Systematic review of opportunistic parasites among Egyptian immunocompromised individuals from 2010 to 2020

Review Article

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ABSTRACT

Opportunistic parasites are commonly linked with immunocompromised individuals due to weakness in their immune system. Alteration in their cellular and humoral responses leads to hindrance of T and B lymphocytes from efficiently acting against opportunistic pathogens. Accordingly, immunocompromised patients present increased susceptibility to different microorganisms including viral, bacterial, fungal, and parasitic infections. Several conditions are commonly associated with host immune system impairment. Among them enrolled in the present review were malignancy, chronic liver diseases, diabetes mellitus, renal failure, organ transplantation, and inflammatory bowel disease. The most common reported opportunistic parasites include species of *Cryptosporidium*, *Blastocystis*, and *Microsporidium*, as well as *T. gondii*, *C. cayetanensis*, *I. belli*, and *S. stercoralis*. The objective of the present systematic review is to increase awareness concerning opportunistic parasitosis among Egyptian immunocompromised individuals from 2010 to 2020 with particular reference to their relative detection rates and risk factors of infection.

Keywords: *Blastocystis, Cryptosporidium, Microsporidium*, opportunistic, *T. gondii*

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INTRODUCTION

The immune system is composed of B and T lymphocytes, phagocytic cells and complement system. Immunodeficiency occurs when one part of the immune system is not efficient or has lost its function, and it may be either primary (congenital) or secondary (acquired). Primary immunodeficiency diseases (PID) are hereditary disorders, caused by mutations of specific genes. They result in increased susceptibility to infections and a predisposition to autoimmune diseases and malignancies. While secondary immunodeficiency diseases are caused by infectious agents such as human immunodeficiency virus (HIV), or corticosteroid chemotherapy, organ transplants, metabolic diseases, irradiation, malnutrition, and environmental conditions[1-3]. According to the component of the immune system, PIDs are classified as adaptive or innate immunity disorders[4]. More than 150 different types of PID were recorded to date[1]. Disorders of adaptive immunity include cellular and humoral immunodeficiency disorders due to defects in both T and B lymphocytes development, differentiation, and maturation. Since B cell mediated-antibody production requires intact T lymphocyte function, so any defects in the T lymphocyte will lead to combined immunodeficiency disorders. Disorders of innate immunity are due to failure of the innate system resulting in delay in the induction of the immune response and may worsen outcomes of infections[5,6].

On the other hand, several studies revealed that interleukins (IL) 12, and 18, and interferon gamma (IFN-γ) may play a role in improvement of the protective immunity against cryptosporidiosis[7-9]. The major source of IL-12 is the dendritic cells that are involved in mediating the immune responses in the host[10]. They have a potentially important role in protection against infection, and they are also involved in degradation and transport of antigens to the lymph nodes, and release chemokines in response to cryptosporidiosis[11]. Therefore, opportunistic parasites are common in immunocompromised individuals when the $CD4^+$ T lymphocyte counts fall below 200 cells/μl[12-14].

Childhood and elderly populations are susceptible to opportunistic infections due to depression of their cellular immunity that leads to increase in disease morbidity[15]. The relationship between protein-energy malnutrition and immunity increases vulnerability to infectious diseases causing immunological impairments[16]. Alcohol slows down the functions of the phagocytes as well as changes the production of cytokines; hence alcohol is considered an immunosuppressant factor[17,18]. Besides, alcohol affects the humoral and cellular system resulting in dysregulation of the immune system. That renders the patient susceptible to infectious pathogens, resulting in increased risk of opportunistic infections in the lungs; infections after surgery and liver diseases[17,19].

Viral infections, in general, induce the production of IFN-α, that inhibits G1 phase of the cell cycle leading to temporary immunosuppression. Besides, HIV can suppress the immune system by destruction of the

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$CD4^+$ T lymphocytes[20]. Meanwhile, cytotoxic drugs impair the immune system by destroying all cells, not only cancer and proliferating cells, thus causing non-specific immunosuppression[20,21].

