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Coronavirus Pandemic

A single-center experience in home management of mild and moderate COVID-19 cases

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Abstract

Introduction: The use of telemedicine for treatment of coronavirus disease 2019 (COVID-19) infection has been effective in lowering the risk of infection and relieving strain on the healthcare system. This study aimed to describe the clinical characteristics of COVID-19 cases, their follow-up, risk factors of disease severity, and predictors of hospital admission while using telemedicine.

Methodology: The study included 611 Egyptian patients with mild and moderate COVID-19 disease. The patients were isolated at home and monitored daily.

Results: Based on the World Health Organization classification, 79% of studied patients had mild illness while 20.5% had moderate illness. The initial symptoms included cough (51.7%), fever (50.8%), fatigue (45.9%), sore throat (41.1%), dyspnea (35.2%), and headache (34%); 25.2% patients had prolonged symptoms (≥ 21 days). Dyspnea was the most frequent (15.5%) long-term symptom. Age, co-existing diabetes, and COVID-19 infection with moderate severity, were associated with the need for hospitalization. We compared patients with COVID-19 infection who required hospital admission (n = 37) versus patients who continued in home isolation (n = 574). High neutrophil/lymphocyte ratio, transaminases, and ferritin significantly correlated with the need for hospitalization. 18.9% of the patients who required hospital admission had diabetes. Multivariate analysis described age and diabetes as independent predictors of disease severity. Age and high neutrophil/lymphocyte ratio were independent predictors of hospital admission.

Conclusions: Telemedicine is effective in-home management of mild/moderate COVID-19 patients, which may ease the pressure on the healthcare system, even beyond the pandemic.

Key words: COVID-19; home management; telemedicine.

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was a public health emergency and a global pandemic. Consequently, 323,000 people died and 4.8 million cases of COVID-19 were recorded worldwide [1-3].

When the healthcare systems were overburdened during the pandemic, manpower and infrastructure were on the brink of collapse. To combat the inevitable threat of failure and to curb virus spread routes, the World Health Organization (WHO) [4] and the Egyptian Ministry of Health (MOH) [5] advocated home isolation for mild/moderate cases of COVID-19 infection [4,5]. Telemedicine was used to manage the surging number of COVID-19 cases worldwide. It was considered an indispensable tool that helped with patients' surveillance, cut down on disease transmission, and, most importantly, ensured the continuity of care of frail patients with multiple chronic diseases [6]. Telemedicine was described by WHO as one of the crucial services in "strengthening the health systems response to COVID-19" [4].

In the current study, we describe our experience in using telemedicine for home management and follow-up of mild and moderate COVID-19 patients. This study aimed to describe the clinical characteristics of COVID-19 cases, follow-up, risk factors of COVID-19 disease severity, and the predictors for hospital admission while using telemedicine.

Methodology

The study included 611 Egyptian patients who tested positive for COVID-19 infection by reverse transcription polymerase chain reaction (RT-PCR) and classified as having mild or moderate COVID-19 disease according to the clinical management guidelines of COVID-19 published by WHO [8]. All patients were referred from Kasr Al-Ainy COVID-19 out-patient clinic, Faculty of Medicine, Cairo University, and were followed up from July 2020 to March 2021. The patients included medical team members, in addition to non-medical academic and administrative staff and their families.

Eligibility criteria included patients aged 18 to 65 years and classified as having mild/moderate COVID-19 disease [8]. All patients consented to home isolation and follow-up. Exclusion criteria included severe cases of COVID-19 who required hospital admission and children or adolescents less than 18 years old. Patients aged more than 65 years and those who refused follow-up were excluded.

The protocol of therapy was decided according to the protocol published by the Egyptian MOH [5]. All COVID-19 cases who consented to home isolation were followed by phone, WhatsApp, emergency hotline, and Zoom meetings. All patients received a home isolation instructions brochure (approved by the MOH) [5] in addition to a medication list, and a follow-up plan.

