

# Parasitic Infections in COVID-19 Hospitalized Patients in Bandar Abbas City, Iran

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## ABSTRACT

**Background and Aim:** COVID-19 has led to a wide range of clinical symptoms, which are increasing in low- and middle-income countries. Parasitic infections are the reasons for the concomitant effect of this disease in these regions, which can reduce or increase the severity of the disease. The present study aimed to determine the clinical features, laboratory findings, and frequency of the intestinal parasites in the COVID-19 patients.

**Materials and Methods:** In this descriptive cross-sectional study, the clinical features, laboratory findings, and frequency of the intestinal parasites in the stool specimens of 150 COVID-19 patients, confirmed by PCR and hospitalized in Bandar Abbas hospitals during 2020-2021, were evaluated using direct wet methods with Lugol and physiological saline, formalin ethyl-acetate concentration technique (FECT), modified Ziehl-Neelsen staining, and trichrome staining.

**Results & Conclusion:** Eighteen (12%) out of 150 patients with COVID-19 were infected with intestinal parasites, among whom the highest frequencies belonged to the intestinal *Blastocystis spp.* (10 %), and then *Giardia lamblia* (1.3%), and *Trichomonas hominis* (0.7%), and some cases with no intestinal helminths were observed. According to the findings, patients with COVID-19 and simultaneous parasite infections had substantially greater rates of decreased appetite ( $P=0.015$ ), stomach ache ( $P=0.002$ ), and flatulence ( $P=0.002$ ) than those without parasitic infections. Based on the laboratory findings, no significant relationship was observed between the two groups of parasites and no parasites. More epidemiological and clinical studies are needed to better understand the status of intestinal parasitic infections (IPIs) in the hospitalized COVID-19 patients in Bandar Abbas city, Iran.

**Keywords:** Clinical Features, COVID-19, Intestinal Parasites, Iran, Laboratory Findings

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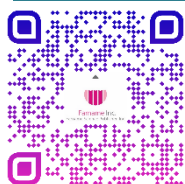
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## 1. Introduction

Over the past two decades, the world has encountered the emergence of three coronaviruses, including SARS-CoV, with mortality rate of 9.5% in September 2003, the new MERS-CoV, which causes

respiratory diseases, and first appeared in the Middle East 9 years later, and also a group of patients with pneumonia of unknown cause was observed in Wuhan, China on December 30, 2019. A week later, on

January 7, 2020, a novel coronavirus (SARS-CoV-2) was discovered in these patients in Wuhan, China. The virus was formerly known as the novel coronavirus 2019 (2019-nCoV), but on February 11, 2020, the disease was officially renamed to COVID-19 by the World Health Organization (WHO). The COVID-19 was more contagious compared to the previous two generations and infected more people with much more fatalities (1). Examining the laboratory parameters in order to determine the severe or less severe cases of COVID-19, identifying patients who are at higher risk of mortality, and increasing awareness for the appropriate action in improving the clinical situation will be useful (2).

The intestinal parasitic infections (IPIs) are major public health problems with disproportionately high prevalence rates in low- and middle-income countries (LMICs) (3.5 billion people suffering) (3). Four hundred fifty million people develop symptomatic clinical forms, and more than 200,000 deaths are annually reported (4). The IPIs comprise both pathogenic and non-pathogenic protozoa and helminths, which produce a variety of symptoms, including malnutrition, weight loss, growth retardation, malabsorption, anemia, stomach ache, nausea, and vomiting (5). About half of the COVID-19 patients experienced gastrointestinal symptoms, including nausea, diarrhea, vomiting, and abdominal pain, which often precede respiratory symptoms, all of which are signs of the intestinal parasites (6). The concomitant parasitic infections in COVID-19 patients may not have any significant association (7). However, concurrent parasite infections with COVID-19 in the patients may alter the host's immune response to the SARS-CoV-2 with either advantageous or deleterious consequences, like a double-edged sword (8, 9). Indeed, parasite-induced immunomodulatory responses may mute the hyper-inflammation associated with the severe COVID-19 and, in contrast, co-infections may suppress an efficient immune response against SARS-CoV-2 early stage of the infection and increase the complications caused by COVID-19 (10). Since SARS-CoV-2 infection can contribute to the spread (11) or reactivation of infectious diseases and given that many patients with COVID-19 will have some degrees of immunosuppression, it is expected to be at risk of reactivation of dormant/latent parasitic infections, especially in endemic areas (12). Therefore, the present study aimed to evaluate the parasitic infections in the patients hospitalized with COVID-19 in Bandar Abbas city, Iran, in 2020-2021.

