

## Research Article

# The Relationship between Soil-Transmitted Helminthic Infections and the Behavior of Elementary School-Aged Children

Primadiati Nickyta Sari<sup>1</sup>, Bambang Soebagyo<sup>1</sup>, Husnia Auliyatul Umma<sup>1</sup>

### Author's Affiliation:

1- Department of Pediatrics, Dr. Moewardi Hospital/Faculty of Medicine Sebelas Maret University, Surakarta, Indonesia.

### Correspondence:

Primadiati Nickyta Sari, Email: primadiatinickytasari24@gmail.com

Received on: 23-Aug-2021

Accepted for Publication: 20-Dec-2021

### ABSTRACT

**Background:** Soil-transmitted helminthic (STH) infection among elementary school-aged children can cause long-term effects on brain development, including future behavioral disorders. Currently, there are no studies that reveal the effect of STH infection on behavioral development disorders in elementary school-aged children.

**Objective:** To analyze the relationship between STH infections and the behavior of elementary school-aged children.

**Methods:** An analytical observational study with a cross-sectional approach in children aged 7-13 years with STH infection from February-August 2020 at the State Elementary School. Behavior disorders were assessed using the Pediatric Symptoms Checklist 17 Items (PSC-17) filled out by the parents. A multivariate regression test was applied, a p-value < 0.05 was considered as statistically significant.

**Results:** STH infection was shown to be significantly associated with internalizing behavioral disorders ( $Z = -2.064$ ;  $p = 0.039$ ), attention ( $t = -3.720$ ;  $p = 0.001$ ), and externalizing ( $Z = -3.664$ ;  $p < 0.001$ ) (Table 2). STH infection had a significant relationship with internalizing, attention, and externalizing behavioral disorders with a coefficient of regression of  $B = 1.809$  (0.281 to 3.337),  $p = 0.022$  (Table 3);  $B = 2.507$  (1.189 to 3.825),  $p < 0.001$  (Table 4);  $B = 3.608$  (1.956 to 5.260),  $p < 0.001$  (Table 5).

**Conclusion:** STH infection is significantly associated with internalizing, attention, and externalizing behavioral disorders in elementary school-aged children.

**Keywords:** Soil-transmitted helminthic infection, Children's behavioral disorders

## INTRODUCTION

Intestinal parasitic infection is a major health problem in developing countries, especially in children, often causing mortality and morbidity. The main cause of intestinal parasitic infection is soil-transmitted helminths (STH), namely roundworms (*Ascaris lumbricoides*), whipworms (*Trichuris trichiura*), and hookworms (*Ancylostoma duodenale* and *Necator americanus*). The World Health Organization (WHO) estimates that more than two billion people with STH infection in the world experience severe morbidity that causes 9,000 to 135,000 deaths per year. The prevalence of worms in Indonesia reached 31.8%. The Ministry of Health of the Republic of Indonesia in 2005 explained that the results of a survey on worms in primary schools showed a prevalence of around 60% - 80%. In previous studies, there were 40.4% of 183 elementary school students infected with worms in one sub-district in Boyolali Regency, where 52.7% were infected with *Ascaris lumbricoides*, 4.1% *Trichuris trichiura*, 29.7% Hookworm, 4.1% Oxyuris, and 9.5% *Ascaris lumbricoides* and Hookworm.<sup>1</sup>

Although STH infection occurs in all age groups, WHO states that school-aged children are one part of the population with a high risk of morbidities related to STH infection. Morbidities associated with STH infection include iron deficiency anemia, malnutrition, growth and development disorders including short stature and cognitive developmental disorders.<sup>2</sup>

Several meta-analysis studies have shown an association between STH infection and impaired cognitive and mental development in children. A longitudinal experimental trial in Brazil showed improvements in children's cognitive, mental, and concentration development after receiving anti-helminthic therapy. STH infection can affect the synaptogenesis process in the brain, causing disorders that can have long-term effects on brain development, including future behavioral disorders.<sup>2-4</sup>

Currently, there are not many studies that reveal the relationship between STH infection and behavioral disorders in elementary school-aged children in more detail. This becomes important and interesting to research so that it can add reference sources related to the effect of STH infection on the behavior of children at elementary school age. This study aimed to analyze the relationship between STH infection and the behavior of elementary school-aged children.

