Prevalence of Parasitic Infections and Related Morbidity in Pediatric Patients on Regular Hemodialysis in Ain Shams University Pediatric Hospital, Cairo, Egypt

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Background and study aim: Opportunistic parasitic infections have been documented to cause serious complications among immunocompromised patients, including those undergoing hemodialysis (HD). Therefore, this study aimed to determine the prevalence of common parasitic infections and associated morbidity among the HD pediatric patients at Ain Shams University Pediatric Hemodialysis Unit.

Patients and Methods: A comparative cross-sectional study was conducted on 50 HD patients and 20 apparently healthy individuals from January 2018 to March 2019. Stool samples were examined for parasites using direct smear, formol ether concentration, and staining with modified Ziehl- Neelsen stain. The serological analysis for anti-*Toxoplasma* IgM and IgG and complete blood count was performed. The results were correlated with the history, physical, and demographic data of the study groups.

Results: The overall prevalence rate of intestinal parasitoses among patients with HD was a little bit higher than the control group (70% versus 60%, respectively) but this was statistically insignificant. *Blastocystis hominis* (30%), *Entamoeba histolytica* (28%), and *Giardia lamblia* (20%) were the most frequent among children with HD, with a statistically significant difference in *Blastocystis hominis* infection rates between patients and their counterparts. Moreover, the overall *Toxoplasma gondii* seroprevalence rate among patients with HD was (22%) and the anti-*Toxoplasma* IgM was (2%).

Conclusion: The overall rate of opportunistic parasitic infections and related clinical symptoms in children with HD was slightly more frequent than in the control group. So, stool examination for intestinal parasites and *Toxoplasma gondii* screening should be incorporated into routine clinical care for children with HD.

INTRODUCTION

Although the continuous progress in sanitation infrastructure, intestinal parasitic infection still be considered a problem at the community level, especially in poor countries. Around 3 billion people (mostly children) are infected with intestinal parasites all over the world **[1,2]**.

Patients on HD usually suffer from disturbed kidney functions with subsequent retention of uremic toxins in their blood. These toxins interfere with humoral and cellular immunity functions causing enhanced individual vulnerability to infections **[3]**. Immune deficiency accompanied by the accumulation of uremic toxins is considered the 2nd most important factor responsible for the high disease and death rates among chronic renal failure patients after cardiovascular diseases **[4]**. End-stage renal disease (ESRD) as an immunosuppressive condition, increases patients' susceptibility to infections. Parasitic infections are one of the significant causes of morbidity and mortality in patients with HD **[5]**. Intestinal

parasites, in particular, *Entamoeba histolytica (E. histolytica)*, *Giardia lamblia (G. lamblia)*, opportunistic *Cryptosporidium* species, *Cystoisospora belli (C. belli), Cyclospora cayetanensis, Blastocystis hominis (B. hominis), Toxoplasma gondii (T. gondii), microsporidia*, and *Strongyloides stercoralis* are prevalent in developing countries, especially among patients with chronic kidney disease (CKD) e.g. chronic glomerulonephritis, congenital anomalies of the kidney and urinary tract (CAKUT), steroid-resistant nephrotic syndrome (SRNS) and thrombotic microangiopathic disorders e g. hemolytic uremic syndrome (HUS) who are undergoing HD **[3,6,7]**. The patients with HD are highly vulnerable to parasitic infections more than the cancer patients receiving chemotherapy. The main parasites found were *B. hominis*, *Entamoeba coli*, *Iodamoeba butschlii*, *Endolimax nana*, *Chilomastix mesnili*, *Strongyloides stercoralis*, and *Taenia* species **[8]**. There is a consensus that the *T. gondii* parasite has a widespread distribution all over the world and may cause dangerous morbidity in immunodeficient patients. The higher prevalence of *T. gondii* infection in HD patients anticipate that these patients are at risk for toxoplasmosis and screening for toxoplasmosis before dialysis is mandatory **[9]**.