Opportunistic parasitosis may not cause severe pathological disorders in immunocompetent individuals, because of their normally functioning immune system[22]. In contrast, in immunocompromised patients, impairment of host immune system alters cellular and humoral responses and hinders T and B lymphocytes from acting efficiently against the infection[23]. Hence, immunocompromised patients are a vulnerable group to microbial infections especially opportunistic parasites[24,25]. Immunosuppression establishes favorable conditions for opportunistic parasites to flourish against the host system causing clinical diseases[26]. Impaired host immune systems are observed in different disease conditions such as malignancy, acquired immunodeficiency diseases (AIDS), organ transplants, corticosteroid chemotherapy, autoimmune and metabolic diseases, irradiation, malnutrition, environmental conditions, as well as in the elderly, and young children[22].

In developing countries, intestinal parasitosis represents a major public health problem due to the low standard of personal hygiene and inadequate sanitation. Opportunistic parasites play an important role in eliciting diseases especially among immunosuppressed patients and children[27]. The WHO reported that about three billion people are globally infected with intestinal parasites because all opportunistic parasites inhabit the gastrointestinal tract except *T. gondii* and *Microsporidium* spp. on some occasions[28,29]. A major cause of morbidity and mortality among severely immunocompromised patients is partially attributed to opportunistic intestinal infections due to watery diarrhea and/or disseminated pathological manifestations[30]. Detection rates of enteric protozoa among immunocompromised patients ranged from 26.5% to 100% in different governorates of Egypt[31,32].

The aim of the present systematic review is to determine the extent of opportunistic parasitosis detected among immunocompromised patients in Egypt throughout the last decade.

Detection rates of opportunistic parasites in Egyptian immunocompromised hosts

Egypt is in the north eastern part of Africa and in 2020 it was recorded to have the highest population density of ~ 104 million inhabitants[33]. It is comprised of 27 Governorates. and over 90% of the population live in 10% of the whole area along the River Nile and Nile Delta in the northern part of the country.

Table (1) shows the prevalence of opportunistic parasites in Egyptian Governorates. In Cairo, a study conducted in 2010 reported a high rate of opportunistic parasites among immunocompromised patients as compared to healthy controls (30% and 10%, respectively). The highest rate was detected among patients suffering from malignancy (18%), followed by equal rates (6%) among chronic liver failure (CLF) and diabetes mellitus (DM)[34]. Four years later, El-Mahallawy *et al*.[35] revealed that the overall parasitic infection was 50.6% among children with cancer compared to diarrheic immunocompetent cases (41%) attending the National Cancer Institute (NCI), Cairo University. Another study conducted by Wassef *et al*.[24] recorded a higher rate of opportunistic parasites in cancer patients (57%) than in control group (43%). Higher rates were observed among patients suffering from solid tumor as compared with those having hematological malignancies (63% vs 46%, respectively). In addition, those under radiotherapy showed higher infection rate than those under chemotherapy (68% vs 52%, respectively). The investigators attributed their results to reduction in local and cell-mediated responses in immunosuppressed patients[24].

In Alexandria Governorate, Hassanein *et al*.[32,36] conducted two studies among patients suffering from inflammatory bowel disease (IBD) and acute lymphocytic leukemia (ALL) in children. Both studies detected the highest rates of opportunistic parasitosis (100% and 90.6%, respectively) as compared to their controls (72.5% and 58.1%, respectively), and the investigators attributed their results to immunosuppression, susceptibility to infection with opportunistic pathogens and diagnosis using a combination of different techniques[32,36].

In addition, two other studies were conducted among immunocompromised patients. The first in 2019 in which Shehata *et al*.[37] reported that the prevalence rate of intestinal parasitosis among hemodialysis (HD) patients was significantly high as compared to apparently healthy individuals (52.5% vs. 12.0%, respectively) and no helminths infection was found. In the second more recent report, Elsayad *et al*.[38] revealed high parasitic infections in 79% of all samples obtained from patients with renal disorders; 40% in patients undergoing HD and 39% in those with chronic renal diseases (CRD), as compared to healthy control (10%).