## 2. Materials and Methods

The current cross-sectional study was done with the informed consent of the patients tested positive with COVID-19 by polymerase chain reaction (PCR) who were hospitalized at Shahid Mohammadi Hospital in Bandar Abbas County, Hormozgan Province, Iran, between December 2020 and July 2021. The study was approved by the Ethics Committee of the Deputy of Research and Technology of the Hormozgan University of Medical Sciences-Iran with an ethical code (IR.HUMS.REC.1399.428).

The following data were extracted from each patient's medical record by the trained research team of Hormozgan University of Medical Sciences: social demographic, clinical data, laboratory data, underlying diseases, treatment regimens, duration of treatment, and disease outcome.

Fresh fecal samples were collected from the COVID-19 patients to evaluate IPIs. First, the macroscopic and then the microscopic examinations of the samples were conducted through wet mount (WM) (direct wet method with Lugol and physiological saline), and formalin ethyl-acetate concentration technique (FECT). Modified Ziehl-Neelsen and trichrome staining methods were used to increase the sensitivity of the parasite detection (13).

### Data analysis

Data were analyzed by the SPSS 26 software using descriptive statistical techniques, including tables of frequency distribution and percentages, sketching qualitative variables, and utilizing statistical indices like mean and standard deviation of quantitative variables. The Chi-square test and Fisher's exact test were utilized to examine the qualitative variables. The non-parametric Mann-Whitney test (two groups) and Kruskal-Wallis test (three groups and more) were used to compare the quantitative variables of age and length of hospitalization among the groups in terms of the abnormal distribution of these two variables in the groups.

## 3. Results & Discussion

The role of fungal and bacterial infections in COVID-19 is known and included in the routine diagnostic workup, but the parasitic infections remain unknown (12). Although, there is possibility for the parasitic infections to reduce the severity of COVID-19 through direct modulation of the immune system along with indirect parasite-driven microbiome balance, they can damage the immune system, raise microbiome dysbiosis, support viral infection, and also reduce the effectiveness of vaccination (6).

The present descriptive and cross-sectional study evaluated 150 fecal samples of the COVID-19 patients

who were confirmed by PCR and admitted to the Shahid Mohammadi Hospital in Bandar Abbas in 2020-2021. The stool specimens of these patients were examined. Eighty-eight participants (58.7%) were female, and the education level of most participants (59.3%) was high school diploma and lower. The demographic characteristics are shown in [Table 1](#). There was no significant difference between individual demographic variables and parasite prevalence in the stool samples.

The macroscopic examination of the stool samples indicated that the highest frequency of color and consistency of feces were formed (72.0%) and brown (87.3%), respectively. The overall prevalence of IPIs was estimated to be 12% ([Table 2](#)). According to the similar studies before the COVID-19 epidemic in Bandar Abbas, Turki *et al.* (14) reported the prevalence of IPIs to be 6.5% among primary school children in Bandar Abbas. Mohammadi-Meskin *et al.* (15) reported 55.2% IPI prevalence in intellectually disabled individuals and rehabilitation personnel in Bandar Abbas. Heydari-Hengami *et al.* (16) reported their prevalence at about 34.9% in food operators in Bandar Abbas. Their findings differed from ours in terms of the frequency of the intestinal parasites owing to the varied demographics. Also among the causes of this decrease in the frequency of intestinal parasites, it could be the general hygiene rules that were observed much more in the period of COVID-19 and decreased interpersonal contact (17). Furthermore, in other parts of the world, Wolday *et al.* (9) reported a prevalence of 37.8% for IPI in the study of COVID-19 patients in Ethiopia. Al-Khaliq *et al.* (18) in Baghdad, the capital city of Iraq, reported the prevalence of 1.1% for the intestinal parasites in COVID-19 patients, which were different from our study.

