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SOME INTESTINAL PARASITES AND PSYCHIATRIC DISEASES: IS THERE A POSSIBLE LINK?

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Abstract

The study assessed the risk of intestinal parasitic infections (IPIs) among psychiatric patients in comparison with controls. A case-control study was conducted on 983 psychiatric patients and another 983 non-psychiatric controls attending the Psychiatry and Neurology outpatient clinic of Minia University Hospital, Egypt, during the period from October 2017 to September 2019. A single fecal sample was collected from each participant and examined by direct saline wet mount, formol-ether concentration. Modified trichrome and Kinyoun acid-fast staining were used to confirm suspected cases of protozoa. Our results showed that the rate of IPIs was significantly higher in psychiatric patients (35%) than in control (10.8%). Multiple IPIs were found in nine (0.9%) psychiatric patients, but not in controls. *Blastocystis hominis* was the most prevalent infection followed by *Cryptosporidium parvum*. Patients suffering from depression had the highest prevalence of infection (32.6%).

Keywords: Egyptian patients, Psychiatric disorders, Intestinal parasites, Depression.

Introduction

Psychiatric disorders are a group of disorders characterized by combination of abnormal thoughts, emotions, behaviors, and relationships with others (Khalili *et al*, 2013). Globally, psychiatric disorders rank the 3rd most common disease, just after cancer and cardiovascular diseases (WHO, 2017), it was estimated that more than 25% of individuals; especially in developing countries develop one or more mental or behavioral disorders in their lifetime (Daré *et al*, 2019). About 16.93% of the Egyptian population suffered from psychiatric disorders (Ghanem *et al*, 2009).

The etiology of psychiatric disorders is poorly understood (Insel, 2010) Besides, biological, psychological, and environmental factors, increased evidence for the role parasitic infections in the development of some psychiatric disorders (Boltoni and Robertson, 2016). Studies suggested the association between psychiatric disorders and parasitic infections, especially those with neurological tropism (Ozaki *et al*, 2011; Alvarado-Esquivel, 2013; Tesfaye *et al*, 2014; Wiwanitkit, 2014; Esshili *et al*, 2016; Chen *et al*, 2019). Besides, meta-analysis study proved such a relationship (Daré *et al,* 2019).

Intestinal parasitic infections (IPIs) are among the most widespread human infections; especially in developing countries, affecting approximately one-fourth of the world populations (Torgerson *et al*, 2014). In Egypt, despite the improvements in the quality of medical services and hygiene status (Youssef and Uga, 2014), protozoa were responsible for significant morbidity (Hussein *et al*, 2017). Man acquires the intestinal infection by feco-oral ingestion of the infective stages (Ayele *et al,* 2019), contaminated food and drinking water (Negm, 2003). But, the blood parasites are transmitted by arthropod-vector (El-Bahnasawy *et al*, 2013). Also, the biological, environmental, and socio-economic factors, behavioral factor influence the risk of parasitosis (Gelaw *et al*, 2013).

This study aimed to assess the risk of intestinal parasites in patients with psychiatric disorders compared to control and to analyze parasites in different psychiatric disorders.

Material and Methods

Study design: This case-control study was carried out at the Psychiatry and Neurology Outpatient Clinic of Minia University Hospitals, Egypt, during the period from October 2017 to September 2019. A total of 983

patients with different psychiatric disorders were included.

Inclusion criteria for psychiatric patients were (a) patients aged from 18 to 70 years; (b) male & female patients and (c) patients who agreed to participate in the study and undergo required investigations. Exclusion criteria were (a) Parasitic patients on treatment, (b) Psychiatric disorder patients due to psychoactive substance use, and (c) Psychiatric patients with combined neurological disorders or with emerging psychiatric manifestations. All the patients were interviewed and diagnosed according to the semi-structured psychiatric interview based on the clinical interview for DSM-5 and confirmed by a consultant of psychiatry. Also, 983 cross-matched patients attended the Neurology Outpatients Clinic without past or present psychiatric disorders were used as controls.

