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Research Article

Is co-infection of intestinal parasites with COVID-19 virus infection affecting its severity?

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Abstract
Corona Virus Disease-2019 (COVID-19) is a global pandemic disease with a spectrum of clinical presentations ranging from asymptomatic to acute respiratory distress syndrome, and multi-organ failure. A case-control study was carried out on 250 COVID-19 patients. Socio-demographic data, clinical features, laboratory findings, and co-parasitic infections were screened to assess the effect of parasitic co-infection on COVID-19 severity. Patients were classified as 135(54%) moderate, 82 (32.8%) severe, and 33(13.2%) critical, according to the National Health Commission. COVID-19 was more prevalent in ages between 60ys and 90ys (38.4%), males (56.8%), rural areas (52.8%), workers (52.8%), and non-married subjects (54.4%). Lymphopenia and anemia increased with increasing severity of COVID-19. Regarding parasitic co-infection, 49.6% of patients had parasitic infections. The percentage of co-parasitic infections was 71.9%, 29.3%, and 12.1% in moderate, severe, and critical COVID-19 patients, respectively. Co-infections were more common in ages between 20 ys and 40 ys (54.0%), males (65.3%), urban patients (61.3%), workers (65.3%), and married patients (57.3%). The most detected parasites were *Blastocystis hominis, Cryptosporidium* spp., *Entameba coli*, and *Cyclospora cayetanensis,* which were almost mixed parasitic infection. There was an inverse correlation between co-infection with intestinal parasites and COVID-19 virus severity. Parasite-driven immunomodulatory responses may mute the hyperinflammation associated with severe COVID-19 virus infection.

Keywords: COVID-19, intestinal parasites, severity.

Introduction
Corona Virus Disease-2019 is a global pandemic disease with a spectrum of clinical presentations ranging from asymptomatic or mild illness to acute respiratory distress syndrome (ARDS), sepsis, and multi-organ failure[1]. The National Health Commission classified COVID-19 patients according to the clinical symptoms, severity of pneumonia, respiratory failure, shock, and/or other organ failure, etc. The mild COVID-19 type experienced mild clinical symptoms without pneumonia in imaging, while the common type showed fever, respiratory tract symptoms, and other symptoms with pneumonia in imaging. Severe type manifested by respiratory distress, respiratory rate ≥ 30 times/min; in resting state, oxygen saturation ≤93%; PaO_2/FiO_2 ≤ 300 MMHG. The critical-type patients suffered from respiratory failure requiring mechanical ventilation, shock, and other organ failure requiring Intensive Care Unit (ICU) monitoring and treatment[2]. Many risk factors affect the severity of the COVID-19 disease, including older age, immune compromise, underlying co-morbidities, and co-infection with intestinal parasites[3,4].

In Africa, COVID-19 patients were suffering from significantly fewer serious symptoms than those in industrialized countries. Researchers explain this phenomenon by co-infection with parasites, which are common in low-income countries. In Egypt, some studies documented a high prevalence of intestinal unicellular organisms, including *Entamoeba* spp**.,** *Giardia lamblia*,*Cyclospora*, and *Cryptosporidium*[5]. These infections may play an important role in

the modulation of the host's immune response and, so, alter the clinical outcomes of COVID-19 patients[6-9]. These infections can induce a balance between pro-inflammatory and anti-inflammatory responses[10]. Furthermore, these infections can skew the immune system towards TH2 responses, thus preventing TH1 hyper-immune activation that is characteristic of COVID-19 severity[4,7].

The correlation between parasitic infections and SARS-CoV-2 infection has research interest because of the high influence of co-infection and the impact of parasitic infections on immune modulation. Thus, this research aimed to assess the effect of co-infection with intestinal parasites on the severity of COVID-19 virus and compare the clinical outcomes of COVID-19 virus infection in patients with or without parasitic co-infection.

Methodology:

Ethical considerations:

The study protocol was approved by both the scientific ethical committee of the Medical Parasitology Department and the Institutional Committee of Research Ethics, Faculty of Medicine, Minia University, Egypt (approval No. 208:1/2022). Written informed consent was obtained from the participants after a full explanation of the purpose and technique of the study.

