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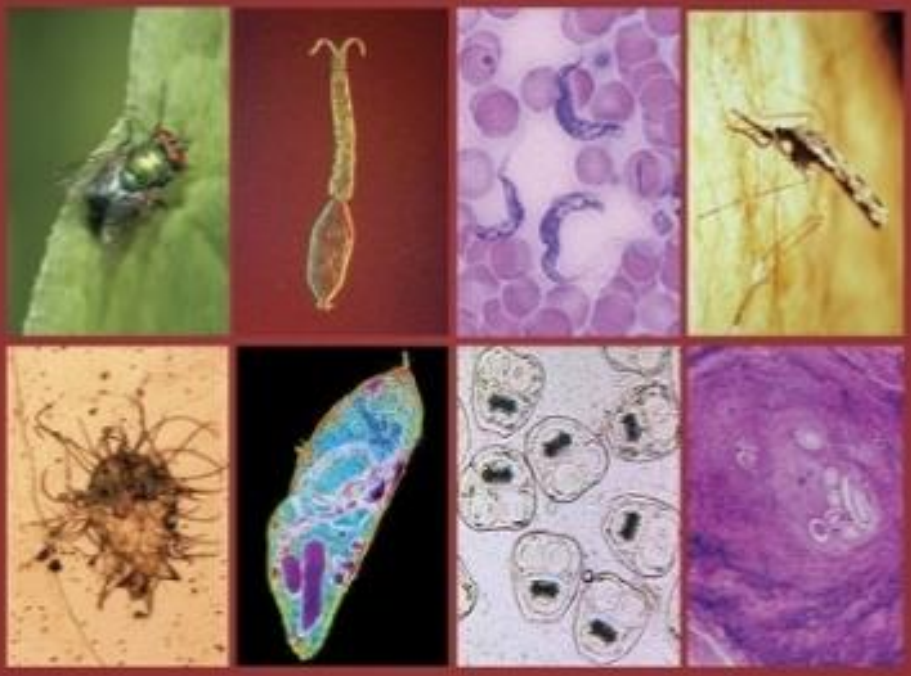

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Prevalence of Parasitic Infections Among Patients with Autoimmune Disorders in Menoufia University Hospitals, Egypt

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ABSTRACT

Some studies can explain how parasitic agents may contribute to the development of autoimmune diseases while others focus on developing a parasite component that may treat autoimmune illnesses. Consequently, the goal of the study was to identify the prevalence of parasitic infections among individuals with various autoimmune disorders and how such infections affect the pathophysiology of these diseases. In the current study, A total of 154 adult patients who had a confirmed diagnosis of autoimmune disease recruited from Menoufia University Hospitals, Egypt, were included. A cross-sectional study design was conducted on the participants who were chosen for history taking, clinical examination, laboratory investigations, and ultrasonography. The results revealed that intestinal parasites such as *Enterobius vermicularis*, *Entamoeba histolytica*, *Giardia lamblia*, and *Ascaris lumbricoides* were found to be prevalent in 56.5% of the subjects in this study. Immune thrombocytopenia (ITP) patients had intestinal parasites in 100% of cases while parasites were present in 52.6% of autoimmune hemolytic anemia (AIHA) and 47.6% in rheumatoid arthritis (RA) patients. Seroprevalence of toxoplasmosis in the studied cases revealed 15.6% positive IgM and 35.1% positive IgG. The IgM-positive cases were perceived in patients with systemic lupus erythematosus (SLE), Hashimoto thyroiditis (HT), and ITP. Whereas, occurrences of IgG positivity were mainly presented in SLE then AIHA, ITP, and RA patients. Less clinical manifestations were observed in autoimmune disorder patients having intestinal parasitic infections. In conclusion, high parasitic prevalence is common in autoimmune disease patients, which alters the pathogenesis and clinical course of these illnesses.

INTRODUCTION

According to the World Health Organization, over 1.5 billion individuals, or 24% of the world's population have intestinal parasites. Tropical and subtropical regions are home to a large number of those parasites where Africa, China, the Americas, and East Asia having the highest concentrations (WHO, 2020).

The helminthic species like *Ascaris lumbricoides*, *Trichuris trichiura*, *Enterobius vermicularis*, *hookworm*, and *Taenia* species as well as protozoan species like *Entamoeba histolytica* and *Giardia lamblia* are the main parasites of worldwide public health (Haque, 2007; Lozano *et al*., 2012).

Many people around the world are impacted by *Toxoplasma gondii*. In immunocompetent hosts, the primary infection is followed by a self-limited febrile illness, but in immunocompromised individuals, such as those with HIV, it is generally known that it puts individuals at risk for developing severe toxoplasmosis (Robert-Gangneux *et al*., 2018).

Autoimmunity is characterized as the immune system's inability to distinguish between infections and self-antigens, which results in injury to healthy tissue (Gutierrez-Arcelus *et al*., 2016).

Self-reactive immune components are what distinguish autoimmune illness from autoimmunity, which also includes pathology. In many areas of the world, autoimmunity and autoimmune illnesses are both sharply on the rise. This is probably due to changes in how exposed we are to environmental variables (Miller, 2023).

In the United States, tens of millions of people are affected by autoimmune illnesses, which are thought to be the third leading cause of morbidity in the developed world (Chang *et al*., 2023). In Egypt, the estimated adult SLE prevalence rate was 6.1/100,000 people (Gheita *et al*., 2021).

Helminthic infection is typically associated with diminished cellular immunological responses and a switch from T-cell to Th2 immune responses. Additionally, a negative correlation between the prevalence of helminthic infections and autoimmune diseases was shown, raising the possibility that "helminthic therapy" may be helpful for those with autoimmune diseases. With few adverse effects, the clinical signs of autoimmune diseases can be reduced by helminthic treatment, which can also lessen the intensity of inflammatory responses. Some intracellular protozoan infections, on the other hand, skew immune responses towards the T helper 1 type and may result in the emergence of an autoimmune disease (Abdoli *et al*., 2022).