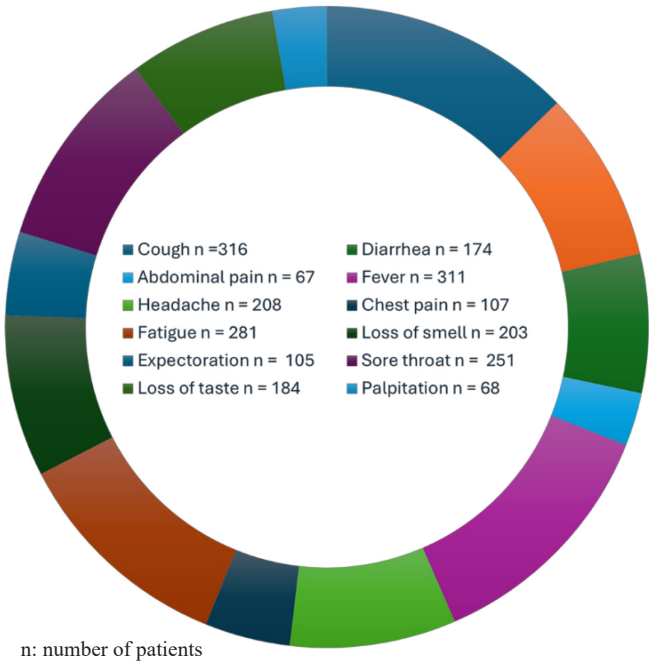
All studied patients underwent computed tomography (CT) and laboratory investigations in the form of complete blood count (CBC), liver and kidney function tests, C-reactive protein (CRP), D-dimer, and serum ferritin.

Daily patient follow-up included review of fever charts, symptoms, and any emerging red flags that require re-evaluation or hospitalization. Red flags included dyspnea, hemoptysis, disturbed consciousness level, persistent high-grade fever not responding to antipyretics, bleeding tendency, chest pain, and blurring of vision. Out of 611 patients, 393 patients were followed for three months. The total duration of symptoms was calculated, and symptoms that persisted for ≥ 21 days were categorized as prolonged duration symptoms.

Statistical methods

Data collection and cleaning were done using Google Forms, then exported through Google Spreadsheets to Microsoft Excel 365©. IBM SPSS 26 (IBM Corp, Armonk, NY, U.S.A.) was used for statistical analysis. Descriptive statistics were calculated to explore, summarize and present the data. We used Mann-Whitney tests and Chi square tests for hypothesis testing, with a significance level of 5%. Multivariate analysis was also done fitting a logistic regression model using the Enter method. Missing data were excluded from the analysis.

Figure 1. Frequency of symptoms among patients.



n: number of patients

Results

Demographics and clinical characteristics of the study population

The study population included 486 cases with mild illness (79.5%) and 125 cases with moderate illness (20.5%); 258 (42.2%) were males and 353 (57.7%) were females; with mean ± SD age 38.5 ± 12 years. Other clinical characteristics of the study population were summarized in (Table 1).

Patients were divided into two groups according to their need for hospitalization during follow-up in home isolation. Group I (n = 37) included patients who required hospital admission; while group II (n = 574) included patients who continued home isolation without the need for hospital admission.

Frequency of symptoms reported among patients

The most reported symptoms among the study population were cough, fever, fatigue, and sore throat, which were reported in 51.7%, 50.9%, 45.9%, and 41.1%, respectively. Other symptoms in the form of shortness of breath with exertion, headache, loss of smell and loss of taste were described in 35.2 %, 34.0%, 33.2% and 30.1%, respectively. Symptoms in the form of diarrhea, chest pain, expectoration, palpitation, and abdominal pain were less frequent (Figure 1).

Table 1. Demographics and clinical characteristics of the study population.

