Clinical and Nutritional Outcomes of Schistosomiasis on Maternal and Child Health

Francees Raphaiel Cabaltera[1], Arienne Therese Evangelista[1], Ramon Joaquin Isaguirre[1],
Mary Jane Flores [1,3,4,*], Bridget Co-Arellano[1], Jessica Joyce De Guia[1], Frumencio Co[2]

[1] Department of Biology, De La Salle University, 2401 Taft Ave., Manila 0922, Philippines
[2] Department of Mathematics and Statistics, De La Salle University, 2401 Taft Ave., Manila 0922, Philippines
[3] Biological Control Research Unit (BCRU), Center for Natural Sciences and Environmental Research (CENSER), College of Science, De La Salle University, 2401 Taft Ave., Manila 0922, Philippines
[4] Ehime University - De La Salle University International Collaborative Research Laboratory, De La Salle University, Laguna Campus, Laguna Province, Philippines
*Corresponding Author: mary.jane.flores@dlsu.edu.ph

Abstract: Schistosomiasis has been a prevalent health concern within endemic nations having affected over a third of the global population, with both pregnant women and children being the most vulnerable in contracting the disease. Despite this, little is known about the specific clinical presentations and deficient micronutrients commonly exhibited by those affected. With this, the study aimed to determine the most prevalent clinical presentations, deficient micronutrients, and risk factors closely associated with the prevalence of schistosomiasis in pregnant women and children. A chi-square test with 95% confidence level was done to assess the significance of the association of infection to the identified conditions, micronutrients, and factors. Positivity rates were also calculated and compared through a chi-square test to determine the most prevalent condition and affected micronutrient. The association strength was also determined by calculating the Cramer's V values. Statistical testing revealed that schistosomiasis in both target populations more commonly exhibits conditions related to the gastrointestinal area (e.g. diarrhea and abdominal pain), but children manifest other presentations such as hematuria and anemia. A weak association was found between micronutrient deficiency and schistosomiasis ($V = 0.0564$), having vitamin A deficiency as the most prevalent. Illiteracy ($p = 0.0013$) and poor water quality ($p < 0.0001$) were also the factors that were found to be directly linked with schistosomiasis. Overall, this review highlights the capability of schistosomiasis to induce broad clinical effects on host health and nutrition. The prevalence of infection is influenced by sociodemographic and environmental factors. Given these findings, cost-effective interventions, proper education, and sufficient research must therefore be done to provide sustainable defense and reduction of infections.

Key Words: Clinical Presentation; Micronutrient; Positivity Rate; Schistosomiasis

1. INTRODUCTION

Schistosomiasis is one of the world's most significant neglected tropical diseases (NTDs) caused by blood flukes under genus *Schistosoma,* and is amongst the most prominent chronic human infections in pregnant women and children aged 4-12 years old globally, with about 40 million of the former being recorded positive for this parasitic disease, and 50 million recorded in the latter (Thayer et al. 2017; Friedman et al., 2018; WHO, 2020). Included within these numbers are tropical countries such as the Philippines which were able to present an 88.4% prevalence in women and a 94.6% prevalence in children under 10 alone, emphasizing the need to control this disease within the affected localities in tropical nations (Gordon et al., 2015). Aside from the many pathologies that were previously identified with

this infection, such as diarrhea, anemia, and abdominal pain, schistosomiasis has also given rise to many cases of malnutrition and nutritional deficiencies globally due to the parasite's ability to interfere with nutrient absorption (Kramer & Allen, 2015). This essentially denotes that its presence within the human body does not exclude the possibility of nutritional complications (i.e. micronutrient deficiencies) to arise along with other complications if a healthy individual gets infected and is left untreated. In spite of this, very little is known on the specifics of the infection's clinical presentations in vulnerable groups which are also more at risk for malnutrition and helminth infection (Arinola et al., 2015).

