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Intestinal Parasitic Infections in Beta Thalassemia Major and Aplastic Anemia in Diwaniyah Province

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ABSTRACT

Background: Beta- thalassemia major (B-TM) and aplastic anemia are among the most complex chronic diseases because they are associated with serious complications as microbial infections. Current study aimed to isolation Intestinal parasite and evaluation their role in B-TM and Aplastic Anemia complications in Diwaniyah Province. **Methods**: This study included 50 children with B-TM and 53 children with aplastic anemia, we confirmed the clinical examinations by Lab diagnosis in Thalassemia Center, and the Maternity and Children Teaching Hospital. Lab diagnosis included; Complete blood count and blood film method, Hemoglobin electrophoresis, Reticulocyte count ,iron test, blood groups and general stool examination. **Results**: The current study included 50 children B-TM their ages ranged from 2 to 11 years, with an average age of 4.13 years and 53 children suffering from aplastic anemia, their ages ranged from 2 to 12 years, with age mean is 6.22 years. The results of the isolation and diagnosis of intestinal parasites showed that 70% of thalassemia patients suffer from intestinal parasitic infections represented by *Entamoeba histolytica, Giardia lamblia, Blastocystis hominis, Ascaris lumbricoide, Ancylostoma duodenale* and *Strongyloides stercoralis* by percentage 14%, 37%, 14%, 20% and 9% and 6% respectively. We also found that 62% of anemic patients suffered from intestinal parasitic infections that included *Entamoeba histolytica, Giardia lamblia, Blastocystis hominis, Ascaris lumbricoide, Ancylostoma duodenale* and *Strongyloides stercoralis* in rate 6%, 15%, 18%, 30%, 6% and 24% respectively. **In conclusion:** Intestinal parasites pose a significant risk of B-TM and aplastic anemia patients.

Introduction

An imbalance in the production of one of the four chains of amino acids that make up hemoglobin, an oxygen-carrying protein present in red blood cells, results in a set of hereditary illnesses known as thalassemia (1). Though the symptoms of each kind of thalassemia are similar, they differ in severity. Mild anemia without symptoms is a feature of alpha and beta thalassemia minor. People with alpha thalassemia major experience moderate to severe anemia-related symptoms, such as exhaustion, shortness of breath, pallor, and an enlarged spleen that causes a bloated sensation and abdominal pain (2,3).

People who have beta thalassemia major, also known as Cooley anemia, frequently experience severe anemia-related symptoms like weakness, fatigue, and shortness of breath. They may also experience jaundice, skin ulcers, and gallstones (3-5). Their spleen may also be enlarged, and some bones, particularly those in the head and face, may thicken and grow due to the bone marrow's excessive activity. When it comes to the long bones in the upper and lower limbs, they could deteriorate and break easily (6). Beta thalassemia major can cause sluggish growth and later puberty in children. Despite the body having too much iron, excess iron can accumulate and be deposited in the heart because it may be absorbed more easily and regular blood transfusions are required. This eventually leads to iron overload disease, heart failure and early death (7,8).

Rarely, when the body stops making enough new blood cells, aplastic anemia develops. You become fatigued and more prone to infection and excessive bleeding as a result of this disorder (9,10). A uncommon and deadly illness called aplastic anemia can strike anyone at any age. It could start out gradually or unexpectedly and worsen over time. It might be mild or harsh (11). The immune system destroying bone marrow stem cells is the most frequent cause of aplastic anemia. Other elements, such as radiation and chemotherapy treatments, exposure to hazardous substances, virus infections, and usage of specific medications, can harm the bone marrow and have an impact on the creation of blood cells (12,13). There are also some medications that can cause anemia, such as medications used for the treatment of rheumatoid arthritis and some antibiotics. In addition, there are unknown factors where in many cases, doctors cannot determine the cause of aplastic anemia (aplastic anemia of unknown cause (14).

Thalassemia or aplastic anemia is one of the diseases that is associated with a significant deterioration of the immune system, which makes the patient more vulnerable to microbial infections, in addition to the exposure of the person infected with these diseases to microbial infection, especially viral infections as a result of blood transfusion (15,16). Where bacterial infections are considered one of the most important problems that threaten the lives of people with thalassemia or aplastic anemia. Most studies have focused on isolating and diagnosing microbes that circulate with blood, especially viral hepatitis, as well as bacteria (17,18). We have noticed a great disregard for microbial infections that occur to these patients in other organs such as the intestines, urinary tract, brain, etc. we considered that parasites are among the most important pathogens. Therefore, the current study aims to isolate and diagnose parasites that infect the intestinal tract of patients with beta thalassemia major and aplastic anemia in additional to evaluate their effects on health conditions of patients.