## METHODS

This research is an analytic observational study with a cross-sectional approach. This research was conducted at the State Elementary School in Banyudono District, Boyolali Regency from February-August 2020. The subjects of this study included children aged 7-13 years with STH infection. The samples in this study were determined by the consecutive sampling method. The exclusion criteria include the subject did not return the fecal sample container and were suffering from other infectious diseases. Furthermore, the subjects were screened early for developmental disorders using the Pediatric Symptoms Checklist 17 Items (PSC-17) questionnaire form that was filled out by the parents. For children who are proven to have STH infection, they will be given anti-worm medication. Children who have been detected with developmental disorders will be treated further. This research was conducted during the offline learning trial period due to the COVID-19 pandemic. Researchers have obtained permission from the principal by implementing health protocols. This research had received an ethical clearance recommendation from the Ethics Committee of Dr. Moewardi Surakarta. Bivariate analysis was carried out using the t-test. Multivariate analysis using logistic regression was carried out to assess the role of several risk factors in influencing the effect. P-value <0.05 was considered statistically significant.

## RESULTS

### 1. Basic Characteristics of Research Subjects

This research was conducted on 67 students in Public Elementary Schools in Banyudono District, Boyolali Regency who met the inclusion and exclusion criteria, resulting in 42 subjects. The basic characteristics of research subjects are described in table 1.

From 42 subjects, 17 children (40.5%) had behavioral disorders, which were divided into 3 children with internalizing disorders; 2 children with attention disorders; 5 children with externalizing disorders; 1 child with impaired internalizing and attention; 2 children with internalizing and externalizing disorders; 3 children with internalizing, attention and externalizing disorders; and 1 child with attention and externalizing disorders. Meanwhile, the other 25 children (59.5%) did not experience any behavioral problems at all.

The STH infection occurred in 17 children (40.5%), whom 13 children (76.5%) experienced behavioral disorders: 1 child with internalizing disorder; 2 children with attention disorders; 4 children with externalizing disorders, 1 child with attention and internalizing disorders; 1 child with internalizing and externalizing disorders; 1 child with attention and externalizing disorders; and 3 children with internalizing, attention, and externalizing disorders. Only 4 children (23.5%) with STH infection had no behavioral problems at all.

The highest score of internalizing behavior disorder occurred in children infected with STH ( $4.12 \pm 2.89$ ), as well as attention behavior disorder ( $5.18 \pm 2.92$ ), and externalizing behavior disorder ( $6.29 \pm 3.26$ ). Thus, children who are infected with STH are more likely to have an increase in the score of high behavioral disorders in internalizing, attention, and also externalizing.

Out of 25 subjects (59.5%) who were not infected with STH, there were 4 children with behavioral disorders, which consisted of: 2 children with internalizing disorders; 1 child with externalizing disorder; and 1 child with

