

ORIGINAL RESEARCH

DETERMINANTS OF PNEUMONIA IN TODDLERS IN JAMBI CITY

Determinan Kejadian Pneumonia Pada Balita di Kota Jambi

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ABSTRACT

Background: Pneumonia is an acute respiratory infection and the second leading cause of toddler deaths in Indonesia. Nutritional status, immunization status, and humidity in the house constitute risk factors for the incidence and prevalence of pneumonia. **Purpose:** The objective of this research is to analyze the determinants of nutritional status, immunization status, and air humidity against the incidence of pneumonia in toddlers in Jambi City. Methods: This was an observational study. A case-control design approach was adopted. The research location was the Public Health Center of Talang Bakung in Jambi City, which has the highest prevalence of pneumonia cases. This study was conducted from January 2019 to August 2019. The number of samples in this study was 66 toddlers, with a 1:1 ratio of cases. Data was collected using a multistage random sampling technique. Primary and secondary data obtained was analyzed with a logistic regression test method. Results: The highest proportion of pneumonia cases was observed in toddlers between the ages of 12 and 35 months (75.76%). The proportion of female toddlers was 57.58%, with the number of siblings being ≥ 1 (93.94%). The proportion of people who completed secondary level maternal education was 60.61%, which was higher than the proportion of people who completed secondary level paternal education (54.55%). The employment status of fathers was 96.97%. Underweight status was with pneumonia (AOR=5.81; 95%CI=1.07-31.68). associated Inadequate air humidity was associated with the incidence of pneumonia 95%CI=1.80-30.13). (AOR=7.37; **Conclusion:** Nutritional status and air humidity were identified as determinants of pneumonia in toddlers in Jambi city.

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ABSTRAK

Latar Belakang: Pneumonia merupakan penyakit infeksi saluran

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https://dx.doi.org/10.20473/jbe.v9i22 021.157-165 pernapasan akut dan menjadi penyebab kematian balita ke-2 di Indonesia. Status gizi, status imunisasi dan kelembapan udara dalam rumah sebagai faktor risiko penentu insiden dan prevalens pneumonia. **Tujuan:** Penelitian ini bertujuan untuk menganalisis determinan status gizi, status imunisasi, dan kelembapan udara terhadap kejadian Pneumonia pada balita di Kota Jambi. Metode: Penelitian ini merupakan penelitian observasional dengan rancangan case control. Lokasi penelitian di Pusat kesehatan masyarakat Talang Bakung, Kota Jambi dengan kasus pneumonia tertinggi. Penelitian ini dilaksanakan pada bulan Januari-Agustus 2019. Jumlah sampel dalam penelitian ini adalah 66 balita dengan perbandingan kasus terhadap kontrol 1: 1 yang diambil dengan menggunakan teknik multistage random sampling. Data diperoleh dari data sekunder dan primer, di analisis dengan metode uji regresi logistic. Hasil: Proporsi kasus pneumonia terbanyak pada usia 12-35 bulan (75.76%), berjenis kelamin perempuan (57.58%), saudara kandung (≥ 1) (93.94%), pendidikan ibu tingkat menengah (60.61%), pendidikan ayah tingkat menengah atas (54.55%) dan status pekerjaan ayah (96.97%). Status gizi berhubungan dengan kejadian pneumonia (AOR=5,81; 95%CI=1.07-31.68), dan kelembapan udara yang tidak memenuhi syarat berhubungan dengan kejadian pneumonia (AOR=7,37; 95%CI=1.80-30.13). Kesimpulan: Status gizi dan kelembapan udara merupakan determinan terhadap pneumonia pada balita di Kota Jambi.

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INTRODUCTION

Acute respiratory infections (ARIs) can be divided into two types: upper respiratory infections and lower acute respiratory infections. Acute lower respiratory tract infections are usually noticed in different forms; however, the most frequently encountered form is pneumonia. Pneumonia is an acute respiratory infection that affects the lung parenchyma, distal to the terminal bronchioles, which include respiratory bronchioles and alveoli. Pneumonia can cause lung tissue conciliation and disrupt the process of local gas exchange (Cilloniz, Martin-Loeches, Garcia-Vidal, Jose, & Torres, 2016).

