Tuijin Jishu/Journal of Propulsion Technology
ISSN: 1001-4055
Vol. 45 No. 1 (2024)

Multiple Soil-Transmitted Helminths Infection in 5-Year-Old Girl Presenting As Severe Anemia, Rectal Prolapse, and Stunting: Complicated Neglected Tropical Disease in Ende, East Nusa Tenggara, Indonesia

Danny Jaya Yacobus[1], Irene Ratridewi[2], Kurniawan Taufiq Kadafi[3], Ardanta Dat Topik Tarigan[1]

[1]*Department of Pediatric Ende General Hospital, Ende Regency, East Nusa Tenggara, Indonesia*

[2]*Infection and Tropical Disease Division, Department of Pediatric Dr. Saiful Anwar General Hospital, Malang, East Java, Indonesia*

[3] *Pediatric Critical Care Division, Department of Pediatric Dr. Saiful Anwar General Hospital, Malang, East Java, Indonesia*

Abstract

BACKGROUND: Soil-transmitted helminth (STH) infections in the pediatric population are still prevalent and spread in various regions in Indonesia. It is associated with a disease burden of over 3.3 million disability-adjusted life years and a global prevalence of 1.7 billion cases. East Nusa Tenggara is one of the provinces that have severe endemicity of STH infection. STH infections frequently coexist with anemia and malnutrition brings negative impacts on child growth and development. Here we present the case of multiple STH infections with its consequences in a 5-year-old girl in Ende, East Nusa Tenggara.

CASE: A 5-year-old girl suffering from pale and fatigue. Her physical examination showed pale conjunctiva, tachycardia, rectal prolapse and anthropometrics status concluded as stunting. Laboratory examination showed severe anemia (Hemoglobin 1.5 gr/dl) with eosinophilia, the fecal smear showed egg form of Ascaris lumbricoides, Ancylostoma duodenale, and Trichuris trichiura. The screening for parasite research on her parent's stool was negative, the patient never wears footwear in daily activity. The patient was treated successfully with triple dose Albendazole, packed red cell (PRC) transfusion, heart failure management, nutritional intervention, and discharged from the hospital in stable condition.

CONCLUSION: STH infection still being the burden of disease in endemic area like Indonesia. Increased awareness of STH in daily practice can reduce the serious complication like severe anemia, and stunting. Environmental health should be identified to asses the risk factor of STH infection.

Keywords: *Soil-Transmitted Helminth Infection, Severe Anemia, Rectal Prolapse, Stunting*

Background

Soil-transmitted helminths (STH) including *Trichuris trichiura*, *Ascaris lumbricoides*, and hookworm (*Ancylostoma duodenale and Necator americanus*) influences almost 1,7 billion people globally.[1] Indonesia has ranked second in the world with 70.642.364 cases, one-third of those are found in preschool-age children (PSC).[2] The risk factors of helminthic infection among PSC are poor hygiene, poor environmental sanitation, and socioeconomic factors.[3] East Nusa Tenggara has one of the highest endemicity of STH infection in Indonesia.[4] The prevalence of STH infection in East Nusa Tenggara is approximately 66% of adults suffered from at least one type of STH, including hookworm (51,7%), *Ascaris lumbricoides* (21,8%) and *Trichuris trichiura* (19,7%).[5] There is no particular data on helminthic infection on pediatric population in East Nusa Tenggara. But the research of STH infection among PSC in Nangapanda, Ende East Nusa Tenggara predominated by *Ascaris lumbricoides* 47,4% PSC, followed by *Trichuris trichiura* 36,8% PSC, and hookworm 9,2% PSC.[6]

STH infection in PSC age are at higher risk of mortality and morbidity associated with anemia, malnutrition, disturbance of growth and development, and poor school performance.[6,7,8] Elaboration on another etiological factor such as the quality and quantity of nutrient intake as well as natural enteropathy can play a role as a contributing factor to malnutrition and anemia.[9] The research from the Nangapanda subdistrict in Ende showed the prevalence of underweight at 33.1%, stunting at 40.2%, wasting at 17.1%, and anemia at 60.3%.[6] East Nusa Tenggara becomes the province with high prevalence of wasting and stunting, followed by the statement that infection of STH and malnutrition and its consequences frequently coexist.[6]

Here we present the case of multiple STH infections in a 5-year-old girl presenting with severe anemia, rectal prolapse, and stunting in Ende, East Nusa Tenggara. We also review the literature report on STH infection and its consequences, to help discuss the major clinical results and also the challenges of diagnosis and therapeutic in limited resources area.

