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BASIC IMMUNIZATION STATUS CORRELATED TO MORBIDITY AND MORTALITY OF SEVERE PNEUMONIA IN TODDLERS

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ABSTRAK

Pneumonia adalah infeksi paru akut yang sering menyerang balita dan menjadi penyebab utama morbiditas serta mortalitas. Imunisasi rutin menjadi upaya pencegahan penting. Penelitian ini bertujuan menganalisis hubungan status imunisasi dengan morbiditas dan mortalitas balita pneumonia berat di PICU RSUD dr. Moewardi. Desain penelitian analitik retrospektif cross sectional menggunakan data rekam medis dan Kartu Menuju Sehat pada 34 balita. Status imunisasi dinilai lengkap bila sesuai usia. Morbiditas dilihat dari lama rawat inap, mortalitas dari status hidup/meninggal. Analisis menggunakan chi square/fisher dan regresi logistik. Hasil menunjukkan balita dengan imunisasi lengkap 90% dirawat <10 hari, sedangkan 82,6% dengan imunisasi tidak lengkap dirawat ≥10 hari (p<0,001). Mortalitas lebih tinggi pada imunisasi tidak lengkap (90,0%) dibanding lengkap (45,8%) (p=0,024). Imunisasi DPT3 dan cacar berhubungan dengan morbiditas, sedangkan polio dan cacar dengan mortalitas. Kesimpulan: imunisasi dasar merupakan prediktor independen morbiditas dan mortalitas pneumonia berat balita setelah dikontrol faktor usia, ASI eksklusif, dan paparan asap rokok.

ABSTRACT

Basic Immunization Status Correlated to Morbidity and Mortality of Severe Pneumonia in Toddlers. Pneumonia is an acute lung infection that often affects toddlers and is a major cause of morbidity and mortality. Routine immunization is an important preventive measure. This study aims to analyze the relationship between immunization status and morbidity and mortality of toddlers with severe pneumonia in the PICU of Dr. Moewardi Regional Hospital. The retrospective cross-sectional analytical study design used medical record data and the Menuju Sehat Card in 34 toddlers. Immunization status was considered complete if appropriate for age. Morbidity was seen from the length of hospitalization, mortality from the status of alive/dead. Analysis used chi-square/Fisher and logistic regression. The results showed that 90% of toddlers with complete immunization were hospitalized for <10 days, while 82.6% with incomplete immunization were hospitalized for ≥10 days (p<0.001). Mortality was higher with incomplete immunization (90.0%) than with complete immunization (45.8%) (p=0.024). DPT3 and smallpox immunization were associated with morbidity, while polio and smallpox were associated with mortality. Conclusion: Basic immunization is an independent predictor of morbidity and mortality in severe pneumonia in toddlers after controlling for age, exclusive breastfeeding, and cigarette smoke exposure.

INTRODUCTION

Pneumonia is an acute respiratory infection of the lungs that can affect all ages, but is more common in younger children.[1,2] Pneumonia is even considered the single most common infectious contributor to mortality in children in the world.[3] Pneumonia accounts for around 120 million cases per year globally, 12% of which develop into severe pneumonia, most of which end in death.[4] Severe pneumonia also contributes to high morbidity rates, as well as complication rates and prolonged hospital stays of around 21% to 54%.[5] Identification of patients at high risk for severe pneumonia is very important. Patients with severe pneumonia require longer ventilator use, especially if associated with corona virus disease 2019 (COVID-19).[6]

The prevalence of pneumonia in toddlers in Indonesia is relatively high, where out of 503,738 cases, 16,819 were confirmed as severe pneumonia. Indonesia ranks ninth with the highest mortality rate due to pneumonia in toddlers, which is 32 per 1000 live births. This shows that 2-3 children die every hour due to pneumonia. Pneumonia in toddlers in Indonesia in 2017 reached 447,431 cases (46.34%) and caused the death rate of 1,351 toddlers.[7] Based on Riskesdas, it was reported that pneumonia incidents experienced a spike in the last month in 2013.[8]