Stool examination: A fecal sample from each participant was collected in labeled, plastic containers with tight-fitting covers, and immediately transported to the Parasitology Department, Faculty of Medicine to be examined for intestinal parasites. Samples were initially examined macroscopically for color, consistency, presence of adult worms, mucous and/or blood. The slides were prepared for microscopic examined direct smear in saline, and in iodine as well as formol-ether sedimentation (Cheesbrough, 2009). Also, modified trichrome stain and Kinyoun acid-fast staining were used (Garcia, 2007).
The intestinal parasites rate was calculated as ratio of patients' number with at least one positive parasite to participant's total number per group (Mohtashamipour *et al*, 2015).

Ethical approval: The study protocols and the consent forms were reviewed and approved by the scientific ethical committee of Department of Parasitology and Department of Psychiatry and Neurology Faculty of Medicine, Minia University on the monthly meeting in September 2017. All participants provided written informed con-sent after the study procedures were explained.

Statistical analysis: Data entry and analysis was done using SPSS version 21. Quantitative data were expressed as mean ± SD. Qualitative data were expressed as number and percentage. Chi square test, Z test were used. Logistic regression analysis determined the relationship between the IPIs rate and the psychiatric disease subtypes. Odds ratios (OR) and 95% confidence intervals (CI = 95%) were calculated. $P < 0.050$ was considered significant.

Results

Among the 983 confirmed psychiatric patients (45.5% male aged 36.2±19.1years) & the non-psychiatric (control) ones (44.9% male aged 35.4±18.3years), without significant differences between psychiatric and control groups as to age (χ^2= 0.20, p=0.9), sex (χ^2= 0.40, p=0.5) and residence (χ^2= 0.13, p=0.7).

The intestinal parasites was significantly more in psychiatric patients (344, 35%) than in controls (106, 10.8%) (COR=4.4; 95% CI = 3.5-5.8, P = 0.001).

Among psychiatric patients, the parasites were *Blastocystis hominis* (16%) followed by *Cryptosporidium parvum* (9.6%). But, intestinal ones were non-pathogenic *Entameba coli* and *Entrobius vermicularis* without significantly different (p = 0.1, p = 0.08 respectively) between patients and controls. Multiple IPIs were found in nine (0.9%) psychiatric patients, but none in controls. The predominant co-existent parasite was *B. hominis* and *C. parvum* (0.4%).

The psychiatric patients were subtypes categorized. However, there was a significant higher prevalence of the intestinal parasitic infections (IPIs) in the patients suffered from depression (OR: 1.3; 95% CI: 1.001-1.7, P = 0.04) compared to the control group, regarding to the protective association existed between the anxiety, bipolar, and somatoform disorders on one hand and IPIs on the other hand.

The details were given in tables (1, 2 & 3)

Table 1: Demographic characteristics of psychiatric patients and control.

Variable	Psychiatric patients, n=983(%)	Control, n=983 (%)	χ^2	P value
Male	447 (45.5)	441 (44.9)	0.40	0.5
Female	536 (54.5)	542 (55.1)		
Age groups (years)				
Range	18-70	18-69	0.20	0.9
Mean ±SD	36.2 ± 19.1	35.4 ± 18.3		
18 -30 years	276(28.1)	280(28.5)		
31-50 years	494(50.3)	491(49.9)		
>50 years	213(21.7)	212(21.6)		
Residence			0.13	0.7
Rural	557 (56.7)	560 (57)		
Urban	426 (43.3)	423 (43)		

Table 2: Frequency of intestinal parasites among psychiatric patients and control.