The investigation of parasitic infections in patients with HD, followed by the desired treatment if tested positive, can, therefore, play a significant role in the process of restoring better quality of life for these patients **[10]**. This work aimed to study the prevalence of common parasitic infections and associated symptoms and signs among pediatric patients undergoing HD at Ain Shams University Pediatric Hemodialysis Unit (PDU).

PATIENTS AND METHODS

This cross-sectional study was conducted in the Pediatric Hemodialysis Unit, Children`s Hospital, Ain Shams University, Cairo, Egypt. The study period was from January 2018 to March 2019.

Study groups:

Patients` group: 50 patients on hemodialysis.

Control group: 20 children with no renal disease.

Out of our 50 cases, we found 17 patients who had CAKUT as a primary etiology of CKD e.g. renal dysplasia, posterior urethral valve, and vesicoureteral reflux, 12 patients had a history of chronic glomerulonephritis e.g. IgA nephropathy, chronic Henoch Schonlein purpura, and lupus nephritis, 4 patients with a history of congenital nephrotic syndrome, 5 patients with a history of HUS, 4 patients who had SRNS, 2 cases of Joubert syndrome, 3 cases of primary hyperoxaluria and 3 cases of drug-induced chronic interstitial nephritis.

The mean age of cases was 14.35 ± 4.44 years after the exclusion of those who were receiving antiparasitic medications at the time of the study, those who were receiving immunosuppressive drugs at the time of the study or 4 weeks before the onset of the study, and children who were having additional disease-causing an immunocompromised state e.g., DM, malignancy and 1ry immunodeficiency.

A detailed history was taken that included age, sex, residence, resources of drinking water, a history of recent travel to foreign countries, and recent exposure to animals during the last three months. Moreover, some clinical data including symptoms e.g., diarrhea, nausea, vomiting, fever, mucous or blood in the stool, abdominal pain, bloating, flatulence, general fatigue, tender lymph nodes, and loss of weight. A complete physical examination was recorded including enlarged lymph nodes and abdominal examination.

Three fecal samples were collected from each study participant. Stool analysis for parasites was done using direct wet smear (saline and Lugol's iodine) of the fresh samples **[11][12]** and concentrated ones using formol ether concentration techniques to detect protozoa and ova of helminths **[13]**. Also, staining of stool samples using the modified Ziehl-Neelsen stain was performed to detect coccidian parasites like *Cryptosporidium parvum (C. parvum), C. belli*, and *Cyclospora* species **[14]**. ELISA test was done to detect anti-*toxoplasma* IgM and IgG antibodies using (Stat Fax 2100, Awareness Technology, Inc., USA).

Complete blood picture was done for all patient with HD using (Nihon kohden 5-Part Complete Blood Count Machine, Indiamart, India)

Vascular access: it is well known that vascular access is needed for CKD children on regular hemodialysis and its complications is a very important issue when dealing with such category of patients. Three known types of vascular accesses are commonly used for HD: A-V fistula, A-V graft, and central venous catheters (CVCs). Most of our patients who had been on chronic HD for years had either A-V fistula or A-V graft that are much more suitable and less problematic for long-term HD. CVCs were met more in patients who had problems in using their fistulas or grafts and so CVCs were used transiently till getting a well-functioning fistula or graft [15].

Ethical consideration: The study was approved by the regional ethical committee of the Department of Pediatrics, Faculty of Medicine, Ain Shams University. Also, all of the recruited patients or their legal guardians were fully informed about the study.

Statistical analysis: Data entry and analysis were performed using IBM SPSS Statistics, version 20.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies and percentages and were compared using the chi-square test or Fisher's exact test, whichever convenient, while continuous variables were presented as means with standard deviations and were compared using t-test. P-values < 0.05 were considered statistically significant to identify differences and associations.

RESULTS

The mean age of the study cases was 14.35±4.44 years. 88% of the study cases were residents in urban areas in contrast to 75% only of the controls.