Some inflammatory disorders have been related to a loss of helminths such as inflammatory bowel disease, asthma, atopic eczema, type 1 diabetes, multiple sclerosis (MS), and rheumatoid arthritis (RA) (Maizels, 2020).

MATERIALS AND METHODS

Study Area and Period:

In this study, 154 adult participants who had confirmed diagnosis of autoimmune diseases; were recruited from Menoufia University Hospitals, Shebin El-Kom, Egypt during the period from December 2022 to May 2023.

Study Design:

A cross-sectional study design was conducted among all participants who were chosen for history intaking, clinical examination, and laboratory investigations (blood, serum, stool, and urine examination) during the research period.

Sample Size Estimation:

According to Shapira *et al*. (2012), it was documented that in 42% of autoimmune illness patients, serum ATxA IgG was positive, at alpha margin 0.05 and 95% confidence interval and according to the following formula $[Z^2_{\alpha/2}\ P(P-1)\ /D^2]$

$Z^2_{\alpha/2}$ = the Z score corresponding to the degree of confidence

P = prevalence of the indicator

D= the desired precision

The estimated sample size was 154 autoimmune patients

Ethical Consideration:

All procedures were completed in accordance with global ethical standards. After receiving approval from the Institutional Ethical Committee of Menoufia University's Faculty of Medicine (IRB: 12-2022 PARA20).

Inclusion Criteria:

All patients (> 18 years), clinically and laboratory-confirmed autoimmune diseases according to; systemic lupus erythematosus (SLE) (Aringer *et al*, 2019), autoimmune hemolytic anemia (AIHA) (Bass *et al*, 2014), immune thrombocytopenia (ITP) (Neunert *et al*, 2019), rheumatoid arthritis (RA), Sjogren diseases (SD), and mixed connective tissue disease (MCTD) (Aletaha *et al*, 2010), Hashimoto thyroiditis (HT), and ankylosing spondylitis (AS) (Rudwaleit *et al*, 2011). The usual history-taking and clinical examination procedures were applied to all patients.

Exclusion Criteria:

Patients who are under 18 years old, patients with other commodities especially which cause secondary immune deficiencies like diabetes mellitus, patients with chronic liver or kidney diseases, pregnant females, and patients with any other signs of infections other than parasitic infections.

Laboratory Investigations:

Complete blood count (CBC), aspartate aminotransferases (AST), alanine aminotransferases (ALT), total and direct bilirubin, blood urea nitrogen, creatinine, and lactate dehydrogenase (LDH) are standard blood tests. ESR, ferritin, and CRP are relative biomarkers of infections.

Anti-*Toxoplasma gondii* IgG and IgM Antibodies in the Serum by ELISA Immunoassay:

Simple vacutainer tubes and needles were used aseptically to take the individuals' venous blood, yielding around 2mL. All samples were delivered to Faith Alive Foundation in ice boxes from various healthcare facilities. Prior to analysis, serum was kept at -80°C after being centrifuged at 14000 rpm for 10 minutes. According to the manufacturer's instructions, kits for ELISA tests (Nantong Voyage Medical Co., Ltd., Jiangsu, China) were used to analyze serum samples for IgM and IgG antibodies against *T. gondii*. The approach recommended by the manufacturer was used to compute the cut-off point. A negative response was considered to be an indication that there were no detectable *Toxoplasma* antibodies. A positive *Toxoplasma* IgG/IgM response was considered to be a sign of either a current or prior infection, depending on the case (Nwachukwu *et al*., 2023).

Stool Sample Collection and Process:

Fresh stool samples were taken for examination to check for parasites. About 2 g of fresh feces were collected from each participant after sufficient instruction, clean dry labeled collection containers, and applicator sticks were provided. The following information was collected for each subject at the time of collection: the sample date, the participant's name, age, and sex. The stool sample was transferred to the laboratory after being preserved in 10% formalin. Following the steps outlined in the WHO standards, a 1g sample of each feces was processed and intestinal parasites were identified and detected microscopically utilizing direct wet-mount and formal-ether concentration procedures (WHO, 1992).

Study Outcomes:

The outcomes of this study, which were obtained through evaluating medical records, largely included the following:

Statistical Analysis:

Statistical Package for Social Science (SPSS) (version 20, SPSS Inc., Illinois, Chicago, USA) was used to enter, classify, and analyze data.

Mean and standard deviation were the terms used to describe quantitative data. Comparatively, qualitative data was expressed as numbers and percentages. Chi-squared test was used to compare qualitative variables. Quantitative variables were compared between the four studied groups by analysis of variance (ANOVA test) (for data that are normally distributed) and the Kruskal-Wallis test (for data that are not normally distributed). P-value <0.05 was considered statistically significant.

RESULTS

This study documented a prevalence of intestinal parasites (56.5%) and a prevalence of toxoplasmosis (15.6% positive toxoplasmosis IgM & 35.1% positive toxoplasmosis IgG) **(**Table 1 & Fig. 1**).**

Table 1: Prevalence of intestinal parasites and toxoplasmosis in autoimmune disease patients.

Serum IgM		Serum IgG		Intestinal parasites	
Positive	Negative	Positive	Negative	Positive	Negative
24 (15.6)	130 (84.4)	54 (35.1)	100 (64.9)	87 (56.5)	67 (43.5)
P value		P value		P value	
<0.001		<0.001		<0.001	

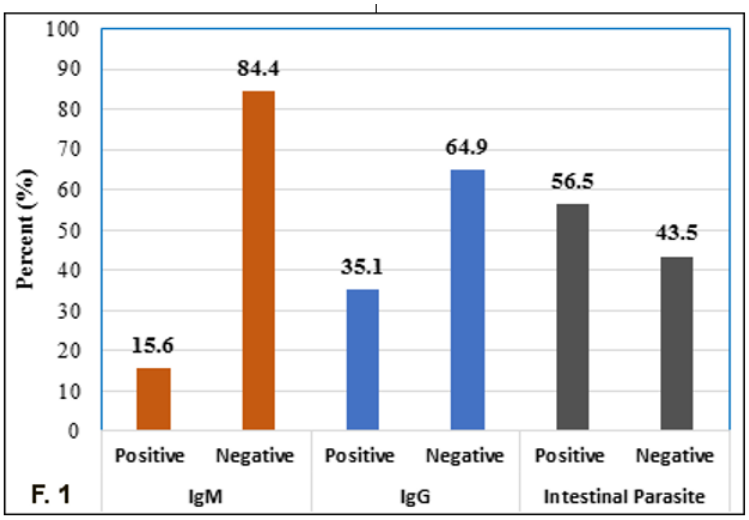

Fig. 1: Intestinal parasites and toxoplasmosis prevalence in autoimmune disease patients.

