

Risk Factors of Bacteremia in Children with Community Acquired Pneumonia

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Abstract

Background: Pneumonia is the leading cause of infectious death in children worldwide. Community Acquired Pneumonia (CAP) is pneumonia obtained in communities where bacteria are the most common cause in children. Bacteremia accompanied by pneumonia has the potential to threaten life in children but the risk factors for bacteremia with pneumonia are not yet clear.

Objective: To study the risk factors of bacteremia in children with CAP

Methods: This was a case control observational study used pediatric inpatient medical records from January 2014-December 2018

Results: There were 275 subjects who met inclusion and exclusion criteria and 45(16.4%) of them had positive blood cultures. Therefore, 90 subjects were included in this study with a mean (\pm SD) age of 23.57(\pm 43.28) and most of them were male (60%). *Klebsiella pneumonia* was the causative pathogen of most cases (22.2%). In bivariate analysis, it was found that malnutrition (OR 35.2; 95% CI 4.45-278.25; $p=0.000$), congenital heart disease (OR 6.83; 95% CI 2.09-22.4; $p=0.001$) and hematological disease (OR 12.57; 95% CI 1.54-102.97; $p=0.004$) were the risk factors of bacteremia in children with CAP. Meanwhile, multivariate analysis showed only malnutrition that had relationship with bacteremia in children with CAP (Exp(B) 0.027; CI 95% 0.003-0.231; $p=0.001$)

Conclusion: Malnutrition was significant risk factors of bacteremia in children with CAP

Key words: *Pneumonia, Community-Acquired Pneumonia, bacteremia, risk.*

Introduction

Community Acquired Pneumonia (CAP) is defined as an acute symptomatic lower respiratory tract infection (LTRI) in patient outside hospital or long-term treatment facilities with new pulmonary infiltrates¹ and majority are caused by bacteria.² Pneumonia is a leading cause

of death of infectious diseases in children throughout the world and contributes around 15% of all deaths of children under 5 years old.³ In Indonesia, the 2014 Sample Registration System results stated that pneumonia was the 3rd leading cause of death in children under five in Indonesia, amounting to 9.4% of the number of under-five deaths.⁴ Pneumonia with bacteremia is life threatening for children² and children under five years old have a greater incidence of bacteremia.⁵ The previous study conducted in Surabaya reported that the incidence of bacteremia in children with pneumonia varies from 4%-18%.² Bacteremia can lead to septicemia with a high mortality rate that varies between 30-70% depends on several factors, such as pathogenic virulence and host factors.⁶ There are still uncertainties about risk factors

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that affect bacteremia in pneumonia.⁷ By knowing these risk factors, it is expected that health professionals can quickly and accurately identify and provide prompt management and evaluation to reduce mortality and morbidity of pneumonia. Therefore, this study aim is to study risk factors of bacteremia in children with CAP.

Methods

This case control observational study conducted in Dr. Soetomo General Hospital, Surabaya, Indonesia. This study used pediatric medical records who were diagnosed with CAP clinically period of January 2014-December 2018. The inclusion criteria were children aged 1 month old–18 years old, diagnosed with CAP based on WHO criteria, confirmed by chest radiography,⁸ and underwent blood culture within 48 hours after hospital admission. The subjects whose incomplete medical

records and the blood culture showed fungal infection were excluded. The subjects were divided into case group and control group. Case group, who had positive blood culture. Control group consisted negative blood culture. Matching was done based on age with case groups. After age grouping, subjects for control group were chosen randomly at ratio of 1:1 to the number of subjects from case group. Those data were collected as risk factors: age, sex, low birth weight, prematurity, and comorbid diseases such as malnutrition,^{9,10} congenital heart disease, neuromuscular diseases, hematologic disease, and HIV (Human Immunodeficiency Virus) infection. After all data collected, bivariate analysis would be performed on each risk factor by Chi-square and the risk factors which had p value<0.25 would be further analyzed by logistic regression. All analysis was