Among the cases, 36(72%) were symptomatic, most frequently with abdominal pain, vomiting, and diarrhea in proportions of (54%, 18%, and 54%, respectively), in contrast to the control group were 15(75%) symptomatic with a significant statistical difference in the diarrhea symptom; p-value (<0.001). Patients with HD showed that 8(16%) had lymph node enlargement but no significant statistical difference with the control, 14 (28%) had organomegaly and 11(22%) were exposed recently to animals with a significant statistical difference compared to the control with p-values 0.007 and 0.027 consequently. Among 50 pediatric patients with HD, we could detect *B. hominis* infection in 15 patients (30%) with a significant statistical difference compared to the control group; p-value (0.004), *C. parvum* in 5 patients (10%), *E. histolytica* trophozoite in 14 patients (28%), *G. lamblia* cysts in 10 patients (20%), *Enterobius vermicularis (E. vermicularis)* in one patient (2%) and *Vampirolepis nana (V. nana)* in none of them (0%) with no significant statistical difference compared to the control group. Among cases, anti-*toxoplasma* IgM was positive in one patient (2%) and reactive anti-*toxoplasma* IgG was found in 10 cases (20%) with no significant statistical difference when compared to the control group (Table 1).

Among cases positive for parasitic infections, male patients were 17 (48.6%) with 30 (85.7%) of the cases had an urban residency, the mean age was (14.22±4.61) years, and the mean duration of dialysis was (7.15±5.64) years but in negative cases, male patients were 6 (40%) with 14 (93.3%) had an urban residency, the mean age was (14.67±4.14) years, and mean duration of dialysis was (7.60±3.11) years. Among cases positive for parasitic infections; abdominal pain, vomiting, and diarrhea were found in 22(62.9%), 4 (11.4%), and 18(51.4%) respectively, with no significant statistical difference compared to the negative cases for parasitic infections. Lymph node enlargement, organomegaly, and animal exposure were found in 5(14%), 8(22.9%), and 7(20%) respectively, with no significant statistical difference when compared to the negative cases for parasitic infections. The mean Hb was (10.53±1.99) g/dl, the mean platelet count was (191.38 ±87.2 $x10^3$/UL), the mean total leucocytic count (TLC) was (6.55±2.09 $x10^3$/UL), the mean neutrophil count was (3.68±1.63 $x10^3$/UL), the mean lymphocyte count was (2.11±.89 $x10^3$/UL) and the median eosinophilic count was (0.39 $x10^3$/UL) with no significant statistical difference compared to the negative cases for parasitic infections regarding all the blood picture parameters (Table 2).

In cases positive for *B. hominis*, 11(73.3%) had an urban residency, in contrast to 33(94.3%) in negative cases. In cases positive for *B. hominis*, the mean duration of dialysis was (8.77) years, abdominal pain, vomiting, and diarrhea was found in 10 patients (66.7%), one patient (6.7%), and 6 patients (40%) respectively with no significant statistical difference when compared to cases with HD negative for the same parasite.

In positive patients, the median eosinophilic count was (0.40 x10^3/UL), but in negative cases, the median eosinophilic count was (0.20 x10^3/UL) with no significant statistical difference when compared to cases with HD negative for the same parasite (Table 3).

In positive cases for *C. parvum*, 5 patients (100%) had an urban residency, but in negative cases, 39 patients (86.7%) had an urban residency. In positive cases for *C. parvum*, the mean duration of dialysis was (5.2) years, abdominal pain, vomiting, and diarrhea were found in 3 patients (60%), 0 case (0%), and 3 cases (60%) respectively, with no significant statistical difference, compared to cases with HD who were negative for the same parasite. The blood picture parameters for cases with HD who were positive for *C. parvum* showed no significant statistical difference compared with cases with HD who were negative for the same parasite (Table 4).

Among cases with reactive anti-*Toxoplasma* IgG; the mean age was (13.95±4.35) years, the mean duration of dialysis was (7.65±4.75) years and 9 patients (90%) had an urban residency, with no significant statistical difference compared with cases with non-reactive anti-*Toxoplasma* IgG. In cases with reactive anti-*Toxoplasma* IgG; animal exposure was found in 3(30%), vascular access included 9 (90%) A-V fistula and 1 (10%) central venous catheter (CVCs), positive lymph node enlargement was found in 2 cases (20%) with no significant statistical difference compared to cases with non-reactive anti-*Toxoplasma* IgG but organomegaly was found in 6(60%) that showed a significant statistical difference compared with the non-reactive cases; p-value (0.020). The blood picture parameters for cases reactive for anti-*toxoplasma* IgG showed no significant statistical difference compared to non-reactive cases (Table 5).

