Post-COVID syndrome: Clinical pattern and impact on health related quality of life

Ashraf Zin EL-Abdeen Mohamed, Lamiaa Hassan Shaaban, Mostafa Mahmoud Attia, Waleed Gamal Elddin Khaleel

Chest Department, Faculty of Medicine, Assiut University, Assiut, Egypt

Correspondence to Waleed Gamal Elddin Khaleel, Pulmonology, Chest Department, Faculty of Medicine, Assiut University, Assiut, Egypt, 71515Tel (office): +020882413720; Mobile: +201006519722; e-mail: waleedgamalddin@yahoo.com

Received: 11-Jan-2024
Revised: 11-Mar-2024
Accepted: 15-Mar-2024
Published: 08-Jul-2024

The Egyptian Journal of Chest Diseases and Tuberculosis 2024, 73:248–260

Background
COVID-19 management has changed from just dealing with a novel respiratory viral illness to unraveling the mystery of a systemic disease. This study aimed to assess clinical pattern for post-COVID survivors and impact on quality of life.
Methods
115 Patients suffering from COVID-19 affection were recruited in this study. The assessment included clinical history with special attention to symptoms attributable to post-COVID manifestations. Evaluation for presence of insomnia, anxiety and depression were done using insomnia severity index (ISI), Hamilton's anxiety (HAM-A) and depression rating scales (HAM-D), respectively. Laboratory investigations included complete blood count (CBC), kidney function test, liver function test, C-reactive protein (CRP), and inflammatory markers including ESR, CRP and Ferritin level. EQ-5D-5L and EQ visual analogue scale (EQ-VAS) were used to assess participants' overall health status and quality of life.
Results
COVID-19 patients suffered from cough (76%), fever (72.9%), fatigue (72.9%), dyspnea (69.8%) and muscle/joint pain (66.1%) as the most distressing symptoms during period of acute infection. Regarding post-COVID syndrome (PCS); Dyspnea (32.2%), fatigue (26.1%), muscle/joint pain (22.6%), loss of taste (16.5%) and loss of smell (15.7%) were the most prevalent at 3 month evaluation. 46.9% patients developed manifestations attributable to post-COVID syndrome. Fever, cough, loss of smell and taste, fatigue, anxiety and insomnia persisted significantly for longer periods among severe cases (Group 2). EQ-5D-5L domains were significantly impaired among severe COVID patients. Significant positive correlation noticed between age and increased duration of dyspnea, muscle/joint pains and depression. Also, CT chest severity scores showed significant correlation with dyspnea, fatigue, muscle/joint pains (P=0.023, 0.012 and <0.001; respectively).
Conclusion
High prevalence of Post-COVID syndrome is a challenge to health care resources. PCS directly impacts mobility, self-care, usual activities, pain perception and anxiety and therefore is associated with lower quality of life among post-COVID patients.

Keywords:
anxiety, EQ-5D-5L, long COVID, post-COVID syndrome, quality of life

Egypt J Chest Dis Tuberc 2024, 73:248–260

2090-9950

Background

Since occurrence of COVID-19 outbreak in Wuhan City; our practice is changing from managing a respiratory viral illness to dealing with a systemic illness.

Majority of patients who develop symptoms suffer mild to moderate disease, 5–8% develop severe disease with Mortality as well-defined acute sequelae [1]. However; 10–20% of cases suffer a variety of long term symptoms after recovery from acute infection status resulting in increased morbidity [2].

Persistence of clinical symptoms more than 4 weeks post infection resulted in defining Post-acute COVID-19 syndrome. The Center for Disease Control (CDC) described persistent symptoms beyond 4 weeks as 'post-COVID conditions'. These include Effects of COVID-19 treatment/hospitalization, Multi-organ effects of COVID-19 and Long COVID [3].

The typical clinical symptoms in 'long COVID' are persistent loss of smell or taste, tiredness, muscle pain, and joint pains, dyspnea, palpitations, dizziness, fatigue, brain fogginess, autonomic dysfunction, cough, headache, depression, low-grade fevers [3].

Based on the duration of symptoms post COVID-19 infection, Nalbandian *et al.* proposed two definitions; persistent symptomatic COVID-19 symptoms (from acute infection and up to 12 weeks) and post-COVID syndrome (PCS) (symptoms present beyond 12 weeks and not attributable to other diagnosis) [4].

The combined prevalence of post COVID symptoms (CDC definition) is about 43%. The corresponding rate among hospitalized patients, including those admitted to the intensive care unit, is approximately 54%, and around 34% among non-hospitalized subjects [5]. This study aims to; evaluate pattern, prevalence and persistence of clinical symptoms post-COVID infection, and the impact of such clinical pattern on health related quality of life (HRQOL).

Methods

115 patients with COVID-19 infection were enrolled in this prospective cohort study. The current Study was carried out in isolation wards and post-COVID clinic of Chest Department, Assiut University Hospitals from June 2021 to Jan 2023. Patients were recruited if age > 18 and COVID-19 infection confirmed with RT-PCR [6]. Informed written consent was obtained from participants and ethical committee of Medicine Faculty, Assiut University approved the study. Exclusion criteria were absence of symptoms and if patients were unwilling to participate in the study.

Clinical, and laboratory data

Enrolled patients were subjected to history taking, clinical examination, and comorbidities evaluation including associated pulmonary (COPD, Asthma and pulmonary embolism), DM, Systemic Hypertension and gastro esophageal reflux disease (GERD). Special attention and detailed assessment of symptoms which could be attributable to COVID-19 infection and its sequelae after 1, 3 and 6 months post COVID-19 acute infection. Symptoms included fever, fatigue, cough, expectoration, vomiting, diarrhea, and loss of smell, loss of taste, muscle/joint pain, headache and sore throat.

Dyspnea was evaluated using mMRC dyspnea scale with Grades 2, 3 and 4 considered as positive for dyspnea detection [7]. Fatigue was assessed using Fatigue Assessment Scale (FAS) which is a 10 item scale to assess both physical and mental symptoms of fatigue. FAS total score ranges from 10 to 50 with score ≥ 22 as a cut-off value for considering fatigue is significant [8].

Hamilton Anxiety Rating Scale (HAM-A) was used to assess anxiety status which is a 14 item based questionnaire with a total range from 0–56 and with score ≥ 18 indicative of presence of anxiety [9]. Depression among participants was evaluated using Hamilton Depression Rating Scale (HAM-D) which consists of 21 items with scores more than 8 considered positive for presence of depression [10,11]. Assessment of Insomnia done using Insomnia severity index (ISI), with total score ≥15; indicative of moderate to severe insomnia [12,13].

The need for oxygen therapy was evaluated for all participants at presentation, 1 and 3 month interval after the acute presentation and measurement of Oxygen saturation and assessment if there is any desaturation (SpO_2≤90%). 6 min walking test (6MWT) done with oxygen saturation assessment (low complexity, safe test, the patient is asked to walk as far as possible along a 30-meter minimally trafficked corridor for a period of 6 min with measurement of nadir oxygen saturation) [14].

Laboratory investigations recorded at time of admission of the patient included complete blood count (CBC) with neutrophil to lymphocyte ratio assessment, renal function test, liver function test, serum electrolytes including sodium, potassium, calcium and magnesium, ESR, coagulation profile (Prothrombin time, Prothrombin Concentration, INR and D-Dimer) and inflammatory markers including serum ferritin, LDH, CRP.

