# Left to right shunt congenital heart disease as a risk factor of recurrent pneumonia in under five-year-old children: a single centre experience in Bandung Indonesia

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# ABSTRACT

Aim Children with congenital heart diseases are at the greater risk of respiratory tract infection such as pneumonia. Recurrent pneumonia is one of the most major challenge for paediatric physicians. The aim of this study is to investigate risk factors of congenital heart diseases to recurrent pneumonia children.

**Methods** This was a retrospective study of under five-year-old children hospitalized in Hasan Sadikin General Hospital Bandung Indonesia from 2015 to 2018. Congenital heart diseases and pneumonia, as well as recurrent pneumonia, were identified. Congenital heart diseases diagnosis with and without pneumonia were reviewed.

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**Results** Of 6997 hospitalized children, in 1258 (18.0%) congenital heart diseases were found, of which 232 (18.4%) had recurrent pneumonia. Most of those had left to right (L to R) shunt, 213 (91.8%). Congenital heart diseases in children aged under 1 year, 144 (62%) were more preponderant than in those aged 1–5 years. More than a half, 119 (51.3%) were males. Left to right shunt was documented as having recurrent pneumonia, of which patent ductus arteriosus and ventricular septal defect were the most common type in congenital heart diseases. Ventricular septal defect had a possibility for recurrent pneumonia by 1.551 times, and malnutrition 2.591 times.

**Conclusion** Ventricular septal defect and malnutrition were identified as risk factors for recurrent pneumonia. Those patients require multidisciplinary approach to prevent respiratory complications.

**Key words**: cardiac defect, child, complication, heart murmur, ventricular septal defect

# INTRODUCTION

The incidence of congenital heart diseases is about 1% in the general population and ranges from 4-50 cases per 1000 live births (1). In Indonesia, incidence for live birth is around 4,6 million every year (2). It is estimated that every year many babies were born with congenital heart diseases. The frequency of CHD is almost the same in every ethnic group and region of the world (3). Left to right (L to R) shunt was the most common type of congenital heart diseases, with ventricular septal defect at least 20% from all defects, atrial septal defect up to 2% and patent ductus arteriosus approximately 10% (4).

The presence of congenital heart diseases caused a significant defect of structure or function of the circulation system, which will then also affect the respiratory system function (5). Direct pulmonary complications of congenital heart diseases are either by structural impact on the airways, abnormal pathophysiological mechanisms leading to increased lung water and/or significant pulmonary disease (5).

Patients with congenital heart diseases often come to hospital with non-cardiac complications such as infection, especially respiratory tract infection like pneumonia (6). Pneumonia as the comorbidity in the paediatric patient of congenital heart diseases may extend the length of stay and complicate the treatment for the congenital heart disease (6). In developing countries infants with hemodynamically significant congenital heart diseases at 70% had recurrent pneumonia (7). The incidence of left to right shunt with recurrent pneumonia has not been studied yet.

In developing countries, mortality of the children with congenital heart disease and pneumonia is increasing (8). A lack of epidemiological studies from developing countries, including Indonesia, makes it difficult to plan even national/local strategies for the prevention and treatment.-

The aim of this study was investigate left to right shunt type of congenital heart disease as a risk factor of the recurrent pneumonia in the children.

# PATIENTS AND METHODS

# Patients and study design

This was a retrospective study of under five-year-old children hospitalized in Hasan Sadikin General Hospital from 2015 to 2018. Hasan Sadikin Hospital, Bandung, Indonesia is the largest tertiary hospital in West Java, Indonesia, serving more than 38 thousand population every year. This hospital is a referral hospital, where most of the paediatric heart problems are referred to. Paediatric cardiac interventions are performed by one paediatric cardiologist. Catheterization is only done 2 days in a week.

This study was approved by the Health Research Ethics Committee of Hospital Dr Hasan Sadikin Bandung Indonesia.

#### Methods

This study was conducted by identifying congenital heart diseases (Q20–Q26 and pneumonia children (J18) (International Statistical Classification of disease ICD-10) (9). Further, recurrent pneumonia, defined as the repeated pneumonia more than one time in a year with clinical improvement but without documented clearance of chest x ray, was identified.

We reviewed congenital heart disease diagnoses with and without pneumonia, a type of congenital heart diseases including left to right (L to R) shunt type (isolated atrial septal defect, ventricular septal defect and patent ductus arteriosus), cyanotic type (tetralogy of fallot and transient great artery, obstruction type (aorta stenosis) post correction surgery/intervention, and epidemiology data (gender and age, cerebral palsy, nutritional status, breastfeeding, low birth weight history and environmental factors - smoke exposure).