Variable	Average	Score Results		
		Internalizing	Attention	Externalizing
<b>Total</b>	42	3,05 ±2,65	3,57 ±2,64	4,00 ±3,25
<b>Children's Age</b>	9,76 ±1,74			
<b>Gender</b>				
Man	25 (59,5%)	3,72±2,95	3,80±2,55	4,56±3,31
Women	17 (40,5%)	2,06±1,78	3,24±2,82	3,18±3,07
<b>Mother's Education</b>				
SD	9 (21,4%)	3,89±3,86	5,00±2,78	5,56±3,57
Junior High	12 (28,6%)	3,00±2,70	3,33±2,46	4,50±3,42
High school	19 (45,2%)	2,58±1,95	3,11±2,64	3,00±2,94
College	2 (4,8%)	4,00±2,83	3,00±2,83	3,50±0,71
<b>Mother's work</b>				
Does not work	17 (40,5%)	3,35±2,03	4,59±2,32	3,76±2,82
Work	25 (59,5%)	2,84±3,02	2,88±2,67	4,16±3,56
<b>Parents' Income</b>				
<1.5 million	32 (76,2%)	2,88±2,79	3,47±2,54	4,16±3,40
1.5-2.5 million	7 (16,7%)	3,71±2,29	3,29±2,43	2,86±2,79
> 2.5 million	3 (7,1%)	3,33 ±2,31	5,33 ±4,51	5,00 ±2,65
<b>Playing gadgets</b>				
No gadgets	15 (35,7%)	3,07 ±3,39	2,67± 2,35	4,00 ±4,02
1-2 hours	19 (45,2%)	2,63 ±2,17	4,00 ±2,87	4,16 ±3,13
> 2 hours	8 (19,0%)	4,00 ±2,14	4,25 ±2,43	3,63 ±2,00
<b>Playing outdoors</b>				
<1x / week	3 (7,1%)	3,33 ±1,15	6,00 ±3,46	4,67 ±2,89
> 1x / week	39 (92,9%)	3,03 ±2,74	3,38 ±2,53	3,95 ±3,30
<b>STH infection</b>				
No STH infection	25 (59,5%)	2,32 ±2,25	2,48 ±1,78	2,44 ±2,16
STH infection	17 (40,5%)	4,12 ±2,89	5,18 ±2,92	6,29 ±3,26

**Table 1 Basic characteristics of research subjects**

internalizing and externalizing disorders. The others 21 children (84%) did not experience any behavioral disorders.

In regards to the types of STH infection, there were 11 children with ascariasis infection, 2 children with Trichuriasis infection, and 4 children with hookworm infection.

## **2. Bivariate Analysis of the Relationship between Soil-Transmitted Helminthic Infection and Behavioral Disorders in Children**

Based on table 2, it is known that the variable that has a significant relationship with internalized child behavioral disorders is the incidence of STH infection ( $Z = -2.064$ ;  $p = 0.039$ ). The incidence of STH infection is significantly associated with internalizing behavioral disorders, where children infected with STH tend to have higher scores of internalizing behavioral disorders.

The variables that were significantly associated with behavioral disorders in children with attention were the incidence of STH infection ( $t = -3,720$ ;  $p = 0.001$ ) and maternal occupation ( $Z = -2.366$ ;  $p = 0.018$ ). Children who were infected with STH tend to have higher attention behavioral disorders. Children of mothers who do not work tend to have high scores of behavioral disorders of children with attention compared to children of working mothers.

Variable	Internalizing		Attention		Externalizing	
	Statistic	p-value	Statistic	p-value	Statistic	p-value
STH infection <sup>a</sup>	Z= -2,064	0,039*	t= -3,720	0,001*	Z= -3,664	<0,001*
<b>Confounding Variable:</b>						
Gender <sup>a</sup>	Z= -1,843	0,065	t=0 ,675	0,503	Z= -1,355	0,176
Children's Age <sup>b</sup>	r=0,144	0,362	r=0,046	0,773	r=0,171	0,278
Mother's education <sup>b</sup>	r=-0,059	0,712	r=-0,253	0,105	r=-0,280	0,073
Mother's work <sup>a</sup>	Z= -1,220	0,222	Z= -2,366	0,018*	Z= -0,116	0,908
Parents' Income <sup>b</sup>	r=0,149	0,345	r=0,067	0,674	r=-0,032	0,840
Playing gadgets <sup>b</sup>	r=0,164	0,298	r=0,269	0,085	r=0,044	0,783
Playing outside the house <sup>a</sup>	Z= -0,470	0,638	Z= -1,454	0,146	Z= -0,639	0,523

Note: a t-test (t) if it meets the normality assumption, the Mann Whitney (Z) test if it does not meet the normality assumption; b Spearman rank test; \* significant at  $\alpha < 0.05$

**Table 2 Bivariate analysis of the relationship between Soil-Transmitted Helminths infection and Child Behavioral Disorders**

The variable that was significantly associated with externalizing child behavioral disorder was the incidence of STH infection ( $Z = -3.664$ ;  $p < 0.001$ ). Children infected with STH tend to have higher scores for externalizing behavioral disorders.

