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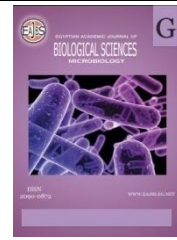
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**Investigation of the Association between COVID 19 Infection, Gastrointestinal Manifestations, Parasitic Diseases and Antiparasitic Treatment:
An Electronic Data Compilation**

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ABSTRACT

Background: COVID 19 pandemic has posed great challenges to national and international health organizations. This health burden is exaggerated in middle and low-income countries, due to the endemicity of parasitic diseases. Pre-existing parasitic infections and antiparasite drug therapy may modify the host's immune response to infection with SARS-CoV-2 and can attenuate the severity of disease presentation. **Methods:** A cross-sectional analytical study was done to investigate the possible association between COVID-19 syndrome, gastrointestinal manifestations, parasitic diseases and antiparasitic treatment. A non-probability convenient sampling technique was used to recruit participants, through electronic data collection. **Results:** The mean age of the survey respondents reporting a positive history of COVID 19 infection was 35.69±12.24 years. Study participants with a positive COVID 19 history have reported a positive history of gastrointestinal disorders in 40.9% of 93 patients responding to that question. Twenty-six out of 95 (27.4%) participants reporting a positive history of COVID 19 also reported a previous history of parasitic infection, while 22 (15.6%) subjects out of 141 individuals with a negative history of COVID 19 infection had a past experience of parasitic infection (P=0.028) Among the parasitic infections stated was amoebiasis, giardiasis and enterobiasis. **Conclusions:** The higher incidence recorded of parasitic infections among subjects with a positive history of COVID-19 suggests that parasite co-infection may lead predispose to a high incidence of COVID-19, which conflicts with other literature data reporting a protective effect of parasitosis against SARS CoV-2 infection. More extensive survey studies targeting larger populations are of crucial importance, especially in developing countries.

INTRODUCTION

Viral infections are important causative agents of epidemics and pandemics that have burdened humanity throughout history. Viral agents causing such health burdens include coronaviruses, such as the severe acute respiratory syndrome coronavirus (SARS-CoV), the Middle East respiratory syndrome coronavirus (MERS-CoV) and most recently, the SARS CoV-2 virus (Piret and Biovin, 2021). The most recent of these pandemics is the coronavirus disease of 2019 (COVID 19) caused by the SARS CoV-2 virus. Despite the various vaccination campaigns, COVID 19 continues to challenge national and international health organizations. Rapid research and investigation strategies are required to keep pace with the rapid spread of this pandemic. Survey studies are valuable research tools that can provide rapid information over a wide base of respondents with different backgrounds (Geldsetzer 2020).

The SARS CoV-2 virus enters epithelial cells by binding to the angiotensin-converting enzyme-2 (ACE-2) receptor. Viral entry and fusion with the host cell membrane are facilitated by the transmembrane serine protease (TMPRSS2). This enzyme serves to cleave the viral S protein, allowing the virus to release its fusion peptide. In addition to the respiratory tract, expression sites of both ACE-2 receptors and TMPRSS2 include the esophagus and the enterocytes of the small and large intestine, which renders the gastrointestinal tract (GI) a target for SARS CoV-2 entry (Zhang *et al.*, 2020).

One of the challenges of COVID 19 is the diversity of clinical manifestations, since it may present with a variety of GI symptoms such as diarrhea, nausea, vomiting and gustatory dysfunction (Han *et al.*, 2020; Tong *et al.*, 2020). Fecal shedding of the SARS CoV-2 virus has been reported to persist even after respiratory tract samples became negative

(Parasa *et al.*, 2020) GI symptoms among COVID-19 patients could be attributed either to the direct binding of the virus to the ACE-2 receptors present in the intestinal epithelial cells (Hunt *et al.*, 2021), or to the association of SARS COV-2 infection with other GI conditions, such as parasitic infections (Hillyer, 2020). Chronic and/or persistent parasitic infections are common in low and medium-income countries (LIMCs). Such chronic infections were shown to alter the clinical outcomes to other infections possibly by modulating the host's immunity. Hence, pre-existing parasitic infections may also impact the host's immune response to infection with SARS-CoV-2, which could result in beneficial and detrimental effects (Woldaya *et al.*, 2021).

Antiparasitic drugs such as chloroquine and ivermectin have been included in various anti-COVID drug regimens. However, till now there is no clinical evidence that any therapy possesses prospective outcomes in suspected or confirmed COVID-19 patients. There are more than 300 clinical treatment and prophylactic trials underway (Caly., *et al.*, 2020).