The prevalence of *Blastocystis* was 10% ([Table 2](#)), which was inconsistent with microscopic studies obtained by Turki *et al.* (14), Heydari-Hengami *et al.* (16), and Mohammadi-Meskin *et al.* (15) all in Bandar Abbas with the prevalence of *Blastocystis* at 2.1%, 24.3% and 30.2%, respectively. Furthermore, in comparison with other studies from other parts of the world; Aydemir *et al.* (17) in Turkey reported the prevalence of *Blastocystis* in the period of COVID-19 as 11.86%, which was relatively similar to our study.

Regarding *giardiasis*, the microscopic examination of our study indicated its prevalence at 1.3% ([Table 2](#)), which was similar to the previous studies in Iran before the COVID-19 pandemic conducted by Turki *et al.* (14) with the prevalence of 2.9%. Our result was inconsistent with the results of studies conducted by Heydari-Hengami *et al.* (15) and Mohammadi-Meskin *et al.*, (15) in Bandar Abbas that reached the prevalence of 6.8% and 5.6%, respectively. Compared to the other parts of the world; Aydemir *et al.* (17) in Turkey reported the prevalence of *giardiasis* in the period of COVID-19 as

1.60%, which was similar to our study. The prevalence of *Trichomonas hominis* was obtained 0.7% ([Table 2](#)).

Even though the parasitic diseases are on the way to decline in Iran compared to the earlier decades, intestinal parasites, particularly protozoa, still remain a difficult public health concern in the areas where there are few healthcare measures (19). Regarding the intestinal helminths infections in our study, no infection was detected among people with COVID-19, but previous studies by Mohammadi-Meskin *et al.* (15) reported the prevalence of *Strongyloides stercoralis* at 16.6% in intellectually disabled patients in Bandar Abbas. Since dexamethasone (a corticosteroid) was in use to treat some COVID-19 patients, there was a risk for increased incidence of severe *Strongyloides* infections by increasing dexamethasone usage (20). Hence, specific parasite detection methods should be examined that was not in the line with our study.

Clinical symptoms were evaluated in individuals with and without parasites ([Table 3](#)). Decreased appetite (83.3%), stomach ache (44.4%), and flatulence (22.2%) were significantly higher in individuals with parasites infection compared to those without parasites ( $P < 0.05$ ). There was no significant difference between the presence of the parasite and the other symptoms such as fever and chills ([Table 3](#)). Furthermore, no correlation was found between the existence of comorbidities and the patient's condition with the presence or absence of the parasite. Wolday *et al.* (9) found that concomitant parasitic infections (protozoa and helminths) might protect against progression to the severe COVID-19 in terms of parasitic immune system modulatory responses. Al-Khaliq *et al.* (18) also showed in their 2021 study an inverse relationship between parasitic infection and COVID-19 infections, however, the possible relationship cannot be reliably speculated and it requires extensive future studies.

So far, the laboratory parameters have been less used for the definitive diagnosis of COVID-19 due to their low sensitivity and specificity, but they have been considered as valuable prognostic indicators and provide useful information regarding the severity of the disease, the course of the disease, and the response to treatment (21). Our laboratory findings of the participants indicated no significant difference in the laboratory results between parasite and non-parasitic groups, however, Tao *et al.* (22) discovered that various coagulation, cardiac, renal, and hepatic functions such as PT, LDH, Total bilirubin, CRP, and ESR increased in the parasite group. In our study, no significant difference was found between COVID-19 patients with any concomitant parasitic infection compared to the patients without parasitic infection during hospitalization, and no death was reported among the participants ([Table 4](#)).