Intestinal parasites	Psychiatric patients (n=983)			Controls (n=983)			Z test	p-value
	Single	Mixed	Total (N, %)	Single	Mixed	Total (N, %)		
Blastocystis hominis	150	7	157 (16)	51	-	51(5.2)	7.9	0.008*
Cryptospo. parvum	89	5	94 (9.6)	22	-	22 (2.2)	6.8	0.004*
E. histolytica /dispar	37	-	37 (3.8)	9	-	9 (0.9)	3.3	0.003*
Entameba coli	8	2	10 (1)	16	-	16 (1.6)	1.1	0.1
Giardia intestinalis	18	1	19 (1.9)	4	-	4 (0.4)	3.1	0.009*
C. cayetanensis	13	1	14 (1.4)	3	-	3 (0.3)	2.6	0.003*
Ascaris lumbricoides	14	1	15 (1.5)	1	-	1 (0.1)	3.4	0.002*
Entrobius vermicularis	-	2	2 (0.2)	-	-	-	1.4	0.08
Hymenolepis nana	6	-	6 (0.6)	-	-	-	2.5	0.005*
Total patients	335	9	344 (35)	106	-	106 (10.8)	13.7	0.001*

Mixed infection: *Blastocystis hominis* and *Cryptos. parvum* (4cases), (*B. hominis* & *Entrobius vermicularis*), (*B. hominis* & *Giardia intestinalis*), (*C. parvum* & *Ascaris lumbricoides*), (*Entameba coli* & *Entrobius vermicularis*) one case each. Triple infection was detected in a case (*B. hominis, Entameba coli* & *Cyclospora cayetanensis*).

Table 3: Association of clinical subtypes and duration of illness with IPIs among psychiatric patients.

Psychiatric Disorders	Psychiatric patients		COR (95%CI)	P- value
	Parasitized N= 344 (%)	Negative N= 639 (%)		
Schizophrenia spectrum and other psychotic disorder	94 (27.3)	120 (18.8)	1.1(0.8-1.5)	0.3
- Anxiety disorders	73 (21.2)	221 (34.6)	0.36(0.27-0.49)	0.001*
- Depressive disorder	112 (32.6)	127 (19.9)	1.3(1.001-1.7)	0.04*
- Obsessive-compulsive disorder and related disorders	16 (4.7)	35 (5.5)	0.63(0.34-1.1)	0.1
- Bipolar disorder	21 (6.1)	58 (9.1)	0.49(0.29-0.82)	0.006*
- Somatoform disorders	28 (8.1)	78 (12.2)	0.47(0.30-0.74)	0.001*
Duration of illness:				
- Less than one year	93 (27)	230 (36)		
- 1-5 year	139 (40.4)	264 (41.3)	1.3 (1.1-1.6)	0.001*
- More than 5 years	112 (32.6)	145 (22.7)		

Discussion

The present study showed that the risk of infection with intestinal parasites was 4.4 times greater for patients with psychiatric patients than controls. This agreed with Sirivichayakul *et al*, (2003); Mohammadi-Meskin *et al*, (2019) & Otu-Bassey *et al*, (2019). In this study, the 35% prevalence recorded agreed with Eze *et al*. (2019). But, it was higher than 8.4% recorded among mental patients in North Taiwan (Cheng and Wang, 2005), 13.5% among patients of a Ghanaian Psychiatry Hospital (Duedu *et al*, 2015) & 29.5% among institutionalized mental patients in Northern Iran (Saeidinia *et al*, 2016). But, less than 49.2% recorded among mental persons in Nigeria Neuro-psychiatric Hospital (Otu-Bassey *et al*, 2019), 54.7% in mental retardation center of Bandar Abbas, Southern Iran (Mohammadi-Meskin *et al*, 2019) and 68% as well as type of psychiatric disorders.

In the present study, nine different parasites were identified six protozoa (*B. hominis, C. parvum*, *Entameba histolytica/dispar, Cyclospora cayetanensis, Giardia intestinalis, &*