Characteristics		Mild [n = 486]	Moderate [n = 125]	*p* value
Age in years (Median ± IQR)		36 (28–45)	44 (33-51)	0.0001
Gender	Males	204 (42%)	54 (43.2%)	0.839
	Females	282 (58.0%)	71 (57%)	
Diabetes	Yes	28 (5.7 %)	26 (20.8 %)	0.0001
	No	458 (94.3 %)	99 (79.2 %)	
Hypertension	Yes	37 (7.6 %)	23 (18.4 %)	0.001
	No	449 (92.3 %)	102 (81.6 %)	
Chronic heart disease	Yes	10 (2.1%)	9 (7.2%)	0.007
	No	476 (97.9%)	116 (92.8%)	
Chronic liver disease	Yes	6 (1.2%)	3 (2.4%)	0.399
	No	592 (96.9 %)	480 (98.8%)	
Chronic lung disease	Yes	14 (2.9%)	5 (4%)	0.562
	No	472 (97.1)	120 (96%)	
Other comorbidities *	Yes	22 (4.5 %)	10 (8 %)	0.12
	No	464 (95.5 %)	115 (92 %)	
Smoking	Yes	75 (15.4 %)	23 (18.4 %)	0.41
	No	411 (84.6 %)	102 (81.6 %)	
Health care providers	Yes	226 (46.5 %)	57 (45.6 %)	0.92
	No	260 (53.5 %)	68 (54.4 %)	
Required admission to hospital	Yes	13 (35%)	24 (65 %)	0.0001
	No	473 (82.4%)	101 (17.6 %)	
Fever	Yes	224 (46%)	87 (69.6%)	0.0001
	No	262 (54%)	38 (30.4%)	
Cough	Yes	223 (46%)	93 (74.4%)	0.0001
	No	263 (54%)	32 (25.6%)	
Expectoration	Yes	64 (13.2%)	41 (32.8%)	0.0001
	No	422 (86.8%)	84 (67.2%)	
Chest pain	Yes	70 (14.4%)	37 (29.6%)	0.06
	No	416 (85.6%)	88 (70.4%)	
Dyspnoea	Yes	143 (29.4%)	72 (57.6%)	0.001
	No	343 (70.6%)	53 (42.4%)	
Palpitation	Yes	42 (8.6%)	26 (20.8%)	0.009
	No	444 (91.4%)	99 (79.2%)	
Sore throat	Yes	191 (39.3%)	60 (48%)	0.0001
	No	295 (60.7%)	65 (52%)	
Loss of taste	Yes	137 (28.2%)	47 (37.6%)	0.07
	No	349 (71.8%)	78 (62.4%)	
Loss of smell	Yes	155 (31.9%)	48 (38.4%)	0.03
	No	331 (68.1%)	77 (61.6%)	
Headache	Yes	151 (31.1%)	57 (45.6%)	0.1
	No	335 (68.9%)	68 (54.4%)	
Diarrhea	Yes	130 (26.7%)	44 (35.2%)	0.8
	No	356 (73.3%)	81 (64.8%)	
Abdominal pain	Yes	46 (9.5%)	21 (16.8%)	0.4
	No	440 (90.5%)	104 (83.2%)	
Fatigue	Yes	199 (40.9%)	82 (65.6%)	0.005
	No	287 (59.1%)	43 (34.4%)	
Laboratory data (Median ± IQR)	WBC x 10^3/UL	6.1 (5.08-8.12)	6.7 (5.39–8.32)	0.148
	Hb (g/dL)	13.6 (12.4–14.8)	14.1 (13–14.8)	0.264
	NLR	1.2 (0.87–1.7)	1.3 (1–2.2)	0.022
	Platelets (× 10^9/L)	213 (173–254)	193 (124–243)	0.368
	CRP (mg/L)	2.8 (1.06–8.32)	4.7 (1.8–7.4)	0.034
	Ferritin (ng/mL)	79 (39.8–151.7)	110 (55–195.8)	0.217
	Creatinine (mg/dL)	0.83 (.73-.96)	0.86 (0.8–0.99)	0.854
	Urea (mg/dL)	24 (20–30)	25 (22.5–32.5)	0.287
	ALT(IU/L)	29 (16–41)	32 (22–45.5)	0.058
	AST(IU/L)	25 (20–32)	27 (23–33)	0.087

ALT: alanine aminotransferase; AST: aspartate aminotransferase; CRP: C-reactive protein; IQR: interquartile range; Hb: hemoglobin; NLR: neutrophil-lymphocyte ratio; WBC: white blood cell count. *p* values < 0.05 were considered significant.

Figure 2. Onset of occurrence of COVID- 19 symptoms during the disease course.

Symptoms starting week	1st week	2nd week	3rd week	4th week
Fever	300	10	1	0
Cough	297	18	1	0
Expectoration	96	5	4	0
Sore throat	236	10	5	1
Headache	197	9	2	0
Fatigue	273	5	1	2
Dyspnoea	192	16	6	1
Haemoptysis	4	2	0	0
Chest pain	99	5	3	0
Palpitation	60	6	1	1
Diarrhoea	146	19	7	2
Abdominal pain	48	13	4	2
Leg swelling	10	3	0	0
Loss of taste	171	10	2	1
Loss of smell	186	14	2	1
Haematuria	1	3	0	0
Purpura	0	2	1	0
Blurring of vision	6	2	1	0