Determining the specific conditions that arise in schistosomiasis and its specific micronutrient interaction is vital for vulnerable populations, particularly pregnant women and children. Research on this disease must be continued in spite of the limitations of the COVID-19 pandemic. Therefore, the current study aimed to assess schistosomiasis' clinical and nutritional outcomes on maternal and child health in African countries through collectively analyzing available published research in the last 15 years to help illustrate how this parasitic disease's effect on nutrition may also take shape in the Philippines. Specifically, this meta-analysis was conducted to determine the following: (1) to determine the most prevalent clinical presentation of schistosomiasis in pregnant women and children of African ethnicity; (2) to identify the most common micronutrient affected by schistosomiasis in African pregnant women and children; and (3) to distinguish the risk factors associated with the prevalence of infection.

2. METHODOLOGY

2.1 Inclusion and Exclusion Criteria

Published data from studies focusing on schistosome infection amongst children and pregnant women were gathered from various electronic databases such as PubMed, MEDLINE, and Google Scholar. The eligibility criteria for these studies included the following conditions: (1) pregnant women of any gestational stage, age, race, and nationality; (2) preschool-age children (PSAC) (ages 3-5 years) and school-age children (SAC) (ages 5–14 years) of any gender, race, and nationality; and (3) literature published in the last 15 years. Exclusion criteria included the following: (1) studies that were conducted outside of the African continent; (2) studies of schistosomiasis on non-human subjects or in vitro

studies; (3) studies with unreliably extracted, duplicated, or overlapping data; (4) abstract-only papers or articles without full-text availability; and (5) literature not published in the English language.

2.2 Statistical Analysis

All the data were tabulated, statistically analyzed, and graphed using Microsoft Excel with the PHStat extension. A chi-square test was done to assess the significance of the association of infection to the identified clinical presentations, micronutrients, and factors. This analysis was executed using a 95% confidence level, with differences considered insignificant at the 0.05 significance level. Positivity rates were then calculated to determine the most prevalent clinical presentation and affected micronutrient of infection. Lastly, the Cramer's V coefficient was calculated to determine the overall strength of association between schistosomiasis and the independent variables of interest. Corresponding descriptive interpretations of the Cramer's V values were then made based on the ranges formulated by Akoglu (2018).

3. RESULTS AND DISCUSSION

3.1 Clinical Presentations in Pregnant Women

Only five clinical presentations were identified to be related to schistosomiasis infection in pregnant women of African ethnicity. Results from the initial chi-square analysis show that there is a significant association between the various clinical presentations being presented by pregnant women and the manifestation of schistosomiasis within the same group ($p < 0.0001$) (Table 1). The calculated Cramer's V value (V = 0.4712) also shows that the data collected from various areas within the African continent presents a very strong association between the two variables being analyzed, indicating that all these specific conditions are highly likely to present themselves altogether within an affected individual.

Table 1. Chi-square Analysis of the Clinical Presentations Displayed by Pregnant Women of African Ethnicity vs the Positivity Rate of Schistosomiasis

Clinical Presentation	n	Positivity Rate (%)	χ^2	p-value

Anemia	824	209 (25.30)	425.03	$p <$ 0.0001***
Diarrhea	342	251 (73.40)		
Hematochezia	342	160 (46.90)		
Abdominal pain	342	272 (79.60)		
Dyspareunia	64	9 (14.60)		

