Meta-Analysis: Relationship of History of Acute Respiratory Infections and Low Birth Weight with Stunting in Toddlers

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ABSTRACT

Basic Health Research (2018) and National Socio-Economic Survey (2019) showed a high incidence of stunting in Indonesia. History of acute respiratory infection (ARI) and low birth weight (LBW) were studied as factors associated with stunting in under-five children. The research's objective was to analyze the association between the history of ARI and LBW with the incidence of stunting in under-five children. This study was a meta-analysis. Literature searching was conducted in reputed and accredited journals in PubMed and Google Scholar, published between 2016-2020, analytic observational study design, contained OR/PR/RR with 95% confidence interval, written in English or Indonesian, and available in full-text. The meta-analysis was conducted with RevMan 5.4 application. We included 14 studies. Results showed there was a significant association between history of ARI and the incidence of stunting in under-five children, with pooled OR = 2.48 (95%CI = 1.82-3.40, p < 0.00001, I2 = 0%, p for heterogeneity = 0.66). This study showed there was a significant association between LBW and incidence of stunting, with pooled OR = 2.15 (95% CI = 1.58-2.93, p < 0.00001, I2 = 61%, p for heterogeneity = 0.005). The conclusions were there were significant associations between the history of ARI and LBW with the incidence of stunting in under-five children.

Keywords: Acute respiratory infection, low birth weight, stunting, under-five children

INTRODUCTION

Stunting is a health problem associated with a disturbance in the growth of children which is characterized by a child's height less than -2 SD (standard deviation). The incidence of stunting in Indonesia is still a challenge in health problems to date. This is a health problem that is a challenge in developing countries. Based on the results of the Basic Health Research (Riskesdas) in 2018, the proportion of very short and short nutritional status (stunting) in toddlers is still at the number 30.8%¹, while the results of the 2019 National Socio-Economic Survey (SUSENAS) showed a decline to 27.67% or 3.1% lower compared to 2018. However, the stunting rate is still quite high, so efforts must be made to implement health programs to reduce the incidence of stunting in Indonesia².

Stunting has a bad impact on the future of the nation because it can cause harm to individuals, families, communities, and the state. The Ministry of Health of the Republic of Indonesia in 2018 stated that the impact of stunting is generally divided into two, namely the impact that can occur relatively quickly and the impact that occurs relatively long. The impact of stunting that occurs relatively quickly is an increase in morbidity and mortality, and an increase in spending on health costs. The impact of stunting in a relatively long time is not achieving optimal body size as an adult, increasing the risk of degenerative diseases, declining reproductive health conditions, low ability to learn in school, and low productivity and work capacity³. Children with stunting scored 16.1% lower on vocabulary tests and 48.8% lower on quantitative assessment tests at 8 years of age compared to children who were not stunted³.

Risk factors for stunting include lack of food intake and the presence of infectious diseases that are often experienced by toddlers. Several risk factors affect nutritional intake in children, namely not implementing breastfeeding for 6 exclusive months, inadequate complementary feeding (MPASI) at weaning age, and irregular feeding. In addition, other risk factors that have an opportunity for stunting are acute respiratory infections (ARI), low birth weight babies (LBW), asthma, diarrhea, and body abnormalities⁴.

ARI is an infectious disease that is often experienced by Indonesian people, both toddlers, and adults. Based on the results of Riskesdas 2018, ARI in toddlers is an infectious disease with the highest prevalence compared to other infectious diseases such as pneumonia and diarrhea. The prevalence of ARI among children under five in Indonesia is 12.8%, while pneumonia is 4.8% and diarrhea is 12.3%¹.

The results of a study conducted by Himawati (2020) on children aged under 5 years in Sampang showed a significant relationship between acute respiratory infections (ARI) and stunting (OR = 3.115, p = $(0.029)^5$. This is in line with research conducted by Natalia and Evitasari (2020) which showed that there was a relationship between a history of ARI disease and the incidence of stunting $(OR = 7.07, p = 0.008)^6$. Meanwhile, a study by Sahitarani et al (2020) on children aged 24-59 months in Sedayu District, Bantul Regency showed that there was no relationship between stunting and the frequency of ARI disease⁷. Likewise, the results of research from Setiawan et al (2018), which showed that there was no significant relationship between the average frequency of ARI and diarrhea with the incidence of stunting⁸.

The condition of LBW is one of the challenges that are often faced by newborns in developing countries. The proportion of low birth weight (LBW) infants in Indonesia is still at 6.2%. Based on the initial survey, 80% of the articles found contained discussions about the relationship between LBW and the incidence of stunting in children under five. Therefore, LBW needs attention considering the causes and effects are very complex, including fetal, placental, maternal factors, and a combination of the three¹.

The results of a study conducted by Fitri (2018) at the Lima Puluh Pekanbaru Health Center prove that there is a relationship between LBW and the incidence of stunting (p = 0.000)⁹. This is in line with the results of research by Nasution et al (2014) which states that there is a relationship between LBW and the incidence of stunting in children aged 6-24 months (OR = 5.60; 95% CI: 2.36-13.32)¹⁰. Meanwhile, the results of a study conducted by Hamzah et al (2021) stated that there was no relationship between LBW and the incidence of stunting (p = 0.106)¹¹. Similar results from the study of Hairunis et al (2016) also stated that there was no relationship between LBW and the incidence of stunting (p = 0.980)¹².

