Effect of Intestine Parasite Infection on Stunting in Children: A Meta-Analysis Study

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Abstract: Stunting is a child health problem that describes a chronic nutritional problem. One of the causes of stunting is intestinal parasitic infection. Research related to the risk factors for stunting has been widely carried out, but related to intestinal parasite infection as one of the determinants is still limited and still being debated. Therefore, it is necessary to make a meta-analysis study. Search for published and unpublished articles according to the flow on the Prisma diagram online through PubMed, Science Direct, Google Scholar, Hindawi, Cochrane library, DOAJ, JSTOR, Public Library of Science (PLoS), UI repository, Unila and USU in a timeframe 2016 to 2021 with Indonesian and English versions. The keywords used were intestinal parasitic infection, soil transmitted helminth infection, intestinal protozoan, stunting, growth disorders, children, intestinal parasitic infections, intestinal protozoa, short stature and children. The article search was carried out using keywords and Mesh terminology using the Quatation mark "", the boolean operators "OR" and "AND". The search results obtained 1042 journals and 2 theses. Then, screening and review were carried out to obtain 6 suitable journals to be analyzed using review manager 5.4 software. The combined p-value of the meta-analysis results was p=0.02 with an OR of 1.48 (95% CI 1.06-2.07). This means that there is an effect of intestinal parasitic infection on the incidence of stunting in children.

1 INTRODUCTION

Stunting is a child health problem, not only in the world, but also in Indonesia. In 2015, around 23.2% or 159 million children under five experienced stunting (Shekar, 2017). Data from 2017 shows that 55% of children under five are stunted in the world originate from Asia and 39% live in Africa. The order of proportion of stunted children under five in Asia is South Asia (58.7%), Southeast Asia (14.9%), East Asia (4.8%), West Asia (4.2%) and Central Asia (0.9%). According to data from *the World Health Organization* (WHO), the prevalence of stunted toddlers in Indonesia in 2005-2017 was the third highest in the Southeast Asia region or *South-East Asia Regional* (SEAR), namely 36.4% (Ministry of Health of the Republic of Indonesia, 2018; UNICEF, 2020).

Based on Nutrition Status Monitoring (PSG) data, the highest prevalence of nutritional problems in Indonesia is *stunting*, namely 27.5% in 2016 and 29.6% in 2017, while Basic Health Research (Riskesdas) in 2018 produced prevalence data of 30.8% (Ministry of Health of the Republic of Indonesia, 2018). Nutritional problems do not only occur in toddlers, but also in children and adolescents. Nationally, the prevalence of *stunting* in children aged 5-12 years is 23.6% and in adolescents aged 13-15 years is 25.7% (Ministry of Health of the Republic of Indonesia, 2018).Handling *stunting* has been designated as one of the priority programs (Ministry of Health of the Republic of Indonesia, 2018; CPM, 2020).

Stunting is divided into two categories, namely short with a Z score threshold of -3.0 to -2.0 standard deviation (SD) and very short with a *Z score* threshold of less than -3.0 SD (Ministry of Health of the Republic of Indonesia, 2020; Harjatmo, 2017). *Stunting has serious impacts both in the* short and long term, including increasing child morbidity and mortality. The incidence of *stunting* at an early age can continue and there is a risk of short growth in adolescence. Therefore, interventions to prevent *stunting growth* are still needed even after exceeding the First 1000 Days of Life (HPK) (Ministry of Health of the Republic of Indonesia, 2018; Aryastami, 2017).

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The causes of *stunting* consist of several factors, namely *basic causes, underlying causes* and *immediate causes*. *Basic causes* are adequate household quality support (such as housing, education, work, income and technology), socio-cultural, economic and political conditions. *Underlying causes* include household food security conditions, parenting patterns, sanitation and health of the household environment, and health services. *Immediate causes* include food intake and infectious diseases. [9] One of the infectious diseases is caused by intestinal parasites which often affect children, especially in tropical areas such as Indonesia (Ministry of Health of the Republic of Indonesia, 2018; Aryastami, 2017; Torlesse, 2016; Setiawan, 2018).

Intestinal parasitic infections can be caused by intestinal protozoa and intestinal worms. The intestinal protozoa that are often found are *Giardia lamblia, Blastocystis hominis, Entamoeba* and *Cryptosporidium*. The prevalence of intestinal protozoan infections is still relatively high. Research in Ethiopia on 500 children aged 1 to 5 years found a prevalence of intestinal parasitic infections of 47% and the highest was *Giardia lamblia infection (22* %) (Osman, 2020). Children with giardiasis are 3.5 times more likely to be malnourished than those without *Giardia lamblia infection* (Osman, 2020). Likewise, in Mexico, 34% of children aged 6 months to 5 years were infected with intestinal parasites, namely *Ascaris lumbricoides, Entamoeba histolytica* and *Giardia lamblia (*Gutiérrez-Jiménez, 2019). Research in Bekasi, West Java, Indonesia also provided data on the prevalence of *Blastocystis hominis* at *60.8%, Giardia lamblia* at *33.8%* and *Entamoeba histolytica* at 1.4% (Winita, 2016).

Intestinal protozoal infections are generally *water-borne diseases* that are transmitted via the oral-fecal route (Mahardianti, 2020). Transmission can occur easily, especially in areas with low sanitation and hygiene conditions. This causes high morbidity rates which of course affect the sufferer's quality of life. Manifestations of this disease can include nausea, vomiting, abdominal pain and diarrhea (Pramestuti, 2017). Intestinal protozoal infections can cause problems with digestion and absorption of nutrients. This is partly due to shortening and *dystrophy* of the intestinal microvillus or the formation of ulcers (Herbowo, 2016).

Intestinal worm infections are most often caused by *soil transmitted helminth* (STH) worm parasites. *Ascaris lumbricoides, Trichuris trichiura,* and hook worms (*Necator americanus* and *Ancylostoma duodenale*) are nematodes that include STH (Jourdan, 2018; Sutanto, 2008). Intestinal worm infections generally are chronic and asymptomatic. This parasite can affect the intake, digestion, absorption and metabolism of food in the host's body.