### 3. Multivariate Analysis of the Relationship between Soil-Transmitted Helminthic Infection and Behavioral Disorders in Children

Based on table 3, it is known that STH infection has a significant relationship with internalizing child behavioral disorders ( $p = 0.022$ ). The regression test results obtained a regression coefficient of  $B = 1.809$  (0.281 to 3.337), which means that children infected with STH tend to have scores of internalizing behavior disorders of 1.809 (0.281 to 3.337) higher than children who are not infected with STH. Gender was a confounding variable that had a significant relationship with internalizing child behavioral disorders, with a  $p$ -value = 0.020. The results of the linear regression test revealed a regression coefficient of  $B = -1.867$  (-3.430 to -0.305), which means that girls tend to have scores of internalizing behavioral disorders of 1.867 (0.305 to 3.430) lower than boys.

Variable	Internalizing	
	B (95%CI)	p-value
STH infection	1,809 (0,281 s/d 3,337)	0,022*
<b>Confounding Variable:</b>		
Female gender	-1,867 (-3,430 s/d -0,305)	0,020*
Mother's Job (working)	-0,883 (-2,445s/d 0,680)	0,260

Note: Linear Regression Test; \* significant at  $\alpha < 0.05$

**Table 3 Multivariate Analysis of the Relationship between Soil-Transmitted Helminths Infection and Behavioral Disorders Score (Internalizing)**

Based on table 4, it is known that STH infection has a significant relationship with attention behavioral disorder, with  $p < 0.001$ . The regression test results obtained a regression coefficient value of  $B = 2.507$  (1.189 to 3.825), which means that children infected with STH tend to have an attention behavioral disorder score of 2.507 (1.189 to 3.825), higher than children who are not infected with STH. The confounding variable that had a significant relationship with the attention behavioral disorders was playing gadgets ( $p = 0.035$ ). The regression test resulted in a regression coefficient of  $B = 0.970$  (0.070 to 1.870), which means that the longer the child plays gadgets, the internalizing behavior disorder score will increase by 0.970 (0.070 to 1.870).

Based on Table 5, it is known that STH infection has a significant relationship with externalizing child behavioral disorders ( $p < 0.001$ ). The regression test results obtained a regression coefficient of  $B = 3.608$  (1.956 to 5.260), which means that children infected with STH tend to have scores of externalizing behavior disorders of 3.608 (1.956 to 5.260) higher than children who are not infected with STH.

Variable	Attention	
	B (95%CI)	p-value
<b>STH infection</b>	2,507 (1,189 s/d 3,825)	<0,001*
<b>Confounding Variable:</b>		
Mother's Education	-0,658 (-1,418 s/d 0,102)	0,088
Mother's Job (work)	-1,199 (-2,586 s/d 0,188)	0,088
Playing gadgets	0,970 (0 ,070 s/d 1,870)	0,035*
Playing outdoors (> 1x/week)	-2,214 (-4,840 s/d 0,412)	0,096