Our study aimed to investigate the possible association between the COVID-19 manifestations and management, gastrointestinal manifestations (GI) and parasitic infections in Middle Eastern countries, particularly Egypt.

The present study aimed at exploring the prevalence of COVID 19 among the study participants and the possible association with GI manifestations, with special reference to parasitic diseases and anti-parasitic drugs.

MATERIALS AND METHODS

1-Study Type:

A cross-sectional analytical study was done to investigate the possible association between COVID-19 syndrome, gastrointestinal manifestations severity, frequency, and parasitic diseases. The study

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was conducted during the period from November 2020 till May 2021.

2-Sample Size and Technique:

A purposive sample of 236 participants was targeted mainly through electronic data collection. The sample size was estimated based on evidence from a previous study assessing the percentage of gastrointestinal manifestations among COVID-19 syndrome patients, and by reviewing the results of other studies (Tharwat Sulaiman *et al.*), Epi-calc 2000 (version 1.01) was used to calculate the sample size of this study. Assuming 80% power, 0.05 level of significance, an estimated proportion of 23.6 %, the sample size was estimated to be 150 participants. After adding a non-response rate of 40% for online surveys, so the estimated sample size was 210, but the final sample included 236 participants.

3-Ethical approval and consent to participate approved by:

- 1-The Research Ethics Committee of Faculty of Pharmacy, Modern University for Technology and Information, Egypt approval number CS884
- 2- Family Medicine Department Council, Faculty of Medicine, Cairo University.

4-Study Population and Setting:

The study was conducted on all people willing to participate in this study (1 to 70 years) from different Egyptian Governorates. Surveys from children were filled by their guardians after consenting to their participation.

5-Inclusion Criteria:

All persons, who could access the internet and who approved participating in the study, were recruited.

6-Exclusion Criteria:

Persons who refused to participate in this study or couldn't access the internet or could not complete the questionnaire were excluded.

7-Data Collection Tool:

A self-administered structured questionnaire composed of 60 questions was designed. Questions were presented in

the Arabic language. Content and face validity was checked by the authors. An online data collection method was used in line with lockdown measures conducted in Egypt and neighboring countries to achieve social distancing. A Google form was created, and participants were requested to complete and submit it. A questionnaire link was shared with groups on social media forums (Facebook, Twitter, and WhatsApp). Furthermore, the authors shared the link personally in their network areas.

The questionnaire enclosed the following items (I) Demographic characters. (II) Medical history for covid-19 if present. (III) History of GI manifestations. (IV) History of respiratory symptoms and finally (V) History of parasitic diseases. Original google form link https://docs.google.com/forms/d/e/1FAIpQLSc-_HkIcSJiqSkPKJlqvjV_QP2bXbI3-W70aiL-7CKXu8GUVw/viewform?usp=sf_link.

8-Ethical Consideration:

The objectives of the study were explained to the participants (by a statement before the initiation of the online survey) and they were completely free to accept or refuse. Participants who refused were excluded from the study results and online consent was taken from those who accepted to participate. Strict confidentiality about participants' personal data (this was secured by the questionnaire being anonymous) was maintained throughout data collection, entry and analysis (according to the Helsinki declaration, and approved by the Research Ethics Committee at the Faculty of Pharmacy, Modern University for Technology and Information, Egypt and Family Medicine Department Council, Faculty of Medicine, Cairo University.

9-Data Analysis:

The data were coded and exported on a data sheet prepared on Microsoft Excel program, version 2013. The statistical package for social science (SPSS) version 24 was used for data analysis. Simple

descriptive statistics were used for the summary of quantitative data and frequencies used for qualitative data. The bivariate relationship was displayed in cross-tabulations, and a comparison of proportions was performed using the chi-square and Fisher's exact tests where appropriate. Independent T-test and one-way ANOVA were used to compare normally distributed quantitative data. The level of significance was set at probability P-value <0.05.

RESULTS

Personal History:

The mean age of the survey respondents reporting a positive history of COVID 19 infection was 35.69 ± 12.24 years, the minimum age being 1 year and the maximum being 70 years. Five individuals were under 18 years of age (5.3%), 71 individuals were between the ages of 18 and 40 years (74.7%), 14 persons were in the age group between 41 and 60 years (14.7%), and 5 persons were above 60 years of age (5.3%). The mean age among COVID 19 negative subjects was 35.27 ± 14.25 years. No significant

difference was found between the two age groups ($P=0.812$).