The World Health Organization estimates that worldwide STH infection sufferers are more than 1.5 billion people (24%). More than 600 million school-age children and 270 million preschool-age children live in areas with intensive parasite transition and are therefore at high risk of infection (WHO, 2020). In 500 children aged under 5 years in Ethiopia, 15% were infected with *Ascaris lumbricoides* (Osman, 2020). The prevalence in Indonesia varies, but is still in the high range. Research conducted by Mutiara in 2014 at several state elementary schools in one sub-district in the West Java region, found that the prevalence of STH infection was 23.2% (Mutiara, 2014). Meanwhile, the prevalence in one of the state elementary schools located in South Lampung Regency was 43.1%. This infection is included in *neglected tropical diseases* (NTDs) so attention regarding its management, including management and elimination efforts, is not yet optimal.

Research regarding risk factors for *stunting* has been widely carried out, however regarding intestinal parasitic infections as one of the determinants is still limited and still debated (Hailegebriel, 2018; Yoseph, 2020). In addition, treating intestinal parasitic infections has not been a priority in implementing *stunting management programs* in Indonesia. Therefore, it is necessary to carry out *systematic reviews* and meta-analysis research to synthesize data related to the influence of intestinal parasite infections on *stunting* in children.

2 THEORETICAL REVIEW

2.1 Child Nutritional Status

Stunting is a child health problem, not only in the world, but also in Indonesia. *Stunting* is nutritional status based on body length (PB) or body height (TB) index according to age. This indicator provides an indication of chronic nutritional problems. Another anthropometric indicator for assessing the nutritional status of toddlers is weight for height (WW/TB), which provides an indication of acute nutritional problems. The BB/TB and BMI/U indicators can be used to identify thin and fat. The problem of being thin and fat at an early age can result in the risk of various degenerative diseases in adulthood (Ministry of Health of the Republic of Indonesia, 2018). Anthropometry is the measurement of the human

body, while nutritional anthropometry relates to various measurements of body dimensions and body composition as well as age and nutritional levels. The nutritional status assessment categories are presented in table 1.

In growth there are 4 interrelated periods, namely fetus, infancy, childhood and puberty. Age 6 to 24 months determines linear growth. Inadequate nutrition can cause irreversible damage and lead to impaired physical and cognitive growth. The first thousand days have been declared a critical period for nutritional interventions and addressing problems that interfere with nutritional adequacy (Budge, 2019). The combined effects and interactions of infection, environmental and dietary factors as determinants of *stunting* in children have long been considered very important.

Table 1: Categories and Thresholds for Children's Nutritional Status Based on Index (Minister of Health of the Republic of Indonesia, 2020)

Index	Nutritional Status Category	Threshold (Z-score)
Body weight according to age (WW/U) Children aged 0-60 months	*Extremely* underweight	<-3 SD
	Underweight	-3 SD to <-2 SD
	Normal weight	-2 SD to +1 SD
	Risk of being overweight	> +1 SD
Body length according to age (PB/U) or Height according to age (TB/U) Children aged 0-60 months	Very Short (*severely stunted)*	<-3 SD
	Short (*stunted)*	-3 SD to <-2 SD
	Normal	-2 SD to +3 SD
	Tall	> +3 SD
Body weight according to body length (BB/WW) or according to height (WW/TB) Children aged 0-60 months	Malnutrition (*severely wasted)*	<-3 SD
	Malnutrition (*wasted*)	-3 SD to <-2 SD
	Good (normal) nutrition	-2 SD to +1 SD
	Risk of overnutrition (*possible risk of overweight)*	> +1 SD to +2 SD
	Over nutrition (*overweight*)	> +2 SD to +3 SD
	Obesity (*obese)*	> +3 SD
Body mass index according to age (BMI/U) Children aged 0-60 months	Malnutrition (*severely wasted)*	<-3 SD
	Malnutrition (*wasted*)	-3 SD to <-2 SD
	Good (normal) nutrition	-2 SD to +1 SD
	Risk of overnutrition (*possible risk of overweight)*	> +1 SD to +2 SD
	Over nutrition (*overweight*)	> +2 SD to +3 SD
	Obesity (*obese)*	> +3 SD
Body mass index according to age (BMI/U) Children aged 5-18 years	Malnutrition (*severe thinness)*	<-3 SD
	Malnutrition (*thinness*)	-3 SD to <-2 SD
	Good (normal) nutrition	-2 SD to +1 SD
	Over nutrition (*overweight*)	+1SD to +2 SD
	Obesity (*obese)*	> +2 SD

Diarrhea or parasitic infections are infections that occur frequently and repeatedly and are associated with an increased risk of *stunting* (Milward, 2017). Exposure to pathogens can cause disruption of intestinal structure and function. This condition is known as *environmental enteric dysfunction* (EED) which is characterized by villous atrophy of intestinal mucosal cells, crypt hyperplasia, increased permeability, and inflammatory cell infiltration. This EED condition can result in disruption of the intestinal immune response, reducing the delivery, absorption and utilization of nutrients resulting in a state of nutritional deficiency (Budge, 2019; Dewey, 2011).

2.2 Intestinal Parasitic Infections

Soil transmitted helminthiasis is an intestinal worm infection that often occurs in children in tropical areas, including Indonesia, especially in areas with poor sanitation. This group of intestinal worms requires moist and warm soil as a medium for the egg stage to develop into an infective stage, either infective eggs or infective larvae. Intestinal worms included in this group are *Ascaris lumbricoides, Trichuris trichiura* and hook worms *(Ancylostoma duodenale* and *Necator americanus)* (Hadidjaja, 2011).