Table 1. Characteristic of Subjects

| Characteristic of Subjects | Case Group (N=45) N(%) | Control Group (N=45) N(%) |
|----------------------------|---------------------------|------------------------------|
| Age <3 months old | 12 (26,7) | 12 (26,7) |
| 3 months-1 year old | 18 (40,0) | 18 (40,0) |
| >1 year old | 15 (33,3) | 15 (33,3) |
| Sex Male | 30 (66,7) | 24 (53,3) |
| Female | 15 (33,3) | 21 (46,7) |
| Low Birth Weight | 8 (17,8) | 8 (17,8) |
| No | 37 (82,2) | 37 (82,2) |
| Premature | 5 (11,1) | 5 (11,1) |
| No | 40 (88,9) | 40 (88,9) |
| Nutritional Status | | |
| Severe malnutrition | 9 (20,0) | 1 (2,2) |
| Malnutrition | 11 (24,4) | 0 (0,0) |
| Normal | 25 (55,6) | 44 (97,8) |
| Comorbid diseases | 35 (77,8) | 32 (71,1) |
| No | 10 (22,2) | 13 (28,9) |
| Malnutrition | 20 (44,4) | 1 (2,2) |
| No | 25 (55,6) | 44 (97,8) |
| Congenital Heart Disease | 18 (40,0) | 4 (8,9) |
| No | 27 (60,0) | 41 (91,1) |
| Hematologic Diseases | 10 (22,2) | 1 (2,2) |
| No | 35 (77,8) | 44 (97,8) |

Cont... Table 1. Characteristic of Subjects

| | | |
|------------------------|-----------|-----------|
| Neuromuscular Diseases | 17 (37,8) | 22 (48,9) |
| No | 28 (62,2) | 23 (51,1) |
| HIV | 1 (2,2) | 1 (2,2) |
| No | 44 (97,8) | 44 (97,8) |
| Lung infiltrates | 40 (88,9) | 40 (88,9) |
| No | 5 (11,1) | 5 (11,1) |
| Lung consolidation | 17 (37,8) | 18 (40,0) |
| No | 28 (62,2) | 27 (60,0) |
| Pleural effusion | 5 (11,1) | 2 (28,6) |
| No | 40 (88,9) | 43 (95,6) |
| Lung atelectasis | 13 (28,9) | 11 (24,4) |
| No | 32 (71,1) | 34 (75,6) |
| Anemia | 19 (42,2) | 15 (33,3) |
| No | 26 (57,8) | 30 (66,7) |
| Leukocytosis | 21 (46,7) | 20 (44,4) |
| No | 24 (53,3) | 25 (55,6) |
| Thrombocytopenia | 8 (17,8) | 8 (17,8) |
| No | 37 (82,2) | 37 (82,2) |

Table 2. Profiles of Pathogenic Bacteria

| Pathogenic Bacteria (N=45) | N(%) |
|--|-------------|
| Klebsiella pneumonia (ESBL+ 1 patient) | 10 (22,22) |
| Staphylococcus aureus | 8 (17,80) |
| Pseudomonas aeruginosa | 5 (11,11) |
| Staphylococcus haemolyticus | 4 (8,89) |
| Acinetobacter baumannii | 3 (6,67) |
| Staphylococcus epidermidis | 3 (6,67) |
| Micrococcus luteus | 2 (4,44) |
| Streptococcus viridans | 2 (4,44) |
| Escherichia coli (ESBL+ 1 patient) | 2 (4,44) |
| Corynebacterium matruchotii | 1 (2,22) |
| Klebsiella oxytoca ESBL+ | 1 (2,22) |
| Staphylococcus MRSA | 1 (2,22) |
| Sternotrophomonas maltophilia | 1 (2,22) |
| Brevibacterium sp. | 1 (2,22) |
| Achromobacter sp. | 1 (2,22) |