There were 134 females (57%) and 102 males (43%) among the 236 subjects responding to the current questionnaire. Among the respondents, 161 were married (68.2%), 67 were single (28.4%), 7 were divorced (3.0%), and 1 person was a widower (0.4%).

As for the employment status, 174 were employed (74%), while 62 were unemployed (26%) (Fig. 1 & Tab.1).

The majority of study participant were of Egyptian nationality ($n = 197$, 83.47%). The study also included persons from Saudi Arabia ($n = 33$, 13.98%), Yemen ($n = 2$, 0.85%), Kuwait ($n = 2$, 0.85%), Eriteria ($n = 1$, 0.42%) and Syria ($n = 1$, 0.42%).

Among the study subjects, 95 (40.25%) have reported a positive history of COVID 19 infection. Among these 95 participants, 10 (10.53%) have reported having contracted repeated infections. History of contact with a COVID 19 case was reported by 35 (38.5%) out of 91 persons, while 4 persons did not respond to that question.

Table 1: Personal data of the study subjects in relation to the presence or absence of a history of COVID-19 infection.

		Have you had the corona virus?						P-value
		Yes		No		Total		
		Count	Row N %	Count	Row N %	Count	Row N %	
Sex	Male	41	40.2%	61	59.8%	102	100.0%	0.987
	Female	54	40.3%	80	59.7%	134	100.0%	
Marital status	Single	18	26.9%	49	73.1%	67	100.0%	0.027*
	Married	75	46.6%	86	53.4%	161	100.0%	
	Divorced	1	16.7%	5	83.3%	6	100.0%	
	Widow	1	50.0%	1	50.0%	2	100.0%	
Do you work?	Yes	74	42.5%	100	57.5%	174	100.0%	0.233
	No	21	33.9%	41	66.1%	62	100.0%	
Have you traveled recently?	Yes	8	26.7%	22	73.3%	30	100.0%	0.104
	No	87	42.2%	119	57.8%	206	100.0%	
History of smoking	Yes	17	58.6%	12	41.4%	29	100.0%	0.086
	No	77	37.9%	126	62.1%	203	100.0%	
	Ex-smoker	1	25.0%	3	75.0%	4	100.0%	

*Significance at $P < 0.05$; Statistical tests performed: chi-square test

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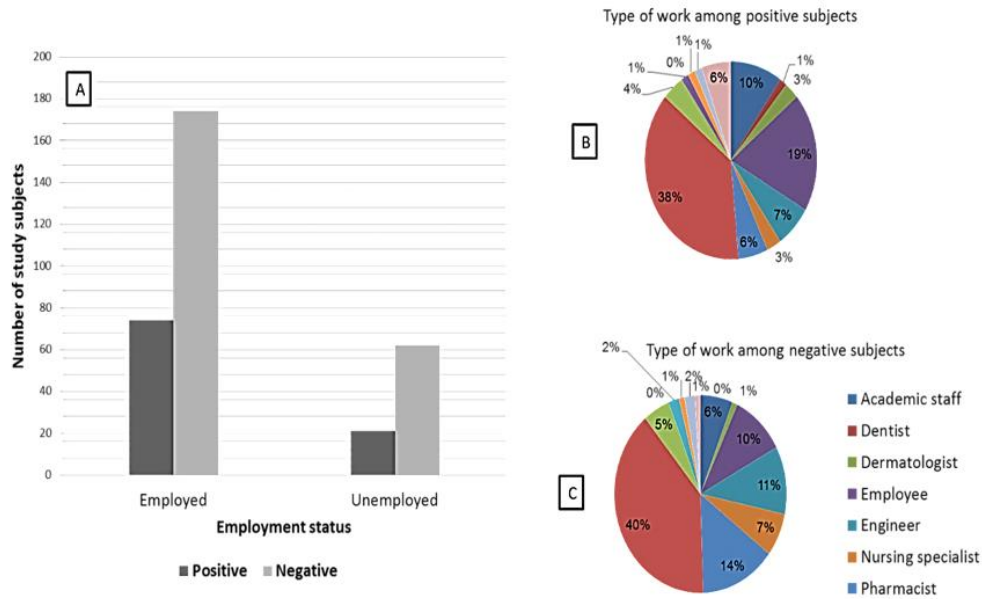


Fig. 1: Employment status among the survey respondents and its relation to the history of contracting COVID 19; positive refers to the positive history of COVID 19 infection; negative refers to a negative history of COVID 19 infection; 1-A: Column chart showing a number of employed and unemployed persons. 1-B: Pie chart presenting the type of work among individuals with a positive history of COVID 19. 1-C: Pie chart presenting the type of work among individuals with a negative history of COVID 19.