Table (1): Comparison between both pediatric patients on regular HD and the control group regarding symptoms of parasitic infections, lymphadenopathy, organomegaly and exposure to animals, Prevalence of intestinal parasitic infections, and helminths, and seroprevalence of anti-toxoplasma IgM and IgG.

			Control (n=20)		Case (n=50)		Test of sig.	
			N	%	N	%	p-value	sig.
Symptoms of parasitic infections	**Vomiting**	No	20	100.0%	41	82.0%	0.052	NS
		Yes	0	0.0%	9	18.0%		
	Diarrhea	No	19	95.0%	23	46.0%	<0.001	S
		Yes	1	5.0%	27	54.0%		
	Abdominal Pain	No	5	25.0%	23	46.0%	0.105	NS
		Yes	15	75.0%	27	54.0%		
Lymphadenopathy, organomegaly and exposure to animals	**Lymphadenopathy**	No	20	100.0%	42	84.0%	0.095	NS
		Yes	0	0.0%	8	16.0%		
	Organomegaly	No	20	100.0%	36	72.0%	0.007	S
		Yes	0	0.0%	14	28.0%		
	Exposure to animals	No	20	100.0%	39	78.0%	0.027	S
		Yes	0	0.0%	11	22.0%		
Prevalence of Intestinal parasitic infections	***B. hominis***	Negative	20	100.0%	35	70.0%	0.004	S
		Positive	0	0.0%	15	30.0%		
	C. parvum	Negative	20	100.0%	45	90.0%	0.312	NS
		Positive	0	0.0%	5	10.0%		
	E. histolytica	Negative	14	70.0%	36	72.0%	0.867	NS
		Positive	6	30.0%	14	28.0%		
	G. lamblia	Negative	14	70.0%	40	80.0%	0.366	NS
		Positive	6	30.0%	10	20.0%		
	E. vermicularis	Negative	17	85%	49	98%	0.07	NS
		Positive	3	15%	1	2%		
	V. nana	Negative	19	95%	50	100%	0.3	NS
		Positive	1	5%	0	0%		
Seroprevalence of anti-*Toxoplasma* IgM and IgG	***Toxoplasma* IgM**	Negative	20	100.0%	49	98.0%	>0.999	NS
		Positive	0	0.0%	1	2.0%		
	***Toxoplasma* IgG**	non-reactive	17	85.0%	40	80.0%	0.744	NS
		Reactive	3	15.0%	10	20.0%		

Table (2): Comparison between positive and negative pediatric patients with HD for parasitic infections regarding demographic data (sex and residency), abdominal symptoms, lymphadenopathy, organomegaly, exposure to animals, the age, and the duration of dialysis, and complete blood count.