#### Statistical analysis

Both descriptive and analytical analysis were conducted. Descriptive analysis was performed with data expressed as frequency and percentage for categorical data. For analytical analysis  $\chi^2$  test or Fisher exact test was used. Bivariate statistical analysis continued with multivariate logistic regression was conducted to analyse prominent risk factors that relate simultaneously to the outcome. Risk was analysed using odd ratio (OR) with confidence interval 95%. Statistical significance of p<0.05 was applied.

#### RESULTS

Of 6997 hospitalized children in the 2015-2018 period, in 1258 (18.0%) congenital heart diseases were identified. Of those, 232 (18.4%) had

recurrent pneumonia. Frequently identified congenital heart diseases type was L to R shunt, 1155 (91.8%). Only the patients with recurrent pneumonia with left to right shunt were included in the analysis, considering only a few patients with cyanotic type, obstructive and post transcatheter closure. Two patients with post patent ductus arteriosus closure were identified as having recurrent pneumonia with cerebral palsy and Down Syndrome as an underlying disease (Figure 1).



Figure 1. Congenital heart disease and recurrent pneumonia in the period 2015 – 2018

Congenital heart diseases among children under 1 year of age were more preponderant than those aged 1-5 years, 144 (62%) and 88 (38%, respectively. More than a half, 119 (51.3%) were males. Ventricular septal defect (VSD) was the most common type of congenital heart diseases followed by patent ductus arteriosus (PDA), and both of those significantly become a risk factor in recurrent pneumonia patients (p=0.001 and p=0.001 respectively) (Table 1).

Table 1. Risk factors and comorbidities in children with and without recurrent pneumonia

No (%) of patients		_
Recurrent pneumonia	Without pneumonia	р
93 (41.7)	143 (24.8)	0.001
41 (19.2)	115 (20.0)	0.823
79 (37.1)	318 (55.2)	0.001
26 (12.2)	146 (25.3)	0.0001
134 (62.9)	252 (43.8)	0.0001
27 (12.7)	82 (14.2)	0.573
28 (13.1)	108 (18.8)	0.064
213	576	
	Recurrent pneumonia   93 (41.7)   41 (19.2)   79 (37.1)   26 (12.2)   134 (62.9)   27 (12.7)   28 (13.1)	Recurrent pneumonia Without pneumonia   93 (41.7) 143 (24.8)   41 (19.2) 115 (20.0)   79 (37.1) 318 (55.2)   26 (12.2) 146 (25.3)   134 (62.9) 252 (43.8)   27 (12.7) 82 (14.2)   28 (13.1) 108 (18.8)

VSD, ventricular septal defect; ASD, atrial septal defect; PDA, patent ductus arteriosus

There were only 26 patients who had history of exclusive breastfeeding; 147 patients had malnu-

trition, only 27 patients were with history of low birth weight (LBW). Cerebral palsy was found in 28 (13.1%) patients.

Of seven risk factors analysed for recurrent pneumonia, two showed statistical significance (p>0.25), namely isolated atrial septal defect and LBW; so that for multivariable analysis with multiple logistic regression these two variables were not included in the analysis.

Ventricular septal defect had a possibility for recurrent pneumonia by 1.551 times greater than atrial septal defect. Patent ductus arteriosus times was by 0.652 lower than atrial septal defect for the possibility of becoming recurrent pneumonia. As other comorbidities, malnutrition had 2.591 times risk for recurrent pneumonia (Table 2).

Table 2. Multivariable analysis of comorbidities in congenital heart diseases left to right shunt in children with recurrent pneumonia (final model)

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Variable	р	OR <sub>adj</sub> (95% CI)	
Isolated VSD	0.042	1.551 (1.020 - 3.201)	
Isolated PDA	0.033	0.652 (0.444 - 0.956)	
Malnutrition	0.001	2.591 (1.791 - 3.749)	
Exclusive breastfeeding	0.001	0.280 (0.172 - 0.456)	

VSD, ventricular septal defect; ASD, atrial septal defect; PDA, patent ductus arteriosus;  $OR_{adj}$  (95% CI), odds ratio adjusted and 95% confidence interval;

# DISCUSSION

This study found 18% of congenital heart diseases from the total number of hospitalized children under five years of age. So far we have not found similar data in any other study. According to one single centre study in Vietnam, 10074 congenital heart diseases patients were hospitalized during the past 6 years (10). To our knowledge, this is the first study to explore congenital heart diseases with recurrent pneumonia in our setting.