Clinical Presentation Among Study Participants Reporting a Positive History Of COVID-19 Infection:

Eighty-eight individuals gave feedback as regards the symptomatology of infection. Among the stated symptoms were fever (77.4%), diarrhea and

abdominal pain (75.0%), difficulty in breathing (78.7%), sore throat and difficulty in swallowing (71.2%), musculoskeletal pain (86.7%), loss of taste and smell (89.3%), and loss of weight (77.8%) (Fig. 2).

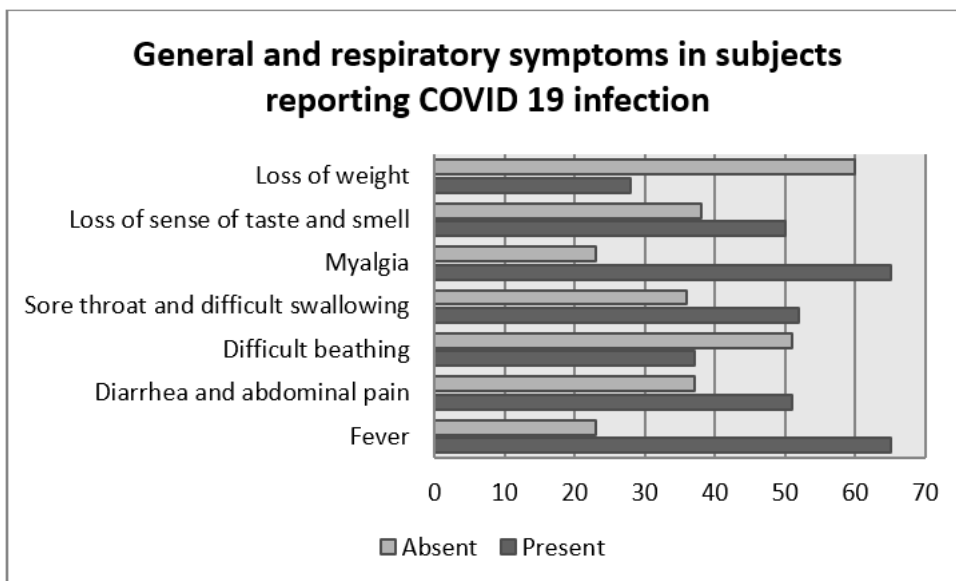


Fig. 2: Bar chart representing the number of COVID 19 positive subjects (X-axis) according to their presentation with general and respiratory symptoms (Y-axis) during infection.

Relation Between Clinical Presentation of COVID 19 and Population Characteristics:

Analysis of the relation between gender and clinical presentation of COVID 19 infection revealed that male patients were more prone to develop loss of taste and smell and loss of weight than female patients (Table 2). A significant association was also found between smoking and loss

of taste and smell, where 16 out of 17 smokers (94.1%) reported suffering from this symptom as compared to 33 out of 70 non-smokers (47.1%) who also reported losing smell and taste during the COVID 19 attack ($P < 0.001$, Pearson's Chi-square test).

Fever was more commonly found among children and young adults and elderly individuals (Table 3).

Table 2: Relation between sex of study participants and symptomatology of COVID 19

Characteristic	Female N = 50 (57%)	Male N = 38 (43%)	p-value	q-value
Fever			0.48	0.56
Present	35 (70%)	30 (79%)		
Absent	15 (30%)	8 (21%)		
Diarrhea			0.075	0.18
Present	33 (66%)	17 (45%)		
Absent	17 (34%)	21 (55%)		
Dyspnea			0.13	0.23
Present	25 (50%)	12 (32%)		
Absent	25 (50%)	26 (68%)		
Sore throat			0.68	0.68
Present	31 (62%)	21 (55%)		
Absent	19 (38%)	17 (45%)		
Myalgia			0.48	0.56
Present	35 (70%)	30 (79%)		
Absent	15 (30%)	8 (21%)		
Loss of smell and taste			0.033*	0.12
Present	23 (46%)	27 (71%)		
Absent	27 (54%)	11 (29%)		
Loss of weight			0.012*	0.087
Present	10 (20%)	18 (47%)		
Absent	40 (80%)	20 (53%)		
¹ Statistics presented: n (%)				
² Statistical tests were performed: chi-square test of independence				
*Statistical significance at $P < 0.05$				

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Table 3: Relation between age group of study participants and symptomatology of COVID 19.