Protozoa are eukaryotic unicellular microorganisms that resemble animals, are heterotrophs and live as parasites in the bodies of other organisms. Protozoa can survive in a free environment by forming cysts, and in the body other organisms move using means of movement in the form of pseupodia, cilia and flagella. Protozoa is a subdivision that comes from Kingdom Protista. Based on movement or locomotion, the Protozoa subdivision is divided into 4 phyla, namely Sarcomastigophora, Ciliophora, Apicomplexa, and Microspora. Protozoa can infect the intestines, blood, lung tissue and other extraintestinal tissues. The species of intestinal protozoa in hosts (humans), especially in children, that are often found include *Entamoeba sp, Giardia sp, Blastocystis sp, Balantidium sp, and Cryptosporidium sp.*

Laboratory examination is an important aspect in diagnosing parasitic diseases. Placing fixation labels, use of special containers, where specimens are collected and how they are disposed of need to be considered. Fresh feces specimens are collected in a clean container, with a wide mouth and a tight lid to prevent spillage and maintain humidity. Stool specimens should not be mixed with water and/or urine. Each specimen sent to the laboratory must be accompanied by the patient's name, identification number, name of the doctor or specimen sender, date and time of specimen collection. The specimen must also be accompanied by a request form for the type of laboratory examination requested. It is better if accompanied by information about possible diagnoses or certain characteristics, such as travel history (Hadidjaja, 2011; Garcia, 2016).

To examine parasites in feces, it is recommended to collect three specimens sent on different days or one day apart but not more than 10 days apart. Two specimens were collected after normal defecation while another specimen was collected after laxative administration. If you suspect intestinal amoebiasis infection, six specimens should be taken. Liquid stool specimens should be examined within 30 minutes of the stool being passed while soft stools should be examined within 1 hour. If this is not possible, then the specimen must be given a preservative. Solid stool specimens may be examined at any time within 24 hours of the stool being passed. Preservatives that can be used include formalin, merthiolate (thimerosal) iodine formalin (MIF), sodium acetate-acetic acid-formalin (SAF), Schaudinn's solution and *polyvinyl alcohol* (PVA) (Garcia, 2016).

Specimen delivery must be carried out using a double container. The inner container is an aluminum cylinder with a screw cap which is then wrapped in cotton to maintain moisture and absorb materials that may escape due to leaks. Next, the container is placed in an outer container made of cardboard.

Intestinal parasite examination methods that can be used are direct preparation, concentration method and removal preparation with permanent smear. Direct preparations were made by mixing about 2 mg of feces with a drop of 0.85% salt solution, then covered with a 22x22 mm glass cover. The entire surface of the cover glass was examined systematically using 100x magnification and low light intensity then with medium magnification (400x). The concentration method is part of the routine parasite examination procedure to detect parasites that may not be found in a direct preparation examination. There are two types of concentration procedures, namely flotation and sedimentation. This method is designed to separate protozoa and worm eggs from feces through differences in specific gravity. Permanent smear preparations not only allow the examiner to store the preparation permanently, but can also be used for further consultations. This preparation is recommended for every stool sample examination. There are several smear techniques, namely the Heidenhain method of iron hematoxylin, trichrome or modified iron hematoxylin.

In providing therapy for intestinal worm infections, especially STH, in children over 2 years, WHO recommends albendazole 400 mg and mebendazole 500 mg given as a single dose orally. For children aged 1 year to 2 years, the dose of Albendazole that can be given is 200 mg. However, it seems that these therapy guidelines need to be updated considering the large number of studies regarding this anthelmintic regimen. It is now known that benzimidazole drugs have limitations, namely their low efficacy against *Trichuris trichiura* and hookworms, as well as the emergence of the risk of resistance. So now multiple drug therapy appears to be a potential solution.

Moser's research on the combination of anthelmintics for hookworm infections showed that the administration of a three-drug regimen (albendazole 400mg, pyrantel pamoate 20mg/kgBB, and oxantel pamoat 20mg/kgBB) had the highest cure rate (84.1%) compared to administration of albendazole and oxantel pamoate or administering pyrantel pamoate and oxantel pamoate at the same dose. Studies in the Philippines also showed that ivermectin plus albendazole had higher efficacy against *T. trichiura infections* than monotherapy. Other studies have also shown the benefit of dual drug therapy including administration of oxantel and tribendimidine in the treatment of infections *with T. trichiura* and other STH species (Brooker, 2018; Eshetu, 2020).

Therapy for intestinal protozoal infections consists of several options. In *Giardia lamblia infection,* metronidazole is an effective treatment. Until 2002, treatment for cryptosporidiosis was unsatisfactory, but now it has shown improvement. Of the many drugs screened for having anticryptosporidial activity, it is known that paromomycin and nitazoxanide show clinical improvement in patients (Farthing, 2006). In the treatment of amoebic colitis, nitroimidazole derivatives are the drugs of choice because they are very effective in treating the trophozoite form. Metronidazole can be given at a dose of 750-800 mg, three times a day for 5-10 days, or tinidazole at a dose of 2 g every day for 3 days. However, this drug has little effect on amoebic cysts so it is recommended that treatment be followed by administration of paromomycin or diloxanide furoate which work on organisms in the lumen (Farthing, 2006). These procedures are summarized in table 2.

Table 2: Therapy for Diarrhea Caused by Protozoa (Farthing, 2006)

Intestinal Protozoa	Therapy	Alternative therapy
Giardia lamblia	Metronidazole 1 g/dose for 3 days	Tinidazole 2 g single dose
Cryptosporidium parvum	Nitazoxanide 500 mg twice daily for 3–14 days	Albendazole 400 mg twice daily for 7–14 days Paromomycin 500 mg four times a day for 7–14 days
Cyclospora cayetanensis	Co-trimoxazole (trimethoprim 160 mg and sulfamethoxazole 800 mg) twice daily for 7 days	Ciprofloxacin 500 mg twice daily for 7 days
Isospora belli	Co-trimoxazole (trimethoprim 160 mg and sulfamethoxazole 800 mg) mg four times a day for 10 days	Ciprofloxacin 500 mg twice a day for 7 days
Entamoeba histolytica	Metronidazole 750 mg three times a day for 5 days Diloxanide furoate 500 mg three times a day for 10 days	Paromomycin 25-35 mg/kgBB three times a day for 7-10 days
Balantidium coli	Metronidazole 400 mg three times a day for 10 days	Tetracycline 500 mg four times a day for 10 days
Blastocystis hominis	Nitazoxanide 500 mg twice a day for 3 days	Metronidazole 800 mg three times a day for 5-10 days Co-trimoxazole (trimethoprim 160 mg and sulfamethoxazole 800 mg) twice a day for 7 days
Encephalitozoon intestinalis	Albendazole 400 mg twice a day for 14-28 days	Not yet available
Enterocytozoon bieneusi	Albendazole 400 mg twice a day for 28 days	Fumagillin 60 mg daily for 14 days