It was the first study on the prevalence of IPIs among the patients with COVID-19 in Bandar Abbas. Microscopic examination of fecal samples of the patients was performed with WM (direct wet method with Lugol and physiological saline) and FECT. Furthermore, modified Ziehl-Neelsen and trichrome staining methods were used for the accurate confirmation to increase the validity of measuring the dependent variable. In this study, no statistically significant difference was shown between different methods in terms of detecting parasites (Table 2), but considering that molecular methods have higher sensitivity than microscopic

methods in detecting intestinal parasites (23), one of the limitations of this study could be not applying this technique and since we examined only one replication of stool sample for each patient, we might underestimate the true prevalence of parasitic infections; hence, it is recommended that at least three consecutive samples should be examined from each patient for three consecutive days. Undoubtedly, studies with larger sample sizes as well as further studies to confirm the association of concomitant parasitic infection in the patients with COVID-19 are needed.

**Table 1.** Socio-demographic characteristics among COVID-19 patients with or without parasitic co-infection

Socio-demographic features	Characteristic	All patients N=150	Without parasite N=132	With parasite N=18	P-value
Sex, N (%)	Female	62 (41.3)	56 (42.4)	6 (33.3)	0.462
	Male	88 (58.7)	76 (57.6)	12 (66.7)	
Age in years [median (IQR)]		49 (23.3)	49 (23.8)	52 (21.8)	0.806
Age group [years, N (%)]	<44	62 (41.3)	54 (40.9)	8 (44.4)	0.737
	45-59	36 (24.0)	33 (25.0)	3 (16.7)	
	60≥	52 (34.7)	45 (34.1)	7 (38.9)	
Occupation	Employee	33 (22.0)	30 (22.7)	3 (16.7)	0.573
	Self-Employment	47 (31.3)	41 (31.1)	6 (33.3)	
	Housewife	51 (34.0)	46 (34.8)	5 (27.8)	
	Retired	19 (12.7)	15 (11.4)	4 (22.2)	
Education level	Illiterate	25 (16.7)	25 (18.9)	0 (0.0)	0.054*
	Diploma and lower college education	89 (59.3)	74 (56.1)	15 (83.3)	
		36 (24.0)	33 (25.0)	3 (16.7)	

\* Fisher's exact test

**Table 2.** Prevalence of intestinal parasite species identified by the wet mount, concentration techniques, and staining methods among COVID-19 patients

		Combined Method	Wet mount		Concentration Techniques	Staining methods	
			Direct fecal smear Pos (%)	LUGOL'S IODINE STAIN Pos (%)	Formalin-Ethyl acetate Concentration Technique (FECT) Pos (%)	Trichrome staining Pos (%)	Modified Ziehl-Neelsen staining Pos (%)
any Parasite	Yes	18 (12.0)	11 (7.3)	11 (7.3)	14 (9.3)	18 (12.0)	0 (0)
	No	132 (88.0)	139 (92.7)	139 (92.7)	136 (90.7)	132 (88.0)	150 (100)
Parasite Species	<i>Blastocystis spp.</i>	15 (10.0)	9 (6.0)	9 (6.0)	11 (7.3)	15 (10.0)	-
	<i>Giardia lamblia</i>	2 (1.3)	1 (0.7)	1 (0.7)	2 (1.3)	2 (1.3)	-

	Combined Method	Wet mount		Concentration Techniques	Staining methods	
		Direct fecal smear	LUGOL'S IODINE STAIN	Formalin-Ethyl acetate Concentration Technique (FECT)	Trichrome staining	Modified Ziehl-Neelsen staining
		Pos (%)	Pos (%)	Pos (%)	Pos (%)	Pos (%)
<i>Trichomonas hominis</i>	1 (0.7)	1 (0.7)	1 (0.7)	1 (0.7)	1 (0.7)	-