High resolution chest computed tomography (HRCT) done when clinically indicated. COVID-19 severity assessed by CT severity score; visual assessment done by responsible radiologist and percentage of involvement of each lobe was scored. Visual severity scoring of CT chest was assessed for each lobe of 5 lobes and classified for each lobe as Score-1 up to Score-5 according to area involved (< 5%, 5–25%, 25–50%, 50–75% or > 75% area involved; respectively). Total score ranged from 0 (no involvement) to 25 (maximum involvement) [15].

COVID-19 cases were classified into Group 1: non severe cases (mild to moderate cases with no need for oxygen therapy or ICU admission), Group 2: severe cases (need for supplementary oxygen during hospital admission; need for invasive mechanical ventilation/ non-invasive mechanical ventilation or ICU admission; respectively) [16–18].

Assessment of health status and QOL

European quality of life- 5 dimensions- 5 level scale (EQ-5D-5L) and EQ visual analogue scale (EQ VAS) which was introduced by the EuroQol Group in 2009; used for health status and quality of life assessment among participants. EQ-5D-5L includes five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each domain has 5 levels: ranging from no problems, slight, moderate, severe up to extreme problems. The EQ VAS range is from 0 (very low) to 100 (very high) where patient self-rates health and their own perception of QOL on a 100 mm vertical VAS [19,20].

Statistical analysis

Statistical analysis was performed using IBM SPSS software version 22.0 (SPSS Inc., Chicago, IL). Data represented as mean±SD, median, interquartile range and numbers (%). Chi square test or fisher's exact test were used for categorical data. Mann-Whitney test was used to compare non parametric values among the studied groups. *P*-value <0.05 will be considered statistically significant. Different correlations of continuous variables in the study were assessed with spearman's correlation.

Results

Females represent 68.7% of the COVID-19 affected patients included in the study. Crowding index median value was 1.5. 40% of patients of the studied group were overweight. DM represented the most common comorbidity (13%) (Table 1).

Table 1 Socio demographic characteristics of COVID-19 patients (*n*=115)

Socio-demographics	115 patients number (%)
Age	
18–30	70 (60.9)
30–40	14 (12.2)
40+	31 (26.9)
Sex	
Male	36 (31.3)
Female	79 (68.7)
Smoking	
Current smoker	11 (9.6)
Non-smoker	93 (80.9)
Passive smoker	9 (7.8)
Ex smoker	2 (1.7)
Crowding index#	
Mean±SD	1.5±0.62
median (IQR)	1.5 (1-2)
BMI	
Mean±SD	27.5±5.57
median (IQR)	27.3 (23.8-30.4)
Comorbidities	**No. (%)**
COPD	4 (3.5)
Asthma	3 (2.6)
DM	15 (13)
Hypertension	11 (9.6)
GERD	10 (8.7)
Pulmonary embolism	2 (1.7)
Received Oxygen Therapy during admission	32 (27.8)

COPD, Chronic obstructive pulmonary disease; DM, Diabetes Miletus; GERD, Gastro-esophageal reflux disease.
#Crowding index: number of family members/number of rooms.

Table 2 shows that most common symptoms of COVID-19 acute infection were cough (76%), fever (72.9%), fatigue (72.9%), dyspnea (69.8%) and muscle/joint pain (66.1%) (Fig. 1). Most common persistent symptoms beyond 28 days were dyspnea (40%), fatigue (37.4%), muscle/joint pain (30.4%), loss of smell and loss of taste (20.9%) (Fig. 2). Also Dyspnea (32.2%), fatigue (26.1%), muscle/joint pain (22.6%), loss of taste (16.5%) and loss of smell (15.7%) were the most prevalent post-COVID symptoms which persisted 90+ days (Fig. 3). Most common symptoms which persisted for 180 days or more were dyspnea (31.3%), fatigue (21.7%), muscle/joint pain (19.1%), loss of taste and smell (13.9%) (Fig. 4).

Age was significantly higher among group 2 (severe COVID-19 cases) with median age 59 vs. 27 among group 1 (non-severe cases). Crowding index and BMI were significantly higher among group 2 cases. VTE were documented among 15.6% of severe cases (Table 3).

Severe COVID-19 cases showed significantly higher leucocyte count and NLR ratio, while absolute lymphocytic count was significantly lower. Inflammatory surrogates were significantly higher for group 2 cases including CRP, ferritin and D-dimer level (*P*<0.001) (Table 4). Significantly longer duration of persistent symptoms regarding fever (*P*=0.012), cough, loss of smell and taste, fatigue, anxiety and insomnia was noticed among severe cases (Table 5).

Significant reduction of all the quality-of-life parameters of EQ-5D-5L score was noticed among severe COVID cases. Also, the severe group show significant decrease in median EQ VAS score (*P*=<0.001) (Table 6). Patients with severe illness showed highly significant desaturation (SpO2<90) at 6MWT oxygen saturation follow up at 1 and 3 months (Table 7).

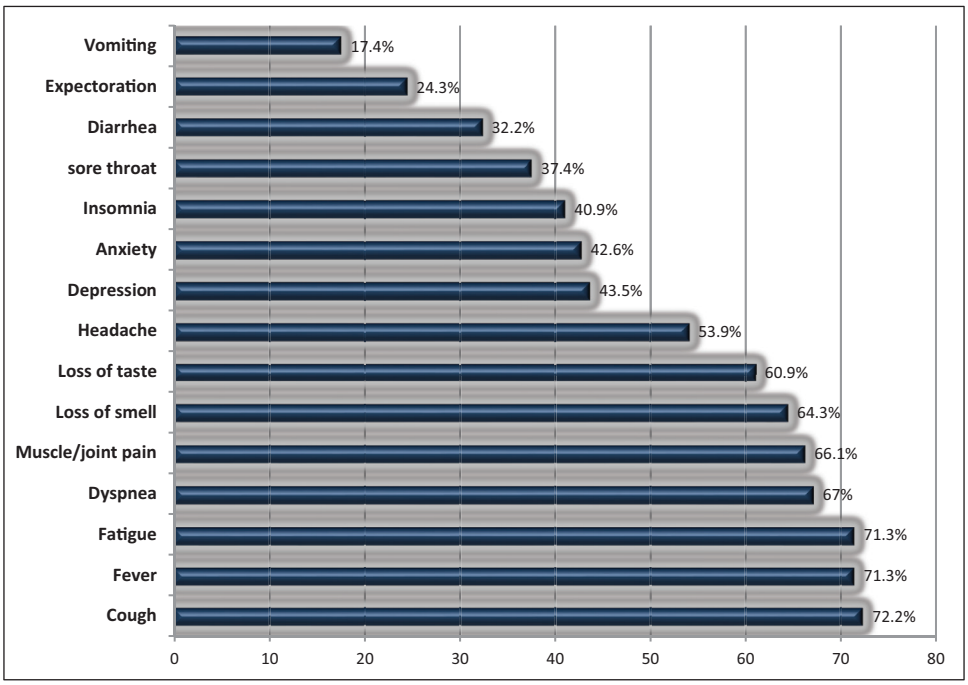
Age showed significant positive correlation with duration of dyspnea (*P*=0.043), muscle/joint pain (*P*=0.012) and depression (*P*=0.009). Significant positive correlation was revealed between BMI and duration of dyspnea (*P*=0.035). Absolute lymphocytic

Table 2 Clinical characteristics of COVID-19 patients during acute infection and at 1, 3 and 6 month follow-up (*n*=115)