3 METHODS

The research was conducted in June 2021 – July 2021. Data or literature collection was carried out through electronic media, namely in the form of published and unpublished results of primary research regarding intestinal parasitic infections on the incidence *of stunting in children.* Literature searches via electronic media were carried out online via the Unila, UI and USU repositories, as well as via PubMed, *Science Direct*, *Google Scholar*, Hindawi, *Cochrane library*, DOAJ, JSTOR, *Public Library of Science* (PLoS). Some of the keywords used are *intestinal parasitic infection, soil transmitted helminth infection, intestinal protozoan, stunting, growth disorders,* and *children*. Key words used in searching through *the repository* were intestinal parasitic infections, *soil transmitted helminths,* intestinal protozoa, short stature, *stunting* and children.

4 RESULT

Article searches were carried out using keywords and *Mesh terminology* for each *PICO component* using *the Quatation mark "", Boolean operators* "OR" and "AND". The results of searching all sources using keywords obtained 1042 journals and 2 theses. Articles that experienced duplication were deleted and then filtered based on the title and 182 suitable journals were obtained. Then verification was carried out through abstracts that met the inclusion criteria and 21 suitable journals were obtained. Then content verification was carried out and 9 appropriate journals were obtained. Then an in-depth review was carried out and it was found that 3 studies were not relevant because the research data was prevalence data and compared data between regions, not between variables, so they did not meet the inclusion criteria. Therefore, 6 articles were obtained that could be analyzed in the meta-analysis. A description of the research search results is presented in Figure 1.

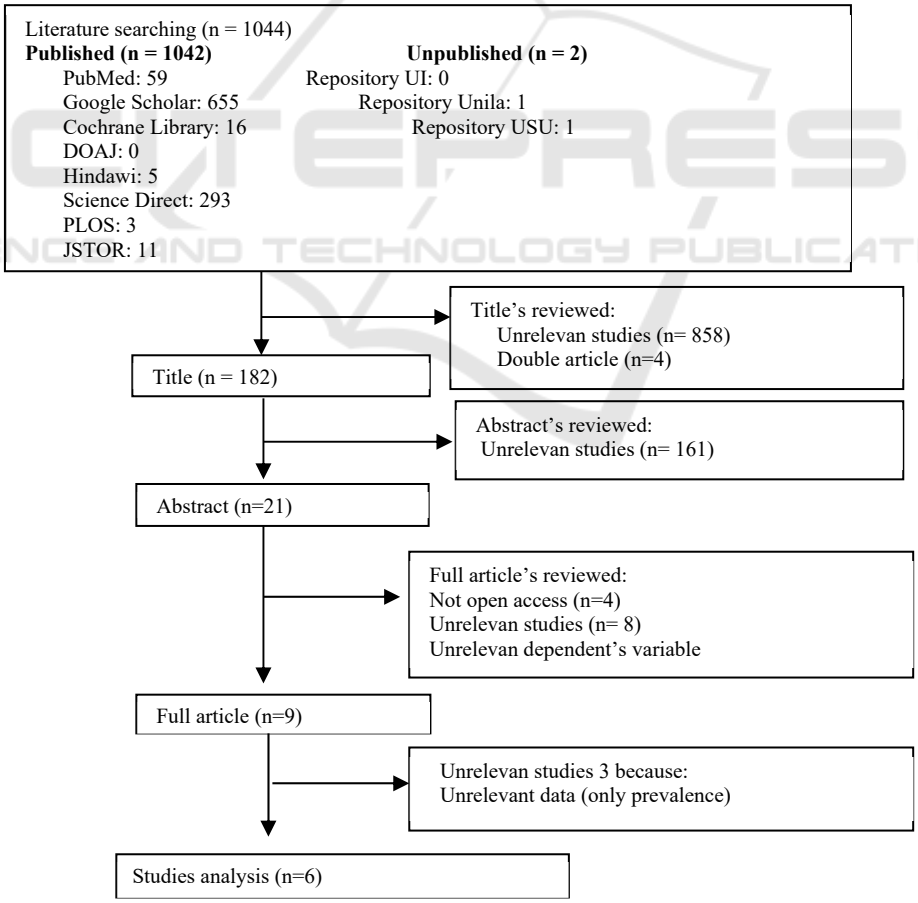

Figure 1. PRISMA diagram of article selection flow

Data analysis was carried out using *review manager 5.4* software. Selected articles were published by PLOS, *BioMed Central Public Health* (BMC), *Sage Open medicine*, and Journal of *Epidemiology and Public Health* (JEPH). The research was conducted in Nangapanda District, Indonesia, Southern Ethiopia, Bahir Dar Ethiopia, Southwest Ethiopia, and Pinrang District, South Sulawesi, Indonesia. All subjects analyzed were 5,687 children aged 6 months to 18 years. The entire study used a *cross sectional design*. The characteristics of the research data in the article are presented in table 3.

Table 3. Characteristics of Research Data

Source	Type	Year of publi-cation	Writer	Title	Loca-tion	n	Sub-ject's age	Inspection		Prevalence		aOR	95%CI
								Stun-ting	Para-site	*Stun-ting*	Para-site		
PLOS	Journal	2021	Djuardi	*Soil-transmitted helminth infection, anemia, and malnutrition among preschool-age children in Nangapanda subdistrict, Indonesia*	Indo-nesia	393	1-5 yrs	HAZ *score*	Kato Katz Metho d	40.2%	58.8%	1.23	0.63-2.39
PLOS	Journal	2017	Grimes	*Sanitation, hookworm, anemia, stunting, and wasting in primary school children in southern Ethiopia: Baseline results from a study in 30 schools*	Ethiop ia	3686	5-18 yrs	HAZ *score*	Kato Katz Metho d	28%	23%	0.99	0.79-1.25
BMC	Journal	2018	Hailege briel	*Undernutrition, intestinal parasitic infection and associated risk factors among selected primary school children in Bahir Dar, Ethiopia*	Ethiop ia	382	7-13 yrs	HAZ *score*	Forma lin-Ether *concen tration metho d*	18.3%	52.4%	1.1	0.65-1.86
SAGE	Journal	2020	Mekonn en	*Soil-transmitted helminth infections and nutritional status of school children in government*	Ethiop ia	404	6-14 yrs	HAZ *score*	*Direct wet mount* and *McMa ster* metho ds	21%	55%	2	1.2-3.33