The World Health Organization (WHO) estimates that under-five deaths are mostly caused by infectious diseases, such as pneumonia (15%), diarrhea (9%) and malaria (7%). Infant mortality is mostly caused by pneumonia, killing 808,694 children in 2017. Pneumonia remains the leading cause of death among children under five years of age, killing approximately 2,400 children per day. Pneumonia accounted for nearly 16% of the total 5.60 million of under-five deaths, killing about 880,000 children in 2018 (United Nations Children's Fund, 2019).

Indonesia is a developing and tropical country. It has the potential to become an endemic area of infectious diseases, which can pose a threat to public health. One of the diseases that poses a threat to public health is pneumonia. Pneumonia is the second leading cause of infant mortality in Indonesia (after diarrhea). The number of pneumonia cases discovered in infants in Indonesia in 2015 was 63.45%. In 2016, the number was 65.27%, and in 2017, this number was 51.19%. The number of toddler deaths due to pneumonia for the years 2015, 2016, and 2017 was 0.16%, 0.11%, and 0.34%, respectively (Ministry of Health RI, 2018).

The data obtained by examining the pneumonia cases in children under five in the Jambi province revealed that the proportion of cases in 2015 was 58.90%. In 2016, the proportion was 45.38%, and in 2017, the number was 50.33%. In 2015, 0.04% of the cases resulted in deaths (Ministry of Health RI, 2018). Based on data obtained from the Jambi City Health Office, for the years 2015, 2016, 2017, and 2018, the prevalence of pneumonia was 3.72%, 1.79%, 1.81%, and 1.83%, respectively. Judging from the above data, an increase in prevalence of pneumonia was observed from 2016 to 2018. The PHC of Talang Bakung is a Public Health Center

(PHC), which saw the highest prevalence of pneumonia in Jambi City in 2018. The prevalence of pneumonia in the PHC of Talang Bakung for the years 2015, 2016, 2017, and 2018 was 1.67%, 3.05%, 3.59%, and 4.42%, respectively (Jambi City Health Office, 2018).

Based on the preliminary survey data that was obtained from the Jambi City Health Office in 2018, the variables related to the incidence of pneumonia were the nutritional status, the immunization status and air humidity. The data obtained revealed that there were still nutritional problems faced by toddlers at the PHC of Talang Bakung, where 1.54% of the toddlers were malnourished. There were still toddlers who could not complete basic immunization, which was 1.02%. This was a possible factor that could cause pneumonia in the work area of PHC of Talang Bakung (Jambi City Health Office, 2018).

From the above description, a high prevalence of pneumonia in the work area of PHC of Talang Bakung was observed, with this trend in prevalence continuing to increase from year to year. There were still problems associated with the nutritional and immunization status. Therefore, researchers were interested in examining the relationship between nutritional status, immunization status, and humidity at home with the incidence of pneumonia in toddlers in Jambi City in 2019.

METHODS

This was an observational study. A casecontrolled design was employed. The case group was toddlers with pneumonia, while the control group was healthy toddlers who had no pneumonia. The inclusion criteria was people residing in the work area of the PHC of Talang Bakung in Jambi City, people having a Maternity and Child Health (MCH) book, and those willing to be the subjects of the research by signing an informed consent form. The minimum sample size was based on hypothesis testing. The sample included two different test proportions of 33 samples each: case sample of 33 toddlers, and a control sample of 33 toddlers (with matching age), so the overall sample size was 66 toddlers. Sampling was conducted through a multistage random sampling technique. This research was conducted from January 2019 to August 2019.

The dependent variable in this study was pneumonia, with the case definition being toddlers diagnosed with pneumonia, and the control group being healthy toddlers and toddlers undiagnosed with pneumonia. The independent variable was nutritional status, which, by definition, is the history of the physical condition of toddlers based on the measurement of body weight with respect to age. The underweight category was defined by the Z score of \leq -2 Standard Deviation (SD). Nutritional status was considered to be normal if the Z score was >-2SD. Immunization status is a history of basic immunization for toddlers and is said to be incomplete if the toddlers do not receive 1 or more than 1 dose of the following: hepatitis B. 1 dose of BCG, 3 doses of DPT-hepatitis B, 4 doses of polio, and 1 dose of measles. Immunization status is said to be complete if you receive all of the following immunization: 1 dose of hepatitis B, 1 dose of BCG, 3 doses of DPThepatitis B, 4 doses of polio, and 1 dose of measles. Humidity is a physical parameter that indicates the moisture content in toddlers' houses. Humidity is said to be inadequate if it is <40% or >70%. Humidity is said to be adequate if it is between 40% and 70%.