Materials and Methods

Study design

The current study is a cross-sectional study that included 50 patients with beta major thalassemia and 53 patients with aplastic anemia with ages range from 2-12 years . Our study

was conducted during the period from April 12 to 5 July, 2022 at the Maternity and Children Teaching Hospital and Thalassemia Center in Diwaniyah province. Consent was taken from all participants before sampling and questionnaire taking, and all patients belonged to the same Arab race, which is consistent with the mentioned hospitals.

Lab diagnosis of B-TM and aplastic anemia

Samples were collected from children previously diagnosed for at least a year with B-TM or aplastic leukemia by specialized doctors. In our current study, we confirmed the diagnosis by laboratory tests, in addition to clinical examinations by specialized doctors in the Thalassemia Center and the Maternity and Children Teaching Hospital. Lab tests included the following:

- **Complete blood count and blood film method:** This examination is based on detecting the size of blood cells of all types, their number, and the extent of their maturity in a specific volume of blood, in addition to knowing the levels of hemoglobin, haematocrit (HCT) in the blood. RUBY system where used for automatic complete blood count whereas blood film method preformed manually for detecting morphology of blood cells.

- **Hemoglobin electrophoresis:** It works to detect the different types of hemoglobin, and in cases of beta thalassemia major, only two types of hemoglobin appear, namely hemoglobin A2 and hemoglobin F. A small amount of blood is used for this procedure, which involves depositing it on specialized paper or a specific gel and exposing it to an electrical current. Varying globins can be distinguished from one another based on how they react to electrical currents, which is due to their different electrical charges.

- **Reticulocyte count:** This test measures the speed of production of red blood cells or retinal cells and the speed of their transmission into the blood. In fact, reticulocytes constitute 1-2% of the total red blood cells in the human body. They spend a day or two in the bloodstream until they mature into red blood cells.

- **Iron test:** to know the cause of anemia, in other words, by detecting the percentage of iron in the blood, it is possible to exclude the person's infection with anemia caused by iron deficiency, as the person with thalassemia does not suffer from iron deficiency. Iron levels are tested using the finger-prick method

- Blood groups: Determination of blood groups using the slide method, which was performed manually.

General stool examinations for identification of intestinal parasites

The current study included the collection of 1 gm of fresh feces in a sterile package, and it was sent directly to the Parasitology Laboratory for the following tests:

- Gross test: We performed this test to look for blood, mucus, worms, and worm segments in the stool. We also noted the color, consistency, and presence of blood.

- Microscopic investigation techniques include: Direct Wet Mounting (Saline and Iodine carriers), Flotation in Saturated Salt Solution, Formol Ether Deposition Technique, Trichrome Staining, Modifier Acid-fast Kenyon Stain.

- Chemical examination: The following examinations typically involve the chemical evaluation of feces:

1. Occult blood, 2.Excess fat excretion (malabsorption), 3.Urobilinogen, 4. Reducing sugars, 5.Fecal osmotic gap, 6. Fecal pH

Statistical analysis

The statistical analysis included tabulation and arrangement of the data by Excel system,

while the probability value, standard deviation, and standard error were calculated using the Statistical Packages for Social Sciences program, and the data were considered statistically different when the probability value (P value) was less than 0.05.

Results

Fifty children with significant thalassemia were enrolled in the current study; their ages ranged from 2 to 11 years, with an average of 4.13 years. Of them, 52% were men and 48% were women. 53 anemic youngsters were also included in this study; their ages ranged from 2 to 12 years, with an average of 6.22 years. The majority of them (53% of them) were females, while the female prevalence rate was 47% as shown in Table 1.

The results of the blood test in Table 2 showed that most of the thalassemia patients had blood types A+, O+, AB+, and B+, with rates of 36%, 24%, 14% and 12%, respectively. Most of the anemic patients had blood types A+, B+, B-, O+, AB+, and O- with a percentage of 17%, 15%, 15%, 13%, 13%, and 11%, respectively

Table (1): Demographical properties of patients

Properties	**B-TM**	**Aplastic anemia**
Age range /year	2 - 11	2 - 12
Mean	4.13	6.22
SD	2.51	3.36
SE	0.35	0.46
Total number	50	53
Gender	**N (%)**	**N (%)**
Male	26 (52)	25 (47)
Female	24 (48)	28 (53)
P value	**0.371**	**0.311**