				elementary schools in Jimma Town, Southwestern Ethiopia									
JEPH	Journal	2020	Muslimah	*Multilevel Analysis Association of Soil Transmitted Helminths and Stunting in Children Aged 6-12 Years Old in Pinrang District, South Sulawesi*	Indonesia	200	6-12 yrs	HAZ *score*	Stool examination (not explained further)	46.5%	41%	2.11	1.11-4.01
BMC	Journal	2020	Joseph	*The high prevalence of intestinal parasitic infections is associated with stunting among children aged 6–59 months in Boricha Woreda, Southern Ethiopia: a cross-sectional study*	Ethiopia	622	6 months-5 years	HAZ *score*	*Direct wet mount* and Kato Katz methods	39.3%	48.7%	2.18	1.36-3.49

Note: HAZ = *Height-for-age-z-score* with classification based on WHO guidelines

Analysis of variations between studies is aimed at determining whether the studies are heterogeneous or homogeneous. Between studies it is said to be homogeneous if the p value in the heterogeneity test is greater than 0.05 or the intuitive index (I^2) and Tau values are small. The results of the analysis show that I^2 of this analysis is 67%, meaning that the variation between studies is heterogeneous, so the model used to calculate the combined effect is *the random effect model*.

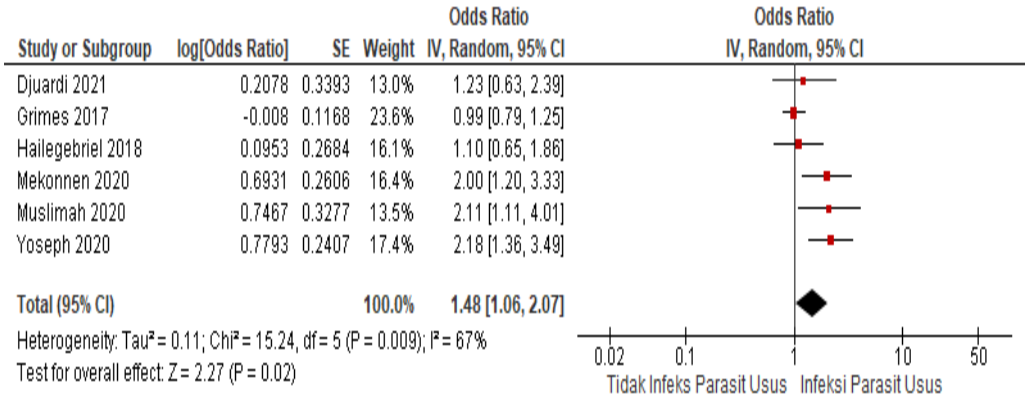

Figure 2. Forest Plot Random Effect Model.

The *forest plot* shows *the odds ratio* for each study with its confidence interval (horizontal line). The combined *odds ratio* is depicted in a diamond shape (black). The combined effect value from the results of the analysis of these six studies was 1.48 with a 95% confidence interval of 1.06-2.07. The combined effect also produces a Z value of 2.27 and a p value of 0.02. This means that there is an influence between intestinal parasitic infections on the incidence of stunting in children. Children with intestinal parasitic infections are 2.27 times more stunted *than* children without intestinal parasitic infections.

Funnel plots can be used to determine research variation and publication bias. If the number of plots on the left and right sides is balanced and the distance between plots is balanced, it means there is no publication bias. This means that if the analysis is carried out on different populations, times, places and conditions, the results will remain consistent. The results of this meta-analysis show a balanced *funnel plot.*

Table 4. *Effect size* of combined studies

Model	Effect Size and 95%CI				Significance test	
	Number of Research	Combined Effects	Lower limit	Upper limit	Z	p
Random	6	1.48	1.06	2.07	2.27	0.02

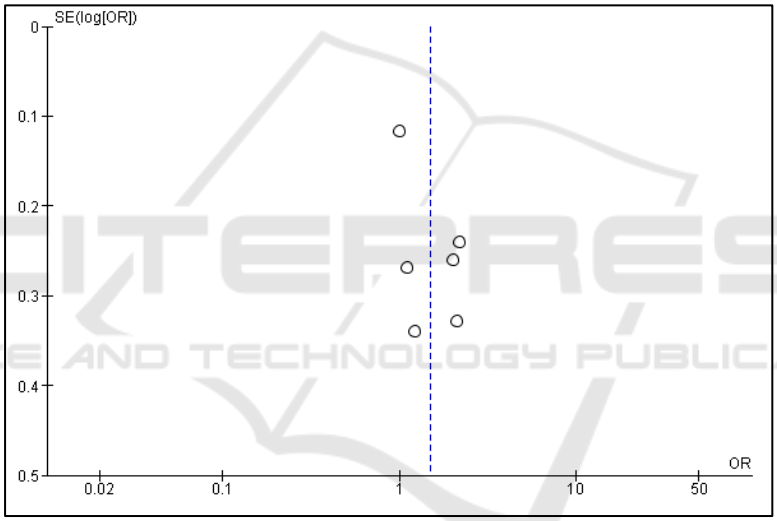

Figure 3. *Funnel Plot*

5 DISCUSSION

Many studies have been conducted regarding intestinal parasitic infections and stunting, but have produced varying results. Therefore, statistical analysis was carried out using meta-analysis to prove the quality of each research so that new quantitative data could be obtained and more accurate conclusions could be drawn.

These six studies were analyzed involving 5,687 research subjects and the combined effect results concluded that there was an influence between intestinal parasitic infections on the incidence of stunting in children with an OR of 1.48 (CI 95%: 1.06-2.07). In determining *stunting status*, all researchers used the same method, namely based on *height-for-age-z-score* which was then classified according to WHO guidelines. Intestinal parasite examination is carried out using stool specimens and then examined in the laboratory. Examination methods in general are *direct wet mount* and the Kato Katz method, except for the Hailegebriel study which used the Formalin-Ether *concentration method* and Mekonnen used *the McMaster method (*Hailegebriel, 2018; Yoseph, 2020; Mekonnen, 2020; Grim, 2017).

