

Intestinal Parasitic Infection Responsible for Undernourishment and Stunted growth in Children of school going age

ABSTRACT

Aim: to discuss about the specific characteristics of intestinal parasitic infection that contributes to the formation of stunting.

Discussion: Intestinal parasites infection (IPI) are one of the global utmost health dilemmas, because they put certain vulnerable member of the population, e.g., children, in danger. Global prevalence rate of IPI varied from 30-60%, especially in developing countries located within the region of tropical and subtropical zone that create a definite public health burden, particularly in low- and middle-income countries, including Indonesia. Basically, IPI divided into helminths- and protozoans; each have different and unique characteristics with helminths have a more sophisticated life cycle compare to protozoan. IPI tends to be chronic and sub-clinical, due to the evasion the host's immune system. This chronic IPI affects the host, directly and indirectly, and in long term when it happen during toddlerhood, it contributes to the formation of undernourishment and stunting via certain pathways. Transmission occurs mainly via food contamination; and it is usually always related with daily socio-economic activity. Persistent transmission exists when source of infection available and practice of poor hygiene supports continuous contamination in the environment. By knowing the details of the life cycle of each gastrointestinal parasite, all stake holder can participate in communal effort to break the chain of transmission.

Conclusion: the presence of infected individuals with poor hygiene practice is the main contributor to the existence of persistent transmission in certain environment and this can then play a role in the formation of stunting.

Keywords: Soil transmitted helminths, intestinal protozoan, persistent contamination, poor hygiene practice, transmission, anthropometric measurement.

1. INTRODUCTION

Intestinal parasitic infections (IPI) are amidst the most prevalent parasitic ailment globally, especially in developing countries [1]. In general, IPI can be classified as helminths based and protozoan based. It is estimated annually by hospital-based affecting up to 3.5 billion individuals and responsible for bring about 450+ million hospital based health consequences [2], ranging from simple diarrhoea, Intestinal gas and abdominal bloating, nausea-vomiting, abdominal discomfort/pain, malabsorption, undernutrition/undernourishment, malaise, febleness, and hindered growth and physical development [4,5].

Millions of children of preschool- and school- age group that reside in endemic zone of soil- transmitted helminths or other intestinal parasite, are in danger [2]. Transmission occurred through foodborne route [6]. Without sufficient anti-parasitic therapy, what may initially be just a simple intestinal parasitic infection can later develop into severe infections resulted in severe disability with cognitive, mental and behavioral sequelae [7,8]. Children are very prone and they often encounter re-infection [9,10]. Parasitologically, this persistent infection can be maintained by several factors, and these will be the focus of this review.

2. PARASITIC AGENTS OF THE GASTROINTESTINAL SYSTEM

Gastrointestinal parasites are either worms (helminths) or one-celled animals called protozoans which live inside the lumen of human intestines. There are four most common species of intestinal helminthic parasites, also known as geohelminths and soil-transmitted helminths: *Ascaris lumbricoides* (roundworm), *Ancylostoma duodenale*, *Necator americanus* (hookworms), *Trichuris trichiura* (whipworm), and *Strongyloides stercoralis*. The diseases caused by these geohelminths are known as ascariasis, ancylostomiasis, necatoriasis, trichuriasis and strongyloidiasis [11,12]. Other non STH species that inhabit the GI tract are less commonly found and will not discuss further.

Among the protozoan group, the most common intestinal protozoan parasites are as follows: *Entamoeba histolytica*, *Giardia lamblia*, *Cyclospora cayatanensis*, and *Cryptosporidium spp.* The diseases caused by these intestinal protozoan parasites are known as amoebiasis, giardiasis, cyclosporiasis and cryptosporidiosis respectively, and they are generally linked with diarrhoea [13,14].

3. THE EFFECT OF INTESTINAL PARASITIC INFECTION TO THE HOST

Each species responsible for IPI's produces characteristic disease syndromes and health problems, ranging from simply asymptomatic [15] to severe condition [13], and that can restricted to only GI tract symptoms including abdominal pain, abdominal bloating, diarrhea, the loss of blood and important macronutrient (protein), even to the point that an anatomical derangement called prolapses recti can occur. Apart from abnormalities that are limited to the gastrointestinal tract, systemic abnormalities may also occur, if the infection lasts for a long time/ persistent, it can caused serious consequences such as malnutrition, stunting, and cognitive retardation [13,16,17].