Study population and design

This case-control study was carried out on 250 COVID-19 patients from the inpatient and outpatient clinics of Chest University Hospital, and Liver University Hospital, , Minia District, Egypt, who were suffering from COVID-19 symptoms from November 2021 to October 2022. Fifty healthy individuals were used as controls.

Patients and controls were subjected to a prepared questionnaire that contained both demographic and clinical data from the studied subjects. The questionnaire included their name, age, gender, occupation, marital status, residence, any chronic diseases such as diabetes millets (DM), hypertension, chronic liver disease, cardiovascular disease, and COVID-19 symptoms such as fever, cough, dyspnea, sore throat, etc.

Stool sample examination:

Fresh stool samples were collected from the studied subjects and placed in clean containers with a tight-fitting lid that contained no preservatives. Stool samples were carefully transferred shortly to the laboratory of the Medical Parasitology Department, Faculty of Medicine, Minia University. Each sample was examined macroscopically and microscopically.

The microscopic examination was done by direct wet smear methods[11] and two staining methods: Giemsa stain [12] and modified Ziehl-Neelsen (ZN) stain[13].

A Complete blood count (CBC) was done for all the studied subjects, especially hemoglobin level, and the total and differential count of white blood cells (WBCs).

Statistical analysis

The analysis of the data was carried out using IBM SPSS 20.0 statistical package software (IBM; Armonk, New York, USA). Data were expressed as mean ± standard deviation (SD), minimum and maximum of range for quantitative parametric measures, in addition to both number and percentage for categorized data. The student t-test was used for comparison between two independent groups for parametric data, and the Chi-square test or Fisher's exact test were used to compare categorical variables. A binary logistic regression analysis was used to analyze the COVID-19 severity associated with patients with intestinal parasites. A *p* value less than 0.05 was considered significant.

Results

Out of 250 COVID-19 patients, 135(54%) were grouped as a moderate group (Group-I) in which patients were suffering from fever and respiratory symptoms such as cough, dyspnea, and sore throats, and CT showed a ground glass appearance. Eighty-two (32.8%) patients were grouped as severe one (Group-II), in which patients had respiratory rates >30, respiratory distress, and O_2 saturation < 93, in addition to the above symptoms. Lastly, 33(13.2%) patients were counted as a critical group (Group-III) in which patients were complaining of respiratory failure and were on mechanical ventilation, with shock, and/or other organ failures such as kidney and liver failure.

The socio-demographic data associated with parasitic infections are summarized in (Table 1). Out of 250 COVID-19 patients, 124 (49.6%) had parasitic infections. Regarding age, COVID-19 virus infection was more common in age group from 60ys to 90ys (38.4%), but most of the patients had no parasitic infection (42.1%), and these data were statistically significant with a *p* value < 0.0001 (Table 1).

Regarding gender, COVID-19 virus infection was more common in males (56.8%), and 65.3% of them had parasitic infections compared to 34.7% of female patients. Regarding residence, COVID-19 virus infection was more common in rural areas (52.8%), and most of them had no parasitic infection (66.7%).

Regarding occupation, COVID-19 virus infection was more common in workers, with 65.3% of them having parasitic infections (Table 1). The COVID-19 virus infection was more common in non-married patients, while parasitic infections were more common in married patients (57.3%) (Table 1).

The rates of co-infection with intestinal parasites in group (I) patients who were presented with fever was (62.1%), cough, dyspnea, and sore throat was (78.2%) (Table 2). On the other hand, the rates of co-infection with intestinal parasites were lower in group (II) and group (III) patients who presented with a respiratory rate > 30, respiratory distress, O_2 saturation > 93, ground glass appearance in CT, respiratory failure (19.4), shock, and organs failure (2.4%) (Table 2).

Regarding associated comorbidities, the rates of co-infection with intestinal parasites in COVID-19 patients associated with either DM or hypertension was high (63.7%), compared to those patients associated with both DM and hypertension (23.4%) or both hypertension and cardiovascular diseases (12.9%) (Table 2).

In this study, patients with a normal lymphocytic count were (61.5%) , in group (I), while it was (20.7%) and (18.2%) in group (II) and group (III) patients, and this difference was significant (*p value* <0.0001). Patients with lymphopenia in these three groups were (38.5%, 79.3%, and 81.8%, respectively), (Table 3).