In research in Nangapanda, there were 58.8% of intestinal parasitic infections which were predominantly caused by *Ascaris lumbricoides*

(47.4%) followed by *Trichuris trichiura* (36.8%) and hookworm (9.2%). A total of 28.7% of subjects experienced multiple infections, namely 20.6% coinfected with *Ascaris lumbricoides* with *Trichuris trichiura, 2.2%* coinfected with *Ascaris lumbricoides* with hookworm and 5.9% coinfected with the three species. A single parasitic infection has been proven to be related to the incidence of *stunting*. The same thing with moderate intensity infections. However, this is not the case with multiple parasitic infections, mild and severe intensity. How this happens has not been explained (Djuardi, 2021). The high prevalence of *A. lumbricoides* and *T. trichiura infections* in this study indicates that oral-fecal transmission is more common than transmission through skin penetration (in hookworm infections) especially in children. Other factors examined in this study were difficult access to health centers and/or midwives (81.9%), lack of access to water sources (13.8%) and poor sanitation (87.3%) which of course could contribute to the high incidence of intestinal parasitic infections and nutritional problems among children in the area (Djuardi, 2021).

Research conducted by Grimers showed that the prevalence of hookworm infection was 18%, *Ascaris lumbricoides* 4.8%, *Trichuris trichiura* 0.6% and *S. mansoni* 0.3%. The high number of hookworm infections in this study is known to be related to inadequate sanitation, namely the absence of latrines and open defecation. Apart from that, data was also obtained on the prevalence of anemia of 23%, *stunting of* 28% and *wasting of* 14%. Statistically, there is no significant relationship between sanitation and hookworms or between hookworms and anemia, *stunting* or *wasting* (Grimes, 2017).

In Hailegebriel's study, 52.4% of subjects were positive for one or more intestinal parasites. The prevalence of multiple intestinal parasitic infections is quite large, namely 6.3%. The most frequently detected intestinal parasitic infections were *E. histolytica/dispar* (16.8%), hookworm (14.7%) and *A. lumbricoides* (13.6%). Based on the multivariate analysis that was carried out, the predictors of intestinal parasitic infection in this study were unclean nails, irregular hand washing habits and maternal education.

Nutritional problems occurred in 41.6% of subjects, consisting of 18.3% *stunting*, 26.7% wasting and 25.9% were underweight. Almost half of the study subjects experienced 2 or more nutritional problems at one time. Of the 18.3% of subjects who experienced stunting, 20% of them experienced severe *stunting* (HAZ<-3SD). Based on further analysis, it is known that subjects born to families with a monthly income of less than 1500 birr (around Rp. 479,000.00), the frequency of eating a maximum of 3 times in 1 day and the presence of intestinal parasitic infections are the main predisposing factors for malnutrition in children (Hailegebriel, 2018).

Mekonnen's research showed that research subjects were infected with 8 species of intestinal parasites, namely *Trichuris trichiura, Ascaris lumbricoides,* hookworm, *H.nana, E.histolytica, E.vermicularis, G.lamblia,* and *S.mansoni* . The highest prevalence of intestinal parasitic infections is infection due to mild intensity STH, namely 55% with the most infections caused by *T. trichiura* (34.9%). *Ascaris lumbricoides* and hookworm were detected in 28.5% and 11.4%. The highest STH infection occurred in children with dirty nails (63.5%). Children who have the habit of defecating in the open (52.7%) have a 1.9 times higher risk of developing STH infection. Likewise, children who are accustomed to not wearing footwear have a 2.2 times higher risk of being infected with hookworms than children who wear shoes. The prevalence *of stunting* is 21%. The results of multivariate analysis show that *T. trichiura infection* is the main predictor of *stunting* in children (Mekonnen, 2020).

Muslimah research in 2020 gave results of a stunting prevalence of 46.5% and intestinal worm infections of 41% in children aged 6 to 12 years. There is an effect of worm infections on the incidence of *stunting* where children with worm infections have a 2.11 times greater probability of experiencing *stunting* than children without intestinal worm infections (Muslimah, 2020).

Yoseph's research stated that the total prevalence of intestinal parasitic infections was 48.7%, consisting of *Giardia lamblia infections* (10.45%), *Entamoeba hystolitica* (4.66%), *Ascaris lumbricoides* (10.77%), hookworms (7.88%). %), *Trichiura trichiura* (6.1%), *Strongyloides stercoralis* (1.6%) and *Taenia sp* (1.3%). About a quarter (22%) of children were moderately infected and 5.94% had multiple intestinal parasitic infections. The prevalence of *stunting* is 39.3% and 3.4% of them experience severe *stunting*. Other nutritional problems are *underweight* 24% and *wasting* 11.6%. The prevalence of *stunting* in children infected with intestinal parasites (59.4%) was significantly higher than the prevalence in uninfected children (20.6%). Almost all (92.53%) children infected with *Ascaris lumbricoides* experienced *stunting*. Likewise, in other intestinal parasitic infections, such as in people with hookworm infections, the prevalence of *stunting* is 89.79%, in *G. lamblia infections* it is 86.20%, *E. histolytica* is 72.24%, *T. trichiura* is 71%, *Taenia sp*.

By 50% and *Strongyloides stercoralis* by 50%. Statistically, there is a significant relationship between *stunting* and infection with hookworms, *G.lamblia* , *E.histolytica* and *T.trichiura* . Children infected with intestinal parasites have a 5.45 times greater risk of experiencing *stunting* compared to those who are not infected (Yoeph, 2020).

Based on the results of these six studies, it is clear that the prevalence of intestinal parasitic infections is still high. Intestinal parasitic infections occur in various ages of children, even in babies as young as 6 months (Yoseph, 2020). The availability of adequate sanitation facilities is very important because otherwise it will be possible for contamination of water and food with human waste, especially if the habit of defecating in open fields continues. The habit of not using footwear can occur because there is still a lack of public knowledge and awareness about how this intestinal parasite can infect humans.