This physico-cognitive retardation due to IPI is a serious consequences of prolonged infection. There is strong clinical evidence that individuals suffer from helminth polyparasitism infections have even worse infections with STHs[12]. Heavily infected individuals are at a higher risk of suffer from more severe form of the disease [18] and are also the prime source of environmental contamination [19] and also persistent transmission [20]. not to mention if the heavily infected individual is also infected by other microorganisms at the same time, a condition known as co-infection, and thus, this preceding parasitic infection appears to open the door for more definitive pathogens and give way to their sites of predilection. [21,22].

3.1. Persistent Transmission

In order to understand persistent transmission, it is necessary to understand the life cycle of intestinal parasites; both worms and protozoa have different life cycle details.

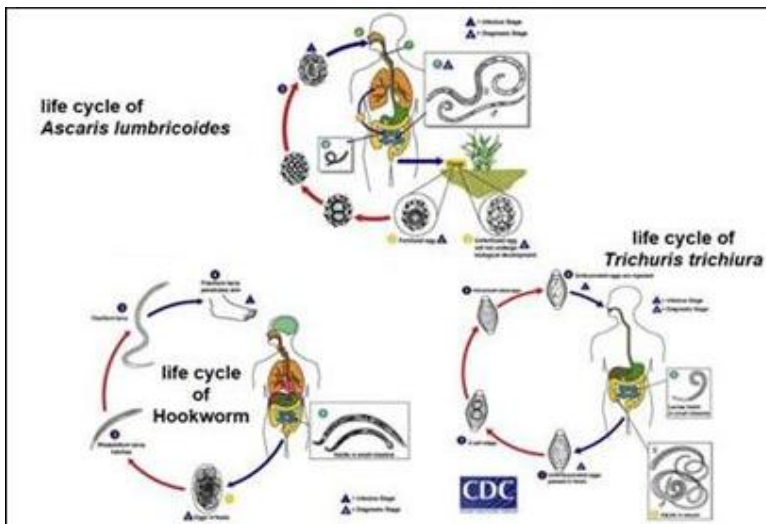


Fig. 1. Illustrative portrayal of the life cycles of *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm [30, with modification].

These geohelminths are disseminated by fertilized eggs that are elapsed in the stool of infected individuals. Mature worms inhabited the host's gut and expelled enormous immature eggs daily. In community with poor practice of sanitation, these eggs surely contaminate the soil. This could take place in several ways: (1) mature eggs that are adhered to raw vegetables or

improperly washed or peeled or cooked food; (2) eggs are unintentionally consumed from **polluted** water springs; and (3) infected eggs are unintentionally consumed by children that have contact with contaminated soil and then unintentionally place their contaminated hands into their mouths without proper washing. These are the most ideal ways of environmental contamination which if occur constantly can lead to persistent transmission of STH to vulnerable members of society, especially children; and this point in the STH life cycles, where there is existence of infected individuals and the potency of environment contamination due to poor practice of hygiene, should be an alternative in efforts to terminate the transmission chain.

These geohelminths (*A. lumbricoides*, *T. trichiura* and hookworms) actually do not accrue in number while they are inside the intestinal lumen of their human host; the possibility of re- infection take place only if direct contact with infective stages (mature and fertilized eggs) in the environment; and this point in the STH life cycles should be an alternative in efforts to terminate the transmission chain. For *S. stercoralis*, its expansion in number can happen

inside the host, and for specific vulnerable group in the society, the immunocompromised patients, its unrestricted proliferation can be deadly.

Other group of intestinal **parasites**, the protozoan, have different but quite simple life cycle compared to helminths. the intestinal amebae have two stages in their life cycles, a motile trophozoite and a cyst. Either stage may serve as the diagnostic form but only the cyst is infectious.

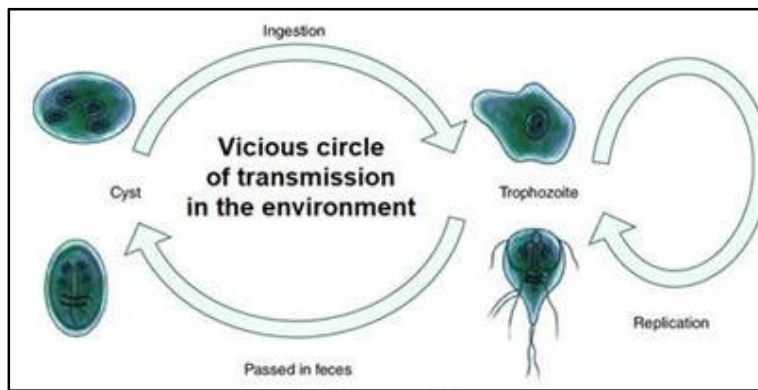


Fig 2. Typical protozoan fecal-oral life cycle [31, with modification]