Characteristic	<18 years N=5 (5.7%)	18-40 years N=67 (76%)	41-60 years N=12 (14%)	>60 years N=4 (4.5%)	p-value	q-value
Fever					<0.001*	0.003
Present	5 (100%)	53 (79%)	3 (25%)	4 (100%)		
Absent	0 (0%)	14 (21%)	9 (75%)	0 (0%)		
Diarrhea					>0.99	>0.99
Present	3 (60%)	38 (57%)	7 (58%)	2 (50%)		
Absent	2 (40%)	29 (43%)	5 (42%)	2 (50%)		
Dyspnea					0.82	>0.99
Present	1 (20%)	29 (43%)	5 (42%)	2 (50%)		
Absent	4 (80%)	38 (57%)	7 (58%)	2 (50%)		
Sore throat					0.29	0.66
Present	4 (100%)	38 (57%)	6 (50%)	4 (100%)		
Absent	0 (0%)	29 (43%)	6 (50%)	0 (0%)		
Myalgia					0.35	0.66
Present	0.35	0.66	8 (67%)	2 (50%)		
Absent	2 (40%)	15 (22%)	4 (33%)	2 (50%)		
Loss of smell and taste					0.86	>0.99
Present	2 (40%)	39 (58%)	7 (58%)	2 (50%)		
Absent	3 (60%)	28 (42%)	5 (42%)	2 (50%)		
Loss of weight					0.38	0.66
Present	3 (60%)	22 (33%)	2 (17%)	1 (25%)		
Absent	2 (40%)	45 (67%)	10 (83%)	3 (75%)		

¹ Statistics presented: n (%)
² Statistical tests were performed: Fisher's exact test
*Statistical significance at P<0.05

Medical Assessment of COVID 19 Infection:

Survey participants reporting a positive history of COVID 19 infection were diagnosed and investigated by various methods including clinical diagnosis (N=25; 27.5%), radiological assessment including CT chest (N=21; 23,1%),

measurement of D-dimer level (N=27; 29.7%), serum iron level (N=23; 25.3%) and molecular diagnosis by PCR (N=51; 56.0%). The total number of respondents to that question was 91 persons (100%).

Management strategies of individuals with a COVID 19 history are summarized in Table 4.

Table 4: Descriptive analysis of different treatment modalities experienced by patients with a positive history of COVID 19.

Management strategies	<u>N(%)</u>
Hydroxychloroquine	
N-Miss	12
Yes	48 (57.8%)
No	35 (42.2%)
Ivermectin	
N-Miss	12
Yes	3 (3.6%)
No	80 (96.4%)
Anti-inflammatory agents	
N-Miss	12
Yes	61 (73.5%)
No	22 (26.5%)
Immune stimulants	
N-Miss	12
Yes	65 (78.3%)
No	18 (21.7%)
Anticoagulants	
N-Miss	12
Yes	21 (25.3%)
No	62 (74.7%)
Antiviral drugs	
N-Miss	12
Yes	1 (1.2%)
No	82 (98.8%)
Home isolation	
N-Miss	4
Yes	90 (98.9%)
No	1 (1.1%)
ICU admission	
N-Miss	1
Yes	5 (5.3%)
No	89 (94.7%)
Respiratory support	
Yes	9 (9.5%)
No	86 (90.5%)
Total number of participants with positive COVID 19 history=95	
N-Miss: Number of participants not responding to the corresponding question	
Anti-inflammatory agents include paracetamol and corticosteroids; immunostimulants include vitamin C and Zinc.	

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Association of Digestive Disorders with COVID 19 Infection:

Study participants that had previously suffered from COVID 19 infection have reported a positive history of digestive disorders in 40.9% of 93 patients responding to that question. Nausea and heartburn were significantly more common among subjects with a positive COVID 19

history (P=0.004 and P=0.002, respectively) (Table 5). Twenty-five patients have reported an increase in the intensity of the whole spectrum of GIT symptoms after acquiring COVID 19 infection. In comparison, 10 participants have reported a decrease in GI disturbance, mainly diarrhea.