Intestinal parasitic infections can cause various impacts on the host. Intestinal worms can reduce a child's appetite and cause competition between hosts and parasites. Lack of carbohydrates, protein, nutrients, and blood can reduce the adequacy needed by the body, thereby reducing the quality of human resources (Muslimah, 2020; Jourdan, 2018). Intestinal protozoal infections often cause complaints of diarrhea. Research shows that 25% of *stunting cases* are associated with five or more episodes of diarrhea (Millward, 2017). Exposure to these pathogens can cause disruption of intestinal structure and function called *environmental enteric dysfunction* (EED). This condition is a *reversible condition*, characterized by villous atrophy of intestinal mucosal cells, crypt hyperplasia, increased permeability, and inflammatory cell infiltration. This can result in disruption of the intestinal immune response, reducing the delivery, absorption and utilization of nutrients resulting in a state of nutritional deficiency. A state of nutritional deficiency can then result in damage to epithelial tissue renewal, maturation and proliferation of intestinal cells and pancreatic b cells, thus disrupting linear growth (Budge, 2019).

Increased intestinal permeability can be determined from the lactose/mannitol ratio (Budge, 2019). Research shows that this ratio tends to be higher in children with infections, especially *Cryptosporidium* infections *sp*. and *Giardia sp* (Budge, 2019). Choudhry's research has shown that *C. parvum infection* can alter intestinal barrier function by reducing the integrity of the intestinal epithelium through reduced TER (*Transepithelial Electrical Resistance*) associated with *downregulation of* the claudin-4 protein (Choudry, 2021). In giardiasis there is malabsorption of fat, xylose and vitamin B12. *Mannose-binding lectin* mediates parasite adhesion to *brush border enterocytes*. Increased apoptosis, loosening of enterocyte adhesions at *tight junctions*, and damage to the enterocyte membrane lumen contribute to impaired digestion and nutrient absorption (Wright, 2012).

The six studies above also provide results that the prevalence of nutritional problems in children is still high, namely in the range of 18.3% to 46.5%. Nutritional problems detected in the research subjects included *underweight, thinness, stunting, wasting* and *anemia*. *Underweight*, can also be called underweight, is the child's nutritional status based on body weight for age with a Z score of -3SD to -2SD. *Stunting* is short stature, a child's nutritional status based on length or height per age with a Z score of -3SD to -2 SD. *Wasting,* which can also be called undernutrition, is a child's nutritional status based on weight per body length, weight per child's height, or body mass index (BMI) per child aged 0 to 60 months with a Z score of -3SD to -2SD . *Thinnes,* also called malnutrition, is a category of children's nutritional status based on BMI per child aged 5 to 18 years with a Z score of -3SD to -2SD (Minister of Health of the Republic of Indonesia, 2020).

Monitoring intestinal parasitic infections and children's nutritional status is very important to pay attention to because it greatly affects their health condition and academic achievement (Hailegebriel, 2018). Apart from carrying out nutritional interventions, it is also necessary to consider the importance of carrying out environmental interventions including water, sanitation and hygiene to prevent the occurrence of infectious diseases, including intestinal parasitic infections (Grimes, 2017).

5.1 Research Limitations

In this research there are still several limitations, including that this research only accesses free published *journals.* Sources for unpublished articles are still limited because they are limited to digital searches due to the COVID 19 pandemic which still limits activities. Apart from that, this research is limited to analyzing the relationship between only two variables, namely intestinal parasitic infections and the incidence of *stunting* in children. There are still other variables such as intensity of parasite infection, Hb levels, body weight and body mass index that can be analyzed in further research.

6 CONCLUSSION

Research that meets the criteria to be tested in meta-analysis is six articles (journals) with heterogeneous variations. The effect size used is *the odds ratio* where the combined effect results show a p value <0.05, which means there is an influence between intestinal parasitic infections, namely intestinal worm infections and intestinal protozoa on the incidence of *stunting* in children. Further research is needed regarding other nutritional status variables such as *underweight, thinness,* and *wasting*. Apart from that, it is also necessary to add reading sources, both *text books* and related journals, to add references for further research.

REFERENCES

Aryastami NK. Policy Study and Overcoming Stunting Nutrition Problems in Indonesia. *Health Researcher Bul* . 2017;45(4):233-240.

Brooker SJ. Soil-transmitted helminth treatment: multiple-drug regimens. *Lancet Infect Dis*. 2018;18(7):698-699.

Budge S, Parker AH, Hutchings PT, Garbutt C. Environmental enteric dysfunction and child stunting. *Nutr Rev*. 2019;77(4):240-253.

CDC. Soil transmitted helminthiases. Available from: https://www.who.int/health-topics/soil-transmitted-helminthiases#tab=tab_3

CDC. domestic intestinal parasites. Available from: https://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/intestinal-parasites-domestic.html#tables1

Choudhry N, Scott F, Edgar M, Sanger GJ, Kelly P. Reversal of Pathogen-Induced Barrier Defects in Intestinal Epithelial Cells by Contra-pathogenic Agents. *Dig Dis Sci*. 2021;66(1):88-104.

CPM. Mother and Child Health Profile 2020. Central Statistic Agency. 2020;53(9):1689-1699.

Dewey KG, Mayers DR. Original Article Early child growth: how do nutrition and infection interact? *Matern Child Nutr*. 2011;7(3):129-142.

Dharma YP, Mutiara H, Suwandi JF, Setyaningrum E. Mapping where infected students live and the relationship between socio-economic factors and parental knowledge level with the incidence of soil-transmitted helminth infections in elementary school students in Natar District, South Lampung Regency. Medulla. 2017;7(5):134-139.

Djuardi Y, Lazarus G, Stefanie D, Fahmida U, Ariawan I, Supali T. Soil-transmitted helminth infection, anemia, and malnutrition among preschool-age children in Nangapanda subdistrict, Indonesia. *PLoS Negl Trop Dis* . 2021;15(6):1-16.