Based on the above background, a contradiction was found between the results of several researchers and other researchers regarding the relationship between a history of ARI and LBW with stunting, so it is necessary to conduct research on the relationship between a history of ARI and LBW with stunting in children under five by conducting a systematic review and meta-analysis. from various research articles.

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METHOD

This study uses a meta-analysis study. The variables of this study were ARI and LBW (independent variable) and stunting (dependent variable). The sample in this study is an article that examines the relationship between a history of ARI and LBW with the incidence of stunting through the PubMed and Google Scholar database sources. The keywords in Bahasa for article search are: "infeksi saluran napas akut", "berat badan lahir rendah", "*stunting*", "balita", "anak-anak". The keywords in English are "acute respiratory infection", "low birth weight", "stunting", "under-

five", "children", "toddler". Article selection criteria include inclusion criteria, namely reputable international journals (indexed by Scopus, Pubmed, and/or Web of Science), accredited national journals (indexed by Sinta 1 to Sinta 4), published in 2016-2020, research subjects are children under five (aged 0-59 months), the research method in the journal is analytical observational, there an are OR/PR/RR values and 95% CI, the language used is Indonesian or English, and can be accessed in full-text. The overall process in article search can be seen in Figure 1.



Figure 1. Article Selection Process

Quantitative analysis was performed using the RevMan 5.4 application. The fixedeffects model will be used if the research has small heterogeneity, and the random-effects model will be used if there is the heterogeneity, based on.²

RESULT AND DISCUSSION

Based on the results of article searches in the Pubmed and Google Scholar databases, it was found that the number of articles included in the inclusion criteria for this metaanalysis were 14 articles out of 1,329 articles found on search engines.

The research articles that met the inclusion criteria and were analyzed in this

study amounted to 14 articles with a crosssectional research design of 6 articles and case-control articles as many as 8 articles. The majority of the research was conducted in Indonesia, namely, 12 studies, and 2 other studies were conducted in Pakistan and Vietnam. Research subjects in these studies varied between infants, toddlers, and toddlers.

Based on the results of a review of all research articles, there is no variation in the definition of the research variables, namely ARI, LBW, and stunting, except for studies that do not define of this variable in the methods section of the published article. Articles included in the meta-analysis can be seen in table 1.

No.	Name of Researcher	Study about ARI	Study about LBW
1.	Candra et al (2016) ¹³	Yes	Yes
2.	Wellina et al (2016) ¹⁴	-	Yes
3.	Yunianingsih et al (2017) ¹⁵	Yes	-
4.	Dewi et al (2018) ¹⁶	-	Yes
5.	Bening et al (2018) ¹⁷	Yes	-
6.	Rahayu et al (2018) ¹⁸	Yes	Yes
7.	Setiawan et al (2018) ⁸	-	Yes
8.	Ramadhani et al (2019) ¹⁹	Yes	-
9.	Giao et al. (2019) ²⁰	-	Yes
10.	Khan et al. (2019) ²¹	-	Yes
11.	Yuniarti et al (2019) ²²	Yes	Yes
12.	Himawati et al (2020) ⁵	Yes	Yes
13.	Sari et al (2020) ²³	-	Yes
14.	Wijayanti et al (2020) ²⁴	-	Yes
	Number of studies	7 studies	11 studies

Table 1. Table of included studies (n = 14 studies)

Figure 2 shows the forest plots for 7 studies that examined the relationship between a

history of ARI and the incidence of stunting in children under five (a total of 965 subjects).

				Odds Ratio		Odds Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Fixed, 95% CI		IV, Fixed, 95% CI	
Bening dkk, 2018	0.8755	0.3537	20.4%	2.40 [1.20, 4.80]			
Candra dkk, 2016	0.8961	0.3041	27.6%	2.45 [1.35, 4.45]		 −- ∎ −-	
Himawati dan Fitria, 2020	1.1362	0.5409	8.7%	3.11 [1.08, 8.99]			
Rahayu dkk, 2018	0.5128	0.4894	10.6%	1.67 [0.64, 4.36]		- +-	
Ramadhani dkk, 2019 (a)	0.5008	0.4994	10.2%	1.65 [0.62, 4.39]			
Ramadhani dkk, 2019 (b)	0.7031	0.4988	10.3%	2.02 [0.76, 5.37]		+	
Yunianingsih dkk, 2017	1.411	0.6713	5.7%	4.10 [1.10, 15.28]			
Yuniarti dkk, 2019	1.9473	0.6248	6.5%	7.01 [2.06, 23.85]			
Total (95% CI)			100.0%	2.48 [1.82, 3.40]		•	
Heterogeneity: Chi² = 5.00, df = 7 (P = 0.66); i² = 0%							50
Test for overall effect: Z = 5.70 (P < 0.00001)						Tidak ISPA ISPA	

Figure 2. Forest plot studies examining the relationship of history of ARI with stunting in children under five

Figure 2 shows the results of data analysis from 7 research articles regarding the relationship of history of ARI with the incidence of stunting in children under five and analyzed using the fixed effects model. The results of the analysis show that the research variation has a small heterogeneity (I2 = 0%, p for heterogeneity = 0.66).