Regarding the total leukocytic count (TLC), leukopenia was more common in group (II) and group (III) of patients (78.0% and 87.9%,), (Table 3).
As regards the hemoglobin level, the percentages of patients with anemia in group (I), group (II) and group (III) were (74.8%, 89.0%, and 93.9%, respectively), with a significant difference (*p value* <0.005), (Table 3).

Upon examination of stool samples of COVID-19 patients by wet mount and staining techniques, the most frequently detected parasites were *Blastocystis hominis* (49.6%), *Cryptosporidium spp.* (44. 8%), *Entamoeba coli* (42.8%), *Cyclospora cayetanensis* (39.6%), and *Isospora belli* (34.4%), followed by *Entamoeba* spp. (16.0%), and *Giardia lamblia* (8.4%) as in (Table 4). Almost all these detected parasites were mixed parasitic infection.

High rate of co-infection with intestinal parasites was detected in group I. They were *Blastocystis hominis* (71.9%), *Cryptosporidium spp.*, (65.9%), *Entamoeba coli* (63.0%), *Cyclospora cayetanensis* (54.1%), *Isospora belli* (51.1%), *Entamoeba* spp. (20.7%), and *Giardia lamblia (*8.9%) (Table 4).

The lowest rate of co-infection with intestinal parasites was detected in group III. They were *Blastocystis hominis (*9.1%), *Cryptosporidium spp.* (6.1%), *Cyclospora cayetanensis* (6.1%), *Entamoeba coli (*3.0%), and *Entamoeba* spp. (3.0%) (Table 4).

Ordinal and adjusted logistic regression analyses were used to determine factors associated with COVID-19 severity. There was an inverse correlation between intestinal parasitic co-infection and COVID-19 virus severity of 0.07 (0.03–0.16). On the other hand, there was a very strong correlation of 2.11 (0.93–4.79) for older patients (60-90 years old). However, there was a moderate correlation of 0.85 for comorbidities, Table 5.

Table (1): Socio-demographic data among COVID-19 patients and parasitic co-infection.

Sociodemographic features:	All patients no.= 250	-ve parasite no.= 126	+ve parasite no.= 124	p value
Age:				
20-40	72 (28.8%)	5 (4.0%)	67 (54.0%)	
40-60	82 (32.8%)	68 (54.0%)	14 (11.3%)	<0.0001*
60-90	96 (38.4%)	53 (42.1%)	43 (34.7%)	
Gender:				
Male	142 (56.8%)	61 (48.4%)	81 (65.3%)	0.007*
Female	108 (43.2%)	65 (51.6%)	43 (34.7%)	
Residence:				
Urban	118 (47.2%)	42 (33.3%)	76 (61.3%)	<0.0001*
Rural	132 (52.8%)	84 (66.7%)	48 (38.7%)	
Occupation:				
Worker	132 (52.8%)	51 (40.5%)	81 (65.3%)	<0.0001*
Not worker	118 (47.2%)	75 (59.5%)	43 (34.7%)	
Marital status:				
Married	114 (45.6%)	43 (34.1%)	71 (57.3%)	<0.0001*
Not Married	136 (54.4%)	83 (65.9%)	53 (42.7%)	

[1)]Chi square test for qualitative data between the two groups.
[2)]Significant level at p value <0.05

Table (2): Clinical features and comorbidities among COVID-19 patients and parasitic co-infection.

Clinical symptoms and sign	All patients no.= 250	-ve parasite no.= 126	+ve parasite no.= 124	p value
Fever	100 (40.0%)	23 (18.3%)	77 (62.1%)	<0.0001*
Cough	134 (53.6%)	37 (29.4%)	97 (78.2%)	<0.0001*
Dyspnea	150 (60.0%)	53 (42.1%)	97 (78.2%)	<0.0001*
Sore throat	135 (54.0%)	38 (30.2%)	97 (78.2%)	<0.0001*
Respiratory rate >30	81 (32.4%)	57 (45.2%)	24 (19.4%)	<0.0001*
Respiratory distress	82 (32.8%)	58 (46.0%)	24 (19.4%)	<0.0001*
O2 saturation >93	82 (32.8%)	58 (46.0%)	24 (19.4%)	<0.0001*
CT: ground glass	82 (32.8%)	58 (46.0%)	24 (19.4%)	<0.0001*
Respiratory failure	33 (13.2%)	30 (23.8%)	3 (2.4%)	<0.0001*
Shock	33 (13.2%)	30 (23.8%)	3 (2.4%)	<0.0001*
Organ failure	33 (13.2%)	30 (23.8%)	3 (2.4%)	<0.0001*
	107 (42.8%)	28 (22.2%)	79 (63.7%)	
	72 (28.8%)	43 (34.1%)	29 (23.4%)	<0.0001*
	60 (24.0%)	44 (34.9%)	16 (12.9%)	
	11 (4.4%)	11 (8.7%)	0	