The positivity of toxoplasmosis IgM among the studied cases with autoimmune disease was significantly related to the female sex, toxoplasmosis IgM positive cases were detected in SLE (37.5%), ITP (20.8%) and Hashimoto thyroiditis (20.8%). Regarding the presenting symptoms, positive cases were presented as 25% recurrent abortion, 20.8% fatigue, 20.8% ecchymosis &, purpura, and 16.7% menorrhagia while in IgM negative, they presented as fatigue 29.2%, bony aches 16.9, arthralgia 15.4% & poly arthritis 10.8%. IgM positive cases showed 20.8% big joint affection and 16.7% both small and big joint affection while IgM negative cases showed 4.6% big joint affection and 26.2% both small and big joint affection. Heart rate was significantly higher in IgM-positive cases. Affected organs were mainly joints, blood, and thyroid in IgM-positive cases meanwhile; in IgG-positive cases, the affected organs were mainly joints and blood, thyroid, lymph nodes, and glands **(**Table 2**)**.

The positivity of IgG was significantly related to the female sex and also showed a higher level of systolic and diastolic blood pressure than IgG negative cases, toxoplasmosis IgG positive cases showed a higher rate of RA while negative cases showed a higher percentage of SLE & ITP. The common presenting symptoms among positive cases were 25.9% poly arthritis, 18.5% fatigue, 18.5% ecchymosis & purpura, and 11.1% recurrent abortion, while in IgG negative, they presented as fatigue 33%, bony aches 17, arthralgia 15% & ecchymosis & Purpura 21%. IgG-positive cases showed 33.3% of big and small joint affection while IgG-negative cases showed 52% small joint affection and 20% of both small and big joint affection. Heart rate was significantly higher in IgG-positive cases. Affected organs were mainly joints and blood (80%) in IgG-positive

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cases meanwhile; in IgG-negative the percentage was 95% **(**Table 2**)**.

Clinical signs and symptoms were generally found to be less severe in autoimmune patients with higher parasite prevalence in the intestine and positive toxoplasmosis IgM and IgG than in people with lower parasite prevalence. According to this, parasite infection may serve as a protective factor and exacerbate the clinical signs of autoimmune illnesses **(**Table 2**)**.

Positive cases of intestinal parasites were significantly related to the females and also showed higher levels of systolic blood pressure than negative cases. Also, the percentage of positive cases was 32.2% ITP but it was 55% SLE in negative cases. Ecchymosis and purpura were of higher rate at 34.5% in intestinal positive cases but fatigue and arthralgia were of higher rate among negative cases. Intestinal positive cases were mainly of no symptoms or small joint affection but in negative cases, they were mainly small joint or both small and big joint affection. The percentage of affected organs intestinal-positive cases was 51.7% blood meanwhile; in intestinal-negative cases, the percentage of joint affection was 85.1% **(**Table 2**)**.

Table 2: Socio-demographic and clinical data in relation to parasitic infection among the studied cases (Total n=154).

