Original Research Article

Post-Covid-19 clinical Symptom Frequency and Associated Factors in a Cohort of Patients discharged from the ICU and Monitored for 12 Months, in Libreville, Gabon

ABSTRACT:

Aims: This study determined the prevalence and evolution of long COVID symptoms in patientshospitalized for severe COVID-19 at the CHUL intensive care unit in Libreville, Gabon.

Study design: Prospective, longitudinal, study

Place and Duration of Study: Infectiology Unit, Libreville University Health Center (CHUL), between January 2021 and January 2022.

Methodology: We included 144 patients (84 men, 60 women; median age 46.4 [16-88] years old) hospitalized in the intense care unit for a RT-PCR- confirmed COVID-19 and who have been accepted a one-year follow-up. All patients were consulted quarterly for 12 months. During the follow-up, existence, appearance and types of symptoms were sought at 3, 6 and 12-months post-hospitalization.

Results: The prevalence of long COVID-19 was 52.1% (n=75/144). Fatigue (21.3%), cough (20.8%), sleep disorders (16.0%) and anxiety (11.1%) predominated at month-3. The main symptoms reported 6-months after the onset of infection were choking sensation (9.7%; n=14), anxiety (7.6%; n=11), fatigue (6.2%; n=9) and cough (3.5%; n=5). One year after, the persistent symptoms were anxiety (6.5%; n=9), dyspnea (1.4%; n=2). Most participants had only one symptom: 60% at month-3, 79.5% at month-6 and 77.8% at 12-months (p=0.04).

Conclusion: The long COVID is frequent among patients hospitalized for severe form of SARS-COV-2 infection. It is imperative to continue generating information for appropriate prevention and monitoring measures to be adopted in Gabon.

Keywords: LONG COVID, severe SARS-CoV-2 infection, Libreville

1. INTRODUCTION

The ongoing SARS-CoV-2 pandemic, which has resulted in enormous global morbidity and mortality, remains an international public health emergency [1]. Although many studies have been able to describe the various serious clinical signs found in the initial phase of the disease, another major aspect of that pathology has become very worrying: long-term events known as LONG COVID [2]. The National Institute for Health and Care Excellence (NICE) describes those events as a set of 'signs and symptoms appearing during or after a COVID-19-compatible infection, persisting for more than 12 weeks and that cannot be explained by an alternative diagnosis' [3]. The post-COVID-19 condition is defined by the World Health Organization (WHO) as a condition that occurs in people with a probable or confirmed history of SARSCOV 2 infection, typically three months after the onset of the first symptoms of COVID-19, with symptoms persisting for at least two months and that cannot be explained

by another diagnosis [4]. Common symptoms in people with long COVID are fatigue and a cognitive dysfunction that daily functioning [4,5]. Approximately 17 million people in the WHO area developed a long COVID between 2020 and 2021 [6]. Prevalence ranging from 10 to 55% was reported [1,7]. Long COVID-19 more frequently occurs in hospitalized patients with very severe forms [7,8]. While many articles report information on long COVID, data from sub-Saharan Africa, especially Central Africa, is very scarce. In Gabon, the number of patients recovering from Sars-cov2 pneumonia continues to grow. More than 45,000 cases of COVID-19 have been reported in the country (COPIL CORONAVIRUS. Epidemiological situation, of 12 January 2023), however no clinical description of the fate of these patients exists in our country. In the light of above, this study aimed at describing the clinical characteristics and socio-economic factors associated with the persistence of COVID-19 Symptoms in Libreville's (epicenter of the epidemic in Gabon) hospitalized resuscitation patients.

2. PATIENTS AND METHODS: This is a prospective, longitudinal, and observational study conducted from January 2021 to January 2022 at the infectiology department of Libreville University Health Center (CHUL). Were included in the analyses, patients of 18 years old minimum, hospitalized in the intensive care unit after an RT-PCR-confirmed COVID-19 and who have been accepted a one-year follow-up.
The following variables were collected on a case report form: age, sex, occupation, alcohol and tobacco use, comorbidities, symptoms and chest CT scan result at admission. All patients were consulted quarterly for 12 months. During the follow-up, existence, appearance and types of symptoms were sought at 3, 6 and 12-months post-hospitalization. Base on the NICE guidelines that define long COVID as the persistence of symptoms beyond 12 weeks [3], new and old symptoms were sought during each visit.