Case Presentation

A 5-year-old girl came to the emergency ward due to pale and easily fatigue. Pale was identified in the palm, conjunctiva, and face 3 months before admission. There was neither a history of fever, jaundice, abdominal pain, nor malignancy. The last month she suffered a lack of appetite, fatigue induced by exercise, and failure to gain weight. There was a history of worm-contained defecation in last three months. She complained of bleeding during defecation followed by rectal prolapse (Fig.1). She is living in a rural area in Ende Regency in East Nusa Tenggara, Indonesia. Her parents work as a farmer and have a history of barefoot during daily activities. She never got medical intervention before coming to our hospital. Her parent's last education degree is junior high school.

Fig 1. Manifestation of rectal prolapse in this patient

On physical examination, the patient looked pale, fully alert, and wake. The heart rate 120 beats per minute, respiratory rate 38 times per minute, blood pressure 95/60 mmHg, and body temperature 36,7^{o}C. Pale in the conjunctiva, face, and both of her palms. Anthropometric measurement showed a body weight 14 kg (WHZ <-2SD to mean), body height 99 cm (-3SD to -2SD), weight age (WA) 37 months of age, and height age (HA) 42

months of age, WA<HA<CA suggest stunting. Laboratory tests showed leucocyte count 8710/ µl, with 11% of eosinophils (958 µl), hemoglobin 1.5 g/dl, mean with peripheral blood smear showed hypochromic anisopoikylocytosis of red blood cells (RBC). Electrolytes, renal function, coagulation test, bilirubin, albumin, serum proteins, and also liver enzymes were normal. Chest radiography and abdominal ultrasound were normal. Electrocardiography (ECG) showed sinus tachycardia.

During hospitalization she suffering worm-contained defecation, we found for about 10-12 adult worms sized 7-12 cm (Fig.2). The microscopic test of stools revealed the incoming of *Ascaris lumbricoides* eggs, *Ancylostoma duodenale* eggs, and *Trichuris trichiura* eggs which were confirmed in two different samples from days. Figure 3A shows the fertilized egg of *Ascaris lumbricoides* in wet stool preparation under the microscope. Figure 3B shows a hookworm egg in wet stool preparation, and Figure 3C shows a *Trichuris trichiura* egg in wet stool preparation under the microscope. Parasitic research on parent's stools resulted negative.