Data collection on nutritional and immunization done status was using questionnaires and observations carried out by recording data from a toddlers' cohort in the MCH book. The measurement of humidity was done using the ATH-02 digital hygrometer thermometer. Data processing was carried out using a computer application program. Data analysis was done using chi square and the logistic regression test method. This study was approved by the Health Research Ethics Committee of the Faculty of Public Health at the University of Jambi. The study bears the certificate number 102/KEPK/2019.

RESULTS

A total of 33 confirmed pneumonia cases were included: 25 toddlers were aged between 12 and 35 months; and eight toddlers were aged between 36 and 59 months. There were 14 males and 19 females. A total of 33 toddlers without pneumonia were included in the study. This recruitment is detailed in a separate study. The 33 toddlers, without pneumonia, were included in the control group. They were matched by age in a similar manner to the case group of pneumonia. The characteristics of the toddlers included in the study are detailed in Table 1.

From Table 2, it can be observed that nine toddlers (27.27%) had a history of being underweight. The number of toddlers having a history of incomplete immunization status was five

(15.15%). The number of toddlers, in whose houses the humidity was classified as inadequate, was 14 (42.42%). Based on the results of the chi-square analysis, nutritional status was observed as p-value=0.04; OR=5.81; 95%CI=1.15–29.44). Air humidity was a significant determinant of pneumonia, with p=0.01; OR=7.37; 95%CI=1.87–29.08). The immunization status did not have a significant relationship with the odds of developing pneumonia and was not a determinant for the incidence of pneumonia in toddlers,

Table	1
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	Characteristi	ics of	toddlers
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wherein p-value = 0.20; OR = 5.71; 95%CI= 0.63<OR<51.89.

Based on the final multivariate logistic regression analysis results indicated in Table 3, it was observed that inadequate air humidity was a determining risk factor for the incidence of pneumonia in toddlers (AOR=7.37; 95% CI, 1.80–30.13; p=0.01). Inadequate air humidity was followed by underweight toddlers as another determining risk factor (AOR=5.81; 95% CI, 1.07–31.68; p=0.04).

endideteristies of todalers						
Characteristics	Cas	se	Cont	rol	Total	
Characteristics	n	(%)	n	(%)	n	(%)
Age (month)						
12–35	25	75.76	25	75.76	50	75.76
36–59	8	24.24	8	24.24	16	24.24
Sex						
Male	14	42.42	18	54.55	32	48.48
Female	19	57.58	15	45.45	34	51.52
Siblings						
No siblings	2	6.06	5	15.15	7	10.61
One or more siblings	31	93.94	28	84.85	59	89.39
Mothers' educational level						
None/primary level	2	6.06	1	3.03	3	4.55
Secondary level	20	60.61	19	57.58	39	59.09
Higher than secondary level	11	33.33	13	39.39	24	36.36
Fathers' educational level						
None/primary	1	3.03	2	6.06	3	4.54
Secondary level	14	42.42	15	45.45	29	43.94
Higher than secondary level	18	54.55	16	48.49	34	51.52
Fathers' employment status						
Unemployed	1	3.03	0	0.00	1	1.52
Employed	32	96.97	33	100.00	65	98.48
Total	33	100.00	33	100.00	66	100.00

Table 2

Data analysis of Nutritional Status, Immunization Status, and Air Humidity in toddlers with pneumonia

Variable	(Case	Co	ontrol	Т	Total OR		n	
vallable	n	(%)	n	(%)	n	(%)	(95% CI)	p	
Nutritional status									
Underweight	9	27.27	2	6.06	11	16.67	5.81	0.04*	
Normal	24	72.73	31	93.94	55	83.33	(1.15 <or<29.44)< td=""><td></td></or<29.44)<>		
Immunization									
Incomplete	5	15.15	1	3.03	6	9.09	5.71	0.20	
Complete	28	84.85	32	97.97	60	90.91	(0.63 <or<51.89)< td=""><td></td></or<51.89)<>		
Humidity									
Inadequate	14	42.42	3	9.09	17	25.76	7.37	0.01*	
Adequate	19	57.58	30	90.91	49	74.24	(1.87 <or<29.08)< td=""><td></td></or<29.08)<>		
Total	33	100.00	33	100.00	66	100.00			