The results of the data analysis displayed on the forest plot show that there is a significant relationship between the history of ARI and the incidence of stunting (*pooled* OR = 2.48, 95% CI 1.82-3.40, p < 0.00001) so it can be concluded that a history of ARI in children under five is associated with a 2,48-fold increased risk of becoming stunted compared to having no history of ARI.

This study proves that a history of ARI is associated with the incidence of stunting. ARI

can affect children's eating patterns that become irregular. Children who have ARI tend to be fussy and lazy to eat, as a result, the nutritional intake that should be fulfilled from daily meals is not achieved. Efforts that can be made so that the risk of stunting can be reduced when children often experience ARI is by ensuring that nutritional intake when children experience ARI is still met by their daily nutritional needs¹³. In addition to inadequate nutritional intake due to lack of appetite, ARI which is an infectious disease is also related to the mechanism of inflammation that occurs. When inflammation occurs, high-sensitivity Creactive protein (hs-CRP) is secreted by the body which has an impact on growth hormone resistance. Inflammation in the body will inhibit the work of the hormone Insulin Growth Factor-1 (IGF-1) which acts as a mediator between growth hormone and the growth of muscle and bone cells in the body¹⁴.

Figure 3 shows a funnel plot for the relationship

between the history of ARI and the incidence of stunting in children under five (total subjects were 965 people).



Figure 3. Funnel plot study on the relationship of history of ARI with the incidence of stunting in toddlers

Figure 3 shows a symmetrical distribution of research, where the distribution of research is balanced between the left and right of the centerline boundary. Therefore, it can be concluded that there is no indication of bias in the publication of studies examining the relationship between a history of ARI and the incidence of stunting in children under five. Thus, this indicates that the results of the metaanalysis of these studies can represent studies on the strength of the risk association between a history of ARI and stunting in children under five.

Likewise, the results of research from Setiawan et al (2018), which showed that there was no significant relationship between the average frequency of ARI and diarrhea with the incidence of stunting.⁸

Figure 4 shows the forest plots for 11 studies examining the relationship between low birth weight and stunting in children under five (a total of 5,420 subjects).





Figure 4 presents the results of data analysis from 11 research articles regarding the relationship between LBW and the incidence of stunting in children under five and analyzed using the random-effects model analysis model. The results of the analysis show that the research variation has moderate heterogeneity (I2 = 61%, p for heterogeneity = 0.005).

The results of data analysis displayed on the forest plot show that there is a significant relationship between LBW and stunting (*pooled* OR = 2.15, 95% Cl 1.58-2.93, p < 0.00001), so it can be concluded that under-fives with a history of LBW in infants are associated with a 2,15 times increased risk of becoming stunted compared to those without LBW.

LBW conditions indicate that the fetus is malnourished while in the womb, and stunting is caused by malnutrition in the long term.

Babies with low birth weight who do not get special attention will experience failure to catch up with growth, so that their growth becomes slower than normal children¹⁵. If it is not supported by adequate nutrition, the risk of nutritional problems will be even greater. This nutritional deficiency is caused by increased growth and development, high metabolic requirements, low nutrient reserves, and immature body physiological systems.¹⁶

In addition to requiring high nutritional intake, LBW infants are also susceptible to infectious diseases. LBW babies are very susceptible to infectious diseases because their serum immunoglobulin levels are still low, so LBW babies should not be in an environment where there is a risk of infection in any form.¹⁷.

Figure 5 shows the funnel plot for the relationship between LBW and the incidence of stunting in toddlers.



Figure 5. Funnel plot studies on the relationship between LBW and the incidence of stunting in toddlers

Meanwhile, the results of a study conducted by Hamzah et al (2021) stated that there was no relationship between LBW and the incidence of stunting (p = 0.106)¹¹. Similar results from the study of Hairunis et al (2016) also stated that there was no relationship between LBW and the incidence of stunting (p = 0.980)¹².

shows Figure 5 an asymmetric distribution of research, where the distribution of research is not balanced between the left and right of the centerline boundary. Therefore, it can be concluded that there is an indication of bias in the publication of studies examining the relationship between LBW and the incidence of stunting in children under five. Based on this analysis, the risk of LBW being stunted may be lower than the pooled OR from the metaanalysis, because there is an opportunity to overestimate the results of this meta-analysis.

CONCLUSION

The conclusion from the meta-analysis of

the relationship between the history of ARI and LBW to the incidence of stunting in toddlers is that there is a relationship between the history of ARI and the incidence of stunting in toddlers, with pooled OR = 2.48 (95% CI = 1.82-3.40, p < 0.00001, I2 = 0%, p for heterogeneity = 0.66), and there is a relationship between LBW and the incidence of stunting in toddlers with pooled OR = 2.15 (95% CI = 1.58-2.93, p < 0.00001, I2 = 61%, p for heterogeneity = 0.005).

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