*significant at 0.05; **significant at 0.01; ***significant at 0.001

Amongst the various conditions that were recorded for this group, these pregnant women were found to be more likely to display abdominal pain when they are positive for the infection based on positivity rate alone, with diarrhea also being considered as one of the more common symptoms of schistosomiasis based on a follow up chi-square test ($p = 0.4655$). The rest of the symptoms, on the other hand, do not share the same recognition since their positivity rates are evidently much lower than the two that were mentioned (Fig. 1).
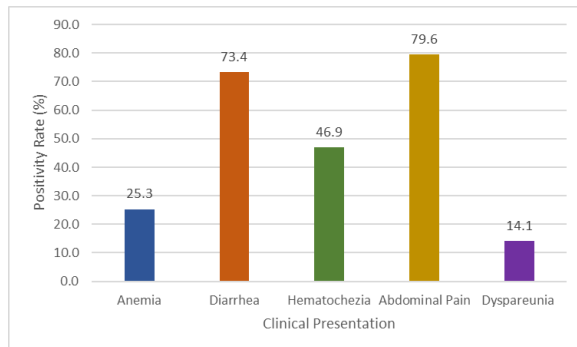

Figure 1. Positivity Rates of Each Clinical Presentation Found in Schistosomiasis-infected Pregnant African Women

The high prevalence of both gastrointestinal complications (abdominal pain and diarrhea) amongst those infected fully supports the parasite's behavior of settling within the vessels of gastrointestinal organs to absorb enough nutrients for producing new offsprings (Centers for Disease Control and Prevention, 2019). The presence of these schistosomes would, therefore, contribute in disrupting the normal function of the GI tract (such as decreased water absorption and increased inflammatory activity within the organ) due to the heavy loads of the parasite within the affected area (Ünal et al., 2020).

3.2 Clinical Presentations in Children

Numerous studies identified a total of thirteen (13) clinical presentations that were linked with schistosomiasis infection in African children. The chi-square analysis reports that there is a significant association between the recorded conditions being presented by children and the manifestation of schistosomiasis among them ($p < 0.0001$) (Table 2). The calculated Cramer's V value (V = 0.3806) for this set of individuals classifies the association between these two variables as being very strong, which means that all the 13 clinical presentations that were identified are very likely to be observed within a single infected child.

Table 2. Chi-square Analysis of the Clinical Presentations Displayed by African Children vs the Positivity Rate of Schistosomiasis

Clinical Presentation	n	Positivity Rate (%)	χ^2	p-value
Anemia	534	314 (58.83)	804.35	$p <$ 0.0001 ***
Stunting	411	194 (47.20)		
Underweight	312	109 (34.93)		
Diarrhea	662	358 (54.05)		
Hematochezia	756	194 (25.61)		
Polyuria	39	10 (25.60)		
Hematuria	358	212 (59.23)		
Dysuria	462	167 (36.21)		
Fatigue	94	15 (15.69)		
Headache	94	21 (22.60)		
Hepatomegaly	403	11 (2.73)		
Splenomegaly	403	16 (4.04)		
Abdominal pain	1026	511 (49.82)		

*significant at 0.05; **significant at 0.01; ***significant at 0.001

Based on numerical value alone, hematuria was identified to be the most common clinical presentation of these children with schistosomiasis (59.23%). However, a follow up chi-square test revealed that both anemia (58.83%) and diarrhea (54.05%) can also be recognized as this as well since their positivity rates are considered very close to that of hematuria ($p = 0.4452$). All the other conditions are less likely to be displayed by schistosome-infected children due to their lower positivity rates, with both splenomegaly and hepatomegaly being the least likely to be observed (Fig. 2.)
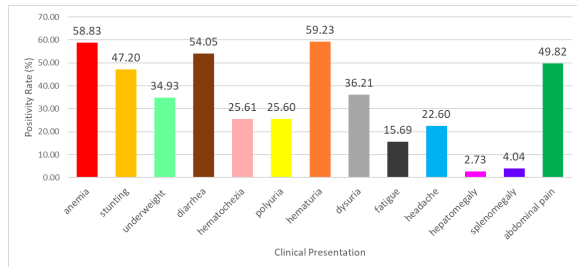
Figure 2. Positivity Rates of Each Clinical Presentation Found in Schistosomiasis-infected African Children

Hematuria was able to obtain the highest positivity rate amongst all the other presentations most possibly due to the overwhelming number of *S. haematobium* cases, which are mainly responsible for urinary-related complications, that are concentrated within the African continent. This, therefore, greatly contributes to the high positivity rate that was recorded from the gathered data (Lai et al., 2015). Along with this, *S. haematobium*'s behavior of depositing eggs into the ureters and bladder, along with the damage caused by the inflammatory response tasked with eliminating the parasite, causes blood to mix with urine, ultimately resulting in the condition we know as hematuria (Paul et al., 2002).