Table (2): Blood groups test of patients

Blood groups	**B-TM**	**Aplastic anemia**	**P value**
A+	18 (36)	9 (17)	0.031
A-	2 (4)	5 (9)	0.518
B+	6 (12)	8 (15)	0.677
B-	0 (0)	8 (15)	0.041
AB+	7 (14)	7 (13)	0.885
AB-	2 (4)	3 (6)	0.818
O+	12 (24)	7 (13)	0.045
O-	3 (6)	6 (11)	0.379
P value	**0.021**	**0.045**	

The results of the isolation and diagnosis of intestinal parasites showed that 70% of thalassemia patients suffer from intestinal parasitic infections represented by *Entamoeba*

histolytica, *Giardia lamblia*, *Blastocystis hominis*, *Ascaris lumbricoide*, *Ancylostoma duodenale* and *Strongyloides stercoralis* by percentage 14%, 37%, 14%, 20% and 9% and 6% respectively. We also found that 62% of anemic patients suffered from intestinal parasitic infections that included *Entamoeba histolytica*, *Giardia lamblia*, *Blastocystis hominis*, *Ascaris lumbricoide*, *Ancylostoma duodenale* and *Strongyloides stercoralis* in rate 6%, 15%, 18%, 30%, 6% and 24% respectively.

Clinical examinations by specialized doctors showed that patients infected with intestinal parasites suffer from obvious complications compared to their peers who are not infected with these parasites where we found that thalassemia patients infected with parasites suffer from diarrhea, fever, rarely intestinal bleeding, abdominal cramps, intestinal colic, flatulence, rarely abdominal pain and constipation and moderate fever while we found anemia patients suffer from high fever, severe anemia, abdominal pain, diarrhea, fatigue, loss appetite, dizziness, dyspepsia (Figure 1 & Table 4).

Table (3): Prevalence of intestinal parasites in studied cases

Intestinal parasites	**B-TM**	**Aplastic anemia**	**P value**
	N (%)	N (%)	
Entamoeba histolytica	5 (14)	2 (6)	0.246
Giardia lamblia	13 (37)	5 (15)	0.043
Blastocystis hominis	5 (14)	6 (18)	0.361
Ascaris lumbricoides	7 (20)	10 (30)	0.048
Ancylostoma duodenale	3 (9)	2 (6)	0.502
Strongyloides stercoralis	2 (6)	8 (24)	0.029
P value	**0.024**	**0.022**	

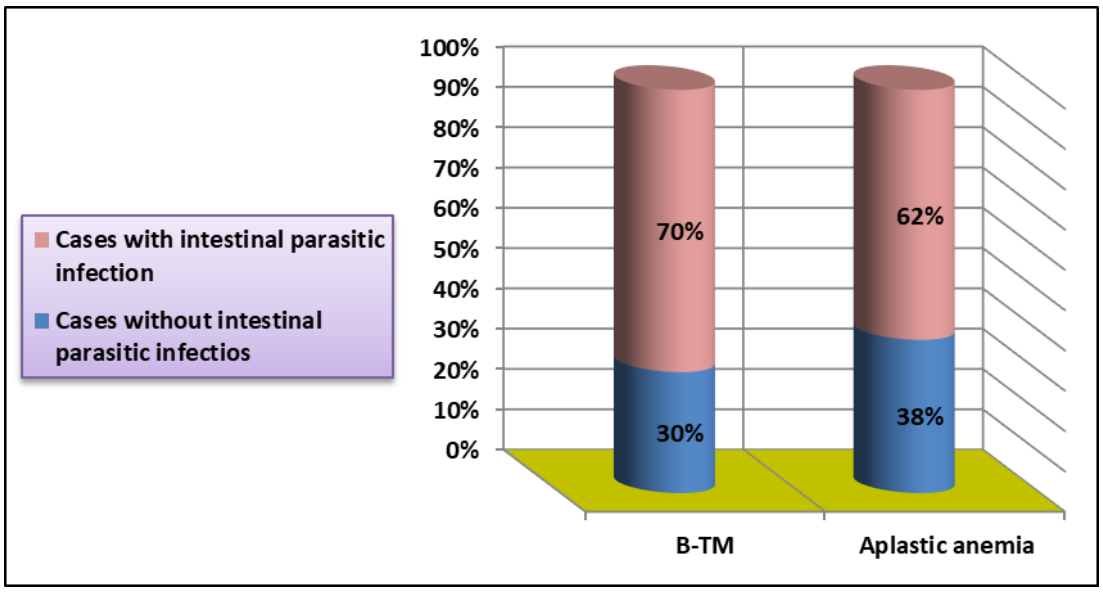

Figure (1): prevalence of intestinal parasites among studied cases

Table (4): signs and symptoms of intestinal parasites in studied cases

Cases	**Symptoms**	
	Positive parasitic infections	**Negative parasitic infections**