In Sohag Governorate, two studies were conducted. In the first study, a high rate was detected among diabetic patients (25%). Type I-DM showed a higher rate of infection as compared to type II-DM (52% and 16% respectively)[39]. The second study was conducted in children and revealed a high rate of intestinal parasitosis in those on chemotherapy as compared to the control group (94% vs 35%, respectively)[40].

In Minya, a study conducted among immunocompromised children showed high prevalence of opportunistic parasites as compared

Table 1. Prevalence of opportunistic parasites in six Egyptian Governorates.

Governorate	Immunocompromised hosts	No.#	%	Reference
Cairo	**Malignancy**	150	57.0	[24]
	Control	50	43.0	
	Solid tumor	100	63.0	
	Hematological malignancies	50	46.0	
	Solid tumor under radiotherapy	50	68.0	
	Solid tumor under chemotherapy	50	52.0	
	Immunocompromised	100	30.0	[34]
	Malignancy	40	18.0	
	CLF	30	6.0	
	DM	30	6.0	
	Control	20	10.0	
	Malignancy and diarrhea	89	50.6	[35]
	Diarrheic immunocompetent	100	41.0	
Alexandria	**IBD**	40	100.0	[32]
	Control	40	72.5	
	ALL	117	90.6	[36]
	Control	117	58.1	
	HD	120	52.5	[37]
	Control	100	12.0	
	Patients with renal disorders	100	79.0	[38]
	HD	50	40.0	
	CRD	50	39.0	
	Control	50	10.0	
Sohag	**DM**	100	25.0	[39]
	Type-I DM	25	52.0	
	Type-II DM	75	16.0	
	Control	100	10.0	
	Children on chemotherapy	100	94.0	[40]
	Control	100	35.0	
Minya	**Immunosuppressed**	200	94.0	[41]
	Immunocompetent	250	60.0	
Menoufia	**Liver transplantation**	50	16.0	[42]
Dakahlia	**Hematological malignancy with diarrhea**	145	85.5	[43]

#: Total number examined; **ALL:** Acute lymphocytic leukemia; **CRD:** Chronic renal disease; **DM:** Diabetes mellitus; **HD:** Hemodialysis; IBD: Inflammatory bowel disease.

with immunocompetent children (94% vs 60%, respectively)[41]. In Menoufia Governorate, Saad *et al*.[42] reported opportunistic parasitic infections (16%) among patients suffering from hepatic diseases. One year later, a study conducted in Dakahlia Governorate showed a high rate of intestinal protozoa (85.5%) that included *G. lamblia* (36.6%), *C. parvum* (30.3%), and *E. histolytica/E. dispar* (27.6%) among hematological malignancy patients with diarrhea[43].

Commonly reported opportunistic parasites

Blastocystis spp.

Blastocystis spp. are anerobic protozoa inhabiting the gastrointestinal tract (GIT) in four different distinct forms: cyst, ameboid, granular and vacuolar forms. Blastocystosis can be acquired by fecal-oral route, although the role of cyst forms is unknown[44]. The main symptoms include acute, chronic, and intermittent gastroenteritis, abdominal pain, abdominal distension, or constipation. A study reported that *Blastocystis* spp. are associated with colonic inflammation[45], and another two studies conveyed that they are not pathogenic[46,47]. *Blastocystis* spp. can be detected in wet mount preparations of fresh stools and cultured stool samples in Jones' media[48]. Iodoquinol and metronidazole are the most common drugs prescribed for treatment[49].

Table (2) shows the reported prevalence of *Blastocystis* spp. in some Egyptian Governorates. In Cairo; El-Shazly *et al*.[50] recorded an infection of 14% among chronic liver diseases (CLD) and that was attributed to possible poor environmental hygiene. A higher rate (28.5%) was reported among neoplastic patients in 2016[24]. Similarly, Ismail and Fadl[51] in 2019 diagnosed blastocystosis in 30% of patients with renal transplantation attending in Nephrology Unit of Kasr Al-Aini, Faculty of Medicine, Cairo University.