Symptoms during acute infection			Symptoms of post-COVID		
Symptoms	Number of patients (%)	Duration in days Median (IQR)	≥28 days No. (%)	≥90 days Number (%)	≥180 days Number (%)
Fever[#]	82 (71.3)	5 (2–10)	1 (0.86)	0	0
Cough	83 (72.2)	12 (7–35)	23 (20)	17 (14.8)	13 (11.3)
Expectoration	28 (24.3)	15 (9.25–180)	11 (9.6)	9 (7.8)	9 (7.8)
Dyspnea	77 (67)	40 (10–180)	46 (40)	37 (32.2)	36 (31.3)
Vomiting	20 (17.4)	4.5 (2–8.5)	0	0	0
Diarrhea	37 (32.2)	6.5 (2–10)	2 (1.7)	2 (1.7)	2 (1.7)
Loss of smell	74 (64.3)	14 (7–64)	24 (20.9)	18 (15.7)	16 (13.9)
Loss of taste	70 (60.9)	14 (7–90)	24 (20.9)	19 (16.5)	16 (13.9)
Fatigue	82 (71.3)	30 (7–180)	43 (37.4)	30 (26.1)	25 (21.7)
Muscle/joint pain	76 (66.1)	15.5 (7–180)	35 (30.4)	26 (22.6)	22 (19.1)
Depression	50 (43.5)	15 (7–180)	20 (17.4)	13 (11.3)	13 (11.3)
Anxiety	49 (42.6)	15 (7–45)	18 (17.4)	8 (7)	8 (7)
Insomnia	47 (40.9)	10 (5–31)	15 (13)	6 (5.2)	6 (5.2)
Headache	62 (53.9)	10 (6-35)	21 (18.3)	11 (9.6)	11 (9.6)
Sore throat	43 (37.4)	7 (3–10.5)	2 (1.7)	0	0
Patients presenting with any post-COVID symptoms			69 (60)	54 (46.9)	48 (41.7)

[#]Grades of fever (38-38.9 low grade, 39-39.9 moderate and ≥40 high grade fever).

Figure 1



Prevalence of symptoms among COVID-19 studied patients during acute infection.

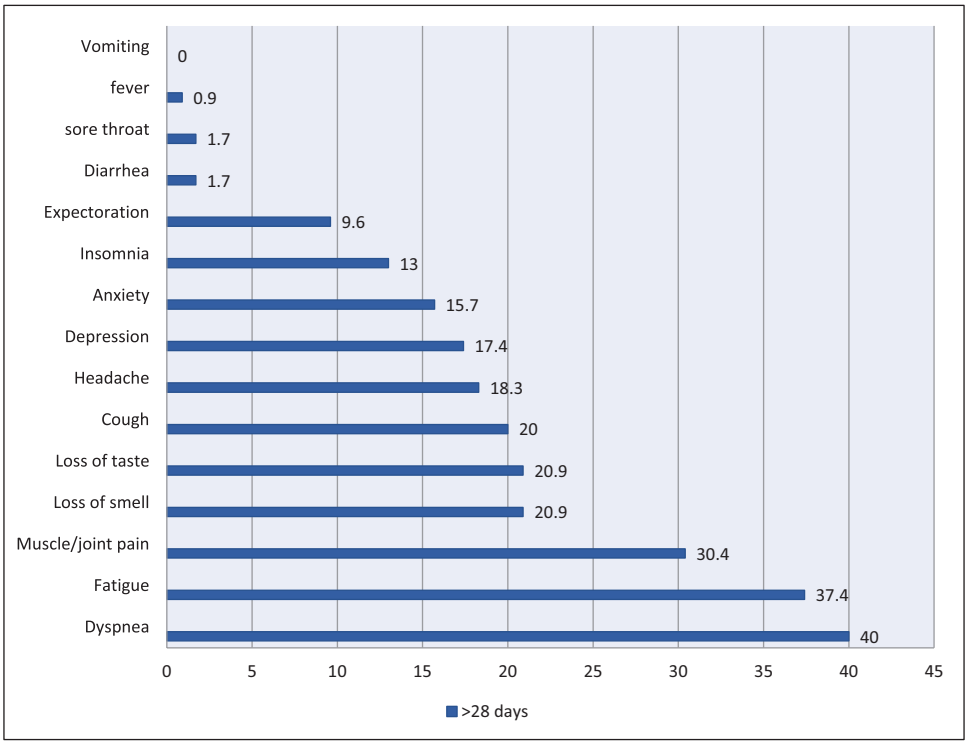
count showed significant negative correlation with symptoms of depression, also CRP value showed significant positive correlation with persistent symptom of expectoration (P=0.017) and symptoms of depression (P=0.015) (Table 8).

All the quality-of-life parameters (mobility, self-care, usual activity, pain/discomfort and anxiety/depression) showed positive correlation with duration of symptoms of dyspnea, fatigue, muscle/joint pain, depression which means the longer the duration of symptoms the worse the quality of life. Positive correlation was revealed between the CT chest severity score and duration of symptoms of dyspnea, fatigue and muscle/joint pain (Table 9).

Discussion

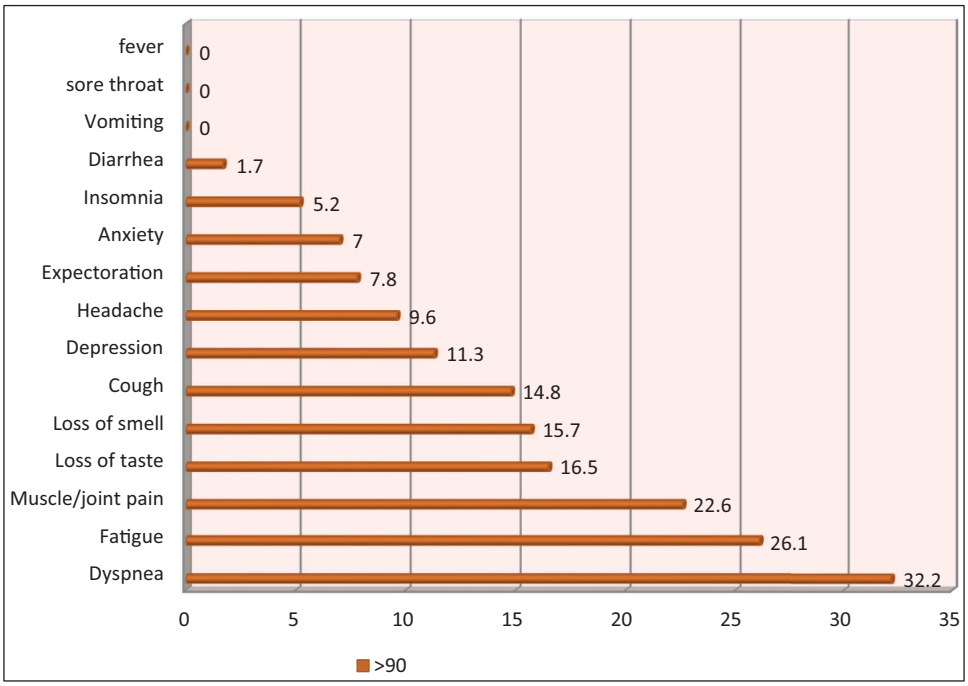
Great variance exists between COVID-19 disease which is a clearly defined disorder and PCS which is still a dilemma. Spectrum of sequelae post COVID

Figure 2



Prevalence of symptoms among COVID-19 studied patients at 28 days follow-up.