*significant if *p*<0.05 (α=0.05)

wultivariate analysis of logistic regression determining the incidence of pheumonia in toddiers					
Variable	Adjusted OR	95% CI	р		
Nutritional status					
Underweight	5.81	1.07-31.68		0.04*	
Normal (Ref.)	-				
Humidity					
Does not qualify	7.37	1.80-30.13		0.01*	
Qualifies (Ref.)	-				

Table 3

Multivariate analy	ysis of log	istic regression	determining th	he incidence of	pneumonia in toddlers
		0			

*significant if p < 0.05 ($\alpha = 0.05$)

DISCUSSION

Nutritional Status

This study revealed that the nutritional status has a significant relationship with the incidence of pneumonia in toddlers. Based on field observations, nutritional needs are influenced by the ability of the mother herself to consume adequate amounts of food; however, the adequacy of nutrients from the food consumed was not being fulfilled, which meant that both the mother and the family were consuming the required quantities, but they were not focusing on the quality of the food being taken (nutrients). Thus, some children under five had a poor nutritional status (Izhar, 2017). Absorption of nutrients from food intake is also influenced by infectious diseases (pneumonia) or other infectious diseases experienced by toddlers. These diseases inhibit (or act as inhibitors to) the fulfillment of nutritional needs in toddlers (Thibault et al., 2015).

The results of this study are in accordance with the theory, which states that there is a relationship between nutritional status and the incidence of pneumonia in infants. A study conducted by Par'i (2014) revealed that the main factor causing nutritional problems is a lack of food intake, which leads to infectious diseases. Toddlers who get a low intake of food show low endurance. Thus, children under five can become incoming infectious vulnerable to agents. Nutritional deficiencies can weaken the immune system of the toddler (as a whole). Protein and energy are required to be consumed in sufficient quantities to strengthen toddlers' immune systems, without which the weakening of the immune system can occur, and the antibody levels may decrease. Consequently, toddlers can easily be attacked by infectious diseases. A lowering of immunity is caused by decreasing leukocyte activity, whereby phagocytes in the immune system will be unable to kill germs. Being underweight can cause immune system disorders. The cells contained in the immune system are

found in specific tissues and organs, such as the lymphoid tissues that support immune responses.

Malnutrition appears to be an important risk factor for causing pneumonia. The results of other studies have shown that there is a relationship between malnutrition and lung infection. Therefore, toddlers who are malnourished are more susceptible to developing pneumonia due to a lack of endurance compared to toddlers who consume nutritious food. Malnutrition can damage the body's defense system against microorganisms and mechanical defenses. This can make the body easily prone to getting infected, leading to a higher mortality rate (Yeo et al., 2019).

In the case of malnutrition or a lack of nutrition, where protein intake is lacking, glucose and cilia in the respiratory system do not function normally. This causes germs to enter the body. During this time, the strength of the abdominal muscles, between the ribs, shoulders, and the diaphragm, is lowered, which can lead to impaired respiration. The ability of the body to expel phlegm becomes damaged. This causes exudate to accumulate in the bronchus. Thus, germs lodged in the respiratory tract can cause infection (Manabe, Teramoto, Tamiya, Okochi, & Hizawa, 2015). This is in line with research conducted by Efni, Machmud, & Pertiwi (2016), who revealed a relationship between nutritional status and the incidence of pneumonia in infants, with p=0.02 and OR=9.10, suggesting that toddlers who were underweight were 9.10 at risk of suffering from pneumonia compared to toddlers who had a normal nutritional status. This study was also in line with research conducted by Sarlis & Filda (2018), who indicated that there was a significant relationship between nutritional status and the incidence of pneumonia in toddlers. They concluded that the state of being underweight is a factor for causing pneumonia, thereby toddlers who are underweight will be more susceptible to pneumonia than toddlers who have a normal nutritional status. Mustikarani, Rahardjo, Qadridjati, & Prasetya (2019) also conducted a similar study, which revealed that there was a significant relationship between nutritional status and the incidence of pneumonia, with p=0.00.