Aplastic anemia	High fever, severe anemia, abdominal pain, diarrhea, fatigue, loss appetite, dizziness, Dyspepsia	Mild fever, constipation, rarely intestinal spams
B-TM	Diarrhea, fever, rarely intestinal bleeding, abdominal cramps, intestinal colic, flatulence	Rarely abdominal pain and constipation, moderate fever

To investigate the role of these parasites in increasing the severity or seriousness of the disease, we evaluated the white blood cell count, where we found the highest rise in the rate of these cells in thalassemia patients with *Entamoeba histolytica*, *Giardia lamblia* and *Blastocystis hominis* (38.5 $\times 10^9$, 28.41$\times 10^9$ and 17.6 $\times 10^9$ respectively) while we found the highest level of WBC in Aplastic anemia cases with *Entamoeba histolytica*, *Ascaris lumbricoides* and *Ancylostoma duodenale* (39.7$\times 10^9$ /L, 30.8$\times 10^9$ /L and 25.41$\times 10^9$L respectively) as in Table 5 .

The results of the hematocrit examination, Table 6, showed that the volume of packed erythrocytes was significantly low in anemia patients with *Entamoeba histolytica*, *Ascaris lumbricoides* and *Blastocystis hominis* (0.097, 0.100, and 0.104 L/L respectively), while we found an increase in this index in thalassemia patients with intestinal parasites, where it was HCT level in infection of *Entamoeba histolytica*, *Giardia lamblia*, *Blastocystis hominis*, *Ascaris lumbricoides*, *Ancylostoma duodenale* and *Strongyloides stercoralis* was 0.201, 0.221, 0.311, 0.316, 0.300 and 0.333 L/L respectively.

We also recorded during our study the treatment that was prescribed for the treatment of these intestinal pathogens, as the approved drug for parasitic infections caused by protozoa such as giardiasis and amoebiasis was metrandazole, with alternative or complementary drugs while the basic treatment for worms such as ascariasis was Vermox added to other alternative or complementary therapies as shown in table 7.

Table (5): White blood cells count in studied cases

Intestinal parasites	**WBC$\times 10^9$ /L (mean + SD)**		**P value**
	B-TM	**Aplastic anemia**	
Entamoeba histolytica	38.5 ± 10.5	39.7 ± 9.11	0.329
Giardia lamblia	28.41± 9.7	22.58 ± 6.41	0.451
Blastocystis hominis	17.6 ± 10	20.2 ± 11.2	0.612
Ascaris lumbricoides	14.88 ± 6.55	30.8 ± 7.81	0.021
Ancylostoma duodenale	14.09 ± 9.52	25.41 ± 4.85	0.048
Strongyloides stercoralis	15.27 ± 5.11	13.72 ± 6.11	0.726
P value	0.042	0.058	

Table (6): HCT level in studied cases

Intestinal parasites	**HCT (L/L) (mean + SD)**		**P value**
	B-TM	**Aplastic anemia**	

Entamoeba histolytica	0.201± 0.09	0.097 ± 0.01	0.005
Giardia lamblia	0.221 ± 0.10	0.111 ± 0.08	0.019
Blastocystis hominis	0.311 ± 0.14	0.108 ± 0.077	0.023
Ascaris lumbricoides	0.316 ± 0.19	0.100 ± 0.03	0.021
Ancylostoma duodenale	0.30 ± 0.17	0.111 ± 0.05	0.025
Strongyloides stercoralis	0.333 ± 0.12	0.104 ± 0.06	0.015
P value	**0.036**	**0.151**	

Table (7): Prescribed drugs to treat intestinal parasites

Intestinal parasites	Prescribed drugs
Entamoeba histolytica	Metronidazole, Tinidazole, Iodoquinol, Paromomycin
Giardia lamblia	Metronidazole, Tinidazole, Quinacrine
Blastocystis hominis	Tindamax, Metronidazole, cotrimoxazole
Ascaris lumbricoides	Vermox , Albendazole, Mebendazole
Ancylostoma duodenale	Vermox, Emverm, folic acid
Strongyloides stercoralis	Vermox, Emverm, Thiabendazole, Ivermectin

