Relationship between Predisposition, Hypoxia and Chest Radiographs Abnormality on Mortality of 2-59 Months Old Children with Pneumonia

Ahmad Zakky Mashuri[1], Retno Asih Setyoningrum[1]

[1]Department of Child Health, Faculty of Medicine, Universitas Airlangga, - Dr. Soetomo General Hospital, Surabaya, Indonesia

Abstract

Background: Pneumonia in children was significant cause of death in world.(1, 2) About 150 million cases of pneumonia in under 5 years old children, 20 million cases include severe pneumonia with a high mortality rate.(3, 4) Based on the 2012 Indonesian Demographic Health Survey, infant mortality rate due to pneumonia was 40/1000 live births.(5) But there are no data describing factors that contribute to pneumonia mortality in Indonesian children.

Objective: To analyze relationship between predisposition, hypoxia and chest radiographs on mortality of 2-59 months old children with pneumonia.

Methods: Retrospective case control study by taking secondary data through medical records for the period 2016-2018 in the Dr. Soetomo Hospital

Results: one hundred and four patients were enrolled, 52 patients were died (case group) and 52 patients were cured (control group). Bivariate analysis show that factor of pneumonia mortality in children were age under 12 months, non-exclusive breastfeeding, overcrowding, incomplete immunization, malnutrition, comorbidities, hypoxia and extensive infiltrates, consolidation, pleural effusions on chest radiographs. Logistic regression analysis show factors that most influenced the pneumonia mortality in children were age under 12 months, malnutrition, overcrowding and extensive infiltrates, consolidation, pleural effusion on plain chest radiographs

Conclusion: Age under 12 months, malnutrition, overcrowding and extensive infiltrate, consolidation, pleural effusion on chest radiographs were the factors that most influence the pneumonia mortality.

***Key words**: Pneumonia, predisposition, hypoxia, chest radiograph.*

Introduction

Pneumonia in children is a significant cause of death and illness in the world, especially in developing countries(1, 2) About 150 million cases of pneumonia in under 5 years of children, 20 million cases include severe pneumonia with a high mortality rate.(3, 4) According to the WHO, pneumonia is the biggest cause of death in children worldwide, which is around 1.2 million under 5 years per year.(6) In poor and developing countries, about 11.5% incidences of severe pneumonia with a high risk of death.(1, 4) Based on the 2012 Indonesian Demographic Health Survey (SDKI), infant mortality rate due to pneumonia was 40 / 1,000 live births. (5) However until now, there are no data describing the factors that contribute to pneumonia mortality in Indonesian children.

Corresponding author:
Retno Asih Setyoningrum
Department of Child Health, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Hospital, Surabaya, Indonesia. Jl. Mayjen Prof. Dr. Moestopo No. 47, Airlangga, Surabaya, East Java, Indonesia
(+62 31) 5501746, E-mail: retnosoedijo@gmail.com

Some study showed that factors related to pneumonia mortality included predisposing factors, hypoxia, chest radiographs and organ dysfunction, young age ≤ 6 month, malnutrition, present of comorbid and sign severe infection (consolidation on chest x ray). [7-10] Identifying factors associated with pneumonia mortality in children are important, because there are many child suffered pneumonia often present with life-threatening complications. This is the reason to analysis of the relationship of predisposing factors, hypoxia and chest radiographs on pneumonia mortality in children aged 2-59 months. By understanding the factors related to pneumonia mortality, it may help health workers diagnose quickly and appropriately provide treatment and evaluation of pneumonia and finally reduce mortality due to pneumonia.

Material and Methods

This was retrospective case-control study. All children diagnosed with pneumonia and treated at the Child Health Department of Dr Soetomo Hospital Surabaya from January 2016 until December 2018. Data were obtained from medical records of children under 2-59 old months treated at Dr Soetomo Hospital due to pneumonia from January 2016 until December 2018. Samples were taken from children with a clinical diagnosis of pneumonia who met the inclusion criteria at the time of the study.

Inclusion criteria in this study is children aged 2 to 59 months with diagnosis of pneumonia. Inclusion criteria for case group is children who died while being treated. Inclusion criteria for control group is children with a diagnosis of pneumonia who cured or recovered. Patients with hospital-acquired pneumonia and incomplete medical record data were excluded from the study.

Various pneumonia predisposing factors, presence of hypoxia, and chest radiographs related to pneumonia were obtained from medical record. Premature was defined as a baby born with a gestational age <37 weeks. Low Birth Weight was baby with birth weight <2500 grams. Exclusive breastfeeding was defined if the children only breast milk for 6 months without supplementary feeding. Exposure to cigarette smoke if the family members have smoking habits. Overcrowding was declared if there are more than 7 people in one house. Comorbidities was defined if one of the cerebral palsy, congenital heart disease, HIV, GERD and Down syndrome were found. The nutritional status cathegorized as malnutrition or well nourished based on the 2006 WHO curve. Immunization status was declared complete if the child has received mandatory immunization against Measles, DPT and Hib according to the age of the patient. Hypoxia was defined with SpO2 or SaO2 below 90%. Radiological features of pneumonia was evaluated by chest radiological examination.