However, this study is not in line with research conducted by Sarv (2017), who indicated that there was no relationship between nutritional status and the incidence of pneumonia in infants (p=0.82). At the time this study was conducted, researchers faced limitations in terms of carrying out measurements, especially in measuring the weight and height of toddlers. It was quite difficult to measure the body weight and height of toddlers independently, so the measurements were carried out together, with the toddler's mother holding her child. The scales were then reduced by the mother's body weight. The results obtained certainly caused some debate and were unexpected. Another research, whose results were also not in agreement, was conducted by Rigustia, Zeffira, & Vani (2019). They stated there was no relationship between nutritional status and the incidence of pneumonia in toddlers, with p value=0.79. Thus, being underweight can reduce the body's immune capacity in responding to incoming infections, including causing an impairment granulocyte functioning, in complement deficiencies, micronutrient and deficiencies. In a state of good nutrition, the body has enough ability to defend itself against infectious diseases. If the nutritional situation becomes poor, the body's immune response will be lowered, so the body's ability to defend itself against infections decreases as well.

Immunization Status

The results of this study revealed that the immunization status has no significant relationship with the incidence of pneumonia in toddlers. These findings are in line with the research conducted by Sary (2017), who suggested that there was no relationship between incomplete immunization status and the incidence of pneumonia in infants (p=0.32, OR=1.61). A similar study was also carried out by Zar et al (2016). The results indicated that the completeness of immunization status was not a risk factor (OR=1.46, 95% CI=0.91-2.35) for the incidence of pneumonia in infants. The results of a similar study conducted by da Silva et al (2018) also revealed that the completeness of immunization status was unrelated and was not a risk factor for the incidence of pneumonia.

However, the results of the current study are not in line with the research conducted by Ningsih, Salimo, & Rahardjo (2019), who revealed a significant relationship between immunization status and the incidence of pneumonia in infants. In this study, toddlers, whose immunization status was incomplete, were more at risk of developing pneumonia compared to toddlers whose immunization status was complete. This study suggested that toddlers' immunity to diseases was influenced by the completeness of immunization status.

Rahmawati (2018) also conducted a similar study and obtained the results of p value=0.01 with OR=22, which meant that there was a relationship between incomplete immunization status, which and the incidence of pneumonia in toddlers, which, according to the results, revealed that toddlers were 22 times at risk of getting pneumonia compared to toddlers whose immunization status was complete. A similar study was conducted by Wahyudi (2017), which revealed that there was a relationship between the completeness of immunization status and the incidence of pneumonia, with p=0.00. Another similar study conducted by Puspitasari & Syahrul (2015) revealed that toddlers who did not receive measles immunization were 10.23 times at risk of suffering from pneumonia compared to toddlers who received measles immunization.

Immunization serves to protect the body, especially infants and toddlers from various infectious diseases, by using vaccines to stimulate the immune response or producing immunoglobulin. Stimulation of the immune system gives the body long-term protection. In the short term, this stimulation protects the body against infections, however, if an infection has occurred. the immune system becomes compromised. Naturally, the body puts forth a defense against various bacteria or viruses that enter. The body's defense is the first, non-specific defense, such as complement and macrophages, which will first play a role when bacteria or viruses enter the body. Thereafter, the second defense is a specific defense consisting of humoral and cellular systems. The defense system only reacts to bacteria or viruses that are similar in shape. The humoral system will produce substances called immunoglobulins (IgA, IgM, IgG, IgE, and IgD), and the cellular system consists of B lymphocytes and T lymphocytes. In the next specific defense system, the body will produce one cell called a memory cell. This cell acts very quickly to protect the body if a disease has entered the body (Pichichero et al., 2016).

The level of education, motivation, and good behavior of mothers in giving special attention to

their children about health care (immunization) can make an impact to prevent the onset of an infectious disease. This is evident from a study conducted, where the population that was observed had good immunization coverage (the universal child immunization status of the village was >95%), which meant that this population could prevent an infectious diseases (Kirolos et al., 2018).

Giving immunization indirectly can provide immunity to a baby against certain diseases in accordance with the antigen in the vaccine; however, the administration of the vaccine depends on the formation of antibodies in the body. Among some children, the antibodies are not formed completely or fail to form. This can be caused by genetic disorders, or it could be due to the quality of the vaccine itself. Immunization is a way to actively boost a toddler's immunity against an antigen, whereby if a toddler is exposed to the same antigen, they can avoid a disease. Immunization does not directly prevent pneumonia. It only provides protection against the factors responsible for triggering pneumonia. Thus, even if a child receives complete basic immunization, the possibility of suffering from pneumonia still exists (Pichichero et al., 2016).