		Cases	Serum IgM		P-value	Serum IgG		P-value	Intestinal parasites		P-value
			Positive N=24	Negative N=130		Positive N= 54	Negative N=100		Positive N=87	Negative N=67	
Age	Mean ±SD	32.81±11.4	31.2±6.8	33.1±12.0	0.44	34.8±11.9	31.8±11.0	0.12	33.0±13.4	32.6±8.1	0.85
Sex	Male	40 (26.0)	0 (0.0)	40(30.8)	0.002	0(0.0)	60(60.0)	<0.001	12(13.8)	28(41.8)	<0.001
	Female	114 (74.0)	24(100)	90(69.2)		54(100)	40(40.0)		75(86.2)	39(58.2)	
Marital status	Single	45 (29.2)	0 (0.0)	45(34.6)	<0.001	10(18.5)	35(35.0)	0.005	27(31.0)	18(26.9)	
	Married	89 (57.8)	24(100)	65(50.0)		39(72.2)	50(50.0)		50(57.5)	39(58.2)	
	Widow	10 (6.5)	0 (0.0)	10(7.7)		5(9.3)	5(5.0)		5(5.7)	5(7.5)	
	Divorced	10 (6.5)	0 (0.0)	10(7.7)		0(0.0)	0(0.0)		5(5.7)	5(7.5)	
Weight	Mean ±SD	71.99±13.6	74.0±6.1	71.6±14.6	0.43	70.8±13.4	72.7±13.8	0.41	72.78±13.8	70.8±13.4	0.19
Systole	Mean ±SD	121.9±14.3	126.3±10.6	121.2±14.8	0.11	127.4±20.4	119.0±8.3	<0.001	119.0±8.3	127.4±20.4	0.002
Diastole	Mean ±SD	77.73±12.8	82.1±10.2	76.9±12.4	0.06	80.9±17.1	76.0±8.0	0.02	76.0±8.0	80.9±17.1	0.87
Type of the disease	SLE	51 (33.1)	9(37.5)	42(32.3)	<0.001	10(15.8)	41(41.0)	<0.001	14(16.1)	37(55.2)	<0.001
	ITP	28 (18.2)	5(20.8)	23(17.7)		9(16.7)	19(19.0)		28(32.2)	0(0.0)	
	RA	21 (13.6)	0 (0.0)	21(16.2)		15(27.8)	6(6.0)		10(11.5)	11(16.4)	
	AIHA	19 (12.3)	0 (0.0)	19(14.6)		5(9.3)	14(14.0)		10(11.5)	9(13.4)	
	AS	9 (5.8)	0 (0.0)	9(6.9)		0(0.0)	9(9.0)		5(5.7)	6(6.0)	
	HT	11 (7.1)	5(20.8)	6(4.6)		5(9.3)	6(6.0)		10(10.5)	1(1.5)	
	MCTD	5 (3.2)	0 (0.0)	5(3.8)		0(0.0)	5(5.0)		0(0.0)	5(7.5)	
	S J	5 (3.2)	0 (0.0)	5(3.8)		5(9.3)	0(0.0)		5(5.7)	0(0.0)	
	ITP+SLE	5 (3.2)	5(20.8)	0 (0.0)		5(9.3)	0 (0.0)		5(5.7)	0(0.0)	
Main symptoms	Fatigue	43 (27.9)	5(20.8)	38 (29.2)	<0.001	10(18.5)	33(33.0)	<0.001	20(23.0)	23(34.3)	<0.001
	Bony aches	22 (14.3)	0 (0.0)	22(16.9)		5(9.3)	17(17.0)		12(13.8)	10(14.9)	
	Arthralgia	20 (13.0)	0 (0.0)	20(15.4)		5(9.3)	15(15.0)		5(5.7)	15(22.4)	
	Poly arthritis	18 (1.7)	4 (16.7)	14(10.8)		14(25.9)	4(4.0)		10(11.5)	8(11.9)	
	Ecchymosis & Purpura	31 (20.1)	5(20.8)	26(20.0)		10(18.5)	21(21.0)		30(34.5)	1(1.5)	
	Loss of weight	10 (6.5)	0 (0.0)	10(7.7)		0(0.0)	10(10.0)		0(0.0)	10(14.9)	
	Menorrhagia	4 (2.6)	4(16.7)	0(0.0)		4(7.4)	0(0.0)		4(4.6)	0(0.0)	
	Recurrent abortion	6 (3.9)	6(25.0)	0(0.0)		6(11.1)	0(0.0)		6(6.9)	0(0.0)	
Joint affection	No	38 (24.7)	5(20.8)	33(25.4)	0.04	15(27.8)	23(23.0)	0.02	33(37.9)	5(7.5)	<0.001
	Small joints	67 (43.5)	10(41.7)	57(43.8)		15(27.8)	52(52.0)		29(33.3)	38(56.7)	
	Big joints	11 (7.1)	5(20.8)	6(4.6)		6(11.1)	5(5.0)		11(12.6)	0(0.0)	
	Small & big joints	38 (24.7)	4(16.7)	34(26.2)		18(33.3)	20(20.0)		14(16.1)	24(35.8)	
Temperature	Mean ±SD	37.52±0.43	37.4±0.5	37.6±0.42	0.06	37.5±0.47	37.55±0.41	0.32	37.55±0.41	37.5±0.46	0.19
Heart rate	Mean ±SD	91.27±14.0	101.04±14.0	89.5±13.4	<0.001	96.4±14.9	88.5±12.9	0.001	88.5±12.9	96.4±14.9	0.50
Organs affected	Joints	84 (54.5)	9(37.5)	75(57.7)	0.008	24(44.4)	60(60.0)	0.008	27(31.0)	57(85.1)	<0.001
	Blood	55 (35.7)	10(41.7)	45(34.6)		20(37.0)	35(35.0)		45(51.7)	10(14.9)	
	Thyroid	10 (6.5)	5(20.8)	5(3.8)		5(9.3)	5(5.0)		10(11.5)	0(0.0)	
	Lymph nodes & glands	5 (3.2)	0(0.0)	5(3.8)		5(9.3)	0(0.0)		5(5.7)	0(0.0)	

SD = Standard deviation

Higher eosinophils, RBCs, hemoglobin, hematocrit, LDH, ferritin, and ESR values were detected in IgM-positive patients, whereas decreased MCV, platelets, and ALT values were found. IgM-positive subjects had higher intestinal parasite rates on stool analysis, as well as higher RBC and albuminuria rates on urine analysis (Table 3**)**.

IgG-positive patients had greater rates of RBCs and albuminuria on urine examination, as well as higher rates of

eosinophils, LDH, ferritin, CRP, and ESR, but had lower levels of ALT. They also had higher rates of intestinal parasite affection (Table 3).

Positive cases of intestinal parasites exhibited greater levels of WBCs, eosinophils, hemoglobin, and hematocrit and indicated lower levels of CRP, ALT, and AST, whereas negative cases showed higher rates of RBCs in urine and albuminuria as well as higher rates of splenomegaly and hepatosplenomegaly (Table 3).

Table 3: Laboratory investigations in relation to parasitic infection among the studied cases.