Occurrence of symptoms during the disease course

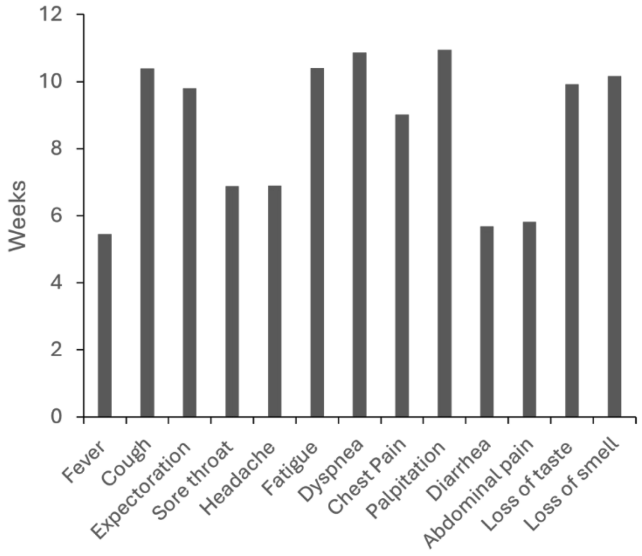
The heat map of symptoms during the one-month follow-up for all 611 patients showed that the most prevalent symptoms reported early during the first week of illness were fever (49%), cough (48.6 %), fatigue (44.6 %), and sore throat (38.6 %) (Figure 2).

Duration of each symptom

Palpitation had the longest duration with 10.9 days. The second longest duration symptom was shortness of breath with exertion, which lasted 10.8 days, followed by cough and fatigue (10.41 and 10.39 days, respectively) (Figure 3).

Patients with COVID-19 infection who required hospital admission versus patients who continued home isolation

Figure 3. Mean duration (in weeks) of each symptom among the study population.



Age and moderate severity of COVID-19 infection at presentation were significantly associated with the need for hospitalization (p = 0.002 and p = 0.0001, respectively). Among the hospitalized patients, 18.9% had diabetes (p = 0.036). No significant association was identified between the need for hospitalization and other comorbidities such as hypertension, chronic heart disease, lung diseases, liver disease, or kidney disease. The patients who required hospital admission had a significantly higher level of neutrophil/lymphocyte ratio (NLR) (p = 0.002), serum ferritin (p = 0.046), urea (p = 0.049), and aspartate aminotransferase (AST) (p = 0.023).

Multivariate analysis to identify risk factors of COVID-19

A stepwise logistic regression was performed using the following variables: patient age; presence of diabetes, hypertension, underlying heart disease, breast disease, liver disease, and NLR. The analysis concluded that patients' age, presence of diabetes, and high NLR were independent predictors of COVID-19 severity (p

Table 2. Multivariate logistic regression for predictors of disease severity.

Variables	Beta	Odds ratio	95% confidence interval	*p* value
Age	0.030	1.031	1.01–1.052	0.003
NLR	0.248	1.283	1.050–1.564	0.015
Diabetes	1.231	3.25	1.753–6.690	0.0001
Hypertension	0.038	1.039	0.491–2.198	0.921
Heart disease	0.781	2.183	0.628–7.588	0.219
Liver disease	-1.047	0.351	0.031–3.950	0.397
Chest disease	0.433	1.542	0.479–4.967	0.468
Healthcare providers	0.279	1.321	0.833–2.096	0.236

NLR: neutrophil-lymphocyte ratio. p values < 0.05 were considered significant.

Table 3. Multivariate logistic regression for predictors of hospital admission.

Variables	Beta	Odds ratio	95% confidence interval	*p* value
Age	-0.056	0.946	0.909–0.984	0.005
NLR ratio	-0.413	0.661	0.503–0.870	0.003
Diabetes	-0.858	0.424	0.143–1.255	0.121
Hypertension	-0.399	0.671	0.211–2.132	0.499
Heart disease	-19.481	0.000	0.000	0.998
Liver disease	-1.047	0.000	0.000	0.999
Chest disease	0.433	0.000	0.000	0.998
Health care providers	-0.929	0.395	0.161–0.965	0.042

NLR: neutrophil-lymphocyte ratio. p values < 0.05 are considered significant.

= 0.003, p = 0.0001, and p = 0.015, respectively). Older age and presence of diabetes increased the odds of disease severity by 1.03 and 3.25 times, respectively. Furthermore, each unit increase in NLR increased the odds of having moderate disease severity by 1.28 (Table 2).