In Alexandria, Hassanein *et al*.[32] reported that blastocystosis was significantly high among patients with IBD as compared to the control (65% vs 17.5%, respectively). More or less similar infection rates were detected in 54.5% of immunocompromised and 67.4%

Table 2. Prevalence of *Blasocystis* spp. among immunocompromised patients in five Egyptian Governorates.

Governorate	Immunocompromised hosts	No.#	%	Reference
Cairo	**Neoplastic patients**	150	28.5	[24]
	CLD	50	14.0	[50]
	Renal transplantation	50	30.0	[51]
Alexandria	**IBD**	40	65,0	[32]
	Control	40	17.5	
	HD	120	24,2	[37]
	Control	100	13.0	
	ALL	55	54,5	[52]
	Control	46	67.4	
Minya	**Immunosuppressed**	200	12.1	[41]
Menoufia	**Liver transplantation**	50	12.0	[42]
Dakahlia	**Hematological malignancy**	145	21.4	[43]
	Malignancy with radiotherapy		38.5	
	Malignancy with chemotherapy		18.5	

#: Total number examined; **ALL:** Acute lymphocytic leukemia; **CLD:** Chronic liver disease; **HD:** Hemodialysis; **IBD:** Inflammatory bowel disease.

of immunocompetent ones[52] and that was attributed to pharmacologic effect of cytotoxic drugs on the parasite among the immunocompromised[53]. Patients undergoing HD showed higher infection rates as compared to their controls (24.2% vs 13%, respectively)[37].

In Minya Governorate, the parasite was detected in 12.1% of immunocompromised children[41], which conformed with the recorded prevalence among liver transplantation patients in Menoufia Governorate[42]. Higher rates were detected in Dakahlia Governorate among patients who had hematological malignancy (21.4%), while those treated with radiotherapy had higher infection rate than those receiving chemotherapy (38.1% vs 18.5%, respectively)[43]. The recorded high prevalence may be due to restriction of the study to diarrheic cases besides other contributing factors such as environmental, socio-economic factors, residence, water source, and food supply.

Cryptosporidium spp.

Cryptosporidium spp. are world wild intracellular zoonotic protozoa and are recognized globally as a major cause of chronic diarrhea in immunocompromised patients resulting in significant morbidity and mortality[54-56]. Sporulated oocysts containing four sporozoites are infective on excretion and therefore transmissible by the fecal-oral route. Complicated AIDS patients with neoplasm and acute leukemia, as well as dairy or cattle farm workers, children in day care and owners of infected dogs or cats are at greatest risk[57]. Cryptosporidiosis is self-limited in immunocompetent individuals meanwhile it may cause severe acute diarrhea in immunocompromised patients, weight loss, nausea, and vomiting[54] leading to malnutrition and cognitive function impairment as well as growth retardation in infants[58]. Cryptosporidiosis is diagnosed using acid fast stain (AF), rapid immunochromatographic test, immunofluorescent microscopy, PCR-restriction fragment length polymorphism, multiplex allele-specific-PCR, and quantitative real-time PCR[59,60].

In Cairo (Table 3), cryptosporidiosis was detected in 23.5% among neoplastic patients[24] and a low rate of 7% was observed among immunocompromised ones[34]. Patients with renal transplantation attending the nephrology unit of Kasr Al-Aini showed 10% prevalence, and the same was found among children suffering from CLD[50,51]. Another study conducted on liver cirrhosis patients revealed only 3.3% *C. parvum* infection by n-PCR and no infection was detected among the control group[61]. Recently, Amin *et al*.[62] detected cryptosporidiosis microscopically among elderly individuals attending outpatient clinics of Internal Medicine Hospital, Cairo University using AF, immunochromatographic test (ICT), ELISA and nested-PCR (3.7%, 6.3%, 6.7% and 3.7%, respectively), and genotype 1 and 2 were reported after using fragment length polymorphism on n-PCR assays.

In Alexandria (Table 3), the high rate of cryptosporidiosis was detected among patients suffering from IBD as compared to control (77.5% vs 20%, respectively)[32]. Meanwhile, lower rates were detected among children having ALL (42.7%)[36], followed by 32.5% vs 11% among HD patients and their counterparts respectively with statistically significant differences[37].