[1)]Chi square test for qualitative data between the two groups.
[2)]Significant level at p value <0.05

Table (3): Laboratory data among different groups of COVID-19 patients

Character	I No.= 135	II No. = 82	III No. =33	p value within groups		
	No. (%)			I vs II	I vs III	II vs III
Lymphocyte level						
20-40%	83 (61.5%)	17 (20.7%)	6 (18.2%)	<0.0001*		
Less than 20%	52 (38.5%)	65 (79.3%)	27 (81.8%)	<0.0001*	<0.0001*	0.757
TLC level ($X10^9$ /L):						
<4	58 (43.0%)	64 (78.0%)	29 (87.9%)	<0.0001*		
4-10	49 (36.3%)	18 (22.0%)	4 (12.1%)			
>10	28 (20.7%)	0	0	<0.0001*	<0.0001*	0.225
Hemoglobin (gm/dl):						
12 – 15	34 (25.2%)	9 (11.0%)	2 (6.1%)	0.005*		
<12	101 (74.8%)	73 (89.0%)	31 (93.9%)	0.011*	0.016*	0.42

[1] Chi square test for qualitative data between the two groups.
[2] Significant level at p value <0.05
[3] I: Moderate II: Severe III: Critical

Table (4): Parasites detected on the examination of the stool samples from the different groups by direct wet mount technique and by Giemsa stain.

parasite	Moderate No.= 135	Severe No. = 82	Critical No. =33	Total No=250	Control No.= 50	P value
Blastocystis hominis	97 (71.9%)	24 (29.3%	3 (9.1%)	124 (49. 6%)	35 (70.0%)	<0.0001*
Cryptosporidium spp.	89 (65.9%)	21(25.6%)	2 (6.1%)	112 (44. 8%)	37 (74.0%)	<0.0001*
Entamoeba coli	85 (63.0%)	21 (25.6%)	1 (3.0%)	107 (42. 8%)	21 (42.0%)	<0.0001*
Cyclospora	73 (54.1%)	24 (29.3%)	2 (6.1%)	99 (39. 6%)	25 (50.0%)	<0.0001*
Isospora belli	69(51.1%)	17 (20.7%)	0	86 (34. 4%)	8 (16.0%)	<0.0001*
Entamoeba spp.	28 (20.7%)	11 (13.4%)	1 (3.0%)	40 (16.0%)	0	<0.0001*
Giardia lamblia	12 (8.9%)	9 (11.0%)	0	21 (8.4%)	0	0.016*

[1]Chi square test for qualitative data between the two groups.
[2]Significant level at p value <0.05.
[3] % of the presented parasites were co infected

Table (5): Factors associated with severe COVID 19.

Variables	Univariate analysis		Multivariate analysis	
	OR (CI 95.0%)	p value	OR (CI 95.0%)	p value
No parasitic infections	0.12 (0.07 – 0.21)	<0.0001*	0.07 (0.03 – 0.16)	<0.0001*
Age: (20 – 40 years)				
40 – 60 years	3.17 (1.57 – 6.42)	<0.001*	0.39 (0.14 – 1.1)	0.075
60 – 90 years	5.83 (2.92 – 11.66)	<0.0001*	2.11 (0.93 – 4.79)	0.074
Comorbidities	0.85	0.206	--------	-------

[1]Dependent: Severity of COVID 19.
[2]OR: Odds ratio (0-0.24 weak, 0.25- 0.49 fair, 0.50- 0.74 moderate, > 0.75 strong)
[3]CI: Confidence interval.