Identification of risk factors for the need for hospital admission during the follow-up of mild COVID-19 patients by multivariate analysis

Stepwise logistic regression was performed using the variables age; NLR; diabetes; hypertension; presence of underlying heart disease, chest disease, and liver disease; and being a healthcare provider. Age, being a healthcare provider, and NLR were identified as independent predictors of hospital admission. It was found that being older and being a medical health provider increased odds of hospital admission by 0.95 and 0.4 times, respectively. Moreover, the analysis showed that each unit increase in NLR increased the odds of hospital admission by 0.66 (Table 3).

Follow-up symptoms after three months and determining prolonged COVID-19

Out of the 611 studied patients, only 393 patients were available for follow-up at 3 months. The loss of patients at follow-up was attributed to non-compliance, patient's refusal to continue to follow-up after recovery, or failure to contact patients through their cellphones (turned off or out of reach). The follow-up for total symptom duration revealed prolonged symptoms (≥ 21 days) in 99 patients (25.2%). Dyspnea was a predominantly prolonged symptom (15.5%), followed by fatigue (10.9%), and bone aches (8.1%).

Discussion

The current study describes the use of telemedicine in management and follow up of home-isolated COVID-19 patients. To our knowledge, this is the biggest single-center research conducted in Egypt to track patients with mild and moderate COVID-19. The overall use of telemedicine in this study followed trends reported in other studies [9,10].

The COVID-19 patients in this study were diagnosed with mild (group A; 79.5%) or moderate illness (group B; 20.5%). The most common pre-existing comorbidities in our study were cardiovascular disease (12.9%), hypertension (9.8%), and diabetes (8.8%). Our findings are in accordance with earlier publications on the frequency of comorbidities in COVID-19-infected patients, where hypertension was described as the most frequent [11,12]. Tabacof *et al.* described cardiovascular disease as the most common associated comorbidity (39.8%) among 112 recruited patients, and hypertension was the most common underlying condition among them (36.3%) [13].

Initial assessment of the patients in our study identified cough, fever, fatigue, and sore throat as the most frequent symptoms (51.7%, 50.8%, 45.9%, and 41.1%, respectively). Other symptoms in the form of shortness of breath with exertion, headache, loss of smell, and loss of taste were less frequent. Diarrhea, chest pain, expectoration, palpitation, and abdominal pain were the least common symptoms. A similar pattern of symptoms was identified in earlier studies where fever, cough, and fatigue were described as the most common symptoms [14,15]. Our findings are consistent with those by Huang *et al*. and Wu *et al.* who discovered that fever, cough, dyspnea, and exhaustion were the most common symptoms in Asia [16,17].

In contrast to the symptoms observed in our study, Lechien *et al.* described headache (70.3%), loss of smell (70.2%), nasal obstruction (67.8%), cough (63.2%), asthenia (63.3%), myalgia (62.5%), rhinorrhea (60.1%), gustatory dysfunction (54.2%), and sore throat (52.9%) as the most common among 1,420 mild to moderate COVID-19 patients [18]. Fever was reported by Lechien *et al.* in only 45.4% of studied patients [18]. The study by Lechien *et al*. was conducted on patients from 18 European hospitals, with healthcare workers accounting for roughly one-third of the patients studied [18]. According to the study by Tabacof *et al.,* the most common symptoms were dyspnea, anxiety,

and chest pain (55.4%, 55.4%, and 42.9%, respectively), while the least common symptoms were difficulty in concentrating, tachypnea, and headache (42%, 34.8%, and 41.1%, respectively) [13].

In the present study, use of telemedicine, including telephone consultations, and patient records allowed us to describe the average duration of each presenting symptom. Palpitation (10.94 ± 4.4 days), dyspnea (10.8 ± 6.83 days), fatigue (10.41 ± 7.13 days), cough (10.39 ± 7.3 days), and loss of smell (10.16 ± 6.11 days) had the longest durations. While fever (5.45 ± 4.25 days) and diarrhea (5.68 ± 3.55 days) had the shortest mean duration among symptoms.

The prolonged palpitation reported among studied COVID-19 patients corroborates with and supports the idea of associated anxiety that may contribute, at least in part, to palpitation symptoms. Huang *et al.* studied the association between psychological distress and resting palpitations in patients who recovered from severe COVID-19 and observed a strong association between the psychological burden and the frequency of palpitation episodes [19]. In contrast to our findings, a previous study reported fatigue (58%) as a long duration COVID-19 symptom [20].