Table 5: Relation between digestive disorders and COVID 19 infection

Study question		Have you had the corona virus?						P-value
		Yes		No		Total		
		Count	Row N %	Count	Row N %	Count	Row N %	
Do you suffer from digestive problems?	Yes	38	40.9%	55	59.1%	93	100.0%	0.878
	No	57	39.9%	86	60.1%	143	100.0%	
Vomiting	Yes	5	55.6%	4	44.4%	9	100.0%	0.486
	No	37	40.7%	54	59.3%	91	100.0%	
Nausea	Yes	14	73.7%	5	26.3%	19	100.0%	0.004*
	No	28	34.6%	53	65.4%	81	100.0%	
Heart burn	Yes	24	61.5%	15	38.5%	39	100.0%	0.002*
	No	18	29.5%	43	70.5%	61	100.0%	
Indigestion	Yes	26	50.0%	26	50.0%	52	100.0%	0.092
	No	16	33.3%	32	66.7%	48	100.0%	
Flatulence	Yes	26	42.6%	35	57.4%	61	100.0%	0.875
	No	16	41.0%	23	59.0%	39	100.0%	
Constipation	Yes	11	30.6%	25	69.4%	36	100.0%	0.082
	No	31	48.4%	33	51.6%	64	100.0%	
Diarrhea	Yes	17	50.0%	17	50.0%	34	100.0%	0.245
	No	25	37.9%	41	62.1%	66	100.0%	

History of Parasitic Infection In Relation to the COVID 19 Infection Status Among Study Participants:

Twenty-six out of 95 (27.4%) participants reporting a positive history of COVID 19 also reported a previous history of parasitic infection, while 22 (15.6%) subjects out of 141 individuals with a negative history of COVID 19 infection had a past experience of parasitic infection (P=0.028) (figure 3). Among the parasitic infections stated were amoebiasis (9 cases among COVID 19 positive patients and 8 cases among negative patients), enterobiasis (6 cases among COVID 19 positive patients and 1 case among negative patients) and giardiasis (5 cases in each study group).

Helicobacter pylori infection was also reported in 8 COVID 19 positive patients and 15 negative patients. Six patients suffered from COVID 19 simultaneously with the occurrence of parasitic infection, the most common being amoebiasis in 3 patients, while one participant suffered from giardiasis and another one from enterobiasis along with the COVID 19 attack. In addition, one respondent reported having been infected with both *Entamoeba* spp and *Enterobius vermicularis* along with the SARS CoV-2 virus. These patients were treated with metronidazole (4 patients), nifuroxazide (1 patient), and nitazoxanide (1 patient).

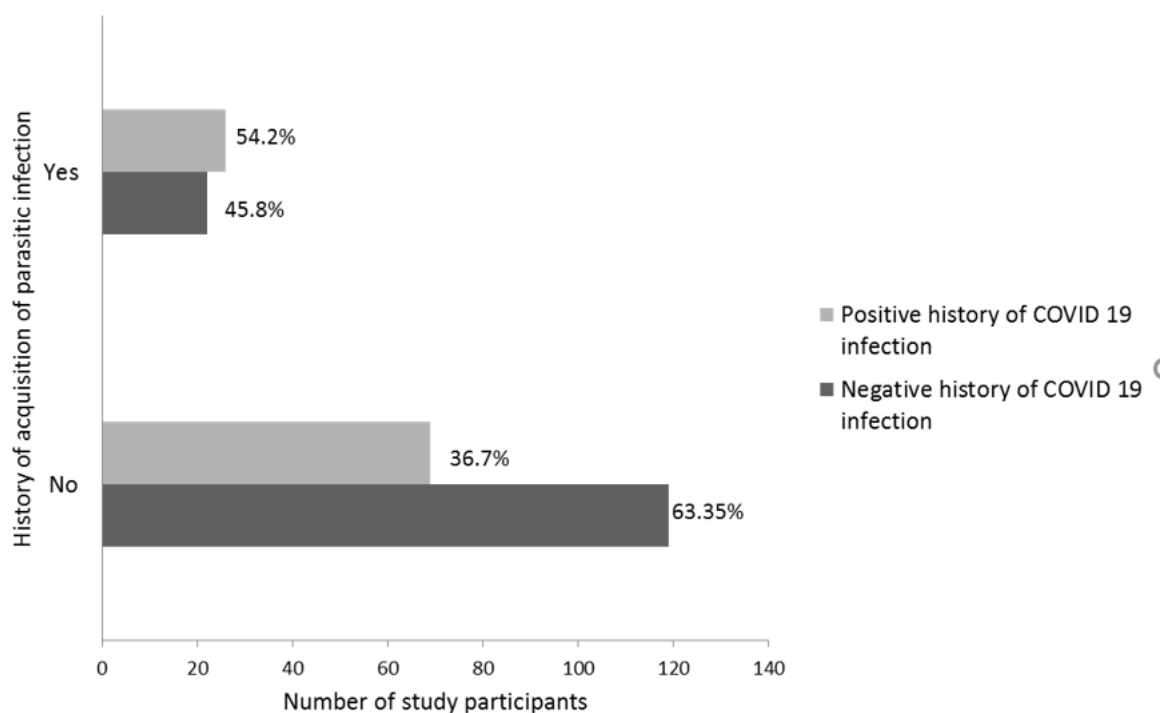


Fig. 3: Bar chart showing number and percent of study subjects reporting history of parasitic diseases in relation to the status of COVID 19 infection. The total number of participants reported a positive history of parasitic infection (N=48; 100%). The total number of participants reporting a negative history of parasitic infection (N=188; 100%); P=0.028. Statistical tests performed: Chi-square test of independence; Statistical significance at P<0.05