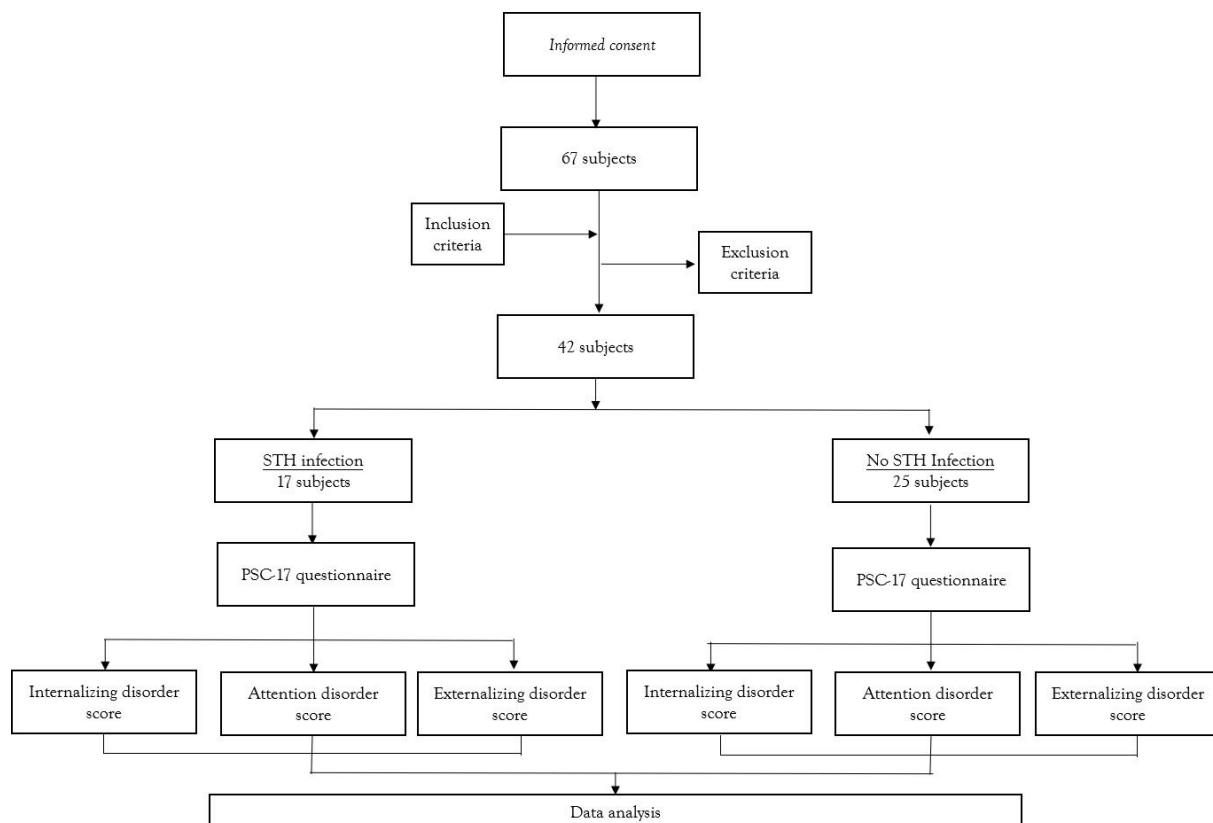
Note: Linear Regression Test; \* significant at  $\alpha < 0.05$

**Table 4 Multivariate Analysis of the Relationship between Soil-Transmitted Helminths Infection and Behavioral Disorders (Attention) Score**

Variable	Externalizing	
	B (95%CI)	p-value
<b>STH infection</b>	3,608 (1,956 s/d 5,260)	<0,001*
<b>Confounding Variable:</b>		
<b>Female gender</b>	-1,474 (-3,092 s/d 0,144)	0,073
<b>Mother's Education</b>	-0,726 (-1,666 s/d 0,213)	0,126

Note: Linear Regression Test; \* significant at  $\alpha < 0.05$

**Table 5 Multivariate Analysis of the Relationship between Soil-Transmitted Helminths Infection and Behavioral Disorders Score (Externalizing)**



**Picture 1. Research chart**

**DISCUSSION**

In this study, girls had lower internalizing behavior disorder scores than boys (Table 3). Internalizing problems are closely related to the time of puberty.<sup>5</sup> Sterba et al. found that girls and boys begin to experience an increase

in internalizing problems at the age of 11 years which coincides with the onset of puberty. In girls, the occurrence of internalizing problems is severe and peaks near the age of 14 or adolescence.<sup>6</sup> Whereas in boys, the peak time for internalizing problems was at the age of 11 years or during the transition period of middle school.<sup>6</sup> Children infected with STH were shown to be significantly associated with behavioral disorders, both internalizing, attention, and externalizing (Table 2). STH infection significantly increased the score of internalizing, attention, and externalizing using the PSC-17 questionnaire (Table 3 to Table 5). STH infection invades the intestinal mucosa and induces the release of inflammatory mediators. This inflammatory reaction can biologically cause behavioral problems in children. In children in a period of rapid brain maturation and development, the strengthening of the gut micro biome and the immune system in the digestive tract can be disrupted due to STH infection, resulting in micronutrient deficiencies, affecting the gut-brain axis by changing the intestinal microbiota, and causing intestinal inflammation.<sup>7</sup>