Among the COVID-19 patients in our study, those with older age, diabetes mellitus and hypertension had significantly moderate COVID-19 illness compared to those with mild illness ($p = 0.0001$, $p = 0.0001$, and $p = 0.001$, respectively). Older patients, patients with moderate illness, and patients with diabetes were significantly more likely to require hospital admission ($p = 0.002$, $p = 0.001$, and $p = 0.036$, respectively). There was no significant association between other comorbidities and the need for hospital admission. Our findings, together with the known increased infection risk associated with diabetes, led us to conclude that diabetic patients are at high primary risk of COVID-19 infection. Most of the COVID-19 infections in previous reports described diabetic patients as being hospitalized or admitted to the intensive care unit (ICU) due to a more severe course of the disease [21]. According to Min Cheol Chang *et al*. patients with clinical features of COVID-19 infection and findings of pneumonia on chest X-ray with co-existing diabetes mellitus were at risk of developing severe COVID-19 infection [22].

In terms of laboratory findings, NLR and CRP were significantly higher in patients with moderate COVID-19. Furthermore, high NLR, AST, and serum ferritin levels were all significantly related to the need for hospitalization. Several studies, including the current study, have highlighted the importance of NLR as an independent prognostic biomarker in determining COVID-19 prognosis and treatment efficacy, in addition to other inflammatory markers like CRP [23,24]. In terms of the patient's need for hospitalization, multivariate analysis revealed that age, the presence of diabetes, and high NLR were independent predictors. Earlier studies, including the study by Hou *et al.*, identified many risk factors of disease progression in patients who were admitted to hospital with COVID-19. Hou *et al*. described patients with older age, higher CRP, and lower lymphocyte count on admission to be associated with in-hospital disease progression [25].

Our findings related to co-existing diabetes, ties well with the study by Holman *et al.* in 2020 which found that during the initial COVID-19 pandemic in England, the severity, and deaths in people with type 1 and type 2 diabetes increased significantly [26]. Other results of meta-analysis done by Emami *et al.* in 2020 presumed that hypertension is the most prevalent underlying disease in hospitalized COVID-19 cases followed by cardiovascular diseases, diabetes mellitus, smoking, COPD, malignancy, and chronic kidney disease [27].

Our findings regarding NLR are consistent with the previous study by Kong *et al*. in 2020 which reported that the NLR was the most important factor affecting the incidence of severe COVID-19 and recommended that patients with high NLR should be hospitalized with respiratory monitoring [28]. Lian *et al*. studied 232 older patients with confirmed COVID-19 in 2020 and reported that high NLR was independently associated with progression to critical illness [29]. Furthermore, Ciccullo *et al.* in 2020 demonstrated that NLR is a reliable prognostic marker for the severity of COVID-19 [30].

COVID-19 infection can result in long-lasting and persistent symptoms [31]. Dyspnea was the most common long-term symptom (15.5 %), which may be due to pulmonary, cardiac, or vascular fibrosis. Prolonged fatigue, and bone and muscle aches were detected in 10.9% and 8.1% patients, respectively. Interestingly, an Italian study found that symptoms persisted in 87.4% of patients discharged from the hospital after recovering from COVID-19. The most reported symptoms were prolonged fatigue (53.1 %) and dyspnea (43.4%), followed by joint pain (27.3 %) and chest pain (21.7 %). The higher percentage in this study in comparison to our findings could be attributed to the inclusion of much more severe cases who were admitted to the hospital and then discharged [32,33].

Conclusions

This study demonstrates the usefulness of telemedicine in home management and follow up of patients diagnosed with mild/moderate COVID-19. The study recounted the independent predictors for disease severity and hospital admission which will provide an efficient tool to better classify the COVID-19 patients. Telemedicine provides better follow-up strategies, decreases the risk of spread of infection, and diminishes the burden on health systems beyond the pandemic.

Authors' contributions

Conception and design: MTH; data collection: HEDI and all participating authors in relevant departments; data analysis and interpretation: MTH and all participating authors in relevant departments; manuscript preparation: MTH and HA.

Ethical approval and consent to participate

The study protocol conformed to ethical guidelines of the 1975 declaration of Helsinki, was approved by the Research Ethics Committee, Faculty of Medicine, Cairo University (REC N-83-2020), 29/7/2020 and was registered on clinicaltrials.gov of the U.S. National Library of Medicine (clinicaltrials.gov identifier: NCT04515199); under the title: Home management of adult Egyptian mild COVID-19 cases (COVID-19). Written informed consent was obtained from all participants.

Availability of data and material

The datasets used and/or analyzed during this study are available from the corresponding author upon reasonable request.

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Annex – Supplementary Items

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