Discussion

COVID-19 is a disease caused by infection of a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with a variety of clinical manifestations. However, most COVID-19 patients only experience moderate or asymptomatic diseases, those with risk factors may experience severe COVID-19 that necessitates hospitalization[3,14,15]. It has been demonstrated that persistent co-infection with intestinal parasites alter the clinical course of COVID-19, potentially through direct manipulation of the host's immune responses[6,9] to SARS-CoV-2 infection, with either advantageous or disadvantageous consequences[8].

By studying the socio-demographic data of COVID-19 patients, infection with COVID-19 virus was more common in the elderly patients from 60 to 90 years old (38.4%). Males (56.8%) were more infected than females (43.2%) and rural patients (52.8%) were more infected than urban patients (47.2%). Also, workers (52.8%) were more infected than non-workers (47.2%), and non-married (54.4%) were more infected than married subjects (45.6%).

These results come in accordance with Chen et al., and Zhou et al., who reported that older ages were more susceptible to infection[14,16].

Moreover, Huang et al., and Lu et al., reported that COVID-19 virus was more common in males than females[15,17]. Further, Abdulateef et al., reported that COVID-19 virus infection was more common in workers than in non-workers[18].

Conversely, Hamed et al., found no significant difference among male and female patients[19]. Abdulateef et al., and Eid et al., reported more infection in females[18,20]. Moreover, Abdulateef et al., reported more infection in married subjects and urban areas[18].
This could be explained by the fact that aging badly affects lung functions and delays the activation of the acquired immune system, thus, the virus replicates rapidly, producing more pro-inflammatory responses and increasing the risk of death[21].

Furthermore, men are more sensitive to SARS-CoV-2[14]. Thus, male sex is one of the risk factors for COVID-19 virus [15,16 and17], which is explained by the fact that community-acquired nature of COVID-19 virus and the fact that men are more likely to be out of the house because of their jobs. It's also important to pay attention to the behavioral disparities that exist between men and women, particularly when it comes to health advice and the issue of social separation that they ignore. Workers were more likely to contract SARS-CoV-2, which makes sense given how quickly the virus may spread outside of the house [22].

Parasitic co-infection with intestinal parasites were more common in ages group between 20ys and 40ys (49.6%), male patients (65.3%) more than female patients (34.7%), urban patients (61.3%) more than rural patients (38.7%), worker patients (65.3%) more than non-worker patients (34.7%). and married patients (57.3%) more than non-married patients (42.7%).

These results come in accordance with Wolday et al., who reported the same finding concerning the age group and gender [4]. Also, Wolday et al., reported more parasitic infections in workers than in non-workers [4]. Moreover, Gebrecherkos et al., reported higher levels of parasitic infection in the age group (20ys-40ys) and in males [23].

Regarding residence, our results contradictory to Wolday et al., who reported more COVID-19 patients in urban areas but most of them were without parasitic infection [4].

In this study, most COVID-19 patients presented with fever, cough, dyspnea, and sore throat (40.0%, 53.6%, 60.0%, and 54.0%, respectively). The rates of co-infection with intestinal parasites in moderate-group patients were higher than in those with severe and critical patients.

It is suggested that parasites may reduce the severity of COVID-19 virus by altering systemic immune responses, although dominant regulatory (Treg) and T-helper (TH) responses are increased[6]. In addition to these defense mechanisms, SARS CoV-2 infection is prevented by the generation of cytokines, increased eosinophilia, and IgE reactions[6,9].

Furthermore, modifications in the gut microbiome caused by parasites may alter the host's immunological response [9].

Our results come in agreement with Hamed et al., [19]. Gebrecherkos et al., and Wolday et al., who reported the same data, but those patients had fewer parasitic infections [4,23].
Regarding associated comorbidities, the rate of co-infection with intestinal parasites in COVID-19 patients associated with either DM or hypertension was high (63.7%) compared to those patients associated with both comorbidities (Table 2).

These data were consistent with Wolday et al.,[4], who found that COVID-19 patients co-infected with parasites had lower proportions of chronic inflammatory conditions, such as hypertension, obesity, diabetes, and inflammatory bowel diseases[24, 25]. Some reports have also demonstrated that parasitic infection correlates with a lower risk of developing diabetes and metabolic syndrome in humans[26].
Here, patients with a normal lymphocytic count were 61.5%, 20.7%, and 18.2% in group (I), group (II), and group (III), respectively, while lymphopenia in these groups was 38.5%, 79.3%, and 81.8%, respectively.