Bivariate analysis was used to see the relationship between independent variables and dependent variables using the analysis of the Chi square test, Fisher's exact test and Mann Whitney test. Multivariate logistic regression test was used to find out the most apropriate factors that influence the mortality. The Level of significant was expressed at 95% confidence interval.

Result

This study was an retrospective case-control study design using secondary data through medical records for the period of 2016-2018. A total of 775 patients were diagnosed with pneumonia during the 2016-2018 period.

Table 1 showed The basic characteristics of our study. The proportion of gender and age of two groups were equal. Table 2 showed results of univariate analysis, the mortality significant factor for children with pneumonia include the age less than 12 months , the presence of comorbidities, non-exclusive breastfeeding, overcrowding, incomplete immunization, malnutrition and hypoxia also chest x rays.

In Table 3, Multivariate logistic regression methode showed that under 12 months of age, high number of people in the family, malnutrition, extensive infiltrates, consolidation and pleural effusion in chest radiographs had significant results in child mortality pneumonia.

Table 1. Subject characteristics.

Karakteristik	Number	%
Gender		
· Male	54	52
· Female	50	48
Age		
· 2 - <12 months	50	48,1
· 12 – 59 months	54	51,9
Gestasional Age		
· Premature	24	23,1
· Term Infant	80	76,9
Birth Weight		
· < 2500 gram	29	27,9
· ≥ 2500 gram	75	72,1
Exclusive breastfeeding		
· No	51	49,0
· Yes	53	51,0
Exposure Cigarette smoke		
· Yes	56	53,8
· No	48	46,2
Overcrowding		
· Yes	23	22,1
· No	81	77,9
Immunization		
· Incomplete	64	61,5
· Complete	40	38,5
Comorbidities		
· Present	53	51
· Non-present	51	49
Nutritional Status		
· With Malnutrition	42	40,4
· Well nourished	62	59,6
Hypoxia		
· < 90 %	21	20,2
· > 90 %	83	79,8
Chest Radiography Finding		
· Minimal Infiltrate	67	64,4
· Extensive Infiltrate	12	11,5
· consolidation	15	14,4
· Pleural Efussion	10	9,6
· Empyema	0	0
· Pneumothorax	0	0
· Lung Abscess	0	0

Table 2. Mortality factor for children with pneumonia using bivariate analysis

Risk Factor	Outcome		P	Odds Ratio	95% CI
	Died	Cured			
Age					
· 2 - <12 months	33	17	0,003	3,576	1,593-8,029
· 12 – 59 months	19	35			
Gestasional Age					
· Premature	15	9	0,245	1,937	0,760-4,939
· Term Infant	37	43			
Birth Weight					
· < 2500 gram	15	14	1,00	1,100	0,467-2,594
· ≥ 2500 gram	37	38			
Exclusive breastfeeding					
· No	36	15	<0,001	5,550	2,394-12,864
· Yes	16	37			
Exposure Cigarette smoke					
· Yes	31	25	0,325	1,594	0,733-3,465
· No	21	27			
Overcrowding					
· Yes	17	6	0,018	3,724	1,330-10,423
· No	35	46			
Immunization					
· Incomplete	39	25	0,009	3,240	1,412-7,435
· Complete	13	27			
Nutritional Status					
· With Malnutrition	34	8	<0,001	10,389	4,036-26,741
· Well nourished	18	44			
Comorbidities					
· Present	40	13	<0,001	10,000	4,065-24,598
· Non-present	12	39			
Hypoxia					
· < 90 %	19	2	<0,001	14,394	3,142-65,937
· > 90 %	33	50			
Chest Radiography Finding*					
· Minimal Infiltrate	19	48	<0,001		0,000-0,028
· Extensive Infiltrate	11	1			
· consolidation	13	2			
· Pleural Efussion	9	1			
· Empyema	0	0			
· Pneumothorax	0	0			
· Lung Abscess	0	0			

*use Mann Whiney test

Table 3. Mortality factor for children with pneumonia using multivariate analysis