Discussion

In developing nations and in those with concomitant conditions, intestinal parasites are a major cause of morbidity and mortality worldwide (19,20). 1.2 billion persons worldwide have *Ascaris lumbricoides*, 795 million have *Trichuris trichiura*, 740 million have hookworms (*Ancylostoma duodenale* and *Necator americanus*), 50 million have *Entamoeba histolytica*, and 2.8 million have *Giardia lamblia* (21). One of the most significant contributing factors to gastrointestinal disorders like diarrhea, dysentery, vomiting, lack of appetite, hematuria, abdominal distension, weight loss, abdominal pain, nausea, and iron deficiency anemia are intestinal parasites. They can also cause other symptoms like itching and scratching in the perianal area, swelling in the lower limbs, coughing, dyspepsia, and pharyngeal irritation (22,23). Poor personal hygiene, environmental factors including feces from humans contaminating soil and water supplies, and improper sewage disposal practices such using night soil as fertilizer all contribute to the fecal oral route, which is important in the transmission of parasite illnesses to humans (24). When the soil is polluted, the eggs can move from the veggies to the hands, then to the mouth, or they can be consumed by eating raw vegetables (25,26). Generally speaking, intestinal parasites no longer pose a life-threatening risk to healthy individuals with a functioning immune system, but they can be deadly for those whose immune systems have been compromised by cancer or other illnesses like organ transplants (26,27).

Blood disorders as B-TM and aplastic anemia are among the most important health problems that children suffer from, and their severity increases with the child's exposure to microbial infections where we found in our current research an increase in the risk and severity of these diseases when they coincide with intestinal infections, especially *Entamoeba histolytica*. Perhaps the reason for the increase in intestinal infection in patients with B-TM and aplastic anemia is due to the weak immune system of these patients, in addition to the deficiency or

dysfunction of red blood cells accompanied by a lack of oxygen, which overshadows the deterioration of all vital activities of the body (28,29). Intestinal parasites cause diarrhea, irritation in the digestive system, and anemia, in addition to the role of some enteroceles, such as protozoa and worms, in causing internal bleeding that poses a direct threat to the life of the child, as we noticed that children with thalassemia or anemia suffer from unfortunate symptoms that increase the risk of the disease and reduce the chance of response to treatment (30). On the other hand, the treatments used for intestinal parasites have a toxic effect on some tissues and organs of the body, such as the liver, spleen, and kidneys, which are already damaged due to the deterioration of the immune system and continuous blood transfusions for patients with thalassemia and anemia and their accompanying health problems (31,32). Here we document that intestinal parasites and their treatments are among the crises that these patients face. Vermox (a common remedy for worms) may cause dizziness, some stomach pain, gas, diarrhea, and some allergic reactions such as rash, itching, redness, swelling of the face and mouth, blisters, and hair loss if Vermox is used for long periods or in larger doses (33,34). Metronidazole maybe associated with dizziness, headache, stomach upset, nausea, vomiting, loss of appetite, diarrhea, constipation, or metallic taste in mouth.. It is recommended, the patient may develop abnormal functions in the kidneys and hepatitis, so this treatment is not an ideal solution for children with thalassemia or anemia (35-37). Despite the importance of this topic, we did not find sufficient studies in this regard.

In an earlier investigation, Gupta et al. discovered that patients with beta-thalassemia major had an intestinal parasite infection rate of 21.9%, whereas patients with aplastic anemia had an infection rate of 26.2%. This study demonstrates that people with beta-thalassemia major frequently have intestinal parasites. The most common intestinal protozoan found was Giardia lamblia, which was followed by Blastocystis hominis and Entamoeba Histolytica/ dispar. Strongyloides stercoralis infection, Ascaris lumbricoides infestation, and Ancylostoma duodenale infestation were all shown to be helminthic infections (38).

Our findings in the current study demonstrated that haematological parameters are changed by parasite infection. Children with aplastic anemia had lower RBC, WBC, and HCT counts due to parasites, however those with Thalassemia had higher WBC counts. According to some research, parasitism causes a decline in RBC, Hb, and HCT. Other research, however, revealed that parasites can reduce haematocrit and trigger the early phases of stress. Additionally, parasite infection promotes catecholamine release, which can mobilize red blood cells from the spleen or cause red blood cell enlargement due to fluid shifting into the intracellular compartment (39,40).

Conclusion

We conclude from the results of our study that intestinal parasites are important pathogens that B-TM and aplastic anemia patients suffer from, as we isolated *Entamoeba histolytica, Giardia lamblia, Blastocystis hominis, Ascaris lumbricoides, Ancylostoma duodenale* and *Strongyloides stercoralis* , so the common infections are giardiasis in B-TM patients and ascariasis in aplastic anemic patients, and these intestinal infections were associated with a clear effect on clinical signs and blood parameters for B-TM and aplastic anemia patients. Furthermore, we did not find sufficient studies about the pathogens that affect this group of patients, so we need more research on the diagnosis and treatment of microbes that affect patients with B-TM and aplastic anemia.

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