In Dakahlia Governorate (Table 3), infection rates were 36%, 32%, 30% and 22% among patients suffering from liver cirrhosis with ascites, hepatocellular carcinoma, CLD and liver cirrhosis without ascites respectively[63]. A similar rate was observed among patients with hematological malignancy attending the Oncology and Radiotherapy Department, Mansoura University Hospital (30.3%)[43]. Liver transplant recipients showed also 20% infection in Menoufia Governorate[42].

Cryptosporidiosis showed a high infection rate among immunocompromised children as compared to immunocompetent children in Minya Governorate

(60.2% vs 42.2% respectively)[41]. This report was followed by a study by ElNadi *et al*.[39] in Sohag Governorate among diabetic patients (5%). Meanwhile, children on chemotherapy in Sohag Governorate[40] showed a high rate of 45%. Later, Mohamed *et al*.[60] detected *Cryptosporidium* oocysts in 45% of diarrheic immunocompromised patients attending the outpatient clinics of pediatric, oncology and internal medicine departments in Sohag University Hospitals. The recorded prevalence rate was ascribed to continued poor personal hygiene, inadequate supply of drinking water, low standard environmental conditions and inadequate waste disposal system[60] (Table 3).

Cyclospora cayetanensis

Cyclospora cayetanensis is an emerging coccidian parasite. The infective disporocystic disporozoic oocyst is unsporulated when passed and therefore is not transmitted by the feco-oral route. Sporulated stages are transmitted by contaminated water and food[64]. The overall number of cases reported in US increased from 2017 to 2019 to attain 2,408 cases possibly due to updating of diagnostic testing procedures, e.g., multiplex molecular test[65]. The infection may be asymptomatic or associated with self-limited or severe diarrhea[66]. Immunocompromised individuals suffer from prolonged diarrhea that lasts up to several months with remission and relapse. Although, the extra-intestinal infection is rare, complications such as Guillain-Barré and Reiter's syndromes were reported[67]. For diagnosis, flow cytometry is more sensitive than AF stain[68]. Renocal-sucrose gradient sedimentation proved to be effective in processing oocysts concentration and purification for flow cytometry[69]. Interestingly, PCR is increasingly used in research and outbreak investigations[70,71]. Trimethoprim-sulfamethoxazole (TMP-SMZ) is the drug of choice used as prophylaxis to prevent recurrent episodes among infected immunocompromised patients[72,73].

Table (3) shows low rates of *Cyclospora* oocysts recorded as 2.5% and 3% among neoplastic and immunocompromised patients, respectively in Cairo[24,34], and 10% among patients with renal transplantation attending the nephrology unit of Kasr Al-Aini, Faculty of Medicine, Cairo University[51]. That was in line with a study done among patients suffering from IBD in Alexandria (10%)[32]. The highest rate of *C. cayetanensis* was detected among children suffering from ALL in Alexandria (22.2%) [36]. In Minya Governorate 7.8% was recorded among immunocompromised children[41], and 6% were positive among liver transplant recipients in Menoufia Governorate[42].

*Cysto**Isospora belli*

Previously known as *Isospora belli*, it is known to cause uncommon diarrheal illness termed cystoisoporiasis. It is an opportunistic protozoan in immunosuppressed human hosts[74,75]. After *in vitro*

Table 3. Prevalence of intestinal coccidia among immunocompromised patients in six Egyptian Governorates.