		Serum IgM		P-value	Serum IgG		P-value	Intestinal parasites		P-value
		Positive N=24	Negative N=130		Positive N= 54	Negative N=100		Positive N=87	Negative N=67	
WBCs	Mean ±SD	7.62±3.59	5.97±3.25	0.10	6.62±3.57	6.02±3.21	0.37	7.25±3.65	4.94±2.38	<0.001
Eosinophils	Mean ±SD	393.3±105.8	292.7±128.6	<0.001	366.5±101.2	277.0±133.8	<0.001	383.7±109.3	213.1±84.1	<0.001
RBCs	Mean ±SD	4.15±0.30	3.76±0.80	<0.001	3.94±0.40	3.77±0.89	0.10	3.93±0.83	3.69±0.64	0.05
Hb	Mean ±SD	11.15±0.88	9.85±2.30	<0.001	10.4±1.3	9.9±2.5	0.09	10.47±2.56	9.52±1.46	0.004
HCT	Mean ±SD	35.25±2.0	31.54±7.66	<0.001	33.5±5.2	31.4±8.0	0.04	33.24±8.20	30.69±5.42	0.02
MCV	Mean ±SD	74.0±4.42	76.85±7.71	0.02	78.4±7.8	75.3±6.9	0.01	75.49±7.94	77.56±6.73	0.08
RDW	Mean ±SD	13.97±0.45	14.62±1.70	0.07	14.6±2.1	14.5±1.2	0.70	14.60±1.85	14.43±1.18	0.52
Platelets	Mean ±SD	112.6±87.67	158.04±59.7	0.02	142.7±83.1	155.4±55.7	0.15	130.8±78.71	176.5±33.0	<0.001
LDH	Mean ±SD	480.8±99.5	297.7±226.3	<0.001	387.8±186.6	293.0±232.6	<0.001	299.4±169.9	360.1±271.1	0.45
Ferritin	Mean ±SD	215.0±93.6	185.8±354.7	<0.001	332.0±420.1	113.9±234.2	<0.001	216.0±363.9	158.0±275.0	0.57
CRP	Mean ±SD	7.67±2.41	9.08±4.46	0.15	9.7±3.7	8.4±4.4	0.01	7.97±3.57	9.97±4.74	0.003
ESR	Mean ±SD	105.42±7.79	84.62±19.88	<0.001	102.4±8.5	80.0±20.0	<0.001	86.39±21.41	89.71±18.0	0.30
Urea	Mean ±SD	28.79±6.16	26.12±6.27	0.06	28.5±8.5	25.5±4.8	0.02	26.21±7.58	26.94±4.77	0.47
Creatinine	Mean ±SD	0.88±0.10	0.84±0.22	0.37	0.89±0.22	0.83±0.19	0.05	0.81±0.23	0.89±0.15	0.01
ALT	Mean ±SD	26.88±3.17	30.19±5.69	0.006	28.6±3.9	30.6±6.0	0.002	27.69±3.88	32.19±6.21	<0.001
AST	Mean ±SD	29.75±2.97	32.92±8.31	0.07	31.0±6.7	33.2±8.3	0.10	31.05±8.51	34.17±6.44	0.01
Albumin	Mean ±SD	3.90±0.21	3.79±0.27	0.06	3.8±0.2.31	3.81±0.23	0.95	3.82±0.31	3.80±0.19	0.55
PT	Mean ±SD	12.40±0.39	12.25±0.42	0.12	12.36±0.44	12.23±0.40	0.06	12.35±0.45	12.17±0.36	0.009
Stool analysis	Negative	4 (16.7)	39 (30.0)		4 (7.4)	39 (39.0)		43 (63.2)	0 (0.0)	
	Enterobius vermicularis	0 (0.0)	40 (30.8)	<0.001	15 (27.8)	25 (25.0)	<0.001	0 (0.0)	40 (46.5)	
	Amoebiasis	10 (41.7)	16 (12.3)		20 (37.0)	6 (6.0)		0 (0.0)	26 (30.2)	<0.001
	Giardia	10 (41.7)	5 (3.8)		10 (18.5)	5 (5.0)		0 (0.0)	15 (17.4)	
	Ascaris	0 (0.0)	5 (3.8)		0 (0.0)	5 (5.0)		0 (0.0)	5 (5.8)	
Urine analysis	Negative	5 (20.8)	110 (84.6)		20 (37.0)	95 (95.0)		59 (86.8)	56 (65.1)	
	Pus cells (8 – 12)	0 (0.0)	5 (3.8)	<0.001	5 (9.3)	0 (0.0)	<0.001	0 (0.0)	5 (5.8)	0.01
	RBCs (>100)	14 (58.3)	0 (0.0)		14 (25.9)	0 (0.0)		4 (5.9)	10 (11.6)	
	Albuminuria	5 (20.8)	15 (11.5)		15 (27.8)	5 (5.0)		5 (7.4)	15 (17.4)	
Abdominal US	Negative	10 (41.7)	50 (38.5)		25 (26.3)	35 (35.0)		29 (42.6)	31 (36.0)	
	Splenomegaly	5 (20.8)	30 (23.1)	0.95	10 (18.5)	25 (25.0)	0.37	5 (7.4)	30 (34.9)	<0.001
	HSM	9 (37.5)	50 (38.5)		19 (35.21	40 (40.0)		34 (50.0)	25 (29.1)	

SD = Standard deviation

Intestinal parasites were present in 100% of ITP patients while presented in 52.6% of AIHA patients, and 47.6% in RA patients. According to the type of parasite, *Enterobius vermicularis* was present mainly in ITP patients followed by AIHA patients, amoebiasis was present mainly in RA followed by SLE & AIHA patients, *Giardia lamblia* was present in SLE & ITP patients and finally *Ascaris lumbricoides* was existed in ITP patients only. RA & AIHA patients were 100% toxoplasmosis IgM positive, while toxoplasmosis IgG was mainly presented in SLE (80.4%) and in AIHA patients (73.7%) **(**Table 4**)**.

Table 4: Intestinal Parasites and toxoplasmosis infection in relation to the type of autoimmune disease among the studied groups.

		cases N = 154	Type of Disease				P-value
			SLE N = 51	ITP N = 28	RA N = 21	AIHA N = 19	
Intestinal parasite	Positive	86 (55.8)	13 (25.5)	28 (100)	10 (47.6)	10 (52.6)	<0.001
	Negative	68 (44.2)	38 (74.5)	0 (0.0)	11 (52.4)	9 (47.4)	
Type of intestinal parasite	*E. vermicularis*	40 (26.0)	2(3.9)	18 (64.3)	0(0.0)	5(26.3)	
	Amoebiasis	26 (16.9)	6(11.8)	0(0.0)	10(47.6)	5(26.3)	
	Giardia lamblia	15 (9.7)	5(9.8)	5 (17.9)	0(0.0)	0(0.0)	<0.001
	A.lumbricoides	5 (3.2)	0(0.0)	5 (17.9)	0(0.0)	0(0.0)	
Toxoplasmosis IgM	Positive	24 (15.6)	42 (82.4)	23 (82.1)	21 (100)	19 (100)	0.045
	Negative	130 (84.4)	9 (17.6)	5 (17.9)	0 (0.0)	0 (0.0)	
Toxoplasmosis IgG	Positive	54 (35.1)	41 (80.4)	19 (67.9)	6 (28.6)	14 (73.7)	<0.001
	Negative	100 (64.9)	10 (19.6)	9 (32.1)	15 (17.4)	5 (26.3)	