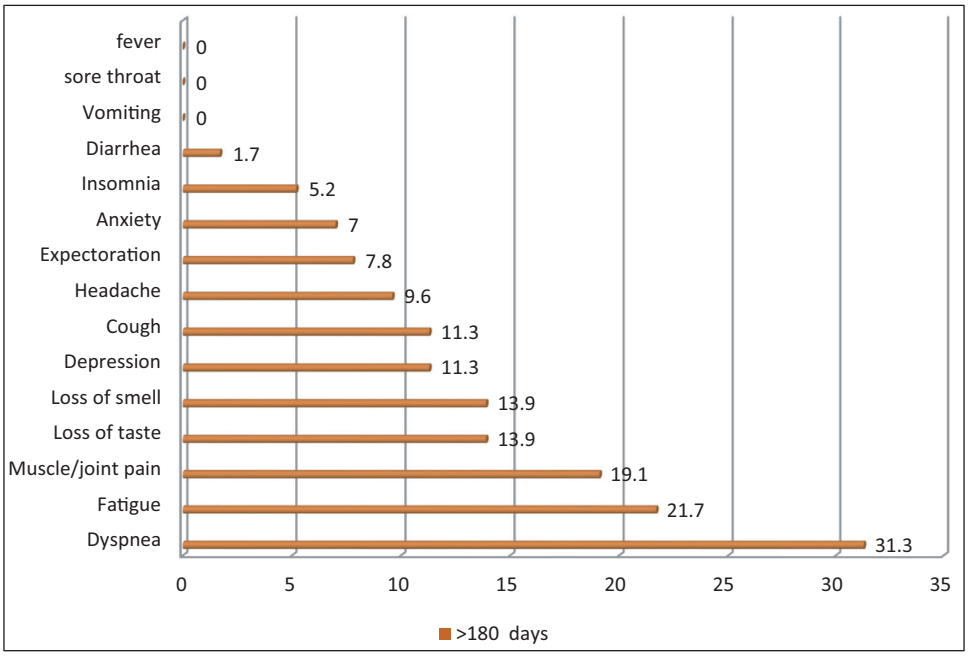
Figure 3



Prevalence of symptoms among COVID-19 studied patients at 90 days follow-up.

infection is variable. There are limited reports and research work regarding information about clinical patterns of presentations in post- coronavirus disease 2019 Syndromes and if there is an impact on HRQOL. Debates about defining PCS still exist. Some reports describe persistent symptoms which continue beyond 12 weeks as PCS, while others use long COVID-19, post COVID-19 conditions to describe ongoing

Figure 4



Prevalence of symptoms among COVID-19 studied patients at 180 days follow-up.

Table 3 Socio-demographic data of COVID-19 patients based on case severity

Socio-demographics	Group 1 (Non-severe cases=83) Number (%)	Group 2 (Severe cases=32) Number (%)	*P* value
Age			
median (IQR)	27 (24–29)	59 (46–69)	0.001*
Sex			
Male	21 (25.3)	15 (46.9)	0.025*
Female	62 (74.7)	17 (53.1)	
Smoking			
Current smoker	6 (7.2)	5 (15.6)	0.058
Non-smoker	70 (84.4)	23 (71.8)	
Passive smoker	7 (8.4)	2 (6.3)	
Ex smoker	0	2 (6.3)	
Crowding index[#]			
median (IQR)	1.3 (1-2)	1.67 (1.3–2)	0.017*
BMI			
median (IQR)	26 (22.9-29.4)	30.7 (26.8-33.2)	0.001*
Comorbidities			
COPD	0	4 (12.5)	0.001*
Asthma	1 (1.2)	2 (6.3)	0.128
DM	5 (6)	12 (37.5)	<0.001*
Hypertension	1 (1.2)	11 (34.3)	<0.001*
GERD	10 (12)	2 (6.3)	0.04*
Pulmonary embolism	0	5 (15.6)	0.022*

COPD, Chronic obstructive pulmonary disease; DM, Diabetes Miletus; GERD, Gastro-esophageal reflux disease.
[#]Crowding index: number of family members/number of rooms.

or new complaints developing 4 weeks post-acute infection [21–24]. 43% is the estimated prevalence of persistent symptoms beyond 4 weeks of acute COVID infection, and prevalence drops to 20% for symptoms existing for 12 weeks or more [5,25,26].

A limited sample of 115 COVID-19 affected patients was recruited and evaluated over 6 months period. Majority was females (68.7%) and patients in the young age range of 18 to 30 years were (60.9%). The findings revealed that Group 2 (severe cases) exhibited a significantly higher median age of 59 years, compared to the Group 1 (non-severe cases) with a median age of 27 years. Prevalence of severe cases was much higher for males (71.4%) versus females (27.4%). Comorbidities such as DM, hypertension, obesity and COPD were

Table 4 Laboratory data of COVID-19 patients according to case severity

	Group 1 (Non-severe cases=83)		Group 2 (Severe cases=32)		*P* value
	Median	IQR	Median	IQR	
CBC					
WBC (10^3/ul)	6	4.35–7.95	9.75	6.13–12.55	0.004*
HB (g/dl)	12.4	11.4–13.7	12.8	11.4–14.3	0.707
HCT (%)	38	34.15–40.3	36.5	33.8–44	0.544
Platelet (10^3/ul)	250	214–324	239	317.25–180.75	0.221
Absolute lymphocytic count (10^3/ul)	1.7	1.1–2.4	0.75	0.545–1.18	<0.001*
Neutrophil/lymphocytic ratio	3	2.56–4.97	12.67	7.37–23.26	<0.001*
Inflammatory markers					
ESR (mm/hr)	38.5	8.75–85.5	50	37.5–107.5	0.462
CRP (mg/dl)	5.5	2.175–10.5	38.5	13.13–71.25	<0.001*
Ferritin (ng/ml)	33.7	11.95–148.8	385	213.43–1006.5	<0.001*
D-Dimer (mg/l)	0.33	0.19–0.44	2.13	0.81–4.9	<0.001*
Liver function test					
Total Bilirubin (umol/l)	6.2	5.1–10	7	5–18	0.882
AST (u/l)	20	18–30	39	27.5–83	0.003*
ALT (u/l)	19	17–31	32	17–80	0.09
Albumin (mg/dl)	41	38–6.75	33	20–37	0.001*
PT (seconds)	11.7	11.25–12.15	12.9	11.77–14.68	0.005*
PC (%)	108.3	97.48–112.33	85.5	66.75–96.75	0.003*
Kidney function test					
Urea (mmol/l)	4.4	3.5–6.6	9.35	5.25–13.38	0.01*
Creatinine (mmol/l)	55	45.5–73	89	67–128.5	0.001*
Electrolyte					
Na (mmol/l)	138	135–140	138	133–141	0.791
K (mmol/l)	4	3.85–4.5	4.2	3.9–4.75	0.389
Ca (mg/dl)	9	8.65–9.3	8.7	8.25–9	0.224
Mg (mg/dl)	1.85	1.69–2.1	2	1.69–2.3	0.685

CRP, C-reactive protein; ESR, Erythrocyte Sedimentation rate; HB, Hemoglobin; HCT, Hematocrit; PC, Prothrombin Concentration; PT, Prothrombin Time; WBC, White Blood Cell Count.