Governorate	Immunocompromised hosts	No.#	Prevalence			Reference
			Cryptosporidium spp.	*C. cayetanensis*	*C. belli*	
Cairo	**Neoplastic patients**	150	23.5	2.5	0.5	[24]
	Immunocompromised	100	7.0	3.0	--	[34]
	CLD	50	10.0	--	--	[50]
	Renal transplantation	50	10.0	10.0	--	[51]
	Liver cirrhosis	60	3.3	--	--	[61]
	Elderly individuals	270	3.7 (AF)*	--	--	[62]
			6.3 (ICT)*	--	--	
			6.7 (ELISA)*	--	--	
			3.7 (nPCR)*	--	--	
Alexandria	**IBD**	40	77.5	10.0	--	[32]
	ALL	117	42.7	22.2	1.7	[36]
	HD	120	32.5	--	--	[37]
Sohag	**Diabetic patients**	100	5.00	--	--	[39]
	Children on chemotherapy	100	45.0	--	--	[40]
	Diarrheic immunocompromised	40	45.0	--	--	[60]
Minya	**Immunosuppressed**	200	60.2	7.8	9.7	[41]
Menoufia	**Liver transplantation**	50	20.0	6.0	--	[42]
Dakahlia	**Hematological malignancy**	145	30.3	--	--	[43]
	Liver cirrhosis with ascites	50	36.0	--	--	[63]
	Hepatocellular carcinoma	50	32.0	--	--	
	CLD	150	30.0	--	--	
	Liver cirrhosis without ascites	50	22.0	--	--	

#: Total number examined; *: Methods used for diagnosis; **ALL:** Acute lymphocytic leukemia; **CLD:** Chronic liver disease; **CRL:** Chronic renal failure; **DM:** Diabetes mellitus; **HD:** Hemodialysis; **IBD:** Inflammatory bowel disease.

sporulation, *C. belli* disporocystic tetrasporozoic oocysts are transmitted through contaminated food or water, so it is not a zoonosis[76]. It may cause mild diarrhea, abdominal discomfort, and low-grade fever in immunocompetent individuals. In contrast infected immunocompromised patients have extreme diarrhea, anorexia, weight loss, abdominal pain, cramps, loss of appetite, nausea, vomiting, and fever, that can last from weeks to months[77]. Molecular tools are more sensitive than microscopic examination for oocyst detection. The extended-range PCR approach, that offers a promising test for diagnosis of parasitic diseases that elude diagnosis using conventional methods, may be applied[78]. For this infection, TMP-SMZ combination are the drugs of choice and are better than antibiotics for treating diarrhea. In patients with AIDS, a single TMP-SMZ double-strength tablet, 3 times a week, was commonly used for long-term suppression of *C. belli*[79]. Table (3) shows that *C. belli* was detected in a small sample (0.5%) among neoplastic patients in Cairo[24]; and higher rates were recorded among ALL children attending El-Shatby Hospital in Alexandria and immunocompromised children in Minya Governorate (1.7% and 9.7%, respectively)[36,41].

Microsporidium spp.

Microsporidium spp. previously considered as obligate unicellular spore forming eukaryotic parasites was recently phylogenetically classified as fungus[80]. It was elicited as an opportunistic infection associated with diarrhea in immunocompromised patients, patients with neoplasms, transplant recipients, diabetics, and in elderly individuals[81-83]. Humans acquire infection through ingestion of contaminated food or water, direct contact with broken skin or eyes, trauma, sexual transmission and trans-placentally[84]. Microsporidiosis in immunocompromised patients is characterized by severe and chronic diarrhea with massive weight loss especially in HIV/AIDS patients, as well as nausea, vomiting, malabsorption, and dyspepsia[85-87]. In 2017, Kazemi *et al*.[88] reported that multiplex nested PCR targeting internal transcribed spacer (ITS), small subunits (SSU) and large subunits (LSU) of ribosomal DNA (rDNA) identified intestinal *Microsporidium* with high sensitivity as compared to traditional techniques such as modified trichrome staining. Albendazole is effective against *Encephalitozoon* (*Enc.*) spp., meanwhile Fumagilin is more broadly effective against *Enc.* spp. and *Enterocytozoon* (*Ent.*) *bieneusi*[89]. In HIV patients, microsporidiosis is treated by anti-retroviral therapy through restoration of immune competence[90].