High positivity rates for anemia in children, on the other hand, can also be related to the parasite's absorption of blood within the venules of the body, which are able to contribute to decreased amounts of ferritin within the affected person's blood, essentially causing the person to become anemic regardless of the intensity of the parasitic infection (Butler et al., 2012).

In the case of diarrhea, the cause of its high positivity rates is mainly similar to that of the adults in which the parasite's behavior within the digestive tract of the affected child leads to decreased water absorption within this specific area of the body (Ünal et al., 2020).

3.3 Micronutrient Deficiency

Deficiencies in iron, vitamin A and vitamin D were identified in both pregnant women and children with schistosomiasis. There is a significant association between the affected micronutrient and positivity rate of schistosomiasis ($p < 0.001$) (Table 3). However, the strength of the association between the two variables was weak using the Cramer's V coefficient (V = 0.0564), indicating that the manifestation of iron or vitamin A deficiency is less likely to be manifested

altogether among pregnant women and children with schistosomiasis.

Table 3. Chi-square Analysis of the Affected Micronutrient vs the Positivity Rate of Schistosomiasis

Clinical Presentation	n	Positivity Rate (%)	χ^2	p-value
Iron	141	31 (21.99)	22.92	$p <$ 0.0001 ***
Vitamin A	6	6 (100)		
Vitamin D	6	4 (66.67)		

*significant at 0.05; **significant at 0.01; ***significant at 0.001

The positivity rates for iron deficiency, vitamin A deficiency (VAD), and vitamin D deficiency (VDD) vary significantly from one another, thus indicating that they have different prevalence. VAD is most observed among pregnant women and children (100.00%) followed by VDD (66.67%). Iron deficiency had the lowest positivity rate (21.99%) indicating that this is the least observed among parasite-infected individuals (Fig. 3). A separate Chi-square test excluding the iron deficiency was conducted to verify the similarity of the prevalence of vitamin VAD and VDD since their positivity rates are closer, and it was found that there is no significant difference between the two variables ($p = 0.1213$).
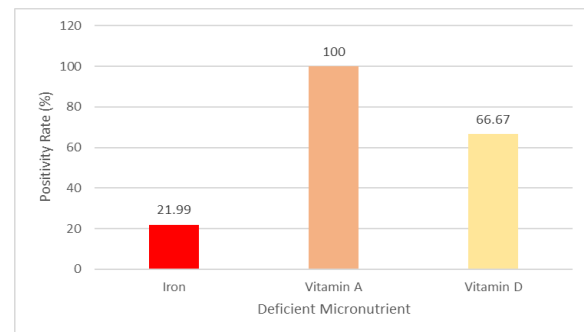

Figure 3. Positivity Rates of Each Deficient Micronutrient Found in Schistosomiasis-infected African Pregnant Women and Children

Since there is only a weak association between the variables, the contribution of schistosomiasis in the reduction of micronutrients is very minimal. *Schistosoma* parasites are known to inhabit digestive organs, specifically in their venules (Kinung'hi et al., 2017). Thus, affecting the micronutrient absorption in the host's body since these parasites compete for these nutrients to survive.

Statistical tests determined that individuals with affected vitamin A levels have the highest positivity rate for schistosomiasis infection. These results were parallel to the study conducted by Friis et al. (1997), where *S. mansoni* may cause the impairment of vitamin A absorption. In the results of the study performed by Reilly et al. (2012), Iron deficiency was most prevalent, affecting approximately half of children and pregnant women in developing countries. While based on the results of this study, iron deficiency serves as the least prevalent among pregnant women and children. The varied results of this study suggest that more research is needed to provide a clear association between schistosomiasis infection and impairment of micronutrient levels among pregnant women and children.