Pneumonia generally has a good prognosis, but the presence of comorbidities such as congenital heart disease, immunosuppression, and chronic lung disease of prematurity also increase the morbidity and mortality of toddlers with pneumonia.[8] Efforts are needed to minimize the morbidity and mortality of toddlers related to pneumonia, including through vaccination or immunization.[2,9]

Five simple interventions have been recommended to reduce the incidence of severe childhood pneumonia, including routine vaccination against measles, pertussis, Hib, and pneumococcus.[8,9] Streptococcus pneumoniae and Haemophilus influenza type-b (Hib) are considered the leading causes of pneumonia deaths in children worldwide. Universal use of conjugated Hib and pneumococcal vaccines is estimated to prevent approximately one million childhood deaths annually.[9]

Immunizations in Indonesia include *Bacillus Calmette–Guérin* (BCG), Hib, DPT, Measles, and *Pneumococcal Conjugate Vaccine* (PCV). These vaccines have been proven to reduce the incidence of pneumonia. For example, Immunization with BCG significantly increases efferocytosis (*clearance of* dead or apoptotic cells) by alveolar phagocytes and provides 100% protection against *lethal influenza A virus pneumonia.*[10] Measles immunization is also known to prevent pneumonia infection.[11] PCV vaccine is also associated with effective protection against pneumonia in infants, indicated by antibody titers >0.35 µg/mL after vaccination.[12] Hib vaccine is also one of the vaccines that can prevent pneumonia. Hib causes more than 350,000 deaths and more than 8 million cases of severe disease each year without universal vaccination.[9,13]

Immunization is very involved in preventive efforts in childhood pneumonia, especially in toddlers as an age group with high morbidity (length of hospitalization) and mortality. However in Indonesia until now there has been no study of this problem in the PICU setting, so this study was conducted to determine the correlation between basic immunization status and morbidity and mortality of toddlers with severe pneumonia treated in the PICU of Dr. Moewardi Surakarta Hospital.

METODE

The type of this study is observational analytical with a retrospective cross-sectional design. Data sources were obtained from medical records and the Road to Health Card (RHC) of toddlers diagnosed with severe pneumonia. The study was conducted at the PICU of Dr. Moewardi Surakarta Hospital from April to December 2024.

The minimum sample size was determined based on the Lameshow formula,[14] using a significance level of 5% with an acceptable confidence level estimate of 15% and the proportion of conditions expected based on previous studies, namely 23%,[15] so a minimum of 34 toddlers were needed after adding the possibility of dropping out by 10%. Subjects were selected consecutively based on the criteria including: subjects aged 0-59 months, diagnosed with pneumonia, requiring treatment in the PICU, having a history of immunization records either from medical records, RHC or other similar documents, obtaining parental consent regarding the use of toddler data.

The variables of this study consist of basic immunization status as an independent variable and toddler morbidity and mortality as dependent variables, plus age, gender, nutritional status, history of exclusive breastfeeding, exposure to cigarette smoke, birth weight, prematurity, ventilator needs, and various comorbidities such as tuberculosis, congenital heart disease, sepsis, shock, and kidney function disorders as confounding variables.

Data analysis consist of univariate analysis to determine the characteristics of the subjects, presented in frequency and percentage; bivariate analysis to determine the correlation between basic immunization status and various confounding factors with morbidity and mortality of toddlers with severe pneumonia using the chi-square test or Fisher's exact; and multivariate analysis to determine which factors were independent predictors of morbidity and mortality of toddlers with severe pneumonia using the binary logistic regression test. The analysis was performed with SPSS version 26 using a significance level of $p < 0.05$.

The research was conducted after obtaining informed consent from subjects' parents and receiving ethical approval recommendations from the Research Ethics Committee of Dr. Moewardi Surakarta Hospital. Surakarta, Indonesia, No. 201/I/HREC/2014, on January 29th, 2024.

RESULT

Characteristics of 34 toddlers with severe pneumonia in this study are presented in Table 1. showed that most (79.4%) were ≤1 years old, 55.9% were male, 61.8% had good nutritional status, 76.5% were exclusively breastfed, 55.9% were exposed to cigarette smoke, almost all (94.1%) were not exposed to tuberculosis, 94.1% had sufficient/normal birth weight, 70.6% did not have comorbid congenital heart disease, 67.6% required ventilators, 55.9% had sepsis, and 55.9% had shock. Almost all subjects (91.2%) did not have impaired kidney function, most (67.6%) were treated for ≥10 days and most (70.6%) still alive (Table 1).