			No parasitic infection (n=15)		Positive Parasitic infection (n=35)		Test of sig.		
			N	%	N	%	p-value	sig.	
Demographic data	Sex	Male	6	40.0%	17	48.6%	0.577	NS	
		Female	9	60.0%	18	51.4%			
	Residency	Urban	14	93.3%	30	85.7%	0.654	NS	
		Rural	1	6.7%	5	14.3%			
Abdominal symptoms	Vomiting	No	10	66.7%	31	88.6%	0.106	NS	
		Yes	5	33.3%	4	11.4%			
	Diarrhea	No	6	40.0%	17	48.6%	0.577	NS	
		Yes	9	60.0%	18	51.4%			
	Abdominal pain	No	10	66.7%	13	37.1%	0.055	NS	
		Yes	5	33.3%	22	62.9%			
lymphadenopathy, organomegaly, and exposure to animals	Lymphadenopathy	No	12	80.0%	30	85.7%	0.683	NS	
		Yes	3	20.0%	5	14.3%			
	Organomegaly	No	9	60.0%	27	77.1%	0.304	NS	
		Yes	6	40.0%	8	22.9%			
	Exposure to animals	No	11	73.3%	28	80.0%	0.713	NS	
		Yes	4	26.7%	7	20.0%			
			Mean	SD	Mean	SD	p-value	sig.	
Age and the duration of dialysis	Age		14.67	4.14	14.22	4.61	0.748	NS	
	The duration of dialysis		7.60	3.11	7.15	5.64	0.719	NS	
Complete blood count and differential count of leukocytes			Mean	SD	Mean	SD	value	p-value	sig.
	Hemoglobin (13–17) g/dl		10.74	1.21	10.53	1.99	t = 0.37	0.712	NS
	Platelets (200-500x10^3)/UL		215.47	71.82	191.38	87.21	t = 0.94	0.354	NS
	TLC (5-15x10^3)/UL		6.76	2.09	6.55	2.09	t = 0.32	0.751	NS
	Neutrophils (2-8x10^3)/UL		3.79	1.65	3.68	1.63	t = 0.23	0.820	NS
	Lymphocytes (1-5x10^3)/UL		2.04	0.71	2.11	0.89	t = −0.24	0.808	NS
			Median	IQR	Median	IQR	Mann-Whitney test		
	Eosinophils (0.2-1x10^3)/UL		0.39	0.25	0.39	0.42	U = 217.5	0.338	NS

Table (3): Comparison between pediatric positive and negative patients with HD for *B. hominis* regarding residency, abdominal symptoms, the duration of dialysis, and CBC with the differential leukocytic count.

		No *B. hominis* (n=35)		**Positive *B. hominis* (n=15)**		**Test of sig.**	
		N	**%**	**N**	**%**	**p-value**	**Sig.**
Residency	Urban	33	94.3%	11	73.3%	0.058	NS
	Rural	2	5.7%	4	26.7%		
Vomiting	No	27	77.1 %	14	93.3%	0.247	NS
	Yes	8	22.9 %	1	6.7%		
Diarrhea	No	14	40.0 %	9	60.0%	0.193	NS
	Yes	21	60.0 %	6	40.0%		
Abdominal pain	No	18	51.4 %	5	33.3%	0.239	NS
	Yes	17	48.6 %	10	66.7%		
The duration of dialysis		**Mean**	**SD**	**Mean**	**SD**	**p-value**	**sig.**
		6.65	4.03	8.77	6.65	0.266	NS

	No *B. hominis* (n=35)		**Positive *B. hominis* (n=15)**		**t-test**		
CBC with the differential leucocytic count	**Mean**	**SD**	**Mean**	**SD**	**value**	**p-value**	**sig.**
Hemoglobin (13-17) g/dl	10.41	1.81	11.02	1.70	t = −1.1	0.275	NS
Platelets (200-500x10^3)/UL	195.00	78.70	208.14	94.84	t = −0.5	0.621	NS
TLC (5-15x10^3)/UL	6.75	1.92	6.31	2.43	t = 0.67	0.504	NS
Neutrophils (2-8x10^3)/UL	3.71	1.66	3.73	1.59	t = −0.04	0.967	NS
Lymphocytes (1-5x10^3)/UL	2.06	0.86	2.16	0.80	t = −0.38	0.705	NS
	Median	**IQR**	**Median**	**IQR**	**Mann-Whitney test**		
Eosinophils (0.2-1x10^3)/UL	0.20	0.1 - 0.5	0.40	0.1 - 0.6	U = 216.5	0.327	NS

Table (4): Comparison between pediatric positive and negative patients with HD for *C. parvum* regarding residency, abdominal symptoms, the duration of dialysis, and CBC with the differential leukocytic count.