Fig 2. The adult worm of *Ascaris lumbricoides*

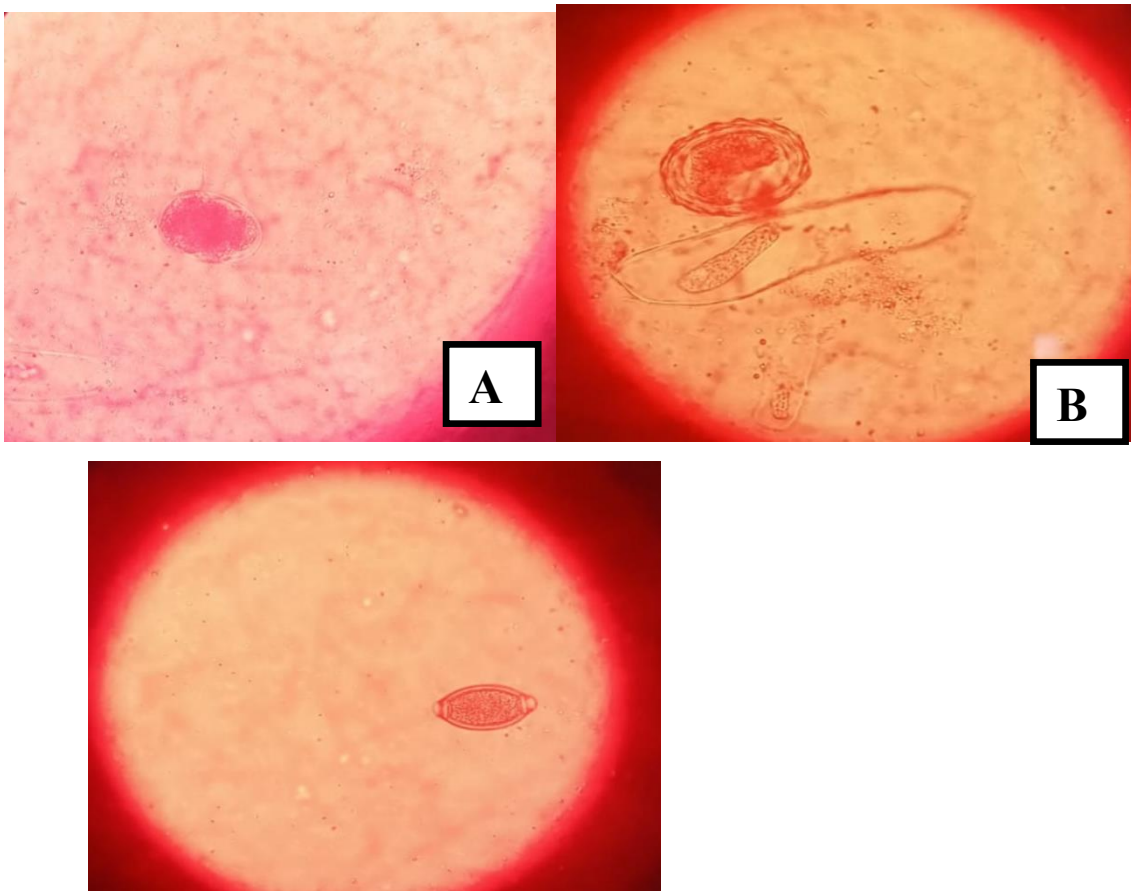

Fig 3. (A) Fertilized egg of *Ascaris lumbricoides* in an unstained wet mount of stool. A larva stage is inside the egg. (B) Hookworm egg in unstained wet mount of stool. (C) *Trichuris trichiura* egg in unstained wet mount of stool

The patient got a triple dose of Albendazole 400 mg/day, packed red cell transfusion, and nutritional intervention by using Protein Energy Ratio (PER) >10%. After 14 days of hospitalization, she was discharged in stable condition, Hb level 11,5 g/dL and stool microscopic there was no worm eggs. The follow-up control after undergoing 1 month, her clinical presentation was good and she gained 2 kilograms of body weight. The laboratory test showed normal results, no anemia was found and the stool microscopic examination was negative.

Discussion

STH is known as a group of intestinal parasites that are frequently affected in tropical and subtropical regions. STH mainly contains *Trichuris trichiura*, *Ascaris lumbricoides*, and hookworm that mainly influence school-age children along with PSC children.[1,10,11,12] STH infections are strongly related to malnutrition, anemia, and impaired physical and congnitive development.[13,14] Risk factors for STH infection such as low socio-economic status, rural, and indigenous communities in tropical and sub-tropical areas.[12,15,16] In this case patient was 5 years old, living in rural area of Ende East Nusa Tenggara and her parents worked as a farmer with low incomes.

Ascaris lumbricoides infected the host by ingesting contaminated food and water.[1] The egg phase of *Ascaris lumbricoides* is mostly asymptomatic infection.[1,18] Adult worms cause symptoms due to the extra-intestinal phase of migratory in the liver and lungs, whereas swallowed dan re-entering the gastrointestinal tract. In the small intestine, *Ascaris lumbricoides* develop into adult worms, and the female releases thousands of eggs per day. *Ascaris* infection causes intestinal obstruction, appendicitis, cholecystitis severe allergy reaction due to eosinophilic asthma, malnutrition, and mucosal bleeding which leads to anemia.[1,18,19] In this case the patient suffering from mucosal bleeding that causes anaemia, and stunting as complications. The manifestation of worm-contained adult *Ascaris lumbricoides* and microscopic finding of *Ascaris lumbricoides* egg to establish the diagnosis.

The main transmission of hookworms is skin penetration.[1,15] Adult hookworms in the intestine use its cutting organs and proteolytic enzyme to damage mucosal and arteriole causing massive intestinal blood loss, and cleave hemoglobin and protein breakdown.[15,19,20,21] This mechanism stimulates adult hookworms to digest hemoglobin and absorb host peptides and amino acids that cause anemia, protein malnutrition, and hypoalbuminemia.[21] Moderate and severe infection has a greater risk of iron-deficiency anemia, especially in PSC age children.[15,22,23] The others long-term impacts are protein malnutrition, stunting, and impaired cognitive capability.[1,15,24] In this case the predisposing factor of hookworm infection in the patient was barefoot habits. Chronic infection of hookworm contributed to severe anemia in this patient, and absorb the patient protein contributed to stunting. The Hb level was 1.5, and she got PRC transfusion during hospitalization.