3.4 Risk Factors

A total of seven (7) factors were identified from multiple studies to have been linked with the manifestation of schistosomiasis amongst various communities across the African continent. Results from the chi-square analysis, however, show that only educational level ($p = 0.0013$) and water source quality ($p < 0.0001$) are associated with the presence of this infection within each community (Table 4). The relationship between both educational level and water source quality, and the manifestation of schistosomiasis were classified as being weak and moderate, respectively, due to the calculated Cramer's V values that were produced (V = 0.0952 for educational level; V = 0.1204 for water source quality).

Table 4. Chi-square Analysis of the Various Risk Factors of Schistosomiasis vs its Positivity Rate

Risk Factor	Type	n	Positivity Rate (%)	χ^2	p-value
Educational level	Literate	845	208 (24.62)	10.41	0.0013 **
	Illiterate	304	104 (34.21)		
Age	≤10 y.o	343	85 (24.78)	0.38	0.5367
	>10 y.o	497	114 (22.94)		
Soil contact	Yes	190	66 (34.74)	0.70	0.4020
	No	958	303 (31.63)		
Toilet presence	Yes	350	68 (19.43)	1.16	0.2825
	No	402	91 (22.64)		
Occupation	Daily Laborer	546	116 (21.25)	1.19	0.2759
	Non-daily Laborer	1302	307 (23.58)		
Water source quality	Safe	1200	215 (17.92)	30.26	$p <$ 0.0001 ***
	Unsafe	888	249 (28.04)		
Proximity to water source	Near	161	18 (11.18)	0.99	0.3200
	Far	243	20 (8.23)		

*significant at 0.05; **significant at 0.01; ***significant at 0.001

The weak association between illiteracy (i.e. inability to read and write; decreased comprehension) and schistosomiasis essentially indicates that the contribution of this specific risk factor to the prevalence of the parasitic disease within each community is very minimal. The moderate association between poor water source quality and schistosomiasis infection, on the other hand, shows that the contribution of this risk factor to the prevalence of schistosomiasis is more significant compared to that of illiteracy, but overall does not exclusively cause the disease in question when one is exposed to it. Nonetheless, while this may be the case based on the data that was collected, both illiteracy and poor water source quality are still considered as being the most likely factors to cause schistosomiasis within each location since the calculated positivity rates of these specific factors are significantly higher than that of their counterparts (Fig. 4).
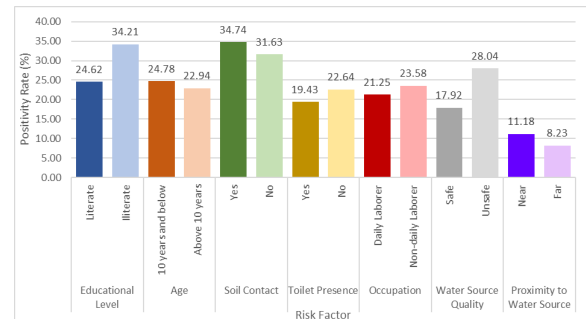

Figure 4. Positivity Rates of Schistosomiasis-infected Individuals Exposed to Each Risk Factor

The prevalence of schistosomiasis infections amongst those with illiteracy can be linked to a lack of awareness, concern, and comprehension that these people may have with this health issue. Since these people lack the knowledge and understanding to comprehend the severity of this infection, they are less likely to follow the necessary preventive measures that are being employed by the concerned bodies in preventing the manifestation of schistosomiasis within

the community they are situated in (Odhiambo et al., 2014).