Table 1. Characteristics of Research Subjects of Toddler Patients with Severe Pneumonia

Characteristics		n	%
Age	≤ 1 year	27	79.4
	>1 year	7	20.6
Gender	Male	15	44.1
	Female	19	55.9
Nutritional status	Good	21	61.8
	Less	11	32.4

Characteristics		n	%
	Poor	2	5.9
Exclusive breastfeeding	Yes	26	76.5
	No	8	23.5
Cigarette smoke exposure	Yes	19	55.9
	No	15	44.1
Exposure to TB Disease	Yes	2	5.9
	No	32	94.1
Birth weight	Low	2	5.9
	Normal	32	94.1
Congenital heart disease	Yes	10	29.4
	No	24	70.6
Ventilator needs	No	11	32.4
	Yes	23	67.6
Sepsis	No	15	44.1
	Yes	19	55.9
Shock	No	15	44.1
	Yes	19	55.9
Kidney function disorders	No	31	91.2
	Yes	3	8.8
Length of hospitalization	<10 days	11	32.4
	≥10 days	23	67.6
Mortality	Alive	24	70.6
	Die	10	29.4

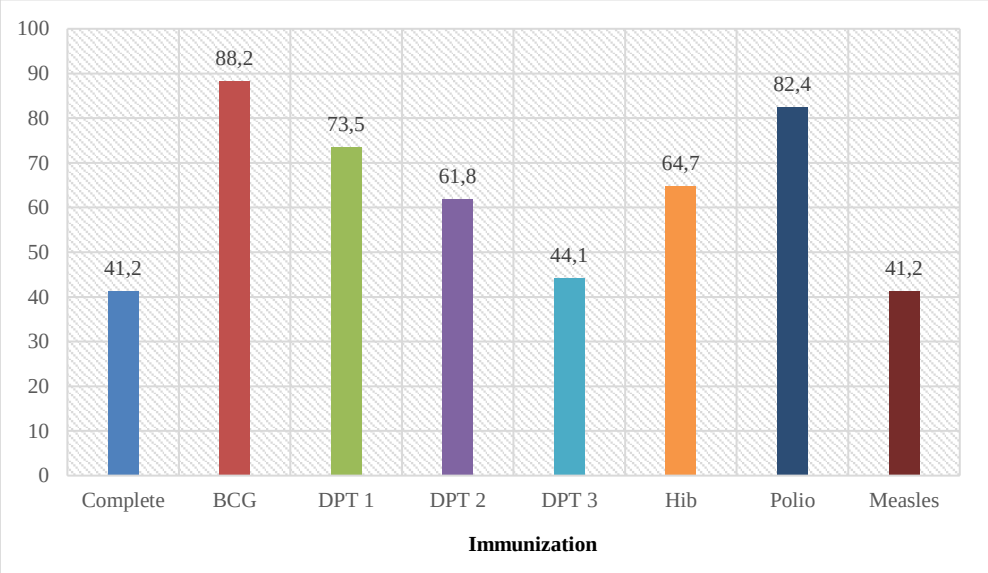

Figure 1. Coverage of basic immunization in toddlers with severe pneumonia

Complete basic immunization status achieved by 41,2% toddler with severe pneumonia. Kind of immunization with highest achievement is BCG (88,2%), followed by polio (82.4%), DPT1 (73,5%), Hib (64,7%), DPT2 (61,8%), DPT 3 (44,1%) and last as the lowest is measles immunization as much as 41,2% similar with complete basic immunization.

There were no characteristic factors correlated to length of hospitalization (p-value of each variables >0.05), but there were two factors were found to be potentially confounding,

namely age with p-value 0.178 and exclusive breastfeeding with p-value 0.227 (Table 2). There were also no subject characteristics that related to subject mortality because each characteristics showed p value >0.05, and there was only one factor that had the potential to be confounding, namely exposure to cigarette smoke with p-value 0.128 (Table 2). This results showed that subject characteristics were homogen.