			No *C. parvum* (n=45)		Positive *C. parvum* (n=5)		Test of sig.		
			N	%	N	%	p-value	Sig.	
Residency		Urban	39	86.7%	5	100.0%	>0.999	NS	
		Rural	6	13.3%	0	0.0%			
Abdominal symptoms	Vomiting	No	36	80.0%	5	100.0%	0.570	NS	
		Yes	9	20.0%	0	0.0%			
	Diarrhea	No	21	46.7%	2	40.0%	>0.999	NS	
		Yes	24	53.3%	3	60.0%			
	Abdominal pain	No	21	46.7%	2	40.0%	>0.999	NS	
		Yes	24	53.3%	3	60.0%			
The duration of dialysis			Mean	SD	Mean	SD	p-value	sig.	
			7.52	4.96	5.20	5.31	0.330	NS	
			No *C. parvum* (n=45)		Positive *C. parvum* (n=5)		t-test		
CBC with differential leucocytic count			Mean	SD	Mean	SD	value	p-value	sig.
	Hemoglobin (13- 17) g/dl		10.61	1.67	10.46	2.84	t = 0.18	0.859	NS
	Platelets (200-500x10^3)/UL		201.50	80.20	174.60	111.09	t = 0.68	0.497	NS
	TLC (5-15x10^3)/UL		6.57	2.15	7.04	1.11	t = −0.48	0.634	NS
	Neutrophils (2-8x10^3)/UL		3.65	1.67	4.30	1.01	t = −0.85	0.397	NS
	Lymphocytes (1-5x10^3)/UL		2.11	0.83	1.89	0.88	t = 0.55	0.583	NS
			Median	IQR	Median	IQR	Mann-Whitney test		
	Eosinophils (0.2-1x10^3)/UL		0.30	0.1 - 0.56	0.12	0 - 0.5	U = 85.5	0.380	NS

Table (5): Comparison between reactive and non-reactive anti-*toxoplasma* IgG in patients with HD regarding residency, vascular access, lymphadenopathy, organomegaly, animal exposure, Age, the duration of dialysis, and CBC with the differential leukocytic count.

		Patients with non-reactive anti-*Toxoplasma* IgG (n=40)		Patients with reactive anti-*Toxoplasma* IgG (n=10)		Test of sig.	
		N	%	N	%	p-value	Sig.
Residency	Urban	35	87.5%	9	90.0%	>0.999	NS
	Rural	5	12.5%	1	10.0%		
Vascular access	Fistula	37	92.5%	9	90.0%	>0.999	NS
	Others	3	7.5%	1	10.0%		
Lymph-adenopathy	No	34	85.0%	8	80.0%	0.653	NS
	Yes	6	15.0%	2	20.0%		
Organomegaly	No	32	80.0%	4	40.0%	0.020	S
	Yes	8	20.0%	6	60.0%		
Exposure to animals	No	32	80.0%	7	70.0%	0.671	NS
	Yes	8	20.0%	3	30.0%		
		Mean	SD	Mean	SD	p-value	sig.
Age		14.46	4.51	13.95	4.35	0.751	NS
The duration of dialysis		7.19	5.10	7.65	4.75	0.798	NS

	Patients with non-reactive anti-*Toxoplasma* IgG (n=40)		Patients with reactive anti-*Toxoplasma* IgG (n=10)		t-test		
CBC with differential leucocytic count	Mean	SD	Mean	SD	value	p-value	sig.
Hemoglobin (13- 17) g/dl	10.65	1.72	10.39	2.08	t = 0.41	0.687	NS
Platelets (200-500x10^3)/UL	199.87	77.19	194.40	106.76	t = 0.18	0.854	NS
TLC (5-15x10^3)/UL	6.55	2.13	6.89	1.91	t = −0.46	0.645	NS
Neutrophils (2-8x10^3)/UL	3.66	1.62	3.94	1.67	t = −0.49	0.629	NS
Lymphocytes (1-5x10^3)/UL	2.09	.79	2.09	1.04	t = 0.01	0.989	NS
	Median	IQR	Median	IQR	Mann-Whitney test		
Eosinophils (0.2-1x10^3)/UL	0.25	0.1 - 0.58	0.37	0.2 - 0.5	U = 172	0.495	NS

DISCUSSION

The overall prevalence rate of common intestinal parasitoses among children with HD in the present study was a little bit higher than among their apparently healthy controls (70% versus 60%, respectively), but this was statistically insignificant. However, the prevalence rate of intestinal parasitic infections was 53% for the Egyptian children with HD in Zagazig University Children's Hospital with a 36% infection rate among the control group **[16]**. Lower infection rates with intestinal parasites among patients with HD were reported in Brazil (45.1%), Turkey (43.7%), and Iran (11.9%-30.7%) **[17]**.

