.05 (SD 10.1) %] was significantly lower than in the group without brain abscess [70.38 (SD 7.6) %], with P=0.02.

We found no significant difference in SpO_2 for mean and median highest level between groups. This inconsistency might have been caused by the high variation in SpO_2 values recorded by pulse oximetry,

caused by certain conditions[9,10] that could not be controlled in this study, such as light (bright light directly to probe may affect the reading), shivering (movement may cause difficulty for the probe to pick up signal), pulse volume (low pulsatile in shock condition and arrhtythmia may also affect the reading), vasoconstriction, and also oxygen supplementation given to the subjects. The weakness of this study was that the data used were based on medical records, therefore, we do not know if such conditions occurred during the SpO_2 recording.

Other possible risk factors for brain abscess incidence were polycythemia, sepsis, pneumonia, dental caries, and restricted pulmonary blood flow. However, polycythemia was not a significant risk factor of brain abscess in this study (P=0.77), a finding similar to a previous study in which no hemoglobin or hematocrit level differences were noted between groups.[5,6]

There were 10/18 (55.5%) subjects with dental caries in the case group, but only 9 (25%) subjects with dental caries in the control group. Dental caries incidence was significantly different between groups, on bivariate analysis (P=0.04). High incidence of dental caries in patients with brain abscess suggests that dental infection might be a bacterial port d'entry to the blood circulation, leading to brain abscess formation.[11] However, this finding should be studied further by comparing the bacterial agents causing the brain abscess and the dental caries.

Multivariate analysis was also done for the significant variables from the bivariate analysis, revealing that only the lowest SpO_2 level consistently had a significant inverse association with the occurrence of brain abscess (P=0.04). The OR point estimate signifies that a 1% decrease of lowest SpO_2 level lowers the odds of developing a brain abscess by 0.93 (95%CI 0.86 to 0.99) times the patient's baseline odds.

A weakness of this study was the small sample size and retrospective design for which complete medical records are very important. The strength of this study was that it was the first of such studies in Yogyakarta, Indonesia. Our intital findings reported here provide basic data on evaluation of risk factors and outcomes of brain abscess in children with cyanotic congenital heart disease in Indonesia. In conclusion, low peripheral oxygen saturation is the main risk factor for brain abscess in children with cyanotic congenital heart disease.

Conflict of Interest

None declared.

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