The correlation between basic immunization status and subject morbidity is shown by the completeness of immunization based on age, DPT3 immunization, and measles. Almost all of the toddlers with complete basic immunization (90.9%) had length of hospitalization for <10 days, while almost all of the toddlers without complete basic immunization (82.6%) had length of hospitalization for ≥10 days (p<0.001 with OR and CI95% 47.5 and 4.7 to 83.9). Type of immunization that contributed to length of hospitalization were DPT3 and measles Toddler with DPT3 immunization most (72.7%) had length of hospitalization for <10 days, while most of them that had not DPT3 immunization (69.6%) had length of hospitalization for ≥10 days (p=0.030 with OR and CI95%: 6.1 and 1.2 to 30.1). Toddlers with measles immunization (72.7%) were hospitalized for <10 days, but most of them (73.9%) without measles immunization were hospitalized for ≥10 days (p-value 0.023 with OR 7.6 and CI95%: 1.23-30.1**).** Meanwhile, the basic immunization status that correlated to subject mortality is the completeness of immunization (p=0.024), with the types of immunization that contributed being DPT3, polio, and measles immunization, with p-values 0.020, 0.005, and 0.024, respectively (Table 3).

Table 2. Analysis of the Correlation between Characteristics of Subjects and Morbidity and Mortality

Variables	Length of hospitalization				p-value	Mortality				p-value
	<10 days		≥10 Days			Alive		Die		
	n	%	n	%		n	%	n	%	
Age										
>1 year	4	36.4	3	13	0.178	4	16.7	3	30	0.394
≤ 1 year	7	63.6	20	87		20	83.3	7	70	
Gender										
Male	4	36.4	11	47.8	0.751	10	41.7	5	50	0.718
Female	7	63.6	12	52.2		14	58.3	5	50	
Nutritional status										
Poor/less	4	36.4	9	37.5	1,000	8	33.3	5	50	0.451
Good	7	63.6	14	62.5		16	66.7	5	50	
Exclusive breastfeeding										
No	1	9.1	7	30.4	0.227	5	20.8	3	30	0.666
Yes	10	90.9	16	69.6		19	79.2	7	70	
Cigarette smoke exposure										
Yes	7	63.6	12	52.2	0.715	11	45.8	8	80	0.128
No	4	36.4	11	47.8		13	54.2	2	20	
Exposure to TB Disease										
Yes	0	0	2	8.7	1,000	1	4.2	1	10	0.508
No	11	100	21	91.3		23	95.8	9	90	
Birth weight										
Low	11	100	21	91.3	1,000	1	4.2	1	10	0.508
Normal	0	0	2	8.7		23	95.8	9	90	
CHD										
Yes	2	18.2	8	34.8	0.437	7	29.2	3	30	1,000
No	9	81.8	15	65.2		17	70.8	7	70	
Ventilator need										
Yes	8	72.7	15	65.2	1,000	16	66.7	7	70	1,000
No	3	27.3	8	34.8		8	33.3	3	30	
Sepsis										
Yes	6	54.5	13	56.5	1,000	13	54.2	6	60	1,000
No	5	45.5	10	43.5		11	45.8	4	40	
Shock										
Yes	7	63.6	12	52.2	0.715	14	58.3	5	50	0.718
No	4	36.4	11	47.8		10	41.7	5	50	
KFD										
Yes	1	9.1	2	8.7	1,000	2	8.3	1	10	1,000
No	10	90.9	21	91.3		22	91.7	9	90	

CHD: congenital heart disease; KFD: kidney function disorders

Table 3. Correlation between Basic Immunization Status with Mortality and Mortality of Severe Pneumonia in Toddler Patients Treated in PICU of Moewardi Hospital