Eshetu T, Aemero M, Zeleke AJ. Efficacy of a single dose versus multiple dose regimen of MBZ agains hookworm infection in a randomized open label trial. *BMC Infect Dis*. 2020; 20:1-8.

Farthing MJG. Treatment options for the eradication of intestinal protozoa. *Nat Clin Pract Gastroenterol Hepatol*. 2006;3(8):436-445.

Garcia LS. *Diagnostic Medical Parasitology*. 6th ed. ASM Press; 2016.

Grimes JET, Tadesse G, Gardiner IA, Yard E, Wuletaw Y, Templeton MR, et al. Sanitation, hookworm, anemia, stunting, and wasting in primary school children in southern Ethiopia: Baseline results from a study in 30 schools. *PLoS Negl Trop Dis*. 2017;11(10):1-18.

Gutiérrez-Jiménez J, Luna-Cázares LM, Martínez-De la Cruz L, Aquino-Lopez JA, Sandoval-Gomez D, Leon-Ortiz AT, et al. Children from a rural region in the Chiapas highlands, Mexico, show an increased risk of stunting and intestinal parasitoses when compared with urban children. Bol Med Hosp Infant Mex. 2019;76(1):18-26.

Hadidjaja P, Margono SS. *Basics of Clinical Parasitology*. FKUI Publishing Agency; 2011.

Hailegebriel T. Undernutrition, intestinal parasitic infection and associated risk factors among selected primary school children in Bahir Dar, Ethiopia. *BMC Infect Dis*. 2018;18(1):1-11.

Harjatmo TP, Par'i HM, Wiyono S. *Assessment of Nutritional Status*. Ministry of Health of the Republic of Indonesia; 2017.

Herbowo H, Firmansyah A. Diarrhea Due to Parasitic Infections. *Sari Pediatri*. 2016;4(4):198.

Jourdan PM, Lamberton PHL, Fenwick A, Addiss DG. Soil-transmitted helminth infections. *Lancet*. 2018;391(10117):252-265.

Mahardianti M, Kurniawan A, Sari IP. Potential Transmission of Cryptosporidium sp. in Ciliwung River Water, Jakarta. *Indonesian Medical eJournal* . 2020;8(2).

Mekonnen Z, Hassen D, Debalke S, Tiruneh A, Asres Y, Chelkeba L, et al. Soil-transmitted helminth infections and nutritional status of school children in government elementary schools in Jimma Town, Southwestern Ethiopia. SAGE Open Med. 2020; 8:1-10.

Millward DJ. Nutrition, infection and stunting: The roles of deficiency of individual nutrients and foods and of inflammation as determinants of reduced linear growth of children Nutrition Research Reviews. *Nutr Res Rev*. 2017; 30: 50-72.

Ministry of Health of the Republic of Indonesia. Stunting Bulletin. Ministry of Health of the Republic of Indonesia. 2018;301(5):1163-1178.

Ministry of Health of the Republic of Indonesia. 2018 Riskesdas Report. 2018 Riskesdas National Report. 2018;53(9):154-165.

Minister of Health of the Republic of Indonesia. Regulation of the Minister of Health of the Republic of Indonesia Number 2 of 2020 concerning Child Anthropometric Standards. Ministry of Health of the Republic of Indonesia; 2020.

Muslimah PA, Salimo H, Dewi YLR. Multilevel Analysis Association of Soil Transmitted Helminths and Stunting in Children Aged 6-12 Years Old in Pinrang

District, South Sulawesi. *J Epidemiol Public Health*. 2020;5(3):372-383.

Mutiara H. Analysis of Tumor Necrosis Factor Superfamily Gene Expression Profiles, Member 13B (TNFSF13B) and Nuclear Factor-B1(NFB1) in Ascariasis Sufferers in State Elementary Schools in Jatinangor District [Thesis]. Bandung. 2014.

Osman KA, Zinsstag J, Tschopp R, Schelling E, Hattendorf J, Umer A, et al. Nutritional status and intestinal parasites among young children from pastoralist communities of the Ethiopian Somali region. Matern Child Nutr. 2020;16(3):1-11.

Pramestuti N, Saroh D. Blastocystis hominis: Potential Intestinal Protozoa Causing Diarrhea. *Cell J Health Researcher*. 2017;4(1):1-12.

Setiawan E, Machmud R, Masrul M. Factors Associated with the Incident of Stunting in Children Aged 24-59 Months in the Andalas Community Health Center Working Area, East Padang District, Padang City in 2018. *J Health Andalas* . 2018;7(2):275.

Shekar M, Kakietek J, D'Alimonte MR, Rogers HE, Eberwein JD, Akuoku JK, et al. Reaching the global target to reduce stunting: An investment framework. Health Policy Plan. 2017;32(5):657-668.

Sutanto I, Ismid I, Sjarifudin P, Sungkar S. *Textbook of Medical Parasitology 4th Edition*. 4th ed. FKUI Publishing House; 2008.

Torlesse H, Cronin AA, Sebayar SK, Nandy R. Determinants of stunting in Indonesian children: Evidence from a cross-sectional survey indicates a prominent role for the water, sanitation and hygiene sector in stunting reduction. *BMC Public Health*. 2016;16(1):1-11.

UNICEF, WHO, World Bank. Levels and Trends in Child Malnutrition: Key Findings of the 2020 Edition of the Joint Child Malnutrition Estimates. 2020;24.

UNICEF. *Improving Child Nutrition The Achievable Imperative for Global Progress*. 2013;18.

World Health Organization (WHO). Soil-transmitted helminth infections. Published 2020. Available from: https://www.who.int/news-room/fact-sheets/detail/soil-transmitted-helminth-infections

Winita R, Huda MK AH. Intestinal Parasite Infections in Children and Their Relationship with Work as a Scavenger Rawina. *Maj FK UKI*. 2016;32(3):113-119.

Wright SG. Protozoan Infections of the Gastrointestinal Tract. *Infect Dis Clin North Am*. 2012;26(2):323-339.

Yoseph A, Beyene H. The high prevalence of intestinal parasitic infections is associated with stunting among children aged 6-59 months in Boricha Woreda, Southern Ethiopia: A cross-sectional study. *BMC Public Health*. 2020;20(1):1-13.