Risk Factor	P	Odds Ratio	95% CI
Age · 2 - <12 months · 12 – 59 months	0,010	11,789	1,820-76,357
Gestasional Age · Premature · Term Infant	0,106	0,147	0,014-1,504
Exclusive breastfeeding · No · Yes	0,403	2,440	0.301-19,782
Overcrowding · Yes · No	0,048	10,155	1,025-100,625
Immunization · Incomplete · Complete	0,467	0,386	0,030-5,028
Nutritional Status · Malnutrition · Well nourished	0,003	20,201	2,842-143,593
Comorbidities · Present · Non present	0,066	5,125	0,898-29,233
Hypoxia · < 90 % · > 90 %	0,765	1,476	0,115-18,931
Chest Radiography Finding · Extensive Infiltrate · Consolidation · Pleural Effusion · Minimal Infiltrate (reference)	0,005 0,034 0,001	107,409 56,926 219,511	4,121-2799,601 1,351-2399,193 8,812-5468,058

*Logistic regression, significant if $p<0.05$

Discussion

In this study, mortality significant factor for pneumonia were age less than twelve months, overcrowding, incomplete immunization, non-exclusive breastfeeding, malnutrition, comorbidities, hypoxia, chest radiographs findings.

Study in India, it was found that the relationship between age and children with pneumonia had died, especially in children aged 2-12 months with p <0.005. There are fewer children who die in the older age groups. This shows that as age increased, the respiratory tract will become wider and the defense mechanism of the respiratory tract more mature.[11]

Non-exclusive breastfeeding was an risk factor associated with the pneumonia mortality in our study. In previous study also showed significant relationship between non-exclusive breastfeeding and the mortality of children suffering from pneumonia with a p value <0.001.[11] Breast milk have effect on systemic immune system with multiple mechanisms including maturational, antimicrobial actions, immuno-modulatory and anti-inflammatory.[12] Malnutrition also as mortality factor has showed in previous study.[13, 14] In our study it was risk factor for determining mortality pneumonia. It is seems malnutrition cause an imbalance production of antibody, decreasing of lymphocytes, complement production, immunoglobulin A, interferon, T cells, and interleukin receptors.[15] This conditions can influence body response against the infection.

Overcrowding at home cause prolonged exposure to pathogen. In our study it was risk factor for determining mortality pneumonia. A study showed a significant relationship between the number of people in the family and the mortality of children suffering from pneumonia with a p value <0.022.[11] Immunizations provide protection againts childhood pneumonia. An study in India, an relationship was found between immunization and the mortality of children suffering from pneumonia with value of p=0.057. [11]

In this study, fifty children with comorbidities, most of them have congenital heart disease. Cardiac complications was also a direct or fundamental cause of death in 27% of pneumonia-related deaths.[16] In our study hypoxia was risk factor for determining mortality pneumonia. A previous study showed significant relationship between hypoxia and the mortality of children suffering from pneumonia with p value <0.001.[11] Mechanism of hypoxia in pneumonia was ventilation and perfusion mismatch in the pulmonary consolidation region. Hypoxia and dehydration caused hemoconcentration, lack of peripheral perfusion, increased metabolic acidosis will worsen general conditions and increase mortality.[17]

In this study showed a significant relationship between mortality with extensive infiltrates (p=0.007) and consolidation (p=0.012) and pleural effusion (p=0.005). An other study found association between abnormal chest radiographs (infiltrates, consolidation) and the pneumonia mortality with a value of p=0.001.[11] Mortality has a statistically significant relationship with bilateral consolidation (p = 0.00) and bilateral pleural effusion (p = 0.01).[18]

Low birth weight, gestational age, exposure to cigarette smoke were not significantly associated with pneumonia mortality in this study. Prematurity and early term have significant relationship with the death of children aged 29 - 364 days, especially deaths caused by infections, respiratory disorders, and other disorders, whereas in 1-5 years old children mortality did not show significant results.[19] Prematurity has significant relationship with child mortality in the first year of age (all cause mortality). Whereas at the age of 1-4 years there was insignificant results and insufficient evidence was found for deaths over the age of 4 years.[20]

Previous study showed low birth weight was associated with mortality in under 1 year old children (HR 0.28; CI 0.27-0.29; p <0.001) and over 15 years old children (HR 0.88; CI 0.78-0.99; p=0.03). While low birth weight was not associated with mortality in 1-14 years old children (HR 0.98; CI 0.82-1.12; p=0.84).[21] There was no significant relationship between pneumonia and exposure to cigarette smoke because the majority of smokers in the family are fathers and the relatively longer time spent by fathers outside the home.[22]

Conclusion

Factors affecting pneumonia mortality were age under 12 months, non-exclusive breastfeeding,

overcrowding, incomplete immunization, malnutrition, the presence of comorbidities, hypoxia, extensive infiltrates, consolidation, pleural effusion on chest radiograph.

Age under 12 months, overcrowding, malnutrition and chest radiographs (extensive infiltration, consolidation, pleural effusion) were the factors that most influence the pneumonia mortality.

Acknowledgments: Many thanks to Atika for statistical assistance.

Funding Acknowledgments: The authors received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict Interest: None declared.