Environmental contamination of vegetables and fruits with intestinal protozoan trophozoites, cysts and oocysts **are** a means of transmitting parasitic agents of public health importance. A possible risk of protozoan infection in humans via unwashed vegetables and fruits. Accidental ingestion of protozoa occurs through consumption of contaminated vegetables and fruits that have been improperly washed and prepared under poor sanitation [31]. **Besides** that, Food handlers with improper personal hygiene practices also have a noteworthy capacity in transmitting foodborne parasites, including intestinal protozoa, right with their own contaminated hand [32]. Preventive effort by (1) using sanitary irrigation water, (2) consuming only properly cleaned and cooked vegetables as fresh as possible, and (3) the most important is practicing good hygiene; these three can all contribute to reduce the risk of protozoa infection; and this point in the intestinal protozoan life cycles should be an alternative in efforts to terminate the transmission chain, e.g., by improving how raw food materials being processed properly and also by giving appropriate therapy to individuals infected with this intestinal protozoans.

3.2 Role of Vulnerable Individuals

The availability of vulnerable individuals in highly endemic area helped transmission of infection to occur continuously [33]. **The** density of a host population in a certain environment is an important parameter that concealed disease transmission, including helminth or protozoan infection. But on contrary, it also has insinuation for the expression of infection to happen through its reverberations on the host's bodily normal function. As a response to the existence of higher ponderosity of the parasite in the environment, people at risk are predicted to either upgrade their immune property as a consequence to the increased risk of parasitism, or furthermore to reduce the immune capability as a direct **effect** of stress regarding overwhelmed environment. However, an individual's health condition is shaped by many different factors, including their genetic history, their latest environmental **milieu**, and history of maternal effects with an emphasize on the time of conception and pregnancy. The latter factor (maternal effect) can open our horizons about when stunting actually started to occur.

3.3 Contribution of Parasitic Infection to Stunting Formation

Undernourishment is a condition of poor energy and nutrient intake in daily individual's meal. Anthropometric measurements are actually the only approved and validated technique for calculating nutritional levels. Wasting hints an individual to a low weight-for-height value for their chronological age. Stunting hints to a low height-for-age value, whereas being underweight refers to a low weight-for-age value. The World Health Organization (WHO) growth standard is frequently used to represent these criteria where measured children that indicate signs of wasting, stunting, or being underweight report values more than two standard deviations below the population standard ($z < -2$).

Due to its causative condition, undernourishment is dichotomized into acute and chronic. Primary acute undernourishment in children is definitely a sequel of insufficient daily food consumption; condition that is chronic and continues to worsen clinically in the absence of external intervention. On the other hand, secondary acute undernourishment is typically a consequence of abnormal macro-nutrient deprivation, elevated energy expenditure, or reduced food intake. These circumstances commonly materialize in the context of previously existing underlying chronic ailment, such as severe infection, cystic fibrosis, chronic liver disease, chronic renal failure, malignancies during juvenility, congenital heart disease, and neuromuscular diseases.

The chief signal of acute undernourishment is called wasting. Chronic undernourishment, on the contrary, is a **consequence** of deficiency of particular element of nutrients at definite times during the phase of early childhood, which reverberates in the defect or at least inhibition of physical and cognitive development. The condition of stunting is the most widely accustomed barometer of chronic undernourishment.

A condition of chronic and/or recurring deficiency of correct nutritious foods, both in quantity and quality, for mother and child during the whole pre- and postnatal periods subsidizes **to the** formation of stunting [34]. Like many illnesses, parasitic infections may result in:

1. withdrawal of food from individuals who are overtly ill [35], or
2. reduce appetite as a result of active abdominal pain and discomfort, the latter being common symptoms of parasitic gastrointestinal infection [36], or
3. Parasites may also influence neuroendocrine control of appetite, for example leptin and adiponectin, and cause anorexia [37]. Enterendocrine cells have the ability to 'notice' the existence of gastrointestinal parasites or their products in the intestine and provoke the cytokine expansion [38]. This eventually changes the expression of taste receptor and let out of satiety hormones. In reality, leptin, a major appetite suppressant has been found to be significantly increased in children **who's** infected with *Entamoeba histolytica*, *Strongyloides spp.*, and also *Giardia lamblia*. Correspondingly, active *Trichuris trichiura* infection that occurs during childhood period has been associated with chronic beneath the recommended portion of intake of energy, protein, iron, and also riboflavin.
4. Prolonged and persistent intestinal parasitic infection (IPI) grants the **development** of stunting. Active IPI can cause direct dysregulation of growth factors which are central for prenatal and postnatal development. Furthermore, IPI opens the door for the entry of a more harmful secondary infections, bacterial and viral, and permitted them to settle definite co-infection; a condition which is responsible for prolonged inflammation, locally and systematically, and make the condition getting worse. Several probable interrelated mechanistic courses also could be related via (1) the host's imbalanced nutritional status, (2) possible environmental enteric dysfunction (EED) due to the combination of (a) chronic and persistent IPI, (b) sustained inflammation, (c) hormonal imbalance, (d) metabolic disturbances, (e) immune instability, (f) the consequences of definite **anemia**, (f) changed microbiota configuration, and also (g) shifted in epigenetic composition. [21]

4. CONCLUSION

Persistent and prolonged IPI supported by constant transmission in the environment triggered both sustained immune activation and also systemic inflammation that opens the door for other infection (bacterial, virus etc) and in long term subsidizes to the development of stunting, directly and indirectly.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Eyayu T, Kiros T, Workneh L, Sema M, Damtie S, Hailemichael W, Dejen E, Tiruneh T. Prevalence of intestinal parasitic infections and associated factors among patients attending at Sanja Primary Hospital, Northwest Ethiopia: An institutional-based cross-sectional study. *PLoS One*. 2021;16(2):e0247075. <https://doi.org/10.1371/journal.pone.0247075>.
2. Fauziah N, Aviani JK, Agriafanny YN, Fatimah SN. Intestinal Parasitic Infection and Nutritional Status in Children under Five Years Old: A Systematic Review. *Trop Med Infect Dis*. 2022;7(11):371. <https://doi.org/10.3390/tropicalmed7110371>.
3. Khurana S, Gur R, Gupta N. Chronic diarrhea and parasitic infections: Diagnostic challenges. *Indian J Med Microbiol*. 2021 Oct-Dec;39(4):413-416. <https://doi.org/10.1016/j.ijmmb.2021.10.001>.
4. Kiani H, Haghghi A, Rostami A, Azargashb E, Tabaei SJ, Solgi A, Zebardast N. Prevalence, risk factors and symptoms associated to intestinal parasite infections among patients with gastrointestinal disorders in nahavand, western Iran. *Rev Inst Med Trop Sao Paulo*. 2016;58:42. <https://doi.org/10.1590/S1678-9946201658042>.
5. Bryan P, Mejia R. Invited Commentary on Growth and Development in Children with Gastrointestinal Parasitic Infections. *Curr Trop Med Rep*, 2015; 2: 233–7. <https://doi.org/10.1007/s40475-015-0059-6>
6. Chávez-Ruvalcaba F, Chávez-Ruvalcaba MI, Moran Santibañez K, Muñoz-Carrillo JL, León Coria A, Reyna Martínez R. Foodborne Parasitic Diseases in the Neotropics - A Review. *Helminthologia*. 2021;58(2):119-133. <https://doi.org/10.2478/helm-2021-0022>.
7. Olopade BO, Idowu CO, Oyelese AO, Aboderin AO. Intestinal Parasites, Nutritional Status And Cognitive Function Among Primary School Pupils in Ile-Ife, Osun State, Nigeria. *Afr J Infect Dis*. 2018;12(2):21-28. <https://doi.org/10.21010/ajid.v12i2.4>.
8. Jasti A, Ojha SC, Singh YI. Mental and behavioral effects of parasitic infections: a review. *Nepal Med Coll J*. 2007;9(1):50-6.