Several studies have shown disruption of the intestinal microbiota and inflammation gut-associated with neuropsychiatric and neurodevelopmental conditions and even personality traits in adulthood.<sup>8-11</sup> Microbial dysbiosis in children has been linked to anxiety and depressive behavior in adulthood through gut-brain axis mechanisms.<sup>11</sup> Not all intestinal parasites have the same pathology or effect on their host. However, these parasites found in the intestine are considered to be pathogens that increase imbalances in the microbiota composition of the gut and dysfunction. Although it is still uncertain whether dysbiosis is the cause or the result of intestinal inflammation as it is associated with a breakdown of the intestinal barrier (gut barrier).<sup>7</sup> The breakdown in the gut barrier then contributes to impaired brain development and psychiatric symptoms.<sup>8-11</sup> The findings of this study may support further developments related to the gut-brain axis theory.<sup>11</sup>

Children with internalizing disorders exhibited significantly higher serum IL-6 levels than those without internalizing disorders.<sup>12</sup> The release of inflammatory cytokines and IL-6 is an early sign of dysregulation of the immune system and gut microbiota. The secretion of IL-6 is also influenced by fluctuations in sex hormones that begin at the onset of puberty with a complex biomolecular mechanism. High IL-6 production can stimulate cytokine secretion by macrophages and dendritic cells in brain neurons. IL-6 is also one of the main astrocytes activators in the central nervous system. Astrocytes are involved in the storage and secretion of glutamate in the brain, which is a neurotransmitter involved in the pathophysiology of depression and other mental disorders.<sup>12</sup> STH infection has been shown to significantly influence the occurrence of attention disorders in children. Research from Ozimek JG et al. has proven that the habit of biting teeth (Onychophagia) in children infected with ascariasis is associated with several psychiatric disorders such as anxiety, obsessive-compulsive behavior, and attention deficit hyperactivity disorder (ADHD).<sup>13</sup> Neuroimmune communication pathways describe how intestinal microbes influence the function and maturation of immune cells in the CNS, where microglia cells play an important role. These cells are activated and produced by pro-inflammatory cytokines which are important regulators of autoimmunity, inflammation nerves, and neurogenesis. These various inflammatory processes can decrease the permeability of the Blood-Brain Barrier (BBB), which in turn causes inflammation of the brain parenchyma. Inflammation of the brain and nervous system plays an important role in the pathophysiology of children's attention disorders.<sup>14</sup> A systematic review supports findings that conclude that patients with ADHD have elevated serum proinflammatory cytokines (IFN gamma and IL-6) in serum.<sup>14-15</sup>

Playing gadgets has been shown to significantly increase attention disorder scores in children. The length or duration of use of gadgets by children can influence their development. The introduction of gadgets too early in children can affect children's social interactions. The ideal length of time for preschoolers to use gadgets is 30 minutes to 1 hour a day. Recent studies have shown that children who use electronic devices are at twice the risk of suffering from ADHD.<sup>16</sup>

Externalizing behavior disorder (impulsive, aggressive, and hyperactive) is one of the symptoms of Autism Spectrum Disorder (ASD). Research by Ferguson et al. has proven an association between gastrointestinal symptoms and externalizing and internalizing behavior problems in children and adolescents with ASD. The inflammatory response due to gastrointestinal disorders including parasitic infections and changes in the intestinal microbiota is thought to be the closest mechanism for activation of the sympathetic nervous system and the hypothalamus-pituitary axis associated with the Blood-Brain Axis.<sup>17</sup>

There are several limitations of this study including the number of samples was limited to 42 subjects according to the calculation of the minimum sample size, but not yet able to represent the population of children with STH infection in general. The identification of puberty that can affect the occurrence of behavioral disorders in children has not been controlled. No data on the severity of STH infection was obtained because there was no quantitative calculation of worm eggs in the stool sample.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ACKNOWLEDGMENTS

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

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