Immunization		Length of hospitalization				OR (IK95%)	p-value	Mortality				OR	p-value
		<10 Days		≥10 Days				Alive		Die			
		n	%	n	%			n	%	n	%		
Complete													
	No	1	9.1	19	82.6	47.50 (4.66-83.94)	<0.001*	11	45.8	9	90	10.64 (1.16-97.59)	0.024*
	Yes	10	90.9	4	17.4	Ref.		13	54.2	1	10	Ref.	
BCG													
	No	0	0	4	17.4	n/s	0.280	1	4.2	3	30	9.86 (0.88-110.43)	0.067
	Yes	11	100	19	82.6	Ref.		23	95.8	7	70	Ref.	
DPT 1													
	No	3	27.3	6	26.1	0.94 (0.19-4.76)	1,000	5	20.8	4	40	2.53 (0.51-12.59)	0.359
	Yes	8	72.7	17	73.9	Ref.		19	79.2	6	60	Ref.	
DPT 2													
	No	3	27.3	10	43.5	2.05 (0.43-9.78)	0.456	8	33.3	5	8	2.00 (0.45-8.98)	0.451
	Yes	8	72.7	13	56.5	Ref.		16	66.7	5	16	Ref.	
DPT 3													
	No	3	27.3	16	69.6	6.10 (1.23-30.09)	0.030*	10	41.7	9	90	12.60 (1.37-115.97)	0.020*
	Yes	8	72.7	7	30.4	Ref.		14	58.3	1	10	Ref.	
Hib													
	No	3	27.3	9	39.1	1.71 (0.36-8.23)	0.705	3	7	29.2	5	2.43 (0.53-11.11)	0.271
	Yes	8	72.7	14	60.9	Ref.		8	17	70.8	5	Ref.	
Polio													
	No	0	0	6	26.1	n/s	0.145	1	4.2	5	50	23.00 (2.18-242.33)	0.005*
	Yes	11	100	17	73.9	Ref.		23	95.8	5	50	Ref.	
Measles													
	No	3	27.3	17	73.9	7.56 (1.49-38.21)	0.023*	11	45.8	9	90	10.64 (1.16-97.59)	0.024*
	Yes	8	72.7	6	26.1	Ref.		13	54.2	1	10	Ref.	

Ref= Reference; OR= Odd Ratio ; *CI= Confidence interval* ; n/s= Not Specified *Significant at p<0.05

Table 4. Multivariate Analysis of Variables Correlated to Morbidity of Toddlers with Severe Pneumonia

Length of hospitalization	B	Ajd OR (CI95%)	p-value
Age (>1 year)	-1.60	0.20 (0.01-3.60)	0.276
Exclusive breastfeeding (no)	1.20	3.32 (0.23-48.28)	0.380
Incomplete immunization	3.82	45.44 (3.93-525.10)	0.002*

Ajd= Adjusted; OR= Odd Ratio; *CI= Confidence interval* ; *Significant at p<0.05

The results of the multivariate analysis showed that incomplete basic immunization (OR=45.44; p=<0.002) was significantly related to the length of hospitalization of toddler patients with severe pneumonia. The risk of hospitalization ≥10 days in subjects with incomplete basic immunization was 45.4 times higher than in subjects with complete immunization. However, age and exclusive breastfeeding do not affect the morbidity of a toddler with severe pneumonia, proven by p-value 0.276 and 0.380, respectively. Thus, complete immunization becomes an independent predictor of patients' morbidity, which is measured by length of hospitalization (Table 4).

Table 5. Multivariate Analysis of Variables Correlated to Mortality of Toddler with Severe Pneumonia

Mortality	B	Ajd OR (CI95%)	p-value
Cigarette Smoke Exposure	1.93	6.86 (1.00-47.28)	0.051
Incomplete immunization	2.68	14.55 (1.40-151.03)	0.025*

Ajd= Adjusted; OR= Odd Ratio; *CI= Confidence interval*; *Significant at p<0.05

The results of multivariate analysis showed that only complete immunization (OR=14.55; p=0.025), which is significantly related to the mortality of toddler patients with severe pneumonia. The risk of death in subjects with incomplete immunization is 14.55 times higher than in subjects with complete immunization. Cigarette smoke exposure did not confound the effect of complete immunization on patient mortality (p=0.051). Thus, complete immunization is the independent predictor of patient mortality (Table 5).