Table 5 Duration of symptoms associated with COVID-19 patients according to case severity

Duration of symptoms (days)	Group 1 (Non-severe cases=83)		Group 2 (Severe cases=32)		*P* value
	Median	IQR	Median	IQR	
Fever	3	2–8	7	4–12	0.012*
Cough	10	7–18	30	12–180	0.002*
Expectoration	7	13–180	22	12–180	0.305
Dyspnea	14	5–180	90	26–180	0.039*
Diarrhea	6	2–10	7	6–12	0.227
Smell loss	10	6–17	90	15–180	0.001*
Taste loss	10	6–17	90	15–180	0.001*
Fatigue	15	7–180	90	21–180	0.048*
Joint pain	14	7–162	90	26–180	0.005*
Depression	15	6–180	17	10–41	0.748
Anxiety	12	5–30	30	13–60	0.052
Insomnia	7	4–12	25	10–60	0.005*
Headache	10	5–30	14	8–60	0.326
throat Sore	6	3–9	10	7–30	0.204
Hospitalization duration					
Isolation (days)	10.5	8–20	14	14–30	0.124

significantly higher among group 2 patients. Kumar and colleagues concluded similar results indicating that advancing age, male gender, and comorbidities like non-asthmatic chronic pulmonary disease and obesity were linked to higher hospital mortality [27].

A related investigation reported a significant association between older age, diabetes and hypertension and the severity of COVID-19 [28]. Additionally, a multi-center, retrospective study indicated that individuals with hypertension

Table 6 Quality of life profile and psychometric properties of COVID-19 patients according to case severity

EQ-5D-5L domains	Group 1 (*n*=83) Number (%)	Group 2 (*n*=32) Number (%)	*P* value
MOBILITY			
Unable to walk about	0	0	<0.001*
Severe problems	0	2 (6.3)	
Moderate problems	0	5 (15.6)	
Slight problems	19 (22.9)	13 (40.6)	
No problems	64 (77.1)	12 (37.5)	
Self-care			
Unable to wash or dress myself	0	0	<0.001*
Severe problems	0	0	
Moderate problems	0	4 (12.5)	
Slight problems	1 (1.2)	10 (31.2)	
No problems	82 (98.8)	18 (56.3)	
Usual activities			
Unable to do	0	0	<0.001*
Severe problems	0	1 (3.1)	
Moderate problems	0	5 (15.6)	
Slight problems	4 (4.8)	12 (37.5)	
No problems	79 (95.2)	14 (43.8)	
PAIN/Discomfort			
Extreme pain	0	0	<0.001*
Severe pain	0	0	
Moderate pain	0	4 (12.5)	
Slight pain	5 (29.4)	18 (56.3)	
No pain	78 (83)	10 (31.2)	
Anxiety			
Extremely	0	0	<0.001*
Severely	0	0	
Moderately	2	5 (15.6)	
Slightly	14	24 (75)	
Not anxious or depressed	67	3 (9.4)	
EQ VAS score			
Median (IQR)	95 (94-96)	75 (65-90)	<0.001*

EQ VAS, EQ visual analogue scale; EQ-5D-5L, The 5-level EQ-5D version (introduced by the EuroQol Group in 2009).

Table 7 CT chest visual severity score and oxygen saturation values for COVID-19 patients according to case severity

	Group 1 (*n*=83) Number (%)	Group 2 (*n*=32) Number (%)	*P* value
CT Chest severity score (at presentation)			
Mild	41 (49.4)	9 (28.1)	<0.001*
Moderate	0	13 (40.6)	
severe	0	10 (31.3)	
Oxygen saturation (at 1 month follow-up)			
SpO_2<90%	0	3 (9.4)	0.02*
Oxygen saturation (at 3 month follow-up)			
SpO_2<90%	0	2 (6.3)	0.76
6-min walking Oxygen saturation (at 1 month follow-up)			
SpO_2<90%	0	6 (18.8)	<0.001*
6-min walking Oxygen saturation (at 3 month follow-up)			
SpO_2<90%	0	4 (12.5)	0.005*

who contracted COVID-19 were more prone to developing severe clinical conditions [29].

Furthermore, Group 2 demonstrated a noteworthy increase in the median crowding index, consistent with a separate study that observed higher mortality rates in homes with a high crowding index [30]. Additionally, Group 2 exhibited a significant decrease in absolute lymphocytic count and albumin, while showing increases in various inflammatory markers including neutrophil/lymphocytic ratio, CRP, ferritin and D-Dimer which is consistent with previous studies [31–33].

The risk of developing PCS was also found to be increased along with a gradient of decreasing age. Subsequently, in a meta-analysis by Quinn and

Table 8 Correlation between socio-demographic characteristics/laboratory profile and post-COVID symptoms duration

Duration of Symptoms (days)	Expectoration	dyspnea	fatigue	Muscle/joint pain	Depression
Socio-demographic characteristics					
Age					
r	–0.012	**0.335**	0.350	**0.445**	**0.467**
P	0.952	**0.043**	0.041	**0.012***	**0.009***
BMI					
r	0.304	**0.238***	0.019	0.007	–0.105
P	0.115	**0.035**	0.866	0.953	0.468
Crowding index					
r	0.277	0.08	0.052	0.107	0.026
P	0.154	0.481	0.642	0.350	0.859
Laboratory results					
WBC					
r	–0.040	0.048	0.072	–0.059	–0.070
P	0.856	0.716	0.579	0.658	0.684
Absolute lymphocytic count					
r	–0.120	–0.047	–0.040	–0.045	**–0.346**
P	0.603	0.725	0.762	0.741	**0.045***
neutrophil/lymphocytic ratio					
r	0.040	0.086	0.105	0.028	0.083
P	0.865	0.529	0.436	0.842	0.634
CRP					
r	**0.670**	0.078	0.303	0.107	**0.657**
P	**0.017***	0.711	0.151	0.618	**0.015***
Ferritin					
r	0.129	**0.410**	0.308	0.230	–0.250
P	0.722	**0.042***	0.135	0.281	0.432
D-Dimer					
r	0.263	**0.509**	0.120	0.109	0.294
P	0.409	**0.025***	0.560	0.595	0.354

BMI, Body Mass Index; Crowding index, number of family members/number of rooms; CRP, C-reactive Protein; WBC, White Blood Cell Count.

Table 9 Correlation between quality of life/6 min walking saturation/CT chest severity score and post-COVID symptoms duration

Duration of symptoms (days)	Expectoration	Dyspnea	fatigue	Muscle/joint pain	Depression
Six-minute walk saturation (at 1 month)					
r	–0.090	–0.108	–0.095	**–0.275***	**–0.244**
P	0.650	0.342	0.392	**0.015**	**0.088**
EQ VAS score					
r	–0.310	**–0.472***	**–0.519***	**–0.491***	**–0.386***
P	0.108	**<0.001**	**<0.001**	**<0.001**	**0.006**
CT Chest severity score					
r	0.197	**0.310***	**0.342***	**0.476***	–0.035
P	0.419	**0.023**	**0.012**	**<0.001**	0.842

colleagues, they identified nine potential risk factors in association with PCS; comorbidities, female gender, asthma, obesity, COPD, DM, age, invasive ventilation and days of hospitalization [25]. Thus, emerging evidence suggests that comorbidities, socio-economic conditions, female gender and health determinants appear to be relevant independent risk factors for the PCS [3].

Post COVID conditions were linked for more than 100 symptoms in various reports. The most frequently observed symptoms were fatigue (23%), memory deficits (14%), dyspnea (13%), depression (13%), anxiety (11%), anosmia (12%), sleep problems (11%), and joint pains (10%) [5].