Ethical approval: The study was approved by the Ethics committee of the "Dr. Soetomo" hospital (number : 1086/KEPK/IV/2019), Surabaya, Indonesia.

References

1. Rudan I, O'Brien KL, Nair H, Liu L, Theodoratou E, Shamim Qazi S, et al. Epidemiology and etiology of childhood pneumonia in 2010 : estimates of incidence, severe morbidity, mortality, underlying risk factors and causative pathogens for 192 countries. J Glob Health. 2013;3:010401.
2. Ebell MH. Clinical diagnosis of pneumonia in children. Am Fam Physician. 2010;82(2):192-3.
3. Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE, et al. Global, regional, and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: an updated systematics analysis. Lancet. 2015;385:430-40.
4. Onyango D, Kikuvi G, Amukoye E, Omolo J. Risk factors of severe pneumonia among children aged 2-59 months in western Kenya: a case control study. Pan African Medical Journal. 2012;13:45.
5. Indonesia KKR. Pedoman tatalaksana pneumonia balita. Direktorat Jenderal Pengendalian Penyakit dan Penyehatan Lingkungan. 2015.
6. WHO. Pocket book of hospital care for children. Guidelines for the management of common illness with limited resources. Geneva: WHO Press; 2013. p. 75-86.
7. Araya S, Lovera D, Zarate C, Apodaca S, Julia Acuna J, Sanabria G, et al. Application of a prognostic scale to estimate the mortality of children hospitalized with community-acquired pneumonia. Pediatr Infect Dis J. 2016;35:369-73.
8. Ramachandran P, Nedunchelian K, Vengatesan A, Saradha S. Risk factors for mortality in community –acquired pneumonia among children aged 1-59 months admitted in a referral hospital. Indian Pediatr. 2012;49:889-95.
9. Patwari A. Risk faktor for mortality in children hospitalized with pneumonia. Indian Pediatr, 49:869-70. Indian Pediatr. 2012;49:869-70.
10. Lupisan S, Ruutu P, Abucejo-Ladesma PE, Quiambao BP, Gozum L, Sombrero LT, et al. Predictors of death from severe pneumonia among children. Trop Med Int Health. 2007;12(8):962-71.
11. Ansari E, Kumar A, Aggarwal K, Meena K, Kamal M. Outcome predictors of severe and very severe pneumonia in children between 2 and 59 months of age admitted in a tertiary care hospital. Indian J Child Health. 2016;14:1-5.
12. Kelly D, Coutts AGP. Early nutrition and the development of immune function in the neonate. Proc Nutr Soc. 2000;59(2):177-85. Proc Nutr Soc. 2000;59(2):177-85.
13. Enarson P, Gie RP, Mwansambo CC, Chalira AE, Lufesi NN, Maganga ER, et al. Potentially modifiable factors associated with death of infants and children with severe pneumonia routinely managed in district hospitals in Malawi. PLoS One.3;8:e0133365. PLoS ONE. 2015;10(8):e0133365.
14. Bokade CM, Madhura AD, Bagul AS, Thakre SB. Predictors of mortality in children due to severe and very severe pneumonia. Niger Med J. 2015;56(4):287–91.
15. Schrimshaw NS, SanGiovanni JP. Synergism of nutrition, infection and immunity: an overview. Am J Clin Nutr. 1997;66:464S-77S.
16. Corrales-Medina VF, Musher DM, Shachkina S, Chirinos JA. Acute pneumonia and the cardiovascular system. Lancet. 2013;381:496-505.
17. Malik S, Gohiya P, Sisodia P. Prevalence of hypoxemia & its determinates in children with acute lower respiratory infection. Int J Pediatr Res. 2015;2(4):122-7.

18. Jain DL, Mishra S, Jain H, Reddy M, Agrawal SB. Role of chest x-ray in assessing severity of pneumonia in children aged 3 months to 59 months. J Pediatr Res. 2017;4(03):242-8.
19. Stephens AS, Lain SJ, Roberts CL, Bowen JR, Nassar N. Association of gestational age and severe neonatal morbidity with mortality in early childhood. . Paediatr Perinat Epidemiol. 2016;6:583-93
20. Juarez S, Goodman A, Stavola B, Koupil I. Birth characteristics and all-cause mortality : a sibling analysis using the uppsala birth cohort multigenerational study. J Dev Orig Health Dis4:374-83. 2016;7(4):374–83.
21. Friedlander Y, Paltiel O, Deutsch L, Knaanie A, Massalha S, Tiram E, et al. Birthweight and relationship with infant, child and adult mortality in the Jerusalem perinatal study. Paediatr Perinat Epidemiol. 2003;4:398–406.
22. Srivastava P, Mishra AK, Roy AK. Predisposing factors of community acquired pneumonia in under five children. Lung dis Treat. 2015;1:101.