Trichuris trichiura is infected through contaminated food and water with *Trichuris* eggs.[1] *Trichuris* worms lay in the large intestine causing colitis and inflammatory bowel disease, and a severe form manifested as *Trichuris* dysentery syndrome that leads to rectal prolapse.[20,24] The pathophysiology of colitis is due to release of stichosomes by adult worms that change host epithelium and allow the anterior end of the parasite to make cellular tunnels to stimulate inflammation and intestinal blood loss.[20,21,24] In this patient suffered from colitis and dysentri syndrome and followed by rectal prolapse which strongly related to Trichuriasis. The fecal microscopy finding of Trichuris eggs prove the diagnosis. The bloody stools contribute to the development of severe anemia in this patient.

Multiple studies showed high prevalence of anemia among children with STH infection.[25] A study in Ethiopia showed children impacted with STH had a high risk of anemia (aOR 8.87, 95% CI 2.28 to 34.58). A metaanalytics research also found a high OR 4.49, 95% CI 1.58 to 12.75, p 0.05 among infants with numerous STH infections.[25,26] Approximately 64% of global cases of STH infection are found in Southeast Asia which is 15% of cases occurred in Indonesia.[27,28] The study found that hookworm-infected children had the highest risk of anemia with OR 3.3, 95% CI 1.98 to 5.49, p 0.05, while *Ascaris lumbricoides* had OR 1.57, 95% CI 1.2 to 2.07, p 0.05, and *Trichuris trichiura* had OR 1.66, 95% CI 1.13 to 2.43, p 0.05.[26] These findings showed that children with multiple STH infection have lower mean hemoglobin levels than single STH infection.[29] The findings on those studies is similar to this patient who suffered from multiple STH infection presenting as severe anemia. Hookworm infection is predominantly causing progressive intestinal blood loss in this patient.

Anemia among children with STH infection was described by nutrition deficiency mechanisms and blood loss.[31] Disturbance of nutrition absorption is often found in *Ascaris lumbricoides* infection interfering absorption of iron (Fe), zinc (Zn), protein, folic acid, vitamin B6, and vitamin B12.[32] The mechanism of blood loss in *Ascaris lumbricoides* is the rupture of capillaries and arterioles within the intestinal tissue.[33-34] Blood loss is also common due to occult bleeding in *Trichuris trichiura* and hookworm infection that led to penetration and disruption in intestinal epithelium that related to hyaluronidase enzyme which is responsible for degrading the mucosal layer.[35] The hookworm has anticoagulant substances secreted to enhance the effect and rate of blood loss and also downregulation of the host immune response. *Ancylostoma duodenale* has the highest rate of blood loss approximately 0.14-0.4 ml of blood loss per day per worm.[1,36] Anemia following *Trichuris trichiura* infection is mainly caused by chronic blood oozing in the caecum and colon through mucosal penetration of adult worms. Estimated blood loss due to *Trichuris trichiura is* approximately 0,005 ml per day per worm.[33] In this case hookworm infection had the greatest contribution to severe anemia in this patient due to rate of blood loss for every hookworm. *Ascaris* lumbricoides distrubing nutrition absorbtion such as Fe and vitamin B12 as a precursor of hemoglobin. Adult worm of *Ascaris lumbricoides* mechanically disrupt the integrity of intestinal capillary. *Trichuris trichiura* increased the degree of severity in anemia by direct penetration of adult worm in colon.

Stunting decrease the intestine villi and number of immunology cells lead to high susceptibility of gastrointestinal infection. An increasing population of IgA-coated bacteria contributed to bacterial dysbiosis in the intestine which disturbed the immune response against parasitic agents like STH.[37] Intestinal helminth infections can impact nutritional status directly or indirectly, leading to malnutrition and stunting.[38-41] STH can cause gastrointestinal tract physiopathology and decreased appetite.[41-43] STH secrete pancreatic enzyme inhibitors, which prevent host nutrient absorption in the small intestine. This infection also increases intestinal permeability consequence as inadequate nutrient absorption.[38] STH can cause intestinal inflammation and persistent blood loss, that lead to malnutrition.[41] In our case this patient might be suffering from chronic malnutrition due to inadequate intake which increases susceptibility to STH infection . But on the other hands, due to risk factors of low socioeconomic, barefoot, and farm activity lead to STH infection, and malnutrition occured after the STH infection.