Lymphopenia was prominent among severe and critical COVID-19 patients. Our study comes in agreement with some studies done by Chen et al., Huang et al., and Qin et al., who reported that lymphopenia was prominent among critically ill patients with COVID-19[14,15 and 27]. Moreover, Fan et al., demonstrated that prominent lymphopenia was more in critical patients as compared to non-critical ones and normal controls [28]. Further analysis showed a significant decrease in T cell counts, especially $CD8^+$ T cells, in severe cases compared with mild cases [29].

Xu et al., provided an explanation for significant lymphopenia by demonstrating that lymphocytes express angiotensin converting enzyme -2 (ACE2) receptors on their surface, which suggests that SARS-CoV-2 virus may directly infect those cells and ultimately cause their lysis [30]. Moreover, tumor necrosis factor (TNF)-alpha levels are noticeably elevated during the COVID-19-induced cytokine storm, which may encourage lymphocyte death [31].
Furthermore, $CD8^+$ T cells are important for killing virus-infected cells, whereas $CD4^+$ T cells are crucial to prime $CD8^+$ T cells by producing cytokines. Excessive elimination of these cells could result in an uncontrolled inflammatory response and severe lymphopenia [27].

Leukopenia was more obvious in group (II), and group (III) of patients (78.0% and 87.9%,), while it was 43.0% in the mild group *(p value* <0.0001). Moreover, the percentages of patients with anemia in group (I), group (II), and group (III) were 74.8%, 89.0%, and 93.9%, respectively. This result was in accordance with Guan et al., [32] and Eid et al., [20] who showed that leukopenia was present in severe vs. non-severe COVID-19 patients (61.1% vs. 28.1%) [32].

Also, our study comes in agreement with a study done by Anai et al., who reported that anemia was correlated with COVID-19 virus severity [33]. Anemia contributes to the development of severe outcomes in COVID-19. This can be explained by the low hemoglobin levels, which serve as a carrier for oxygen to target organs in the body. Thus, the transport of oxygen to several organs in the body will be disrupted. Consequently, hypoxia will eventually result in multiple organ dysfunction, especially respiratory organ dysfunction [33].

Moreover, COVID-19 could worsen anemia, as SARS-CoV-2 can interact with hemoglobin molecules on the erythrocyte through ACE2, Cluster of Differentiation 26, and 147 (CD147 and CD26) receptors. This interaction will cause the virus to attack the heme on the 1-beta chain of hemoglobin and cause hemolysis [34]. On the other hand, this data was in contrast with data reported by Fan et al., [28].

Regarding co-infection with intestinal parasites, there was an inverse correlation between intestinal parasitic infections and COVID-19 severity; the percentage of co-infection with intestinal parasites were 71.9%, 29.3%, and 12.1% in group (I), group (II), and group (III) patients, respectively. The most frequently detected parasites which almost co-infected

were *Blastocystis hominis, Cryptosporidium spp., Entamoeba coli, Cyclospora cayetanensis, Isospora belli, Entamoeba* spp., and *Giardia lamblia*, respectively.

These results come in agreement with Abdel-Hamed et al., who showed that the prevalence of parasitic infections was 72.8% in mild cases compared to 20.7% in severe cases[35]. These results were explained by Can et al., who reported that picoplast proteins of protozoa have immunogenic potential [36]. Also, *Cryptosporidium parvum* oocysts provide a protective immunity at an extremely low dose, which restores the T1-partner mucosal (CD8+T-cells) and their cytokine IFN-γ effectors that otherwise decrease with ongoing protein malnutrition**.** In addition, immunomo-dulation caused by malaria is effective against the extreme manifestations of certain respiratory viruses. Hospitalized children diagnosed with influenza and malaria in Kenya are less likely to suffer respiratory distress than those with influenza alone[37]. Also, the number of positive cases was higher in the severe group than in the moderate one [38].

This data was contradictory to Abdoli [39] who suggested that parasitic infections can increase the susceptibility to intracellular pathogens, including viruses, by potentiating a T-helper 2 immune response.