The previous study in Canada demonstrated that most child patients hospitalized with recurrent pneumonia were known to have an underlying illness at the time of pneumonia recurrence, one of those was congenital heart disease (8). We found 18.4% recurrent pneumonia cases among the children under five years of age with congenital heart disease. The most frequently identified congenital heart disease type was left to right shunt (91.8%).

We are still using "recurrent pneumonia" as terminology in this study, but we cannot conduct radiologic examination after the patients' recovery to confirm the diagnosis due to our limitations such as the cost for patient care and queuing

for X-ray examination by inpatients. A previous study in Turkey in three years of observation demonstrated that 50 patients with congenital heart diseases were hospitalized due to pneumonia, of which acyanotic type was the most common (76%) and 68% of patients were under 1 year of age (1). In our study, there were 62% of children under 1 year of age with congenital heart disease who had recurrent pneumonia comparing to 38% of children aged 1-5 years with the most frequently identified congenital heart disease type left to right shunt (91.8%). In general, our research has a similar result with the study conducted in Turkey (1). A previous study showed the highest incidence of pneumonia occurred in the youngest patients with the incidence decreasing gradually with increasing age: the attack rates for pneumonia are 1/100 in infants (<1 year), 4/100 preschool age, 2/100 at school age (5-9 years), and 1/100 at ages 9-15 years (11).

To diagnose the recurrent pneumonia, clinical evaluation should be conducted carefully. The evaluation also included history of age of the first chest infection, cough nature, duration and pattern, premature delivery, growth history, tuberculosis (TB) history, and parental smoking (12). Recurrent pneumonia is still a diagnostic challenge in paediatrics. Early treatment of the child's underlying condition is crucial in order to stabilize lung disease and thus prevent progressive pulmonary function deterioration (13). We also collected other risk factor data in our study such as smoke exposure, Down syndrome, hypothyroid congenital, TB history and premature delivery but we excluded all those because of incomplete data from medical records.

In this study, there were only 32 (out of 213) patients who were known to have been exclusively breastfed. A previous study in India stated that a lack of breastfeeding had been reported to be associated with an increased risk of the development of severe pneumonia by 1.5 to 2.6 times (14). It was known that lack of exclusive breastfeeding was identified to be an important determinant associated with the need for a change in antibiotics and prolonged hospital stay in severe pneumonia (14). Furthermore, acute malnutrition and lack of breastfeeding are considered to be factors associated with increased mortality in children due to pneumonia (14). In our study malnutrition was the only risk factor the increase 5.556 times for recurrent pneumonia. Previous studies showed that mortality risk increased among severely malnourished children with pneumonia (15). High mortality risk can be linked to immunodeficiency associated with malnutrition, high rates of comorbidities, delayed health-seeking behaviour among families of children with malnutrition, and potential delays in diagnosis due to the insensitivity of clinical signs (15).

History of low birth weight in our study was found in 12 patients. Previous studies showed that low birth weight had been associated with the development of severe pneumonia, as well as to be a risk factor for increased mortality (14).

Initial pulmonary hypertension (PH) that occurs in the L to R shunt, such as VSD, atrial septal defect and PDA, will cause high flow PH; however, if this continues, it will cause damage to the intima media of lung tissue and will be replaced by fibrosis which will cause high PH resistance that has a poor prognosis (5). In our study not all patients with PH performed right heart catheterization to determine PH high flow or PH high resistance, suggesting that it is not known whether the recurrence is caused by a high resistance PH or other lung abnormalities (5).

The most common causes of recurrent pneumonia are L to R shunt of congenital heart diseases, VSD, atrial septal defect and PDA, which cause an overflow to the lungs (5). According to our study VSD had a significant influence for higher prevalence of recurrent pneumonia. In our research VSD was higher comparing to PDA. Other studies explain that hospital admission for pneumonia in young children with haemodynamically significant congenital cardiac disease is mainly associated with non-cardiac conditions, which may be genetic, respiratory or caused by malnutrition (3).

There are some limitations of the study. The single-centre study population may also not be representative of all children with congenital heart diseases and recurrent pneumonia. Besides, we did not further divide malnutrition to subcategories (wasted, severely wasted or obesity).

In conclusion, ventricular septal defect and malnutrition are both risk factors for recurrent pneumonia. Those patients require multidisciplinary approach to prevent respiratory complications.

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# TRANSPARENCY DECLARATION

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