Individuals utilizing water of poor quality, on the other hand, are more at risk for the parasitic infection due to the lack of treatment and cleaning that their main water source is undergoing. A lack of treatment within the water source being utilized by the community permits the schistosome cercariae to freely enter the body systems of the people who unknowingly ingest or bathe in the untreated water, ultimately increasing the possibility that the parasitic infection will develop within the individual exposed to this risk factor (Grimes et al., 2014).

4. CONCLUSIONS

This study presents (1) the clinical presentations both pregnant women and children may possess when infected with schistosomiasis, (2) the different micronutrients affected by the disease, and (3) the risk factors that can predispose to contraction. The high prevalence of gastro-intestinal complications, along with hematuria and anemia in children, within both study groups shows that extra attention must be given in these specific areas when treating those that are infected. This can be done through supplying the communities with medicines made specifically for these conditions, along with anthelmintic medication. In the case of micronutrients, deficiencies in vitamins A and D are observed in these study groups, essentially pointing out that programs focused on micronutrient supplementation must be executed within affected communities. Lastly with the risk factors, the high prevalence of schistosomiasis amongst communities with low educational levels and poor water source quality shows that there is a need for both clean water and proper education on this disease, within each locality. Hence, fortifying this knowledge within each affected community, along with interventions in cleaning their immediate water sources, is a must to lessen the prevalence of the disease.

Generally, schistosomiasis has been associated with a wide range of signs and symptoms in many existing literature. However, prior to the present study, the most common manifestation of the disease had been unknown, especially in vulnerable groups, such as children and pregnant women. This meta-analysis was able to uncover the effects of infection in both macro and micro levels, along with identifying the type of complication that would most likely arise in schistosomiasis patients of a certain demographic. Additionally, it was able to identify the

micronutrient most commonly reduced by the infection. Through combining existing data from multiple studies, it also provided stronger conclusions regarding the factors contributing to the prevalence of the disease. Ultimately, all of these findings contribute further knowledge essential for improving the diagnosis, management, and prevention of schistosomiasis.

The current study was, however, mainly limited by the use of published studies focusing on pregnant women and children of African ethnicity due to the insufficient research conducted outside the African continent. This meta-analysis also specifically utilized quantitative data on the prevalence of schistosomiasis and its associated clinical presentations from literature within the past 15 years. Sources without the complete data necessary for calculating the positivity rates of each clinical presentation were therefore excluded in this study. Along with this, micronutrient deficiency data that was collected from journal articles did not separate the prevalence among pregnant women and children, hence this study was not able to fully distinguish the differences between each target population regarding this factor.

5. REFERENCES

Akoglu H. (2018). User's guide to correlation coefficients. *Turkish journal of emergency medicine,* 18(3), 91–93. https://doi.org/10.1016/j.tjem.2018.08.001

Arinola G.O., Morenikeji O.A., Akinwande K.S., Alade A.O., Olateru-Olagbegi O., Alabi P.E., & Rahamon, S.K. (2015). Serum Micronutrients in Helminth-infected Pregnant Women and Children: Suggestions for Differential Supplementation During Anti-helminthic Treatment. *Annals of global health,* 81(5), 705–710. https://doi.org/10.1016/j.aogh.2015.10.001

Butler, S. E., Muok, E. M., Montgomery, S. P., Odhiambo, K., Mwinzi, P. M., Secor, W. E., & Karanja, D. M. (2012). Mechanism of anemia in *Schistosoma mansoni*–infected school children in western Kenya. *The American journal of tropical medicine and hygiene, 87*(5), 862. https://doi.org/10.4269/ajtmh.2012.12-0248

Centers for Disease Control and Prevention. (2019). *CDC - dpdx - schistosomiasis infection.*

https://www.cdc.gov/dpdx/schistosomiasis/index.html

Friedman J.F., Olveda R.M., Mirochnick M.H., Bustinduy A.L., & Elliott A.M. (2018). Praziquantel for the treatment of schistosomiasis during human pregnancy. *National Library of Medicine,* 1; 96(1), 59. https://doi.org/10.2471/BLT.17.198879