The highest records of microsporidiosis were recorded in Alexandria Governorate. Table (4) shows four studies conducted in Alexandria among patients suffering from IBD, non-HIV immunocompromised patients, children suffering from ALL and HD patients (90%, 77.3%, 60.7%, and 11.7%, respectively)[32,36,37,91]. In contrast, lower rates were reported in Cairo (9.5%) among neoplastic patients[24], and 2% each among immunocompromised patients and patients suffering from CLD[34,50]. In Cairo, stool samples were collected from cancer patients suffering from leukemia and lung, liver, breast, and colon cancer. The samples were examined by different stains (modified trichrome blue, acridine orange, and calcofluor white), together with regular PCR. The latter showed the highest sensitivity rate and diagnosed *Ent. intestinalis* in 17% of the sample examined[92]. In 2016, approximately 5% was recorded among hematological malignancy patients undergoing radiotherapy and chemotherapy in Dakahlia Governorate[43] and 3% among diabetic patients in Sohag Governorate[39]. In the Faculty of Medicine, Ain Shams University, spores were microscopically detected in 13.9% of all individuals examined and only one case was missed by Nested and RFLP-PCR[93]. The infection rate was higher among immunocompromised as compared to immunocompetent (14.5% and 13.3%, respectively) cases. Additionally, a detailed genotyping study showed equal number of immunocompromised

Table 4. Prevalence of *Microsporidia* spp. among immunocompromised patients in four Egyptian Governorates.

Governorate	Immunocompromised hosts	No.#	%	Reference
Cairo	**Neoplastic patients**	150	9.5	[24]
	Malignancy, DM and CRF	100	2.0	[34]
	CLD	50	2.0	[50]
	Cancer patients	100	17.0	[92]
	All samples microscopically	323	13.9	[93]
	Immunocompromised patients	173	14.5	
	Immunocompetent	150	13.3	
Alexandria	**IBD**	40	90	[32]
	ALL	117	60.7	[36]
	HD	120	11.7	[37]
	Non-HIV immunocompromised patients	44	77.3	[91]
Sohag	**Diabetic patients**	100	3.0	[39]
Dakahlia	**Hematological malignancy**			
	Malignancy with radiotherapy	145	5.0	[43]
	Malignancy with chemotherapy			

#: Total number examined; **ALL:** Acute lymphocytic leukemia; **CLD:** Chronic liver disease; **CRL:** Chronic renal failure; **DM:** Diabetes mellitus; **IBD:** Inflammatory bowel disease; **HD:** Hemodialysis.

individuals, five cases, with each of *Ent. bieneusi*, *Enc.* spp., and mixed infection among 15 cases. Meanwhile, six immunocompetent individuals had *Ent. bieneusi*, 3 had *Enc.* spp. and 10 had mixed infection[93].

Strongyloides stercoralis

This nematode worm causes strongyloidiasis and is endemic in 25% of tropical and subtropical regions. In the USA, the highest rates of infection were observed among residents of the southeastern states, immigrants, refugees, travelers, and military personnel[94]. Complications were associated with persistent infection, high worm burden and high mortality[95]. Its life cycle begins by skin penetration with infective filariform larvae, found in soil contaminated with human feces. This is followed by migration to the lungs and penetration into the alveolar air sacs, then ascent to the tracheobronchial tree and swallowing[96]. After that, they mature into adult worms that burrow into the mucosa of duodenum and jejunum. In the GIT lumen fertilized females produce eggs from which hatch noninfectious rhabditiform larvae that pass in the feces[97]. In autoinfection, rhabditiform larvae mature into the filariform form within the GIT and penetrate perianal skin or colonic mucosa leading to increased burden of infection[98]. Among immunocompromised patients, fatal hyperinfection with disseminated disease was attributed to autoinfection[99]. In a case report of angioimmunoblastic T-cell lymphoma, Abdelrahman *et al*.[100] documented, the association of immunosuppressive therapy and steroids as a primary cause of fatal strongyloidiasis hyper infection. Recorded prevalence in table (5) showed high rate of 13.6% strongyloidosis among immunosuppressed children in Minya Governorate[41], as compared to 2.6% estimated by Hassanein *et al*.[36] among leukemic children in Alexandria city, and no infection was found among the control groups.