In the current study, cough (72.2%), fever (71.3%), fatigue (71.3%), dyspnea (67%), muscle/joint pains (66.1%) were the most prevalent symptoms during acute infection period. Reassessment after 4 weeks period revealed great change in pattern of persistent symptoms with dyspnea as the leading disabling symptom (40%) followed by fatigue (37.4%), muscle/joint pains (30.4%), loss of smell and taste (20.9%). Dyspnea and other mentioned symptoms persisted in the same order at 3 months evaluation and 6 months

evaluation with prevalence rates at 6 months of 31.3% for dyspnea, 21.7% for fatigue, 19.1% for muscle/joint pain and 13.9% for loss of smell and taste.

Emerging evidence suggests that a still unknown proportion of individuals will develop chronic disease conditions, such as diabetes [34], autoimmune diseases [35], cerebrovascular and/or cardiovascular disorders, including venous thromboembolism (VTE) [36], psychological distress, or mental illness [37] obviously; Post-COVID condition also affect the respiratory system (e.g., lung fibrosis), all of which subsequently contribute to the burden of persisting symptoms and sequelae following acute SARS-CoV-2 infection [38].

Proposed underlying mechanisms claimed attributable to emergence of PCS can include SARS-CoV-2 persistence on its receptors upon host cells. Adaptive immune system is triggered by viral persistence, there by activating auto-reactive T lymphocytes through antigen-presenting cells. Also, autoantibodies production is increased via the ongoing B cell activation (demonstrated in nearly 50% of patients with post-COVID conditions) can result in autoimmune disorders evolvement (e.g., thyroid disease, lupus erythematosus, antiphospholipid syndrome) [35,39].

Also, persistent hyper inflammation and cytokine storms resulting in cellular damage, immunologic aberrations caused by super antigens, molecular mimicry or epitope spreading, and hemostatic changes, predominantly characterized by coagulation abnormalities; are among the hypothesized theories for emergence of PCS. Profound hemostatic alterations can occur during or following an acute SARS-CoV-2 infection and up to several months post infection. The coagulation system is affected preferentially rather than the megakaryocyte-platelet system and are associated with a high risk of thromboembolic complications [40,41].

VTE were documented among 15.6% of group 2 patients. Previous meta-analysis documented an estimated overall VTE prevalence of 14.1% (95% CI: 11.6–16.9) and a prevalence of 45.6% (95% CI: 31.0–66.2) for patients in the ICU [42]. Jiménez *et al.* and Tan *et al.* revealed that VTE incidence were more near to 7.8% among COVID-19 patients [43,44]. The difference in incidence rates may be inferred to the limited number of patients and the mild degree of severity in the recruited group.

Moreover, Group 2 experienced a significant prolongation in the duration of symptoms such as fever, cough, smell loss, taste loss, fatigue, joint pain, and insomnia. Upper limit for IQR for symptoms as dyspnea, fatigue, joint pain and depression extended to 6 months duration among mild cases. Symptoms lasting beyond 6 months among severe cases included cough, expectoration, dyspnea, loss of smell and taste, fatigue and joint pains. These findings correspond with studies suggesting that the severity of post-COVID-19 manifestations is linked to the severity of the initial COVID-19 illness [45].

Ezzelregal and colleagues assessed 120 post-COVID-19 patients; one month or more after recovery. Body pains (32.5%) were the most distressing symptom. About 61.7% of participants had high-state anxiety and 51.7% had high-trait anxiety [46].

Meta-analysis regarding prevalence of post-acute COVID syndrome (PACS) in Egypt revealed that fatigue was the most commonly reported symptom across various studies of post-COVID survivors (48.1% of all survivors), followed by myalgia at 32.9%, anorexia at 32.8%, and anxiety at 31.5% [47].

Female sex was revealed to be significantly associated with PACS (OR 1.6, 95% CI 1.4 to 1.2, $P<0.001$). Also the combined results showed that severe COVID and the presence of any comorbidity were found to be independent risk factors for PACS, with odds ratios of 2.3 and 1.8, respectively [47].

The study also identified significant negative impacts on all the quality-of-life aspects, as measured by EQ-5D-5L score, in Group 2. This aligns with previous research indicating lower quality of life in COVID-19 patients requiring mechanical ventilation and/or ICU admission in comparison to those who didn't during hospitalization [48].

Additionally, Group 2 demonstrated a heightened severity in CT chest severity scores and desaturation during the 6-minute walk test. These results are in agreement with studies correlating CT severity scores with patient survival and associating lower 6MWT performance with lower PaO2/FiO2 ratios during hospitalization [49].

Furthermore, the data showed positive correlations between age and the duration of certain symptoms [dyspnea (r=0.335, P=0.043), muscle/joint pain (r=0.445, P=0.012) and depression (r=0.467, P=0.009)], as well as between BMI and the duration of dyspnea in post-COVID patients. Significant positive correlation was found between CRP and depression (r=0.657, P=0.015), also; duration of expectoration in post-COVID patient which may be explained by severity

of infection and/or secondary bacterial infection (r=0.670, *P*=0.017). These results aligns with previous studies [50,51].

Correlation studies also revealed significant positive correlation between acute inflammatory markers including ferritin and d-dimer with increased duration of experiencing dyspnea (*r*=0.410, *P*=0.042; *r*=0.509, *P*=0.025; respectively).

Negative correlation was found between the EQ VAS score and increased duration of symptoms of dyspnea, fatigue, muscle/joint pain and depression, this data is consistent with a meta-analysis which found that 58% of the post-COVID-19 patients had reported poor quality of life [51].

Among post-COVID-19 patients, a combined assessment of individual factors using the EQ-5Q-5L questionnaire revealed that 33.9% encountered issues with mobility, 13% experienced problems with self-care, 19.1% suffered problems during usual activities, 23.4% experienced pain/discomfort and 39.1% reported anxiety/depression. Those limitations were more significant among moderate and severe COVID cases. These findings indicate that a significant proportion of individuals recovering from COVID-19 exhibit a diminished quality of life, presenting considerable difficulties for patients, healthcare providers, and public health practitioners [52].

Finally, a positive correlation was identified between the CT chest severity score and the duration of symptoms, highlighting the potential of CT severity scoring in predicting long-term outcomes and PCS development.

Sivan and colleagues explored the correlation between symptom severity, functional disability, and overall health in a largely non-hospitalized PCS cohort. Symptom scores were strongly positively correlated with functional difficulty scores (0.7, 0.6–0.7) and moderately negatively correlated with overall health (−0.4, −0.3, to −0.5). Severity phenotypes might help stratify patients for targeted interventions and planning of care pathways [53].

Given the growing number of people with PCS (already more than one million in the UK alone), the findings of severity phenotypes could have widespread implications for the provision and resourcing of services to support people living with the condition. The stratification based on the severity of cases could help national and local providers to plan services and interventions that might be directed towards this categories [53].

Studying patients with PCS revealed episodic and fluctuating nature for the condition, and that symptom severity can vary over time within the same individual [54]. identifying triggers for this fluctuation (either physical, cognitive, emotional) may help to avoid worsening of symptom severity and decrease its impact on function and HRQOL. We recommend complex multifaceted rehabilitation interventions to manage symptom severity fluctuation seen in PCS.

More contemporary data suggest that self-reported symptoms attributable to PCS showed low rates (between 4.2% and 5.0%) among adults who have had triple vaccination [26]. In addition, Quinn *et al.* reported rates of PCS of 2% to 10% among vaccinated persons [25]. Therefore, in times of emerging variants and widespread vaccination programs, it is suggested that the PCS may now be less frequent (and less pronounced) after acute infection.