Table 3. Bivariate Analysis of Risk Factors of Bacteremia in Children with CAP

| Variables | OR | CI 95% | p |
|------------------------------------|--------|---------------|---------|
| Age <3 months old >3 months old | 1.000 | 0.393-2.546 | 1.000# |
| Sex Male Female | 1.750 | 0.746-4.106 | 0.197# |
| Low Birth Weight | 1.000 | 0.339-2.947 | 1.000# |
| Premature | 1.000 | 0.269-3.724 | 1.000# |
| Comorbid Diseases | 1.422 | 0.548-3.690 | 0.486# |
| Malnutrition | 35.200 | 4.453-278.253 | 0.000*# |
| Congenital Heart Disease | 6.833 | 2.084-22.402 | 0.001*# |
| Hematologic Disease | 12.571 | 1,535-102,970 | 0.004*# |
| Neuromuscular Disease | 0.635 | 0.274-1.470 | 0.635# |
| HIV | 1.000 | 0.061-16.496 | 1.000# |

*p<0.05 was considered statistically significant

#Chi Square test was used

(OR=Odd Ratio)

Table 4. Multivariate Analysis Model of Risk Factors of Bacteremia in Children with CAP

| Variable | Exp(B) | CI 95% | p |
|--------------------------|--------|-------------|---------|
| Sex | 0,344 | 0,112-1,051 | 0,061# |
| Malnutrition | 0,049 | 0,005-0,478 | 0,009*# |
| Congenital Heart Disease | 0,370 | 0,079-1,724 | 0,205# |
| Hematologic Disease | 0,054 | 0,011-1,035 | 0,107# |

*p<0.05 was considered statistically significant

#Logistic Regression test was used

Table 5. Multivariate Analysis Model of Risk Factors of Bacteremia in Children with CAP

| Variable | Exp(B) | CI 95% | p |
|--------------|--------|-------------|---------|
| Malnutrition | 0,027 | 0,003-0,231 | 0,001*# |
| Constant | 4,020 | | 0,004 |

* $p < 0.05$ was considered statistically significant

#Logistic Regression test was used

Abbreviations and Symbols

| | |
|-----|------------------------------|
| CAP | Community Acquired Pneumonia |
| CHD | Congenital Heart Disease |
| CI | Confidence Interval |
| HIV | Human Immunodeficiency Virus |
| WHO | World Health Organization |

performed by IBM SPSS 21.

Results

There were 275 subjects who met criteria. There were 45 (16.4%) patients with positive blood culture results. Therefore, there were 90 subjects included with a mean (\pm SD) age of 23.57(\pm 43.28) months ranging from 1 month old to 15 years old. Most of them were male (60%) and had normal nutritional status (76.7%). Lung infiltrates were presented in majority subjects (88.9%). More than 40% of subjects from case group had anemia and leukocytosis (Table 1). The blood culture results showed 15 types of pathogens found. *Klebsiella pneumoniae* was the causative pathogen of most cases (22.2%) (Table 2).

The risk factors examined were listed in Table 3. In bivariate analysis, malnutrition (OR 35.2; 95% CI 4.45-278.25), congenital heart disease (OR 6.83; 95% CI 2.09-22.4), and hematologic disease (OR 12.57; 95% CI 1.54-102.97) were significantly associated with the occurrence of bacteremia in children with CAP ($p < 0.05$). The first step of multivariate analysis (Table 4) showed that only malnutrition that was associated with bacteremia in children with CAP and suitable for further analysis (Exp(B) 0.049; CI 95% 0.005-0.478; $p = 0.009$). Second step of multivariate analysis also proved that malnutrition significantly had relationship with bacteremia in children with CAP (Exp(B) 0.027; CI 95% 0.003-0.231; $p = 0.001$) (Table 5).