Pos: Positive

**Table 3.** Clinical features among COVID-19 patients with or without parasitic co-infection

	Characteristic	All patients	Without parasite	With parasite	P-value
Clinical symptoms and signs	fever	101 (67.3)	89 (67.4)	12 (66.7)	0.949
	Chills	65 (43.3)	58 (43.9)	7 (38.9)	0.685
	decreased appetite	85 (56.7)	70 (53.0)	15 (83.3)	0.015
	Stomach ache	27 (18.0)	19 (24.4)	8 (44.4)	0.002
	Diarrhea	30 (20.0)	26 (19.7)	4(22.2)	0.802
	Flatulence	9 (6.0)	5 (3.8)	4 (22.2)	0.002
	Respiratory symptoms	93 (62.0)	84 (63.6)	9 (50.0)	0.264
	Loss of smell and/or taste	3 (2.0)	3 (2.3)	0 (0.0)	1.000*
	Head ache	26 (17.3)	21 (15.9)	5 (27.8)	0.212
	Dizziness	9 (6.0)	7 (5.3)	2 (11.1)	0.330
	Cough (any type)	50 (33.3)	43 (32.6)	7 (38.9)	0.594
	Dry cough	8 (5.3)	8 (6.1)	0 (0.0)	0.596*
	Haemoptysis	1 (0.7)	1 (0.8)	0 (0.0)	1.000*
	Vomiting	8 (5.3)	8 (6.1)	0 (0.0)	0.596*
	Chest pain	6 (4.0)	4 (3.0)	2 (11.1)	0.101
	Sore throat	6 (4.0)	6 (4.5)	0 (0.0)	0.356
	Dyspnea	55 (36.7)	48 (36.4)	7 (38.9)	0.835
	Other symptoms	96 (64.0)	83 (62.9)	13 (72.2)	0.439
Comorbidities	Comorbidity (at least 1)	79 (52.7)	68 (51.5)	11 (61.1)	0.444
	Hypertension	30 (20.0)	28 (21.2)	2 (11.1)	0.315
	Diabetes	26 (17.3)	22 (16.7)	4 (22.2)	0.559
	Cardio-vascular diseases	16 (10.7)	14 (10.6)	2 (11.1)	0.948
	Chronic liver disease	5 (3.3)	5 (3.8)	0 (0.0)	1.000*
	Chronic obstructive lung diseases and asthma	4 (2.7)	4 (3.0)	0 (0.0)	1.000*
	Chronic kidney disease	5 (3.3)	4 (3.0)	1 (5.6)	0.447*
	Autoimmune diseases	5 (3.3)	4 (3.0)	1 (5.6)	0.447*
	Tumor	2 (1.3)	2 (1.5)	0 (0.0)	1.000*
	Hepatitis c	1 (0.7)	1 (0.8)	0 (0.0)	1.000*
Patient condition	Hospitalized in COVID-19 ward	148 (98.7)	130 (97.5)	18 (100.0)	1.00

Characteristic	All patients	Without parasite	With parasite	P-value
Hospitalized in ICU ward	2 (1.3)	2 (1.5)	0 (0.0)	0.879
Length of stay (LOS)(Days)	4.0 (2.0)	4.0 (2.0)	4.0 (2.0)	
Death	00 (00)	00 (00)	00 (00)	