DISCUSSION

Complete basic immunization has been shown to be associated with morbidity and mortality in toddlers with severe pneumonia. Especially for measles, DPT-3, and polio immunization. Children who did not receive measles immunization had a 7.56 times greater risk of being hospitalized for longer and a 10.64 times greater risk of dying. This is in line with the results of the 2020 WHO–UNICEF study which stated that the measles vaccine not only prevents measles infection itself, but also reduces secondary complications such as pneumonia which are often the main cause of death in children after measles infection.[16,17]

DPT immunization, especially the 3rd dose, is also closely related to length of hospitalization and death. DPT-3 is an important component in protection against pertussis, which in young children often causes secondary pneumonia. Based on data from the CDC (2019), incomplete DPT vaccination coverage has been shown to increase the risk of severe complications including pneumonia and seizures due to hypoxia.[18]

Polio, which appeared to have a significant association with mortality (OR=23, p=0.005) in this study, must be interpreted cautiously. Although the polio vaccine does not directly prevent pneumonia, polio immunization may be a proxy for good overall immunization status. In addition, children who receive all types of vaccines generally receive better health care, including better nutrition and sanitation. This aligns with herd immunity and "positive health-seeking behavior" associated with children's basic immunization compliance.[17,19]

In contrast, although most subjects had received BCG and Hib vaccines, no significant association was found between the two vaccines and the length of hospitalization and mortality. The heterogenity of the immune response to the vaccines and other factors such as pathogen virulence, previous immunization history, and the possibility of co-infection may explain this. Some literature suggests that the BCG vaccine protects against severe systemic infections more than specific pneumonia.[19,20]

Toddlers who do not receive complete immunization have a 47.5 times greater risk of experiencing a hospital stay of more than 10 days (p<0.001), and a 10.64 times greater risk of death (p=0.024). This shows that immunization is important in forming protective immunity against pathogens that cause severe pneumonia, both directly and indirectly. As explained by Lassi et al., vaccination significantly protects the incidence of severe pneumonia and death in children, especially pneumococcal, Hib, and measles vaccines.[21]

This study reaffirms the importance of preventive approaches in reducing the burden of childhood disease. In the context of severe pneumonia, immunization not only provides direct protection but also reduces the need for intensive care and invasive interventions such as ventilators, which have an impact on the economic burden on families and the health system. This finding is consistent with a meta-analysis by Roussel and Raoult,[16],which showed that high immunization coverage significantly reduces hospitalization and mortality from pneumonia in developing countries. Additional risk factors such as poor nutritional status, exposure to cigarette smoke, and non-exclusive breastfeeding also worsen the clinical

condition. However, these variables did not significantly correlate with morbidity or mortality in this study.

Overall, the results of this study strengthen the evidence that complete basic immunization, especially measles, DPT-3, and polio vaccines, play an important role in reducing severe pneumonia morbidity and mortality in toddlers. Immunization must continue to be encouraged by health workers, especially in high-risk age groups, as part of national efforts to reduce toddler mortality. Increasing public awareness, equal access to vaccination, and strengthening the immunization coverage monitoring system are strategic steps that must be optimized in future child health policies.[22–24]

This study has some limitations, due to being conducted in a single center, thus only a small sample size (n = 34) was used. It may reduce the statistical power and generalizability of the findings, especially in analyzing the association between specific types of immunization and morbidity and mortality. In addition, this study did not consider other variables that could potentially be confounding factors, such as maternal immunization status during pregnancy, housing density, environmental sanitation, parental education level, and the time interval between vaccination and disease onset.

Data collection based only on medical records retrospectively also could cause information bias due to incomplete or inaccurate recording. Assessment of immunization status based on documentation without direct verification with the Maternal and Child Health Book can also pose a risk of misclassification.

CONCLUSION

Complete basic immunization can minimize morbidity and mortality rates in toddlers with severe pneumonia. The hospital can provide health education to families about the importance of complete basic immunizations and their impact on morbidity and mortality in toddlers with severe pneumonia when it was not met. This study's results can also be followed up by prospective or multicenter studies with a larger population, and stricter control designs to strengthen the validity of the findings, because the results of this study have provided useful initial features.

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