In this study, children with HD showed that *B. hominis* was the most prevalent protozoal infection (30%) and *C. parvum was* the least one (10%). On the other hand, Moawad et al. 2020 reported that *C. parvum* was the most prevalent among the patients with HD (13.2%) followed by *B. hominis* (9.6%) with the least prevalence reported for *C. cayetanensis* (1.5%) **[16]**. Gil et al. stated that *Cryptosporidium* species (26.4%) and *B. hominis* (24.5%) were the most widespread parasites that inhabit the intestine of Brazilian patients with HD **[18]**. Another Brazilian study also reported *B. hominis* as the most common parasite in patients with HD (20.1%) followed by *Endolimax nana* (16.3%),

whereas *Cryptosporidium* species was reported among 4.7% of patients **[19]**. This concurs with a study that revealed *B. hominis* (4.2%-14.1%) and *Cryptosporidium* species (11.5%) as the most prevalent parasites among Iranian patients with HD **[17]**.

In this study, children with HD showed that the prevalence of *C. parvum* was (10%), *E. histolytica* cyst (28%), and *G. lamblia* (20%). Compared with these findings, higher infection rates with *Cryptosporidium* species (40.0%), and lower *E. histolytica* (14.0%) and *G. lamblia* (12.0%) have been recently reported among patients with ESRD with HD in Upper Egypt **[3]**, and also similar results were reported in Zagazig city – the capital of Sharqia Governorate- in the eastern part of Egypt where *Cryptosporidium* species (13.2%), *E. histolytica* (5.1%) and *G. lamblia* (2.9%) **[16]**.

Karadag et al. stated that *B. hominis* (23.9%) followed by *G. lamblia* (8.5%) were the most prevalent parasite species among Turkish ESRD patients undergoing HD, while low rates of *Cryptosporidium* species and *E. histolytica* (2.1% each) were detected among patients **[6]**.

These differences in the prevalence of intestinal parasitic infections among children with HD could be to some extent explained by differences in the geographical distribution of parasites in the community due to environmental, climatic, sanitary, water resources differences plus the individual differences in hygienic and behavioral factors. Also, the role of the immune status, duration of HD, and the technique of stool examination in the estimation of infection rate differences could not be excluded. Similarly, variations in the prevalence of intestinal parasitoses among apparently healthy children can be explained by the differences in the same previously mentioned factors with children undergoing HD **[20]**.

The overall *T. gondii* seroprevalence rate for HD patients in this study was (22%) which is lower than those previously reported among patients with HD (61.7%) and renal transplant recipients (70.0%) in the Alexandria governorate in Egypt **[21]**. Uniformly, it is less than the rates recorded in Turkey (56.0%-76.5%), Mexico (56.7%), and Iran (56.7%-73.7%) **[22-24]**. The anti-*Toxoplasma* IgM seroprevalence among patients with HD in this study was (2%) which is lower than that reported among Egyptian patients on regular HD (16.7%) and renal transplant recipients (24.1%) **[25]**. Also, it is lower than those in Iranian patients undergoing regular HD in whom it was (7.8%-13.5%) **[26]**. However, the seroprevalence rate of anti-*Toxoplasma* IgM among patients with HD in this study is slightly close to the rates reported from Turkey (1.7%) **[24].**

Comparisons can be difficult due to several factors, such as the duration of HD and the different environmental conditions. There are many obstacles in the use of molecular techniques for the diagnosis of *T. gondii* infection in developing countries, so, serological detection of anti-*Toxoplasma* antibodies is still the most commonly used approach for screening of the infection among immunocompromised patients **[27].** IgG avidity test is a good technique for serodiagnosis of *T. gondii* as it distinguishes between acute and chronic infections. In this regard, the low avidity of specific anti-*Toxoplasma* IgG indicates a recent primary infection **[26,28]**. Also, the development of kits using immunoreactive proteins and multi-epitope antigens has been proposed for enhancing the diagnosis of *T. gondii* infection **[29]**.