Discussion

The prevalence of bacteremia in this study was 16.4%. It was in line with previous study that stated

prevalence of bacteremia pneumonia patients ranging from 4-18%.¹¹ Lung infiltrates were found in most of subjects that had bacteremia (88.9%). Chest radiology findings are considered as “gold standard” to define pneumonia. However, there are wide variabilities in diagnosing CAP based on chest radiography due to inconsistent interpretation of plain chest radiography among doctors.¹²

More than 40% of subject that had bacteremia in this study presented anemia and leukocytosis. Anemia is one of comorbidity that increases the severity of pneumonia and poor outcome.¹³ Leukocytosis is conventionally thought to be associated with severe bacterial infection, but level of increase cannot be relied upon to distinguish between viral and bacterial pneumonia.¹⁴ This study found that *Klebsiella pneumoniae* was the most frequent causative bacteria. *Klebsiella pneumoniae* is frequently involved in severe infection and nosocomial infection. It is also proved as independent mortality risk factor in CAP and has high incidence in developing countries.¹⁵

This study found that age was not associated with bacteremia in children with CAP. Since age-matching method was used in this study to determine the control group, age could not be proven to be a risk factor of bacteremia in children with CAP. This study also found that sex was not associated with bacteremia in children with CAP. Some studies found that gender has no rule in bacteremia, but on the contrary other studies mentioned that male patients tend to be admitted in hospital compare to female patients,¹⁶ more frequently suffer from LRTI, more severe infection, and have higher mortality.¹⁷

This study found that LBW and prematurity had no relationship with bacteremia in children with CAP. It was in line with previous studies conducted in primary and tertiary health facilities in Surabaya, Indonesia that declared LBW was not associated with pneumonia, even in children under 5 years old.^{18,19} However, LBW babies tend to suffer from respiratory infection due to low immunity and lung disorders.²⁰ Premature babies are more vulnerable to severe bacterial infection due to lack of Immunoglobulin G that originally will be transferred from the mothers through the placenta in the following months.²¹

This study found that malnutrition was a significant risk factor of bacteremia in children with CAP and

independently increased the risk 35 times. These findings support the previous study conducted also in Dr. Soetomo General Hospital.² Pneumonia and malnutrition are known to be the two biggest killers of children.²² Malnutrition is also the most common risk factor for children with CAP in developing countries,⁵ described as mortality predictor of pneumonia in children,²³ increase the risk of mortality 2-3 times,²² and independently affects the mortality of under 5 years old children with pneumonia.²⁴ It was proven by studies that mentioned 55% of deaths among pneumonia patients to be malnourished children²³ and more than 95% of all new cases of pneumonia in children aged less than 5 years occur in developing countries due to the increased prevalence of malnutrition.²⁵ The increase in incidence and severity of infections in malnourished children is mostly due to a decrease in immune function, limited production and/or reduced functional capacity of all cellular components of the immune system.²²

Bivariate analysis in this study found that children with CAP and CHD were 6 times as likely to have bacteremia. Respiratory disease is most common complication of CHD in children, including pneumonia.²⁶ There is a close relationship between respiratory and cardiovascular system. Congenital anomalies of the circulatory system limit the heart's ability to increase systemic and pulmonary blood flow.²⁷ Bivariate analysis also found that children with CAP and hematologic disease had 12 times greater risk to have bacteraemia. Nevertheless, it was not proven by multivariate analysis. Lung infection including pneumonia is known as a common complication and a leading cause of death of haematological malignancies.²⁸

This study found that neuromuscular disease and HIV had no relationship with bacteremia in children with CAP. Patients with neuromuscular disease often develop inability to breathe deeply and cough effectively, and inability to effectively remove phlegm secretion that will lead to lung disfunction, increase airway resistance, and increase ventilation requirements.²⁹ Recently, bacterial pneumonia is claimed as the most frequent infection in children with HIV infection and there were 10-fold increase in incidence of bacterial pneumonia in children with HIV infection.³⁰

Conclusion

Malnutrition was significant risk factors of bacteremia in children with CAP.

Ethical Clearance: Approved by ethical committee of Dr. Soetomo General Hospital No 1496/KEPK/VI/2019

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Conflict of Interest: no

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