Toxoplasma gondii

This obligate intracellular parasite affects about one-third of the world population[101]. It can be transmitted by ingestion of tissue cysts in meat or ingestion of mature disporocystic tetrasporozoic oocysts in contaminated fruits, vegetables and drinking water; besides congenital transmission, organ transplantation, blood transfusion, and accidental inoculation in the laboratory[102]. Retinochoroiditis is the most frequent clinical manifestation of congenital and acquired *Toxoplasma* infections[103,104]. Chronic toxoplasmosis is associated with various autoimmune disorders, including rheumatoid arthritis, systemic sclerosis, inflammatory bowel syndrome and autoimmune thyroid disorders[105]; and causes impairment of the innate immune state that is responsible for proliferation in autoantibodies production[106]. Mori *et al*.[107] reported that loop-mediated isothermal amplification (LAMP) has increasingly appeared as an alternative molecular method to PCR for diagnosis of toxoplasmosis. Currently, recommended drugs act against *T. gondii* tachyzoites, and do not eradicate the bradyzoite. The most effective drug is pyrimethamine because it blocks dihydrofolate reductase that is involved in parasite reproduction[108-110].

Table (6) shows that a low rate of toxoplasmosis was detected among immunocompromised patients in Cairo Governorate (6%)[34]. In Dakahlia Governorate, *Toxoplasma* IgG-antibody showed higher rate of infection (92.6%) as compared to *Toxoplasma* IgM (13.6%) among patients suffering from late stage of liver cirrhosis. Besides, it was higher than in those with chronic non cirrhotic HCV (76.9% and 12.8%, respectively) as compared to the controls (15% and 7.5%, respectively)[111]. In Menoufia Governorate, *Toxoplsama* IgG-antibody showed higher rate of infection as compared to *Toxoplasma* IgM-antibody

Table 5. Prevalence of *S. stercoralis* in two Egyptian Governorates.

Governorate	Immunocompromised hosts	No.#	%	Reference
Alexandria	**ALL children**	117	2.6	[36]
	Immunocompetent	117	0.0	
Minya	**Immunosuppressed children**	200	13.6	[41]
	Immunocompetent	250	0.0	

#: Total number examined; **ALL:** Acute lymphocytic leukemia.

Table 6. Prevalence of *T. gondii* among immunocompromised patients in four Egyptian Governorates.

Governorate	Immunocompromised hosts	No.#	Toxoplasmosis%*	IgG%	IgM%	Reference
Cairo	**Malignancy, DM, CRF**	100	6.0	--	--	[34]
Alexandria	**Liver cirrhosis**	81	--	92.6	13.6	[111]
	Chronic HCV non cirrhotic	39	--	76.9	12.8	
Menoufia	**Liver transplant recipients**	50	--	28.0	18.0	[42]
	DM-type I	--	86.37	--	--	[113]
	DM-type II	--	66.69	--	--	
Qalyoubia	**Rheumatic arthritis patients**	25	54.0	--	--	[112]

#: Total number examined; ***:** Overall prevalence of toxoplasmosis.

among liver transplant recipients (28% and 18%, respectively)[42].

In Qalyoubia Governorate, the overall prevalence of toxoplasmosis showed a high infection rate in rheumatic arthritis patients as compared to the controls (54% and 32.0%, respectively)[112], while in Menoufia Governorate, the rate was higher among DM-type I patients than those of DM-type II (86.37% and 66.69%, respectively)[113].

In conclusion, the highest rates of opportunistic infections were recorded from each of Alexandria, Sohag and Minya Governorates. In Alexandria City, IBD patients presented high rates of *Blastocystis* spp. and *Cryptosporidium* spp., meanwhile children with ALL showed highest rates of *C. cayetanensis*. Both *C. belli* and *S. stercoralis* were largely detected in immunocompromised patients in Minya Governorate. *Microsporidium* spp. was highly demonstrated among non-HIV immunocompromised patients in Alexandria City. Finally, toxoplasmosis was mostly detected among DM-I in Menoufia Governorate, and IgG and IgM antibodies were highly detected among patients with liver cirrhosis in Dakahlia Governorate. Reasons for variations in patterns in parasite distribution are unclear but reflects that parasite colonization in the intestinal tract might be affected by immunosuppression.

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