DISCUSSION

Population studies in the middle eastern region and developing countries are still short of providing satisfactory data on the characteristics of COVID 19 in these regions. We have therefore designed a cross-sectional online survey targeting participants in the Middle East, particularly Egypt. This region is of special research interest, due to the high prevalence of gastrointestinal disorders and parasitic diseases, which affect the immunity of the host, thus modulating the immune response to various pathogens, including viruses (Maizels *et al.*, 2018).

The mortality rates due to COVID 19 are higher among older patients. Levin *et al.* (2020) reported an infection fatality rate of 0.002% in patients 10 years of age as compared to 15% in patients 85% years of age. While this age susceptibility is evident in developed countries, higher

death reports have been reported among younger patients in low-income countries. This could probably be attributed to the higher incidence of infection and decreased management quality (Chauvin *et al.*, 2020). In our study, the mean age of participants with an appositive history of SARS CoV-2 infection was 35.69 ± 12.24 years. The majority of patients were between 18 and 40 years of age (74.7%). Only five patients required ICU admission, all of whom were between the ages of 27 to 37 years.

Jin *et al.* (2020) investigated gender differences in susceptibility to SARS CoV-2 infection and severity of disease presentation. Among 1,019 survivors of COVID 19 infection, the susceptibility among male and female patients was similar. However, data from hospitalized and deceased patients revealed that male patients were more prone to severe infection and also increased mortality rates.

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In the current study, there was no significant difference between the susceptibility to COVID 19 infection among male and female patients. It was observed, however, that male patients reported a higher incidence of loss of taste and smell. The abundance of ACE 2 receptors in the tongue and nasal mucosa can explain the distortion of taste and smell sensations secondary to viral binding to these receptors (Vaira *et al.*, 2020). In the study at hand, we also observed a higher incidence of loss of taste and smell among smokers. There is conflicting data on the susceptibility of smokers to COVID 19, since some studies have reported a protective effect of smoking due to the inhibition of pro-inflammatory cytokine production by nicotine (Korzeniowska *et al.*, 2021). In opposition, other studies suggested an increased risk of COVID 19 among smokers due to the increased expression of ACE 2 receptors in lung cells (Maggi *et al.*, 2021).

Loss of taste and smell was the most frequently reported symptom (89.3%) in our study. Additionally, participants also suffered from fever (77.4%), difficulty in breathing (78.7%), sore throat and difficulty in swallowing (71.2%), musculoskeletal pain (86.7%), loss of weight (77.8%) and diarrhea and abdominal pain (75.0%). COVID 19, although notorious for its respiratory manifestations, has also well-recognized gastro-intestinal symptoms (Pola *et al.*, 2021). These can be attributed to the immune response against viral infection or even the direct action of the virus. This is evidenced by the fact that intranasal inoculation of SARS CoV-2 leads to faecal shedding of viral RNA, while intragastric inoculation leads to lung pathology (Pola *et al.*, 2021). In a study by Tian *et al.* (2020), case reports and retrospective clinical studies were evaluated to analyze the nature of GIT disturbance during COVID 19 infection. Symptoms reported in these studies included anorexia, nausea, vomiting, diarrhea, abdominal pain and GI bleeding.

Diarrhea was more frequently found in adults and children.