This study demonstrates that co-infection with intestinal parasites was associated with lower odds of developing severe COVID-19 in Egyptian patients. Conversely, there was a very strong correlation for older patients and a moderate correlation for comorbidities.
Many reports state that older patients with COVID-19 and comorbidities are at increased risk of death due to the severity of SARS-CoV-2 pneumonia[3,16,23].

Conclusion

To summarize, coinfection with intestinal parasites was associated with a lower probability of developing severe COVID-19. COVID-19 patients without parasitic co-infection were admitted to the ICU and required supplemental oxygen compared to those with intestinal parasitic co-infection.

Conflict of interest: None to declare.

References

1. World Health Organization. WHO Director General's opening remarks at the media briefing on COVID-19. 2020b. Available at < https://www.who.int/director-general/ speeches/detail/who-director-general-s-opening-remarks-atthe-media-briefing-on-covid-1911-march-2020 Accessed Feb. 1, 2022.
2. General Office of National Health Committee. Notice on the issuance of a program for the diagnosis and treatment of novel coronavirus (2019-nCoV) infected pneumonia (trial revised fifth edition). Available at < http://www.nhc.gov.cn/yzygj/s7653p/202003/ 46c9294a7dfe4cef80dc7f5912eb1989.shtml. Accessed 3 Mar 2020.
3. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H et al., Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;20: 30079-5.
4. Wolday D, Tasew G, Amogne W, Urban B, Schallig HD, Harris V, et al., Interrogating the impact of intestinal parasite-microbiome on the pathogenesis of COVID-19 in Sub-Saharan Africa. Front. Microbiol. 2021; 12:766–772.
5. Ahmed AK, Sanadeki MM, Abd Rabou RA, Kamal AM, Abdel-Ghany W M, Abdelrehim MG. Prevalence and associated risk factors of *Cyclospora cayetanensis* and *Cystoisospora belli* infections among adult immune-competent patients with diarrhea attending Minia University Hospitals, Egypt. J. Egypt. Soc. Parasitol. 2021; 51: 17-22.
6. Chabé M, Lokmer AS, Egurel L. Gut protozoa: friends or foes of the human gut microbiota? Trends. Parasitol 2017; 33: 925–934.
7. Bradbury RS, Piedrafita D, Greenhill A, Mahanty S.Will helminth co-infection modulate COVID-19 severity in endemic regions? Nat. Rev. Immunol. 2020;20:342.
8. Hays R, Pierce D, Giacomin P, Loukas A, Bourke P, McDermott R. Helminth coinfection and COVID-19: an alternate hypothesis. PLoS. Negl. Trop. Dis. 2020;14: e0008628.