Albendazole and mebendazole are the most frequently prescribed drugs in STH infection. Single-dose albendazole had high efficacy in eradicating *A lumbricoides* and also hookworm, but unsatisfied in *T.trichiura*.[44-48] Several studies showed better efficacy of triple dose albendazole than single-dose albendazole. But several studies stated moderate efficacy of triple dose albendazole to *T.trichiura* infection.[50-53] Mebendazole had higher cure rate in *T.trichiura* than albendazole alone.[48] Integration of albendazole and also pyrantel pamoate never tend to develop the rate of cure or rate of egg reduction in trichuriasis.[54] In this case of multiple STH infection, our hospital only has albendazole and pyrantel pamoate. We gave a triple dose of albendazole and showed clinical improvement. We decided not to give pyrantel pamoate because of lack of evidence based to eradicate STH especially *Trichuris trichiura*. The stool microscopy examination after a triple dose albendazole there was no worm.

Conclusion

Multiple STH infections among the pediatric population mostly presenting as severe anemia and malnutrition. Awareness of STH infection especially in endemic area should be practiced. Evaluation of environmental hygiene, history of barefoot, usage of latrine, and level of education should be identified. Fecal microscopy examination and antihelmintics like albendazole and pyrantel pamoate were very useful in limited resources area like Ende. The provision of chemoprophylaxis should also be encouraged in endemic area.

References

[1] Parija SC, Chidambaram M, Mandal J. 2017. Epidemiology and clinical features of soil-transmitted helminths. Trop Parasitol. 7: 81-5. https://doi.org/10.4103/tp.TP_27_17 PMID: 29114484

[2] World Health Organization. Soil-transmitted helminthiases: number of children (pre-SAC and SAC) requiring preventive chemotherapy for soil-transmitted helminthiases: 2019 [Internet]. Geneva: World Health Organization. 2020 [cited 2023 Sep 11]. Available from: https://apps.who.int/neglected_diseases/ntddata/sth/sth.html.

[3] Anderson RM, Turner HC, Truscott JE, Hollingsworth TD, Brooker SJ. 2015. Should the Goal for the Treatment of Soil Transmitted Helminth (STH) Infections Be Changed from Morbidity Control in Children to Community-Wide Transmission Elimination? PLoS Negl TropDis 9(8):e0003897.Epub2015/08/21.https://doi.org/10.1371/journal.pntd.0003897 PMID: 26291538

[4] World Health Organization. Indonesia: communicable disease profile. In: World Health Organization [Internet]. 2016 [cited 2023 Sep 9]. Available from: https://www.who.int/nmh/countries/idn_en.pdf?ua=1.

[5] Wiria AE, Hamid F, Wammes LJ, Prasetyani MA, Dekkers OM, May L, et al. 2015. Infection with soil-transmitted helminths is associated with increased insulin sensitivity. PLoS One 10: e0127746. https://doi.org/10.1371/journal.pone.0127746 PMID: 26061042

[6] Djuardi Y, Lazarus G, Stefanie D, Fahmida U, Ariawan I, Supali T. 2021. Soil-transmitted helminth infection, anemia, and malnutrition among preschool-age children in Nangapanda subdistrict, Indonesia. PLos Negl Trop Dis 15(6): e0009506. https://doi.org/10.1371/journal.pntd.0009506.

[7] Truscott J, Hollingsworth TD, Anderson R. 2014. Modeling the interruption of the transmission of soil-transmit- ted helminths by repeated mass chemotherapy of school-age children. PLoS Negl Trop Dis. 8 (12):e3323. Epub 2014/12/05. https://doi.org/10.1371/journal.pntd.0003323 PMID: 25474477.

[8] Makata K, Kinung'hi S, Hansen C, Ayieko P, Sichalwe S, Mcharo O, et al. 2020. Hand hygiene intervention to optimize helminth infection control: Design and baseline results of Mikono Safi–An ongoing school-based cluster-randomised controlled trial in NW Tanzania. 2020. PLoS ONE 15(12): e0242240.