Based on data analysis, it was observed that the status of immunization was not related and was not a determinant of the incidence of pneumonia because a small number of samples of toddlers with pneumonia was studied, and most toddlers had a history of getting complete basic immunization (Ministry of Health RI, 2018).

Humidity

The results of current study revealed that inadequate humidity in houses has a significant relationship with the incidence of pneumonia, with AOR=7.37, 95% CI=1.80–30.13. Thus, it can be concluded that toddlers who live in homes with inadequate humidity are 7.37 times at risk of suffering from pneumonia compared to toddlers living in homes that have adequate levels of humidity.

When the humidity in a house is too high or too low, it can lead to the fertile growth of microorganisms. Humidity can be affected by temperature, lighting intensity, poor ventilation, and watertight flooring. Unhealthy air humidity is the fastest medium for the growth of bacteria and can cause pneumonia. Humidity is a triggering factor for the proliferation of viruses, bacteria, and fungi. Generally, high humidity can also be caused by the non-availability of adequate ventilation (Pusparini, Cahyono, & Budiono, 2017).

The findings of this study were in line with a research conducted by Darmawati, Sunarsih, & Trisnaini (2016), who revealed that there was a significant relationship between the humidity in houses and the incidence of pneumonia in infants (p=0.00, OR=5.95). The humidity at home influences the development of bacteria, germs, and fungi in rooms. If toddlers often sleep for long periods of time in humid rooms, the risk of getting pneumonia will be even greater. Pusparini, Cahyono, & Budiono (2017) also conducted a similar study. The results indicated that toddlers living in homes with inadequate humidity are 8.73 times at risk of suffering from pneumonia. The research conducted by Kusumawati, Suhartono, & Yunita (2015) revealed a p-value = 0.02 with OR = 3.23, which meant that the humidity in houses was a risk factor for the incidence of pneumonia in infants.

Most of the toddlers live and stay indoors. If the physical conditions in a house do not qualify and meet the health requirements (in terms of humidity), there is a risk for microorganisms (e.g., bacteria and viruses) to develop, which can cause pneumonia in infants (Rahmawati, 2018). However, a research conducted by Hidayah, Ummah, & Wulandari (2018) revealed different results. The study indicated that there was no significant relationship between the humidity in houses and the incidence of pneumonia in infants (p=1.00; OR=1.00; 95% CI=0.19-5.40). A study carried out by Kurniasih, Suhartono, & Nurjazuli (2015) also suggested that there was no significant relationship between humidity in homes and the incidence of pneumonia in infants, with OR=0.81. From some of these studies, it can be concluded that humidity is not the main cause of pneumonia; there are other causes that are more dominant.

Thus, the results of current study revealed that inadequate humidity in houses can increase the growth of microorganisms. The following observations were made by researchers in the respondents' homes: A high level of humidity was felt in the houses; in terms of the physical conditions of the houses, they were made of boards and plywood; the walls of the houses were made from bricks, which were not plastered; and the floors of the houses were not plastered. Based on data documented by the PHC in Talang Bakung, out of the 10,109 houses inspected in 2018, the percentage of healthy homes was 5,730 (56.68%). This indicated that the percentage of healthy houses in the working area of the PHC in Talang Bakung was still low. Components of a house must meet physical and biological requirements because not paying attention to these factors can potentially cause discomfort for its inhabitants. It can also increase the risk factors for spreading a disease.

CONCLUSION

This study concluded that the incidence of pneumonia most often occurs in females in the age group between 12-35 months. Toddlers who were underweight were 5.81 times more likely to develop pneumonia compared to toddlers who ate a balanced meal. Toddlers living in homes with inadequate humidity were 7.37 times more likely to develop pneumonia compared to toddlers living homes with adequate humidity. in The incompleteness of immunization status did not have a significant impact on the incidence of pneumonia. Some suggestions for health policy makers in Jambi City include strengthening supplementary feeding programs, focusing on cold chain vaccine management, and healthy home supervision. Further research carried out should examine other factors associated with the incidence of pneumonia with a greater degree of accuracy and by considering a larger sample size based on different study designs.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTION

The author is participating actively in research and article writing and partly responsible for the content of writing.

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