9. Zemene T, Shiferaw MB. Prevalence of intestinal parasitic infections in children under the age of 5 years attending the Debre Birhan referral hospital, North Shoa, Ethiopia. *BMC Res Notes*. 2018;11(1):58. <https://doi.org/10.1186/s13104-018-3166-3>.
10. Monárrez-Espino J, Pérez-Espejo CR, Vázquez-Mendoza G, Balleza-Carreón A, Caballero-Hoyos R. Intervention to prevent intestinal parasitic reinfections among Tarahumara indigenous schoolchildren in northern Mexico. *Rev Panam Salud Publica*. 2011;30(3):196-203. <https://doi.org/10.1590/s1020-49892011000900002>.
11. Mascarini-Serra L. Prevention of Soil-transmitted Helminth Infection. *J Glob Infect Dis*. 2011;3(2):175-82. <https://doi.org/10.4103/0974-777X.81696>.
12. Donohue RE, Cross ZK, Michael E. The extent, nature, and pathogenic consequences of helminth polyparasitism in humans: A meta-analysis. *PLoS Negl Trop Dis*, 2019; 13(6): e0007455. <https://doi.org/10.1371/journal.pntd.0007455>
13. Berhe B, Bugssa G, Bayisa S, Alemu M. Foodborne intestinal protozoan infection and associated factors among patients with watery diarrhea in Northern Ethiopia; a cross-sectional study. *J Health Popul Nutr*. 2018;37(1):5. <https://doi.org/10.1186/s41043-018-0137-1>. Erratum in: *J Health Popul Nutr*. 2019;38(1):16.
14. Yanyan Jiang, Zhongying Yuan, Hua Liu, Jianhai Yin, Yuan Qin, Xiaofeng Jiang, et al. Intestinal Protozoan Infections in Patients with Diarrhea — Shanghai Municipality, Zhenjiang City, and Danyang City, China, 2011–2015 and 2019–2021[J]. *China CDC Weekly*, 2022, 4(8): 143-147. <https://doi.org/10.46234/ccdcw2022.028>
15. Kpene GE, Lokpo SY, Deku JG, Agboli E, Owiafe PK. Asymptomatic Intestinal Parasitic Infestations among Children Under Five Years in Selected Communities in the Ho Municipality, Ghana. *Ethiop J Health Sci*. 2020 Nov;30(6):867-874. <https://doi.org/10.4314/ejhs.v30i6.3>.
16. Parija SC, Chidambaram M, Mandal J. Epidemiology and clinical features of soil-transmitted helminths. *Trop Parasitol*. 2017;7(2):81-85. https://doi.org/10.4103/tp.TP_27_17.
17. Toreyhi S, Vahedi S, Tabatabaei S, Hadighi R. The role of brain waves in distinction children with intestinal parasite diseases and attention-deficit/hyperactivity disorder in Karaj. *Advances in Cognitive Science*, 2021;23(2):59-71. <https://doi.org/10.30514/icss.23.2.5>.
18. Pullan R, Brooker S. The health impact of polyparasitism in humans: are we under-estimating the burden of parasitic diseases? *Parasitology*. 2008 Jun;135(7):783-94. <https://doi.org/10.1017/S0031182008000346>.
19. Ribas A, Jollivet C, Morand S, Thongmalayvong B, Somphavong S, Siew CC, Ting PJ, Suputtamongkol S, Saensombath V, Sanguankiat S, Tan BH, Paboriboune P, Akkhavong K, Chaisiri K. Intestinal Parasitic Infections and Environmental Water Contamination in a Rural Village of Northern Lao PDR. *Korean J Parasitol*. 2017 Oct;55(5):523-532. <https://doi.org/10.3347/kjp.2017.55.5.523>.
20. Lilian Da Silva Santos, Hans Wolff, François Chappuis, Pedro Albajar-Viñas, Marco Vitoria, Nguyen-Toan Tran, Stéphanie Baggio, Giuseppe Togni, Nicolas Vuilleumier, François Girardin, Francesco Negro, Laurent Gétaz, "Coinfections between Persistent Parasitic Neglected Tropical Diseases and Viral Infections among Prisoners from Sub-Saharan Africa and Latin America", *Journal of Tropical Medicine*, vol. 2018, Article ID 7218534, 10 pages, 2018. <https://doi.org/10.1155/2018/7218534>
21. Siagian FE. Role of Intestinal Parasitic Infection in Stunting. *South Asian Journal of Research in Microbiology*, 2023;15(2). pp. 41-50 <https://doi.org/10.9734/SAJRM/2023/v15i2285>