9. White MPJ, McManus CM, Maizels RM. Regulatory T-cells in helminth infection: induction, function and therapeutic potential. Immunology. 2020;160:248–260.
10. Ssebambulidde K, Segawa I, Abuga KM, Nakate V, Kayiira A, Ellis J, et al., Parasites and their protection against COVID-19-Ecology or Immunology? MedRxiv. 2020-05.
11. Estevez EG, Levine JA. Examination of preserved stool specimens for parasites: Lack of value of the direct wet mount. J. clinic. microbiol. 1985; 22:666-7.
12. Garcia LS, Bruckner DA. Diagnostic medical parasitology. Washington, DC: 2001. p.131-135.
13. Henriksen SA, Pohlenz JFL. Staining of Cryptosporidium by a modified Ziehl-Neelsen technique. Acta. Vet. Scand. 1981; *22*: 594
14. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al., Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020; 395: 507-513.
15. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y et al., Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395:497-506.
16. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z *et al.,* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective study. Lancet. 2020; *395*:1054-1062.
17. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al*.,* Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020; 395: 565-574.
18. Abdulateef D S, Rahman HS, Salih JM, Osman SM, Mahmood T A, Omer SHS, et al., COVID-19 severity in relation to sociodemographics and vitamin D use. Open medicine. 2021; 16: 591-609.
19. Hamed AM, Elsebaie EH, Shaheen HA, Mahfouz A, Hasan MD, Abdeltawab MS. Investigation of the Association between COVID-19 Infection, Gastrointestinal Manifestations, Parasitic Diseases and Antiparasitic Treatment: An Electronic Data Compilation. Egypt Acad.J. Biol. Sci. G. Microbiology. 2022; 14:85-99.
20. Eid RA, Attia AM, Hassan M, Shaker M A, Kamal MA. Demographic, clinical, and laboratory characteristics of patients with COVID-19 during the second and third waves of the pandemic in Egypt. J. Infect. Public. Health. 2021; 14: 1358-1366.
21. Opal SM, Girard TD, Ely EW. The immunopathogenesis of sepsis in elderly patients. Clin. Infect. Dis. 2005;41(Suppl. 7): S504-12.
22. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al., Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA.2020;23: 1061-1069
23. Gebrecherkos T, Gessesse Z, Kebede Y, Gebreegzabher A, Tasew G, Abdulkader M, et al., Effect of co-infection with parasites on severity of COVID-19. Med Rxiv. 2021; 2021-2002.
24. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet. Respir. Med. 2020; 8:e21.
25. Hill MA, Mantzoros C, Sowers JR. Commentary: COVID-19 in patients with diabetes. Metabolism. Metab. Clin. Exp. 2020; 107:154217.
26. Sanya RE, Webb EL, Zziwa C, Kizindo R, Sewankambo M, Tumusiime J, et al., The effect of helminth infections and their treatment on metabolic outcomes: results of a cluster-randomized trial. Clin. Infect. Dis. 2020;71:601–613
27. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al., Dysregulation of Immune Response in Patients With Coronavirus 2019 (COVID-19) in Wuhan, China. Clin. Infect. Dis. 2020;71: 762–768.
28. Fan BE, Chong VCL, Chan SSW, Lim GH, Lim KG, Tan GB, et al., Hematologic parameters in patients with COVID-19 infection. Am.J.Hematol.2020;95:131-134.
29. Liu J, Li S, Liu J, Liang B, Wang X, Wang H, et al., Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. E Bio Medicine. 2020; *55*:102763.
30. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, et al., Clinical findings in a group of patients infected with the 2019

novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ. 2020;368.
31. Singh S, Sharma A, Arora SK. High producer haplotype (CAG) of-863C/A,-308G/A and-238G/A polymorphisms in the promoter region of TNF-α gene associate with enhanced apoptosis of lymphocytes in HIV-1 subtype C infected individuals from North India. PloS. one. 2014;9: e98020.
32. Guan WJ, Ni ZY, Hu Y, Liang W H, Ou C Q, He JX, et al., Clinical characteristics of coronavirus disease 2019 in China. N. Engl. J. Med. 2020;382: 1708-1720.
33. Anai M, Akaike K, Iwagoe H, Akasaka T, Higuchi T, Miyazaki A, et al., Decrease in hemoglobin level predicts increased risk for severe respiratory failure in COVID-19 patients with pneumonia. Respir. Investig. 2021; 59:187–193.
34. Cavezzi A, Troiani E, Corrao S. COVID-19: hemoglobin, iron, and hypoxia beyond inflammation. A narrative review. Clinics and practice. 2020; 10: 1271.
35. Abdel-Hamed EF, Ibrahim MN, Mostafa NE, Moawad HS, Elgammal N E, Darwish EM, et al., Role of interferon-gamma in SARS-CoV-2-positive patients with parasitic infections. Gut pathogens.2021;13,1-7
36. Can H, Alak SE, Köseoğlu AE, Döşkaya M, Ün C. Do Toxoplasma gondii apicoplast proteins have antigenic potential? An in silico study. Comput. Biol. Chem. 2020; 84: 107158.
37. Thompson MG, Breiman RF, Hamel MJ, Desai M, Emukule G, Khagayi S, et al., Influenza and malaria coinfection among young children in western Kenya, 2009–2011. J. Infect. Dis. 2012; 206, 1674-1684.
38. Bhadra R, Cobb DA, Weiss LM, Khan IA. Psychiatric disorders in toxoplasma seropositive patients—the CD8 connection. Schizophr. Bull. 2013; 39: 485-489.
39. Abdoli A. Helminths and COVID-19 co-infections: a neglected critical challenge. ACS. Pharmacol. Transl. Sci. 2020; 3: 1039-1041.