[9] Ansuya, Nayak BS, Unnikrishnan B, George A, N SY, Mundkur SC, et al. 2018. Risk factors for malnutrition among preschool children in rural Karnataka: a case-control study. BMC Public Health. 2018; 18: 283. https://doi.org/10.1186/s12889-018-5124-3 PMID: 29482540.

[10] Brooker S, Clements AC, Bundy DA. Global Epidemiology, Ecology and Control of Soil-Transmitted Helminth Infections. Advances in Parasitology 2006; 62: 221-261. https://doi.org/10.1016/S0065-308X(05)62007-6 .

[11] Kurscheid J, Laksono B, Park MJ, Clements ACA, Sadler R, McCarthy JS, et al. Epidemiology of soil-transmitted helminth infections in Semarang, Central Java, Indonesia. PLoS Negl Trop Dis 2020; 14(12): e0008907. https://doi.org/10.1371/journal.pntd.0008907.

[12] Hughes A, Nguyen DN, Clarke NE, Dyer CE, Hii SF, Clements AC, *et al*. Epidemiology of soil-transmitted helminths using quantitative PCR and risk factors for hookworm and *Necator americanus* infection in school children in Dak Lak province, Vietnam. *Parasit&Vectors* 2023; 16:213. https://doi.org/10.1186/s13071-023-05809-x.

[13] Buonfrate D, Bisanzio D, Giorli G, Odermatt P, Fürst T, Greenaway C, et al. The global prevalence of Strongyloides stercoralis infection. Pathogens. 2020;9:1–9.

[14] Gilmour B, Alene KA, Clements ACA. The prevalence of soil transmitted helminth infections in minority indigenous populations of South-East Asia and the Western Pacifc region: a systematic review and meta-analy- sis. PLoS Negl Trop Dis. 2021. https://doi.org/10.1371/journal.pntd.00098 90.

[15] Umbrello G, Pinzani R, Bandera A, Formenti F, Zavarise G, Arghittu M, et al. Hookworm infection in infants: a case report and review of literature. *Italian Journal of Pediatrics* (2021) 47: 26.

[16] Bethony J, Brooker S, Albonico M, Geiger SM, Loukas A, Diemert D, et al. Soil-transmitted helminth infections: ascariasis, trichuriasis, and hook- worm. Lancet. 2006;367:1521–32.

[17] Hotez PJ, Brindley PJ, Bethony JM, King CH, Pearce EJ, Jacobson J. Helminth infections: the great neglected tropical diseases. J Clin Invest. 2008;118:1311–21. https://doi.org/10.1186/s13052-021-00981-1

[18] Jourdan PM, Lamberton PH, Fenwick, Addiss DG. Soil-transmitted helminth infections. Lancet 2018; 20: 391(10117): 252-265. https://doi.org/10.1186/s13052-021-00981-1.

[19] Loukas A, Maizels RM, Hotez PJ. The yin and yang of human soil-transmitted helminth infections. *Int J Parasitol* 2021 December; 51(13-14): 1243-1253. doi:10.1016/j.ijpara.2021.11.001.

[20] Budhathoki S, Shah D, Bhurtyal KK, Amatya R, Dutta AK. Hookworm causes melaena and severe anaemia in early infancy. Ann Trop Paediatr. 2008;28(4): 293–6.

[21] Loukas A, Hotez PJ, Diemert D, Yazdanbakhsh M, McCarthy JS, Correa-Oliveira R, Croese J, Bethony JM, 2016. Hookworm infection. Nat. Rev. Dis. Primers 2 10.1038/nrdp.2016.88.

[22] Brooker S, Bethony J, Hotez PJ. Human hookworm infection in the 21st century. Adv Parasitol. 2004;58:197–288.

[23] Papier K, Williams GM, Luceres-Catubig R, Ahmed F, Olveda RM, McManus DP, et al. Childhood malnutrition and parasitic helminth interactions. Clin Infect Dis. 2014;59:234–43.

[24] Else KJ, Keiser J, Holland CV, Grencis RK, Sattelle DB, Fujiwara RT, *et* al. Whipworm and roundworm infections. Nature Rev. Dis. Primers 2020; 6. 10.1038/s41572-020-0171-3.