Conclusion

The multi-organ manifestations and sequelae of COVID-19 beyond the acute phase of SARS-CoV-2 infection are recognized as a novel disease entity. Based on the evaluation of symptom scores and quality of life assessment among post-COVID acute condition; PCS prevalence rates remain high; and has direct impact on quality of life among those patients.

Limitations of the study

Distinct and rare clinical phenotype patterns recognition may be limited as sample of selected patients were recruited in a single-center study. Symptom based subjective assessment was based upon patient's reported symptoms, which may limit the generalization of the results.

Acknowledgements

None.

Ethics approval and consent to participate

The study was approved by the institutional review board and ethical committee of Faculty of Medicine-Assiut University in compliance with the Helsinki Declaration (IRB: 17101382).

Consent for publication

Not applicable.

Availability of data and material

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

Financial support and sponsorship
None.

Conflicts of interest
The authors declare no conflict of interest.
Trial registration: ClinicalTrials.gov. NCT04561141.

Authors' contributions
AZEM, LHS and WGEK conception and design. MMA and WGEK: data collection. MMA, LHS and WGEK: statistical analysis. LHS and WGEK: medical writing. All authors revised the manuscript.

Ethical Considerations
إستمارة موافقه على الاشتراك في البحث(بيان وصفي للبحث وأخلاقياته:- الغرض(من البحث: تقييم مجموعة من المرضى المصابين بفيروس كورونا المستجد أثناء فترة الإصابة و المتابعة لمدة 3 أشهر. خطوات البحث: كل المرضى سيأخذ منهم تاريخ مرضى و فحص اكلينيكى بحرص و نتائج التحاليل الهامة للحالة المرضية و نتائج الأشعة المقطعية على الصدر مع الاهتمام بمتابعة نسبة تشبع الدم بالأكسجين و معاملات جودة الحياة ما بعد الإصابة بفيروس الكورونا المستجد.لفوائد المحتملة من المشاركة في البحث: تحديد المدى نسبة حدوث متلازمة ما بعد الإصابة بفيروس الكورونا و المظاهر الاكلينيكية و جودة الحياة الصحية...احتمالات المتاعب والآثار الجانبية: لا تذكرمترتبات عدم المشاركة:المشاركة في البحت غير ملزمه و يكون للمريض الحق في الانسحاب من البحث في أي وقت دون أن يحجب عنه أي خدمه طبية وللمشارك الحق في الاحتفاظ بهده الوثيقة و سرية المعلومات مضمونه.'لقد قرأت المعلومات السابقة (أو قرأت علي) وكانت لي الفرصة للسؤال عما أريد وأجيبت أسئلتي جميعا من قبل الطبيب/ مصطفى محمود عطيه بما أرضاني وأوافق بكامل اختياري على مشاركتي في هذه الدراسة وأفهم أنه من حقي الانسحاب من البحث في أي وقت دون أن تحجب عني الخدمة الطبية المقدمه لي'التوقيع:السيد:

List of Abbreviations

6MWT, 6 min walking test;
CRP, C-reactive protein; EQ-5D-5L, The 5-level EQ-5D version (introduced by the EuroQol Group in 2009);
EQ-VAS, EQ visual analogue scale;
FAS, Fatigue assessment scale;
HAM-A, Hamilton's anxiety rating scale;
HAM-D, Hamilton's depression rating scale;
HRQOL, Health related quality of life;
ISI, Insomnia severity index;
mMRC, modified Medical Research Council;
PACS, post-acute COVID syndrome;
PCS, post-COVID syndrome;
QOL, quality of life;
VTE, venous thromboembolism

References

1 Chippa V, Aleem A, Anjum F. Post-Acute Coronavirus (COVID-19) Syndrome. 2023 Feb 3. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. PMID: 34033370
2 Li X, Ma X. Acute respiratory failure in COVID-19: is it 'typical' ARDS? Crit Care 2020; 24:198.
3 Scharf RE, Anaya JM. Post-COVID Syndrome in adults-an overview. Viruses 2023; 15:675.
4 Nalbandian A, Sehgal K, Gupta A, Madhavan MV, McGroder C, Stevens JS, *et al*. Post-acute COVID-19 syndrome. Nat Med 2021; 27:601-615.
5 Chen C., Haupert S.R., Zimmermann L., Shi X., Fritsche L.G., Mukherjee B. Global prevalence of post-coronavirus disease 2019 (COVID-19) condition or long COVID: A meta-analysis and systematic review. J Infect Dis 2022; 226:1593–1607.
6 Tahamtan A, Ardebili A. Real-time RT-PCR in COVID-19 detection: issues affecting the results. Expert Rev Mol Diagn 2020; 20:453-454.
7 Rajala K, Lehto JT, Sutinen E, Kautiainen H, Myllärniemi M, Saarto T. mMRC dyspnoea scale indicates impaired quality of life and increased pain in patients with idiopathic pulmonary fibrosis. ERJ Open Res 2017; 3:4.
8 Michielsen HJ, De Vries J, Van Heck GL. Psychometric qualities of a brief self-rated fatigue measure: The Fatigue Assessment Scale. J Psychosom Res 2003; 54:345-352. 13
9 Hamilton M. The assessment of anxiety states by rating. Br J Med Psychol 1959; 32:50–55. https://doi.org/10.1111/j.2044-8341.1959.tb00467.x
10 Hamilton M. Depression rating scale. Neurol Neurosurg. Psychiatry 1960; 23:56–62.
11 Kendrick T, Pilling S, Mavranezouli I, Megnin-Viggars O, Ruane C, Eadon H, *et al*. Management of depression in adults: summary of updated NICE guidance. BMJ 2022; 378:1557.
12 Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Med 2001; 2:297-307.
13 Morin CM, Belleville G, Bélanger L, Ivers H. The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response. Sleep 2011; 34:601-608.
14 Agarwala P, Salzman SH. Six-minute walk test: clinical role, technique, coding, and reimbursement. Chest. 2020; 157:603–611.
15 Sharma S, Aggarwal A, Sharma RK, Patras E, Singhal A. Correlation of chest CT severity score with clinical parameters in COVID-19 pulmonary disease in a tertiary care hospital in Delhi during the pandemic period. Egypt J Radiol Nucl Med 2022; 53:1-8.
16 The Lancet. Facing up to long COVID. Lancet 2020; 396:1861.
17 Masoud H, Elassal G, Hassany M, Shawky A, Abdel Hakim M, Zaky S. Management protocol for COVID-19 patients MoHP protocol for COVID19. Cairo Egypt: Ministry of health and population; 2020. [Google Scholar]. 2020
18 Kamal M, Abo Omirah M, Hussein A, Saeed H. Assessment and characterisation of post-COVID-19 manifestations. Int J Clin Pract 2021; 75:e13746.
19 Stolk E, Ludwig K, Rand K, van Hout B, Ramos-Goñi JM. Overview, update, and lessons learned from the international EQ-5D-5L valuation work: version 2 of the EQ-5D-5L valuation protocol. Value Health 2019; 22:23-30.
20 Cheng LJ, Tan RL, Luo N. Measurement properties of the EQ VAS around the globe: a systematic review and meta-regression analysis. Value Health 2021; 24:1223-1233.
21 World Health Organization. A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021. World Health Organization; 2021. https://apps.who.int/iris/bitstream/handle/10665/345824/WHO-2019-nCoV-Post COVID-19-condition-Clinical-case-definition-2021.1-rus.pdf
22 COVID-19 rapid guideline: managing the long-term effects of COVID-19. London: National Institute for Health and Care Excellence (NICE); 2020. PMID: 33555768
23 Centers for Disease Control and Prevention. evaluating and caring for patients with post-COVID conditions: interim guidance. https://stacks.cdc.gov/view/cdc/107148
24 Centers for Disease Control and Prevention. Background: Evaluating and Caring for Patients with Post-COVID Conditions. https://pesquisa.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/resource/pt/grc-747267
25 Quinn KL, Katz GM, Bobos P, Sander B, McNaughton CD, Cheung AM, *et al*. Understanding the post COVID-19 condition (long COVID) in adults and the expected burden for Ontario. Science Briefs of the Ontario COVID-19 Science Advisory Table 2022; 3:1-32.
26 Ayoubkhani D, Bosworth M. Self-Reported Long COVID after Infection with the Omicron Variant in the UK: 18 July 2022. Office for National Statistics. 2022 Jul 18
27 Kumar MA, Krishnaswamy M, Arul JN. Post COVID-19 sequelae: venous thromboembolism complicated by lower GI bleed. BMJ Case Rep 2021; 14:1.
28 Abdel-Aaty H, El-Habashy MM, Shedeed IM, Mahrous AH. Laboratory markers and radiological signs of mild versus severe COVID-19 patients. Egypt J Chest Dis Tuberc 2023; 72:194-201.