ITP & RA cases were 100%, female patients. SLE & AIHA patients had significantly higher weight. The age of the patients also varied greatly, being greater in RA & AIHA patients. In RA patients, both systolic and diastolic blood pressure were greater. Patients with RA and SLE had higher body temperatures, and those with AIHA had tachycardia as well (Table 5**)**.

Table 5: Socio-demographic and clinical data in relation to the type of autoimmune disease among cases.

		Type of Disease				P-value
		SLE N = 51	ITP N = 28	RA N = 21	AIHA N = 19	
Age	Mean ±SD	26.9±7.3	26.2±7.2	42.6±15.0	40.6±2.7	<0.001
Sex	Male	20(39.2)	0(0.0)	0(0.0)	5(26.3)	
	Female	31(60.8)	28(100)	21(100)	14(73.7)	<0.001
Marital status	Single	25(49.0)	5(17.9)	5(23.8)	0(0.0)	
	Married	26(51.0)	23(82.1)	5(23.8)	10(52.6)	<0.001
	Widow	0(0.0)	0(0.0)	10(47.6)	0(0.0)	
	Divorced	0(0.0)	0(0.0)	1(4.8)	9(47.4)	
Weight	Mean ±SD	73.5±12.8	60.7±5.1	67.5±16.6	85.1±9.0	<0.001
Systole	Mean ±SD	117.8±9.2	116.8±13.9	139.0±23.9	122.6±4.5	<0.001
Diastole	Mean ±SD	77.5±9.1	66.8±7.7	94.3±15.3	77.4±4.5	<0.001
Main Symptoms	Fatigue	10(19.6)	0(0.0)	1(4.8)	18 (94.7)	
	Bony aches	10 (19.6)	0(0.0)	0(0.0)	1(5.3)	<0.001
	Arthralgia	10(19.6)	0(0.0)	5(23.8)	0(0.0)	
	Poly arthritis	4(7.8)	0(0.0)	14(66.7)	0(0.0)	
	Ecchymosis &	2(3.9)	28(100)	1 (4.8)	0(0.0)	
	Purpura	10(19.6)	0(0.0)	0(0.0)	0(0.0)	
	Loss of weight	0(0.0)	0(0.0)	0(0.0)	0(0.0)	
	Menorrhagia	5 (9.8)	0(0.0)	0(0.0)	0(0.0)	
	Recurrent abortion					
Joint affection	No	2 (3.9)	21(75.0)	1(4.8)	14(73.7)	
	Small joints	45(88.2)	7(25.0)	0(0.0)	5(26.3)	
	Big joints	0(0.0)	0(0.0)	1(4.8)	0(0.0)	<0.001
	Small & big joints	4 (7.8)	0(0.0)	19(90.5)	(0.0)	
Temperature	Mean ±SD	37.7±0.32	37.3±0.4	38.0±0.2	37.1±0.2	<0.001
Heart rate	Mean ±SD	87.1±10.7	88.5±7.9	95.2±9.6	108.7±2.3	<0.001
Organs affected	Joints	49(96.1)	0(0.0)	20(95.2)	0(0.0)	
	Blood	2(3.9)	28(100)	1 (4.8)	19(100)	<0.001
	Thyroid	0(0.0)	0(0.0)	0(0.0)	0(0.0)	
	Lymph nodes & glands	0(0.0)	0(0.0)	0(0.0)	0(0.0)	

SD = Standard deviation

SLE and ITP patients had the lowest white blood cell counts, respectively. In SLE cases, followed by RA cases, eosinophils likewise had the lowest value. In AIHA cases, the lowest levels of RBCs, Hb, and HCT were found, whereas ITP cases had the highest levels of platelets. The LDH value was highest in AIHA cases and lowest in ITP cases. RA patients had the highest levels of CRP and ESR, respectively. Splenomegaly was discovered by abdominal ultrasound in 82.1% of ITB cases, 66.7% of SLE cases, and 47.4% of AIHA patients **(**Table 6**)**.

Table 6: Lab investigations in relation to the type of autoimmune disease among the patients.