2.1 Ethical Considerations

The study was conducted by good clinical practices (GCP), following the Helsinki Declaration, and according to the recommendations of the National Vaccination Committee, under the direction of the COVID-19 Response Steering Committee (COPIL). This study was approved by the scientific committee in charge of regulating studies on COVID-19 in Gabon (PROT-023-CSCOVID-19).

2.2 Statistical Analysis

All data were collected in an Excel file and analyzed using the stat view 5.0 software. Quantitative data expressed as a median (25^{th}-75^{th} percentile) were compared using Mann-Whitney or Kruskall-Wallis tests. Qualitative variables expressed as a percentage were compared using Khi2 and Fischer's exact tests. The significant threshold was set at $p< 0,05$.

3. RESULTS

3.1 General Characteristics of the Study Population

In total, 144 patients met the inclusion criteria and were followed for 12 months. Their general characteristics are summarized in **Table I.**

Table I: General characteristics of study participants

Variables	Sample	
	N	%
Age in years		
<30	18	12,5
30-45	56	39,0
46-60	47	32,6
>60	23	15,9
Gender		
Male	84	58,4
Female	60	41,6
Occupation		
Students	12	8,3
Health workers	19	13,2
Public sector	58	40,2
Informal sector	26	18,1
Metered	12	8,3
None	17	11,8
Smoking		
No	135	93.7

Yes	9	6.3
Alcohol		
Yes	96	66.7
No	48	33.3
Comorbidities	92	63.9
Hyper-voltage	49	34,0
Type II Diabetes	22	15,3
Overweight	56	38,8
Obesity	61	42,3
Renal dysfunction	3	2,1
Sickle cell disease	2	1,4
HIV	4	2,7
Asthma	5	3,4
Duration of hospitalization		
1-5 D	10	19.4
6-10 D	16	47.1
>10	8	23.5
Disease severity		
Hypoxemia	22	41.5
Level of lung damage		
<10%	11	9,2%
11-25%	9	7.5
26-50%	49	41,2
51-75 %	38	31,9
> 75 %	12	10,1

The median age of the patients was 46.4 [16-88] years old and the sex ratio, 1.4. More than a third of (40.3%) were employees. Comorbidities (mostly obesity, overweight, high blood pressure, and diabetes) were found in more than half of them (n=92; 63.9%), see Table I.
Fatigue (100%), fever (72.2%), shortness of breath (50.0%), cough (47.2%) and joint pain (34.0%) were the most common symptoms in patients at hospital admission. The median time between the onset of the symptoms and hospitalization was 8 [6-14] days, 48.8% of the patients were hospitalized for more than 10 days after the onset of the symptoms. The median length of hospitalization was 8 [5-10] days, with half of the participants hospitalized for more than 10 days.
All the patients received a chest CT scan at admission. Lesion involvement between 26 and 50% was the most common (Table I).
No patients were vaccinated against COVID-19. Of the 144 patients, more than half (52.1%; n=75) had a long COVID, 39 (27.1%) still had symptoms at 6 months, and 9 (6.4%) had some persistent symptoms at 12 months.

3.2 Type and Frequency of Symptoms

Three months after hospitalization, fatigue (21.5%; n= 31) and cough (20.8%; n=33) were the most common symptoms. 2 (1.4%) among the patients still had headaches (Figure 1).

Two new symptoms that did not exist in the acute phase of the disease appeared, namely sleep disorders (16.0%; n= 23) and anxiety (11.1%; n= 16) (Figure 1).