GIT manifestations during viral infections might also be due to underlying intestinal disorders. Parasites are major contributors to intestinal disturbances and cause a wide spectrum of upper and lower intestinal tract symptoms. Crossroads between parasitic infections and SARS CoV-2 infection are of particular research interest, due to the wide prevalence of co-infection and the impact of parasitic infections on immune modulation. In the study at hand, the incidence of past parasitic infection was significantly higher among patients with SARS CoV-2 infection history. Six survey respondents had simultaneous SARS CoV-2 and parasitic infection including amoebiasis, enterobiasis and giardiasis. Abdoli (2020) suggested that helminthic infection can increase the susceptibility to intracellular pathogens including viruses by potentiating a T-helper 2 immune response. However, several studies have suggested a protective effect of parasitic infections against SARS CoV-2 infection (Abott, 2018; Desai *et al.*, 2021). One of the potential contributors to such a protective effect is the eosinophilia commonly present with parasitosis (Rosenberg and Foster, 2021). Eosinophils are suggested to play a protective role in SARS CoV-2 infection since patients with low eosinophil count were more likely to develop severe symptomatology and fatal outcome (Yan *et al.*, 2021). Eosinophils are also potential markers for past SARS CoV-2 infection among COVID-19 patients (Li *et al.*, 2021). Further research on the molecular mechanisms of parasite-virus interactions is certainly recommended and can open valuable insights to explain gastrointestinal pathogenesis of microbial co-infection. For example, human galectins 1 and 3 (Gal-1 and Gal-3) were found to be increased during *Entamoeba histolytica* (Petropolis, 2014). These pro-inflammatory mediators inhibit viral adhesion and are potential targets for antiviral therapy (Pourrajab, 2021). Another approach to

antiviral therapy is arginine deprivation since arginine is essential for viral replication. Infection with *Giardia lamblia* causes arginine depletion by consumption of host arginine and metabolism by arginine deaminase thus disturbing the enterocyte cell cycle (Buret *et al.*, 2015).

Another important crossing point between SARS CoV-2 and parasitic infections is the observation that certain anti-parasitic drugs have proven to improve the clinical outcome of COVID-19. In the current study, participants reported using hydroxychloroquine (57.8%) and ivermectin (3.6%) as part of the drug regimen against COVID 19, which also included anti-inflammatory drugs, anticoagulants and immune stimulants. The antimalarial drug hydroxychloroquine was one of the earliest agents to be included in the anti-COVID regimen by several countries. It was found to protect against the development of severe attacks, especially if given early in the disease (Prodromos and Rumschlag, 2020; Weston *et al.*, 2020). Another famous anti-parasitic agent included in the anti-COVID regimen is the macrocyclic lactone ivermectin (Heidary and Gharebaghi, 2020). While its antiparasitic activity is contributed to its action as a glutamate-gated chloride channel blocker, its anti-viral activity is mediated by interfering with SARS CoV-2 protein transport into the nucleus of the host (Caly *et al.*, 2020). Another antiparasitic drug that has been investigated for its potential benefit in SARS CoV-2 infection is nitazoxanide, which inhibits viral replication and potentiates interferon-alpha and beta production (Filho *et al.*, 2020).

Limitations and Recommendations:

The study was conducted before the implementation of widespread vaccination campaigns, so the effect of vaccination on both COVID 19 and digestive disturbances remains uncovered. Repetition of the survey questionnaire with emphasis on the response to vaccination and its possible impact on co-existing intestinal infections is strongly recommended. In addition,

middle eastern and developing countries merit more extensive population studies to explore the effect of endemic parasitic diseases on emerging viral infections and the value of therapeutic repurposing of anti-parasitic drugs in the management of parasite-virus co-infection.

Conclusions

The COVID 19 pandemic is considered to be the highest health crisis worldwide and constitutes an augmented health burden in middle and low-income countries. The current study investigated the association between GIT disturbances, particularly parasitic infections and COVID-19. The higher incidence of parasitic infections among subjects with a positive history of COVID-19 could suggest that parasite co-infection may lead to a high incidence of COVID-19, which conflicts with other literature data reporting a protective effect of parasitosis against SARS CoV-2 infection. In addition, respondents were asked about the treatment regimen against COVID 19 and the inclusion of the antiparasitic drugs hydroxychloroquine and ivermectin. Additionally, other lines of therapy were reported. These included immunomodulatory agents which could be an alternative treatment option under the situation of the lacking of effective antiviral therapy, their high side effects and low patient compliance. However, more experimental and clinical trials are needed to yield sufficient evidence concerning the correlations of COVID-19 and other GIT infections along with the convenient effective therapy. In addition, more extensive survey studies targeting larger populations are of crucial importance, especially in developing countries, to determine the impact of parasitic diseases on SARS CoV-2 infection and the degree of public awareness on common symptomatology and management strategies between these health burdens.

List of Abbreviation:

(ACE-2) angiotensin-converting enzyme-2

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(COVID 19) The coronavirus disease of 2019
(GI) gastrointestinal
(MERS-CoV) Middle East respiratory syndrome coronavirus
(SARS-CoV) sever acute respiratory syndrome coronavirus
(TMPRSS2) the transmembrane serine protease

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