[25] Lebu S, Kibone W, Muoghalu CC, Ochaya S, Salzberg A, Bongomin F, et al. Soiltransmitted helminths: A critical review of the impact of co-infections and implications for control and elimination. PLoS Negl Trop Dis 2023;17(8): e0011496. https://doi.org/10.1371/journal.pntd.0011496.

[26] Alnaz AR, Darlan DM, Andriyani Y, Lubis RR. Hemoglobin Level and Risk of Anemia in Soli-Transmitted Helminths Infections among Children: A Systematic Review and Meta-analysis.

[27] World Health Organization. Eliminating soil-transmitted helminthiasis as a public health problem in children. France: WHO Press; 2012.

[28] Bukhari A, Hamid F, Minhajat R, Sutisna NS, Marsella CP. Non-nutritional and disease related anemia in Indonesia: A systematic review. *Asia Pac J Clin Nutr 2020*; 29(*Suppl 1*):S41-S54.

[29] Degarege A, Animut A, Medhin G, Legesse M, Erko B. The association between multiple intestinal helminth infections and blood group, anemia and nutritional status in human populations from Dore Bafeno, southern Ethiopia. J Helminthol. 2014 Jun; 88(2):152–9. https://doi.org/10.1017/S0022149X12000855 PMID: 23286203.

[30] Sanchez AL, Gabrie JA, Usuanlele MT, Rueda MM, Canales M, Gyorkos TW. Soil-transmitted helminth infections and nutritional status in school-age children from rural communities in Honduras. PLoS Negl Trop Dis. 2013;7(8):e2378. https://doi.org/10.1371/journal.pntd.0002378 PMid:23951385

[31] Salam N, Fareed M. Soil-transmitted helminth infections and its association with haemoglobin levels in India: A meta-analysis. J Clin Diagnostic Res. 2019;13(6):12. https://doi.org/10.7860/jcdr/2019/40681.12950.

[32] Righetti AA, Koua AY, Adiossan LG, Glinz D, Hurrell RF, N'Goran EK, et al. Etiology of anemia among infants, school-aged children, and young non-pregnant women in different settings of South-Central Côte d'Ivoire. Am J Trop Med Hyg. 2012;87(3):425-34. https://doi.org/10.4269/ajtmh.2012.11-0788 PMid:22848097.

[33] Caldrer, S.; Ursini, T.; Santucci, B.; Motta, L.; Angheben, A. Soil-Transmitted Helminths and Anaemia: A Neglected Association Outside the Tropics. Microorganisms 2022, 10, 1027. https://doi.org/10.3390/microorganisms10051027.

[34] Ahmed A, Al-Mekhlafi HM, Al-Adhroey AH, Ithoi I, Abdulsalam AM, Surin J. The nutritional impacts of soil-transmitted helminths infections among Orang Asli schoolchildren in rural Malaysia. Parasites Vectors. 2012;5(1):1-9. https://doi.org/10.1186/1756-3305-5-119 PMid:22704549.

[35] Sungkar S, Tambunan FB, Gozali MN, Kusumowidagdo G, Wahdini S. The effect of albendazole toward anemia in children with soil-transmitted helminths infection in a remote and endemic area. Med J Indones. 2018;27(4):293-8. https://doi.org/10.13181/mji.v27i4.2857.

[36] Conlan JV, Sripa B, Attwood S, Newton PN. A review of parasitic zoonoses in a changing Southeast Asia. Vet Parasitol. 2011;182:22–40. doi: 10.1016/j.vetpar.2011.07.013. Epub 2011 Jul 12.

[37] Fauziah N, Ar-Rizki MA, Hana S, Patahudin NM, Diptyanusa A. Stunting as a Risk Factor of Soil-Transmitted Helminthiasis in Children: A Literature Review. *Hindawi Interdiciplinary Perspectives on Infectious Disease* 2022: 1-14. https://doi.org/10.1155/2022/8929025

[38] Ulukanligil M, Seyrek A. Anthropometric status, anaemia and intestinal helminthic infections in shantytown and apartment schoolchildren in the Sanliurfa province of Turkey. Eur. J. Clin. Nutr. 2004, 58, 1056–1061.

[39] Casapía, M.; Joseph, S.A.; Núñez, C.; Rahme, E.; Gyorkos, T.W. Parasite risk factors for stunting in grade 5 students in a community of extremem poverty in Peru. Int. J. Parasitol. 2006, 36, 741–747. doi: 10.1016/j.ijpara.2006.03.004.