E. coli) and three worms (*Ascaris lumbricoides, Hymenolepis nana, Entrobius vermicularis*). but, the helminthes prevalence among psychiatric patients (2.3%) was much lower than previous reports from Iran (Mohammadi-Meskin *et al*, 2019), Nigeria (Eze *et al,* 2019; Otu-Bassey *et al*, 2019) and Tanzania (Nyundo *et al*, 2017), it was in accordance with the fact that in general, among chronic psychiatric patients in Sina Hospital Shahre-Kord, Iran (Khalili *et al*, 2013). Moreover, Sargent (1983) in USA reported *T. trichiura*, *Ascaris lumbricoides, Giardia lamblia*, and *Entamoeba histolytica* and added that annual examination and treatment could control parasitosis; but, complete eradication might require examination following home visits by the resident population. Rivera *et al.* (2006) reported *E. histolytica* in mentally retarded patients residing in a mental institution in Metropolitan Manila, Philippines. Shokri *et al.* (2012) in Iran reported mentally retarded individuals were infected with *S. stercoralis*, *Blastocystis hominis*, *Entamoeba coli, Giardia lamblia, Enterobius vermicularis*, *Hymenolepis nana*, and *Iodamoeba butschlii.* They recommended that the environment disinfection, training and financing of the staff, increasing the number of workers, recruiting of professionals. The differences might be attributed to sample size, location, sanitation, and low parasites due to massive use of anti-helminthic drugs mainly school-aged children (Dahesh, 2018). In this study, all parasites except for *E. coli* and *E. vermicularis* showed significant different between psychiatric patients and control, due to fecooral transmission and poor personal hygiene. Also, conventional treatment of drinking water was not always sufficient for to kill infective stages, especially with *C. parvum* (Khalifa *et al*, 2014). Generally, blastocystosis is one of the commonest zoonotic parasite (Zanetti *et al*, 2020). The present result showed that *B. hominis* was the most prevalent intestinal parasite among psychiatric patients (16%), which agreed with others (Khalili *et al*, 2013; Mohammadi-Meskin *et al*, 2019).

Enterobius vermicularis is one of the commonest human helminthic parasites especially in children (lee *et al*, 2000). Chao *et al*. (2019) reported that enterobiasis patients had a higher risk of developing psychiatric disorders mainly especially anxiety, depression, and sleep disorders. However, it was detected in only 2 psychiatric patients (0.2%). This agreed with others (Shehata and Hassanein, 2015; Saeidinia *et al*, 2016; Mohammadi-Meskin *et al*, 2019; Otu-Bassey *et al*, 2019). The low rate of infection might be explained as Scotch adhesive tape swab was the gold standard method for diagnosis (Awad *et al,* 1985), was not performed due of compliance issues. So, actual enterobiasis prevalence might be probably higher than given.

Intestinal parasites and psychiatric diseases might be a risk factor one to another (Bolton and Robertson, 2016). Unlike parasites with neurological tropism, intestinal ones may produce psychiatric symptoms indirectly through brain-gut-axis which may clear after effective therapy (Chao *et al*, 2019). Also, some intestinal parasites cause under nutrition and anemia depleting the host's essential nutrients and adversely affect mental health. So, treatment of IPIs may spell a better prognosis for psychiatric patients (Nyundo *et al*, 2017). Defaye *et al*. (2020) experimentally found that *Blastocystis*-infected rats presented both depressive and anxiety-like behaviors. But, the un-hygienic behavioral pattern associated with different psychiatric diseases especially, depression and psychotic disorders contributed to IPIs (Chandrasena *et al*, 2010).

In the present study, patients with depression had highest prevalence of infection (32.6%). Hand-washing before and after eating, and using toilet were significantly protect against IPIs (Geneidy, 2019). Thus, stress increased the susceptibility to parasitic infections by altering oxidant-anti-oxidant state making host' immune system to be in favorable conditions for the opportunistic parasites (El-Sayed and Morsy, 2021).

In the present study, there was a significant of IPIs prevalence in patients with increased duration of psychiatric illness, which agreed with other previous studies (Cheng and Wang, 2005; Otu-Bassey *et al*, 2019). Prolonged exposure to psychological stress increased the IPIs risk (Chandramathi *et al*, 2014).

Conclusion

The outcome data showed that psychiatric patients were at risk to acquire intestinal parasites especially those suffering from the depression. Also, the study highlighted importance of examining psychiatric patients for parasites

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