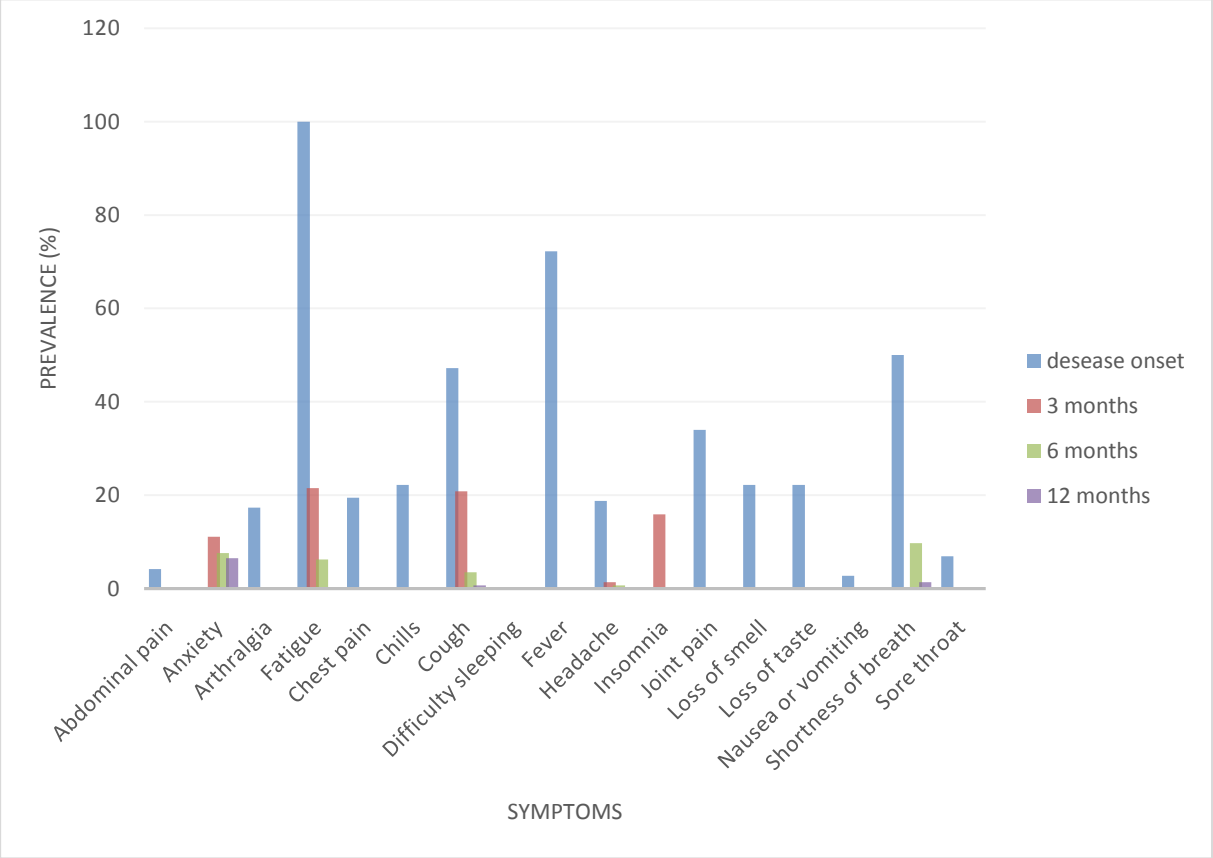

Fig. 1 : Prevalence of self-reported COVID-19 symptoms from hospital admission until month 12.

The symptoms reported six months after the onset of the infection were dyspnea, described as choking sensations (9.7%; n= 14), anxiety (7.6%; n= 11), fatigue (6.2%; n= 9) and cough (3.5%; n= 5).
A year after discharge from hospital, the persistent symptoms were anxiety (6.5%; n=9), dyspnea (1.4%; n=2) and cough (0.7%; n=1). The majority (n=119; 82.7%) of the patients had at least one thoracic CT scan follow-up, and 6 (5.5%) had discrete fibrosis lesions.

3.3 Persistence of symptoms and related factors

More than 50% of males, of obese and/or overweight patients, of patients with duration of symptoms before hospitalization of more than 10 days, and of patients with more than 50% lung damage had persistent symptoms at 3 months (Table II).
All asthmatics (n=5) still had at least one symptom after 3 months. The frequency of long COVID was higher among asthmatics, patients with no comorbidities, and patients with a pre-hospitalization symptom duration of more than 10 days (Table II).
Among the patients with symptoms at month 3; all those over 60 years (n=12/12) still had at least one symptoms at month 6; So did patients with chronic renal failure, nearly two third (62.3; n=5/8) of HIV-positives, 3 out of 4 smokers and 63.4% (n= 14/22) of those who received respiratory assistance (Table I).

A significant decrease in the frequency of long COVID was observed between the 3-month and 6-month visits, that frequency did not exceed 40% in the different groups.

Table II: Relationships between factors of severity and symptoms duration.