		Type of the Autoimmune Disease				
		SLE N = 51	ITP N = 28	RA N = 21	AIHA N = 19	P-value
WBCs	**Mean ±SD**	**4.48±2.68**	**5.80±2.7**	**7.7±4.0**	**6.9±2.6**	**<0.001**
Eosinophils	**Mean ±SD**	**233.7±138.4**	**452.5±68.1**	**299.0±73.3**	**316.8±76.1**	**<0.001**
RBCs	**Mean ±SD**	**3.9±0.53**	**3.95±0.38**	**3.88±0.41**	**2.57±0.47**	**<0.001**
Hb	**Mean ±SD**	**9.95±1.07**	**10.11±1.19**	**10.27±1.13**	**6.76±1.19**	**<0.001**
HCT	**Mean ±SD**	**32.0±5.26**	**32.89±4.27**	**32.48±4.5**	**20.68±5.18**	**<0.001**
MCV	**Mean ±SD**	**74.92±6.81**	**76.79±4.13**	**81.33±7.93**	**78.26±11.84**	**0.01**
RDW	**Mean ±SD**	**14.50±1.35**	**14.14±0.71**	**13.69±0.72**	**16.84±2.59**	**<0.001**
Platelets	**Mean ±SD**	**152.3±54.9**	**69.9±15.5**	**156.33±21.0**	**165.4±20.0**	**<0.001**
LDH	**Mean ±SD**	**273.7±123.2**	**254.6±112.0**	**320.5±218.3**	**637.9±368.6**	**0.005**
Ferritin	**Mean ±SD**	**77.50±69.1**	**82.8±114.2**	**318.1±499.5**	**371.6±495.1**	**0.09**
CRP	**Mean ±SD**	**8.0±2.7**	**5.9±2.1**	**16.3±5.1**	**7.8±2.4**	**<0.001**
ESR	**Mean ±SD**	**84.7±19.0**	**71.8±19.8**	**101.0±8.3**	**101.6±10.7**	**<0.001**
Urea	**Mean ±SD**	**28.0±5.1**	**23.6±4.0**	**32.0±10.1**	**21.5±1.6**	**<0.001**
Creatinine	**Mean ±SD**	**0.85±0.16**	**0.39±0.20**	**1.08±0.19**	**0.75±0.16**	**<0.001**
ALT	**Mean ±SD**	**30.3±2.6**	**27.6±3.3**	**29.6±2.7**	**30.9±9.8**	**0.05**
AST	**Mean ±SD**	**33.3±6.5**	**25.3±5.5**	**30.7±7.7**	**42.1±5.0**	**<0.001**
Albumin	**Mean ±SD**	**3.8±0.19**	**3.8±0.27**	**3.7±0.41**	**3.7±0.17**	**0.08**
PT	**Mean ±SD**	**12.2±0.35**	**12.7±0.48**	**12.5±0.51**	**12.0±0.0**	**<0.001**
Stool analysis						
Negative		**33 (64.7)**	**0(0.0)**	**0(0.0)**	**5(26.3)**	
Enterobius		**2(3.9)**	**18 (64.3)**	**0(0.0)**	**5(26.3)**	
Amoebiasis		**6(11.8)**	**0(0.0)**	**10(47.6)**	**5(26.3)**	
Giardia		**5(9.8)**	**5 (17.9)**	**0(0.0)**	**0(0.0)**	
Ascaris		**0(0.0)**	**5 (17.9)**	**0(0.0)**	**0(0.0)**	**<0.001**
Urine analysis						
Negative		**42(82.4)**	**23(82.1)**	**11(52.4)**	**14 (73.7)**	
Pus cells (8 – 12)		**0(0.0)**	**0(0.0)**	**0(0.0)**	**5(26.3)**	**<0.001**
RBCs (>100)		**9(17.6)**	**0(0.0)**	**0(0.0)**	**0(0.0)**	
Albuminuria		**0(0.0)**	**5(17.9)**	**10(47.6)**	**0(0.0)**	
Abdominal US						
Negative		**15(49.4)**	**5(17.9)**	**15(71.4)**	**5(26.3)**	
Splenomegaly		**2(3.9)**	**23(82.1)**	**0(0.0)**	**5(26.3)**	**<0.001**
HSM		**34(66.7)**	**0(0.0)**	**6(28.6)**	**9(47.4)**	

SD = Standard deviation

DISCUSSION

Immunologists and parasitologists are now and urgently studying the consequences of parasitic infections on the immune system. Many parasitic worms have a tendency to suppress the host's immune response, which permits them to ameliorate some conditions while aggravating others *(*Bashir *et al.*, 2002).

In order to demonstrate the prevalence and effects of intestinal parasitic infections on patients with autoimmune diseases, the current study was carried out.

The present study documented a high prevalence of intestinal parasites and high seroprevalence of toxoplasmosis IgM and IgG in the studied cases of autoimmune disorders. Also, the positivity of toxoplasmosis IgM among cases with autoimmune disease was significantly related to the female sex. Toxoplasmosis IgM-positive cases were detected in SLE, ITP, and HT. Also, the positivity of IgG was significantly related to the female sex and showed a higher percentage in RA patients.

According to Osada and Kanazawa (Osada and Kanazawa, 2010), helminths mostly induce T-helper Type 2 (Th2) cells while reducing T-helper Type 1 (Th1) cells. This theory would only clarify how parasitic worms regulate autoimmune disorders brought on by Th1 cells (Rook, *2008*). Some parasite illnesses reportedly have an anti-inflammatory response. Previous research has demonstrated that helminths like *Necator americans* and *Trichuris suis* can reduce the symptoms of inflammatory bowel diseases such as Crohn's disease and ulcerative colitis (Varyani *et al*., 2017).

Due to the Th2-based immune response they produce; parasitic worms commonly impair the immune system's ability to respond to a vaccine effectively.

This makes the immune system less susceptible to antigens than usual. This is a severe problem in underdeveloped nations where parasitic worms and the need for vaccinations are common *(*Kamal and Khalifa, 2006).

Numerous parasites have the ability to regulate their own immune responses by driving the production of regulatory genes including the suppressor of cytokine signaling (SOCS) gene and immunosuppressive cytokines like IL-4 and IL-10. In another way, they can also hinder the activity of sensitive T-cells that are stimulated by autoimmune conditions including diabetes, arthritis, encephalomyelitis, and multiple sclerosis (MS) (Dhingra *et al*., 2013).

It was revealed that helminths, particularly nematodes and flatworms, viruses, and bacteria can alter the effect of autoimmune illnesses due to their immunosuppressive activity, which is in line with certain recent findings (Saunders *et al*., 2007; Sfriso *et al*., 2010; He *et al*., 2010; Akdis *et al*., 2011).

In the current study, the positivity of toxoplasmosis IgM among cases with autoimmune disease was significantly related to the female sex. Also, positive cases were clinically presented with recurrent abortion, fatigue, ecchymosis, purpura, and menorrhagia. Affected organs were mainly joint, blood, and thyroid in IgM-positive cases. Regarding the positivity of IgG, it was significantly related to the female sex and also showed higher levels of systolic and diastolic blood pressure. In toxoplasmosis IgG-positive cases, the common presenting symptoms were polyarthritis, fatigue, ecchymosis, purpura, and recurrent abortion.