In this study, we found that the prevalence of *E. vermicularis* was (2%) among patients with HD, which was against what has been stated by Rasti et al. and Shehata et al., where helminth larva or ova was not detected **[25,26].**

In this study, among the controls, *E. histolytica* and *G. lamblia* were the most prevalent but *C. parvum* and *B. hominis* were not detected. Alternatively, Gil et al. stated that *B. hominis* was the most prevalent species while *Cryptosporidium* species were not detected among the control group **[18]**.

Regarding *T. gondii*, the prevalence rate of anti-*Toxoplasma* IgG among the control group was (15%) which was lower than that was stated by Aufy et al. but the prevalence rate of anti-*T*oxoplasma IgM was (0%) which was in agreement with that stated in the same study **[25]**.

In this study, among the control group, we found that the prevalence of *E. vermicularis* and *V. nana* was (15%) and (5%) respectively, which was against what was stated by Rasti et al. and Shehata et al., where helminth larva or ova was not detected **[26,30]**.

In this study, approximately half of the patients with HD had a significant increase in the

prevalence of diarrhea but not abdominal pain or vomiting compared with the controls. On the other hand, Gil et al. stated that abdominal pain had a significant increase in patients with HD compared with the controls **[18]**.

In this study, when we compared between cases with positive parasitic infections and those who were negative for parasitic infections, we found no statistically significant association with diarrhea, vomiting, or abdominal pain that is in congruence with what was reported among Brazilian patients with HD, where no significant association was found between parasitic infections and diarrhea **[31]**. Nevertheless, it is unlike the recent finding among patients with ESRD undergoing HD in Upper Egypt, where a statistical significance difference from the control group was found between the prevalence of *Cryptosporidium* species and diarrhea **[3]**.

The lack or presence of association of HD with diarrhea among patients from different studies might be explained by differences in the level of immunosuppression, which determines the presence and severity of diarrhea. It is noteworthy that the differences in the incidence of gastrointestinal symptoms, including diarrhea, among patients with CKD undergoing dialysis could be largely attributed to several factors such as the levels of uremic toxins, presence of other metabolic disorders, intake of medications, and psychosocial factors **[26]**.

In this study, organomegaly and exposure to animals had a significant prevalence in patients with HD when compared to the controls. Alternatively, Bayani et al. stated that their patients showed no significant increase in the prevalence of organomegaly **[31]**.

In this study, the comparison between patients positive for parasitic infections and those who are negative showed no significant difference regarding the duration of HD. This was in agreement with that stated by Mohaghegh et al. **[32]**.

The results of this study revealed that opportunistic parasitic infections and related clinical symptoms in ESRD children undergoing HD were more frequent than in a matched control group. Considering that patients under HD are immunocompromised, parasitic infections may make their situation much more complicated.

We suggest that the stool examination for intestinal parasites, with special attention to *B. hominis*, should be included in the routine clinical care of patients with HD, especially in symptomatic cases. Asymptomatic cases should also undergo regular screening with stool analysis every 3 to 6 months. Measures to prevent the acquisition of intestinal parasites are also recommended. We also recommend studying the value of the prophylactic anti-helminthic treatment program applied to school children under governmental supervision, this is because we observed a low incidence of helminthic infections among the children involved in this study. It's strongly suggested that additional tests should be done, particularly for common bacterial, viral, and fungal agents known to be responsible for symptoms reported in this study. The high *T. gondii* seronegativity rate among patients with HD in this study indicates that the majority of these patients had not been exposed to infection and are vulnerable to the risk of acute infection that may lead to serious complications in those patients, so meticulous screening for *T. gondii* among patients with HD is strongly indicated with the introduction of new accurate tests like IgG avidity test.

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