Friis, H., Mwaniki, D., Omondi, B., Muniu, E., Magnussen, P., Geissler, W., ... & Michaelsen, K. F. (1997). Serum retinol concentrations and Schistosoma mansoni, intestinal helminths, and malarial parasitemia: a cross-sectional study in Kenyan preschool and primary school children. *The American journal of clinical nutrition, 66*(3), 665-671. https://doi.org/10.1093/ajcn/66.3.665

Gordon, C. A., Acosta, L. P., Gobert, G. N., Olveda, R. M., Ross, A. G., Williams, G. M., ... & McManus, D. P. (2015). Real-time PCR demonstrates high prevalence of Schistosoma japonicum in the Philippines: implications for surveillance and control. *PLoS neglected tropical diseases, 9*(1), e0003483. https://doi.org/10.1371/journal.pntd.0003483

Grimes, J. E., Croll, D., Harrison, W. E., Utzinger, J., Freeman, M. C., & Templeton, M. R. (2014). The relationship between water, sanitation and schistosomiasis: a systematic review and meta-analysis. *PLoS neglected tropical diseases, 8*(12), e3296. https://doi.org/10.1371/journal.pntd.0003296

Kinung'hi, S. M., Mazigo, H. D., Dunne, D. W., Kepha, S., Kaatano, G., Kishamawe, C., ... & Nuwaha, F. (2017). Coinfection of intestinal schistosomiasis and malaria and association with haemoglobin levels and nutritional status in school children in Mara region, Northwestern Tanzania: a cross-sectional exploratory study. *BMC research notes, 10*(1), 1-11. https://doi.org/10.1186/s13104-017-2904-2

Kramer C.V., & Allen S. (2015). Malnutrition in developing countries. *Paediatrics and child health,* 25(9), 422-7. https://doi.org/10.1016/j.paed.2015.04.002

Lai, Y. S., Biedermann, P., Ekpo, U. F., Garba, A., Mathieu, E., Midzi, N., ... & Vounatsou, P. (2015).

Spatial distribution of schistosomiasis and treatment needs in sub-Saharan Africa: a systematic review and geostatistical analysis. *The Lancet infectious diseases, 15*(8), 927-940. https://doi.org/10.1016/S1473-3099(15)00066-3

Odhiambo, G. O., Musuva, R. M., Atuncha, V. O., Mutete, E. T., Odiere, M. R., Onyango, R. O., ... & Mwinzi, P. N. (2014). Low levels of awareness despite high prevalence of schistosomiasis among communities in Nyalenda informal settlement, Kisumu City, Western Kenya. *PLoS neglected tropical diseases, 8*(4), e2784. https://doi.org/10.1371/journal.pntd.0002784

Paul, J. F., Verma, S., & Berry, K. (2002). Urinary schistosomiasis. *Emergency medicine journal, 19*(5), 483-484. http://dx.doi.org/10.1136/emj.19.5.483

Reilly, L., Nausch, N., Midzi, N., Mduluza, T., & Mutapi, F. (2012). Association between micronutrients (vitamin A, D, iron) and schistosome-specific cytokine responses in Zimbabweans exposed to Schistosoma haematobium. *Journal of parasitology research, 2012.* https://doi.org/10.1155/2012/128628

Thayer W.M., Clermont A., & Walker N. (2017). Effects of deworming on child and maternal health: a literature review and meta-analysis. *BMC public health,* 17(4), 113-158. https://doi.org/10.1186/s12889-017-4747-0

Ünal, E., Arslan, S., Onur, M. R., & Akpinar, E. (2020). Parasitic diseases as a cause of acute abdominal pain: imaging findings. *Insights into Imaging, 11*(1), 1-19. https://doi.org/10.1186/s13244-020-00892-5

World Health Organization. (2020). *Schistosomiasis.* WHO. https://www.who.int/news-room/fact-sheets/detail/schistosomiasis