\* Fisher's exact test

**Table 4.** Laboratories findings among COVID-19 patients with or without parasitic co-infection

Laboratories findings, (median, IQR)	All patients	Without parasite	With parasite	P-value
WBC, $\times 10^3/\mu\text{L}$	5.8 (4.0)	5.8 (4.0)	6.0 (2.9)	0.694
RBC, $\times 10^6/\mu\text{L}$	4.5 (0.9)	4.5 (0.9)	4.5 (1.2)	0.784
Hb, g/dL	12.4 (2.8)	12.4 (2.8)	13.4 (3.8)	0.726
HCT, %	37.4 (6.6)	37.1 (6.7)	37.8 (9.6)	0.713
Plt, $\times 10^3/\mu\text{L}$	200.0 (106.0)	197.0 (101.0)	203.0 (122.5)	0.611
NEUT, %	75.0 (16.0)	75.0 (16.7)	73.2 (13.5)	0.991
Lym, %	18.8 (13.3)	18.8 (13.5)	19.1 (12.0)	0.724
Mixed, %	5.0 (5.0)	5.5 (5.0)	4.7 (4.4)	0.184
Urea, mg/dL	33.0 (15.0)	33.0 (15.0)	32.5 (14.5)	0.694
Cr, mg/dL	1.0 (0.3)	1.0 (0.3)	1.1 (0.4)	0.286
Na, mEq/L	138.0 (5.0)	138.0 (5.0)	137.5 (4.0)	0.756
K, mEq/L	4.4 (0.8)	4.3 (0.8)	4.6 (0.8)	0.643
LDH, mg/dL	580.0 (340.0)	580.0 (345.0)	618.5 (311.8)	0.701
Ferritin, $\mu\text{g/mL}$	487.0 (766.0)	483.0 (763.0)	599.5 (892.8)	0.995
CRP, mg/Lit	31.0 (48.5)	30.0 (48.0)	36.6 (55.8)	0.931
ESR, mm/h	42.0 (34.0)	41.0 (30.0)	44.5 (46.5)	0.970
BS, mg/dL	118.0 (53.0)	118.0 (55.0)	115.0 (49.0)	0.405
SGOT, U/L	37.0 (17.0)	38.0 (17.0)	36.0 (9.5)	0.890
SGPT, U/L	37.0 (25.0)	37.0 (26.0)	36.5 (26.3)	0.970
ALP, U/L	172.0 (83.0)	172.0 (80.0)	180.5 (110.5)	0.268

Abbreviations: ALP: Alkaline Phosphatase; BS: Blood Sugar (Glucose); CRP: C-Reactive Protein; Cr: Creatinine; ESR: Erythrocyte Sedimentation Rate; HCT: Hematocrit; Hb: Hemoglobin; IQR: Interquartile range; K: Potassium; LDH, Lactate dehydrogenase; Lym: lymphocytes; Mixed: Mixed cell population includes monocytes, basophils, and eosinophils; Na: Sodium; NEUT: Neutrophils; Plt: Platelet; RBC: Red Blood Cells; SGOT: Serum Glutamic Oxaloacetic Transaminase; SGPT: Serum Glutamic-Pyruvic Transaminase; WBC: White Blood Count;

## 4. Conclusion

The relatively low prevalence of IPIs was observed in Bandar Abbas, where *Blastocystis spp.* was the most common intestinal parasite, followed by *Giardia lamblia* and *Trichomonas hominis*, respectively. Considering the high prevalence of *Strongyloides stercoralis* and other opportunistic parasitic infections in Bandar Abbas in the past, the conventional diagnostic methods alone are not sufficient to diagnose the parasitic infections; hence, the specialized methods to diagnose these infections, such as FEC and helminths culture, should be combined with WM as a routine

diagnostic method in the medical diagnostic laboratories, as well as collecting several samples on different days before starting chemotherapy, especially for the COVID-19 patients who are taking immunosuppressive drugs.

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### Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

### Ethical Considerations

The study protocol was approved by the Ethics Committee of the Deputy of Research and Technology of the Hormozgan University of Medical Sciences, Iran (ethical code IR.HUMS.REC.1399.428).

### Authors' Contributions

KS and JS conceived and designed the study. SAM and MN participated in collecting and evaluating the

samples. Analysis was performed by SMM, ER and MF. The first draft of the manuscript was written by KS, JS, and SMM and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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### Conflict of Interest

The authors declare that they have no competing interests.

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