[40] Quihui-Cota L, Valencia ME, Crompton DW, Phillips S, Hagan P, Díaz-Camacho SP, et al. Prevalence and intensity of intestinal parasitic infections in relation to nutritional status in Mexican schoolchildren. Trans. R. Soc. Trop. Med. Hyg. **2004**, 98, 653–659. doi: 10.1016/j.trstmh.2003.12.017.

[41] Degarege A, Erko B, Negash Y, Animut A. Intestinal Helminth Infection, Anemia, Undernutrition and Academic Performance among School Children in Northwestern Ethiopia. Microorganisms **2022**, 10, 1353. https://doi.org/10.3390/microorganisms10071353.

[42] Crompton, D.W.; Nesheim, M.C. Nutritional impact of intestinal helminthiasis during the human life cycle. Ann. Rev. Nutr. **2002**, 22, 35–59. [CrossRef]

[43] Michael, C. Global health impact of soil-transmitted nematodes. Pediatric Infect. Dis. J. **2004**, 23, 663–664.

[44] WHO. Investing to overcome the global impact of neglected tropical diseases: third WHO report on neglected diseases 2015. World Health Organzation, 2015.

[45] Keiser J, Utzinger J. The drugs we have and the drugs we need against major helminth infections. Adv Parasitol 2010;73:197-230. doi:10.1016/S0065-308X(10)73008-6.

[46] Keiser J, Utzinger J. Efficacy of current drugs against soil-transmitted helminth infections: systematic review and meta-analysis. JAMA 2008;299:1937-48. doi:10.1001/jama.299.16.1937.

[47] Speich B, Ame SM, Ali SM, et al. Oxantel pamoate-albendazole for Trichuris trichiura infection. N Engl J Med 2014;370:610-20. doi:10.1056/NEJMoa1301956.

[48] Moser W, Schindler C, Keiser J. Efficacy of recommended drugs against soil transmitted helminths: systematic review and network meta-analysis. BMJ 2017; 358:j4307. doi: 10.1136/bmj.j4307.

[49] Sungkar S, Putri KQ, Taufik IS, Gozali MN, Sudarmono P. The Effectiveness of Triple Dose Albendazole in Treating Soil Transmitted Helminths Infection. *Journal of Parasitology Research* 2019; 6438497: 1-4. https://doi.org/10.1155/2019/6438497.

[50] Steinmann P, Utzinger J, Du ZW, Jiang JY, Chen JX, Hattendorf J, *et al*. Efcacy of singledose and triple dose albendazole and mebendazole against STH and Taenia sp: a randomized controlled trial. PLoS ONE 2011; 6(9): Article ID e25003. https://doi.org/10.1371/journal.pone.0025003.

[51] Adegnika AA, Zinsou JF, Issifou S, Ngoa UA, Kassa RF, Feugap EN, *et al*. Randomized, Controlled, Assesor-Blind Clinical Trial To Asses the Efficacy of Single- versus Repeated- Dose Albendazole To Treat *Ascaris lumbricoides*, *Trichuris trichiura*, and Hookworm Infection. *Antimicrobial Agents and Chemotherapy* 2014; 58(5): 2535-2540.

[52] Gultom DE, Ali M, Pasaribu AP, Pasaribu S. Two or Three Consecutive Days Albendazole Treatment Has Better Efficacy than Single-Dose Albendazole Treatment for Trichuriasis. *Indones Biomed J* 2020; 12(1): 45-50. DOI: 10.18585/inabj.v12i1.920.

[53] Tee MZ, Lee SC, Er YX, Yap NJ, Ngui R, Easton AV, *et al*. Efficacy of triple dose albendazole treatment for soil-transmitted helminth infection. PLos ONE 2022; 17(8): : e0272821. https://doi. org/10.1371/journal.pone.0272821.

[54] Sapulete EJJ, Dwi Lingga Utama IMG, Sanjaya Putra IGN, Kanya Wati D, Arimbawa IM, Gustawan IW. Efficacy of albendazole-pyrantel pamoate compared to albendazole alone for Trichuris trichiura infection in children: a double blind randomized controlled trial. Malays J Med Sci. 2020;27(3):67–74. https://doi. org/10.21315/mjms2020.27.3.7.