A similar study revealed that 49.2% of the patients had cerebral toxoplasmosis and 50.9% of the cases were attributed to reactivation. The highest prevalence associated with autoimmune disease was rheumatoid arthritis (28%) (Durieux *et al*., 2022).

Population-based case-control research for *Toxoplasma gondii* and multiple sclerosis was conducted, and it documented a seroprevalence of anti-*T. gondii* antibodies in 29.5% and 66.7% of the cases. It was hypothesized that *Toxoplasma gondii* and MS had a negative correlation, indicating that this parasite may have a protective function (Nicoletti *et al*., 2020).

By studying the prevalence of CNS toxoplasmosis in individuals with autoimmune disorders, immunocompetent people, and immunocompromised patients, it was discovered that patients with autoimmune diseases have clinical indices of brain toxoplasmosis more frequently than immunocompromised patients (Graham *et al.*, 2021).

Studying the seroprevalence of *Toxoplasma gondii* infection in patients with arthritis in Eastern China in 2017 as a result showed that the prevalence of anti-*Toxoplasma gondii* IgG was significantly higher in patients with arthritis (18.8%) compared to healthy controls. Patients with rheumatoid arthritis had the greatest infection seropositivity, which was subsequently followed by reactive arthritis, osteoarthritis, infectious arthritis, and gouty arthritis (Tian *et al*., 2017).

Furthermore, it was demonstrated that *T. gondii* infection improves experimental autoimmune encephalomyelitis because it modifies the immune response to enhance brain expression suppressor of cytokine signaling (SOCS3) and IL-27. This finding was in line with a prior study (Ham *et al*., 2021).

According to the type of parasites, all ITP patients had intestinal parasites, followed by AIHA patients and RA patients. ITP patients were more likely to have *Enterobius vermicularis* than AIHA patients, RA patients were more likely to have amoebiasis than SLE or AIHA patients, ITP patients were more likely to have giardiasis than AIHA patients, and ITP patients were more likely to have *Ascaris lumbricoides* than AIHA patients. Toxoplasmosis IgM was detected in all RA

and AIHA patients. Although toxoplasmosis IgG was more common in SLE and AIHA patients.

Helminth infection consistently strengthens the immune system, reducing the impact of rheumatoid arthritis. As a result, parasitic helminths can be employed to treat rheumatoid arthritis. Additionally, it is advised that more research be done to make use of these helminth species' immunological qualities and that helminth organisms be considered symbiotic organisms rather than parasites (Ike *et al*., 2020).

According to a former study, through immunomodulation, parasites such *Hymenolepis microstoma*, TPC and ES-62 from *Acanthocheilonema viteae*, *Plasmodium chabaudi*, *Schistosoma mansoni*, and *Toxoplasma gondii* benefit lupus-prone animals with SLE (Jafari *et al*., 2021).

Similarly, employed mouse models were used to examine the impact of a parasite-derived 68-mer peptide on type 1 diabetes and multiple sclerosis, two autoimmune diseases. It was discovered that this parasite with peptide origins can improve various autoimmune conditions (Lund *et al*., 2016). Demonstrated malarial infection in mice decreased pathogenic leukocyte infiltration but had no effect on the autoimmune inflammation of glomeruli, corroborating this finding (Bolland *et al.*, 2018).

Interestingly, one research suggested that cDC2s generated by CCL17 play a crucial role in systemic lupus erythematosus's end-stage lupus nephritis and are inhibited by a parasite infection. Malaria parasite infection did not alter the lupus-causing autoimmune processes, but it did prevent end-stage tissue damage in the kidney and draining lymph nodes (Amo *et al*., 2021).

A prevalence study was carried out in agreement with the current study to detect the frequency of intestinal parasites found in autoimmune illnesses. *Cryptosporidium* (48.0%) was the parasite with the highest prevalence, and it was followed by *C. cayetanensis* (32%), *G. lamblia* (24%), *B. hominis* (20%), and *E. histolytica* (8%). There were 4% for each of *Schistosoma mansoni*, *Microsporidia*, *S. stercoralis*, and *A. lumbricoides* (Hussein *et al.*, 2019).

In a corresponding study for the relationship between intestinal parasites and inflammatory bowel disease (IBD), it was found that *Blastocystis* species, *Entamoeba histolytica* and *Cryptosporidium* species were the most common intestinal parasites in IBD patients compared to healthy controls (Kamal *et al*., 2022).

Conclusion

Numerous autoimmune disorders patients, including those with SLE, ITP, RA, and AIHA, typically had high prevalence rates of toxoplasmosis and intestinal parasites, which changed the clinical course and investigatory indicators of these illnesses. Therefore, more research may be indicated to determine the primary mechanisms by which those parasites might alter the course of several autoimmune illnesses.

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Author contribution

Conceptualization: Salwa Oshiba, Yahya Naguib, Alaa Efat, and Reda Ibrahem. Collection of data, laboratory (blood, stool & urine examination), and radiological investigations (abdominal ultrasound): Alaa Efat, Salwa Oshiba, and Yahya Naguib. Statistical analysis and tabulation of data: Reda Ibrahem. Paper writing and critical revision: Salwa Oshiba, Alaa Efat, Reda Ibrahem, and Yahya Naguib. The final manuscript was reviewed and approved by all authors.

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Corresponding author can provide the data sets used and/or analyzed during the current study upon reasonable request.

Declarations

Competing Interests:

The authors declare no competing interests.

Conflict of Interest:

No authors have disclosed any competing interests. No author is affiliated with any businesses or other organizations that may create a conflict of interest.

Ethics Approval:

This study was carried out in accordance with the guidelines established by the Menoufia University Faculty of Medicine Ethical Scientific Committee (IRB: 12-2022 PARA20). Volunteers made up the entire group. After explaining the purpose of the study, informed written consent was obtained from every patient or family (if the patient was unable to give informed consent or write one).

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