22. Mabbott NA. The Influence of Parasite Infections on Host Immunity to Co-infection With Other Pathogens. *Front Immunol*. 2018 Nov 8;9:2579. <https://doi.org/10.3389/fimmu.2018.02579>.
23. Michel J. Ebert D, Hall MD. The trans-generational impact of population density signals on host-parasite interactions. *BMC Evol Biol*, 2016; 16: 254. <https://doi.org/10.1186/s12862-016-0828-4>
24. Tschirren B, Richner H. Parasites shape the optimal investment in immunity. *Proc Biol Sci*. 2006;273(1595):1773-7. <https://doi.org/10.1098/rspb.2006.3524>.
25. Du H, Bartleson JM, Butenko S. Tuning immunity through tissue mechanotransduction. *Nat Rev Immunol* 2023;23: 174–88. <https://doi.org/10.1038/s41577-022-00761-w>
26. Greimel E, Kato Y, Müller-Gartner M, Salchinger B, Roth R, Freidl W. Internal and External Resources as Determinants of Health and Quality of Life. *PLoS One*. 2016 May 2;11(5):e0153232. <https://doi.org/10.1371/journal.pone.0153232>.
27. Virolainen SJ, VonHandorf A, Viel KCMF. Gene–environment interactions and their impact on human health. *Genes Immun*, 2023; 24, 1–11. <https://doi.org/10.1038/s41435-022-00192-6>
28. Jukarainen S, Kiiskinen T, Kuitunen S. Genetic risk factors have a substantial impact on healthy life years. *Nat Med* 2022;28: 1893–1901. <https://doi.org/10.1038/s41591-022-01957-2>
29. Gibson JM. Environmental Determinants of Health. *Chronic Illness Care*. 2017 Nov 7:451–67. https://doi.org/10.1007/978-3-319-71812-5_37.
30. Truscott JE, Turner HC, Farrell SH, Anderson RM. Soil-Transmitted Helminths: Mathematical Models of Transmission, the Impact of Mass Drug Administration and Transmission Elimination Criteria. *Adv Parasitol*. 2016;94:133-198. doi: 10.1016/bs.apar.2016.08.002.
31. Wiser, M.F. (2021). Nutrition and Protozoan Pathogens of Humans: A Primer. In: Humphries, D.L., Scott, M.E., Vermund, S.H. (eds) *Nutrition and Infectious Diseases*. Nutrition and Health. Humana, Cham. https://doi.org/10.1007/978-3-030-56913-6_6
32. Eslahi VA, Olfatfar M, Zaki L, Saryazdi AK, Barikbin F, Maleki A, et al. Global prevalence of intestinal protozoan parasites among food handlers: A systematic review and meta-analysis. *Food Control*, 2022; 145. 109466. <https://doi.org/10.1016/j.foodcont.2022.109466>.
33. Silk MJ, Fefferman NH. The role of social structure and dynamics in the maintenance of endemic disease. *Behav Ecol Sociobiol*, 2021; 75, 122. <https://doi.org/10.1007/s00265-021-03055-8>
34. Titaley CR, Ariawan I, Hapsari D, Muasyaroh A, Dibley MJ. Determinants of the Stunting of Children Under Two Years Old in Indonesia: A Multilevel Analysis of the 2013 Indonesia Basic Health Survey. *Nutrients*. 2019;11(5):1106. <https://doi.org/10.3390/nu11051106>.
35. Gabain IL, Ramsteijn AS, Webster JP. Parasites and childhood stunting - a mechanistic interplay with nutrition, anaemia, gut health, microbiota, and epigenetics. *Trends Parasitol*. 2023 Mar;39(3):167-180. <https://doi.org/10.1016/j.pt.2022.12.004>.

36. Ünal E, Arslan S, Onur MR, Akpınar E. Parasitic diseases as a cause of acute abdominal pain: imaging findings. *Insights Imaging*. 2020 Jul 20;11(1):86. <https://doi.org/10.1186/s13244-020-00892-5>.
 37. Yahya RS, Awad SI, Kizilbash N, El-Baz HA, Atia G. Enteric parasites can disturb leptin and adiponectin levels in children. *Arch Med Sci*. 2018 Jan;14(1):101-106. <https://doi.org/10.5114/aoms.2016.60707>.
 38. Yu Y, Yang W, Li Y, Cong Y. Enteroendocrine Cells: Sensing Gut Microbiota and Regulating Inflammatory Bowel Diseases. *Inflamm Bowel Dis*. 2020;26(1):11-20. <https://doi.org/10.1093/ibd/izz2>
-