29 Salamanna F, Veronesi F, Martini L, Landini MP, Fini M. Post-COVID-19 Syndrome: The persistent symptoms at the post-viral stage of the disease. a systematic review of the current data. Front Med. 2021; 8:653516.

30 Novak P. Post COVID-19 syndrome associated with orthostatic cerebral hypoperfusion syndrome, small fiber neuropathy and benefit of immunotherapy: a case report. eNeurologicalSci 2020; 21:100276.

31 Greer N, Bart B, Billington CJ, Diem SJ, Ensrud KE, Kaka A, *et al*. COVID-19 postacute care major organ damage: a systematic review. BMJ Open 2022; 12:e061245.

32 Mehandru S, Merad M. Pathological sequelae of long-haul COVID. Nat Immunol Nat Res 2022; 23:194–202.

33 Mallapaty S, Callaway E, Kozlov M, Ledford H, Pickrell J, Van Noorden R. How COVID vaccines shaped 2021 in eight powerful charts. Nature 2021; 600:580–583.

34 Xie Y, Al-Aly Z. Risks and burdens of incident diabetes in long COVID: a cohort study. Lancet Diabetes Endocrinol 2022; 10:311-321.

35 Rojas M, Rodríguez Y, Acosta-Ampudia Y, Monsalve DM, Zhu C, Li QZ, *et al*. Autoimmunity is a hallmark of post-COVID syndrome. J Transl Med 2022; 20:1-5.

36 Katsoularis I, Fonseca-Rodríguez O, Farrington P, Jerndal H, Lundevaller EH, Sund M, *et al*. Risks of deep vein thrombosis, pulmonary embolism, and bleeding after covid-19: nationwide self-controlled cases series and matched cohort study. BMJ 2022; 377:e069590.

37 Wang S, Quan L, Chavarro JE, Slopen N, Kubzansky LD, Koenen KC, *et al*. Associations of depression, anxiety, worry, perceived stress, and loneliness prior to infection with risk of post–COVID-19 conditions. JAMA Psychiatry 2022; 79:1081-1091.

38 Udwadia ZF, Koul PA, Richeldi L. Post-COVID lung fibrosis: The tsunami that will follow the earthquake. Lung India 2021; 38(Suppl 1):S41.

39 Batiha GE, Al-Kuraishy HM, Al-Gareeb AI, Welson NN. Pathophysiology of Post-COVID syndromes: a new perspective. Virol J 2022; 19:158.

40 Castanares-Zapatero D, Chalon P, Kohn L, Dauvrin M, Detollenaere J, Maertens de Noordhout C, *et al*. Pathophysiology and mechanism of long COVID: a comprehensive review. Ann Med 2022; 54:1473-1487.

41 Rossetti CL, Cazarin J, Hecht F, Beltrão FE, Ferreira AC, Fortunato RS, *et al*. COVID-19 and thyroid function: What do we know so far? Front Endocrinol 2022; 13:1041676.

42 Leentjens J, Van Haaps TF, Wessels PF, Schutgens RE, Middeldorp S. COVID-19-associated coagulopathy and antithrombotic agents—lessons after 1 year. Lancet Haematol. 2021; 8:e524-e533.

43 Jiménez D, García-Sanchez A, Rali P, Muriel A, Bikdeli B, Ruiz-Artacho P, *et al*. Incidence of VTE and bleeding among hospitalized patients with coronavirus disease 2019: a systematic review and meta-analysis. Chest 2021; 159:1182-1196.

44 Tan BK, Mainbourg S, Friggeri A, Bertoletti L, Douplat M, Dargaud Y, *et al*. Arterial and venous thromboembolism in COVID-19: a study-level meta-analysis. Thorax 2021;76:970-79.

45 Assar S, Pournazari M, Soufivand P, Mohamadzadeh D. Systemic lupus erythematosus after coronavirus disease-2019 (COVID-19) infection: Case-based review. Egypt Rheumatol 2022; 44:145-149.

46 Ezzelregal HG, Hassan AM, Serag R, Eldin HS. Post-COVID anxiety and its associated factors in Egyptian patients. Egypt J Chest Dis Tuberc 2023; 72:262-267.

47 Azzam A, Khaled H. Exploring the prevalence and factors associated with post-acute COVID syndrome in Egypt: a systematic review and meta-analysis. Egypt J Internal Med 2023; 35:67.

48 Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. Lancet Infect Dis 2022; 22:1293-1302.

49 Mathieu E, Ritchie H, Rodés-Guirao L, Appel C, Giattino C, Hasell J, *et al*. Coronavirus pandemic (COVID-19). Our World Data 2020. Available from: https://ourworldindata.org/coronavirus.

50 Ye Y, Zhang Q, Wei X, Cao Z, Yuan HY, Zeng DD. Equitable access to COVID-19 vaccines makes a life-saving difference to all countries. Nat Hum Behav 2022; 6:207-216.

51 Lopez-Leon S, Wegman-Ostrosky T, Ayuzo del Valle NC, Perelman C, Sepulveda R, Rebolledo PA, *et al*. Long-COVID in children and adolescents: A systematic review and meta-analyses. Sci Rep 2022; 12:9950.

52 Gerritzen I, Brus IM, Spronk I, Biere-Rafi S, Polinder S, Haagsma JA. Identification of post-COVID-19 condition phenotypes, and differences in health-related quality of life and healthcare use: a cluster analysis. Epidemiol Infect 2023; 151:e123.

53 Sivan M, Parkin A, Makower S, Greenwood DC. Post-COVID syndrome symptoms, functional disability, and clinical severity phenotypes in hospitalized and nonhospitalized individuals: A cross-sectional evaluation from a community COVID rehabilitation service. J Med Virol 2022; 94:1419-1427.

54 Adhikari SP, Shrestha P, Dev R. Feasibility and effectiveness of telephone-based telephysiotherapy for treatment of pain in lowresource setting: a retrospective pre-post design. Pain Res Manag 2020; 2020:2741278.