	3 months		6 months	
	N	%	N	%
Age				
≥ 60 years	12	52,2	12	52,2
≤ 60 years	63	51,2	27	22,2
Gender				
Male	46	54.8	22	26.2
Female	29	48.3	17	28.3
Occupation				
Heath workers	8	42.1	5	26.3
no health workers	67	53.6	34	27.2
Smoking				
Yes	4	44.4	3	33.3
No	71	52.6	36	26.7
Presence of comorbidity				
Yes	43	46.7	29	25.0
No	32	61.5	16	30.0
Hypertension				
Yes	24	49.0	9	18.4
No	51	53.7	30	31.6
Type 2 diabetes				
Yes	8	36.4	4	18.2
No	67	54.9	35	28.7
Obesity/overweigh				
Yes	62	52.3	32	27.4
No	13	48.1	7	25.9
Renal dysfunction				
Yes	1	33.3	1	33.3
No	74	52.3	38	27.0
Asthma				
Yes	5	100.0	2	40.0
No	70	50.4	37	26.6
HIV				
Yes	2	50		
No	73	52.1		
Length of stay at hospital				
> 10 days	8	47.1	3	17.7

< 10 days	26	41.9	16	25.8
Symptoms duration before hospitalization (n=109)				
≥ 10 days	24	58,5		
≤ 10 days	54	50		
Ventilation				
Yes	22	41.5	14	26.4
No	53	58,2	25	27.4
Lunch damage				
> 50 %	27	54.0	15	30.0
< 50%	35	50,7	21	22.3

3.4 Number of Symptoms per Patient

Among the patients with at least three persistent symptoms at month 3, 9.8% (n=9/92) had comorbidities compared to 5.8% (n=3/52) with no comorbidities. Two out of five asthmatics still had three persistent symptoms at three months ($p < 0.01$). While 14.3% (n=7/49) of hypertensive patients had three persistent symptoms ($p < 0.04$), only 5.3% (n=5/95) of non-hypertensive patients were concerned.

Of the patients who no longer had symptoms at 6 months, 15 (14.3%) were over 60 years of age, with 6 (50%) patients in this age group having at least two persistent symptoms at 6 months (p=0.06). Most participants with long COVID had only one symptom: 60% (n=45/75) at three months 79.5% (n= 31/39) at 6 months, and 77.8% (n=7/9) at 12 months (p=0.04) (Table III).

Table III : Evolution of the number symptoms presented by the patients during the follow-up

Number of symptoms	Time since symptom onset		
	3 months	6 months	12 months
No symptom, n (%)	69 (47.9)	105 (72.9)	135 (93.7)
One symptom, n (%)	45 (31.3)	31 (21.5)	7 (4.9)
2 symptoms, n (%)	18 (12.5)	7 (4.9)	1 (0.7)
At least 3 symptoms, n (%)	12 (8.3)	1 (0.7)	1 (0.7)

4. Discussion

This study aimed at identifying and determining the prevalence and progression of long COVID in 144 patients, hospitalized for severe COVID-19 at the CHUL intensive care unit. Date on long COVID-19 is scare in sub-Saharan Africa, especially in Central Africa. According to the reported data inpatients the probability of who's long COVID is known it be higher than outpatients were included [9]. These patients are also more likely to participate in post-illness follow-up consultations. More than half of the participants (52.1%) had at least one symptom of long COVID. This high prevalence corroborates that reported in a health center in Nigeria (56.7%) and several other studies that describe a frequency ranging from 10% to over 80% [10-12]. This prevalence has decreased significantly over time. At six months post-hospitalization, it was 27.1%, lower that reported in a meta-analysis (64%), but

comparable to that described in Saudi Arabia [12, 13]. Overall, a difference in long or post COVID symptoms prevalence is described by regions [14].

The prevalence and the number of symptoms decreased significantly over time. The prevalence was twice as low between 3 and 6 months. At 12 months, only 12% of those with post-COVID symptoms still reported. That decrease could be a corollary of the needed for the progressive resolution of tissue and organic lesions in the acute phase of the disease [15]. Bearing in mind that 20% of people tested positive in Libreville were hospitalized, and that among those not hospitalized, a significant proportion (8/%) would develop long COVID (according to the data from the literature), about 10,000 people are living with a reduced quality of life linked to long COVID. Furthermore, the emergence of new symptoms in the study cohort highlights the need for systematic follow-up of patients. It is also necessary to continue collecting information to better describe long COVID, the importance of which may be underestimated in our settings.

Consistent with other studies, fatigue was the most common symptom reported by the participants, with about a quarter to 50% of them being affected [12,16]. The cause and pathogenesis of post-COVID fatigue or muscular weakness are unclear. However, decreased pulmonary diffusion capacity, viral myositis, cytokine disruption, or corticosteroid-related myopathy were incriminated in other SARS infections [17]. Although the reduction in physical capacity was not sought, the high prevalence of fatigue most certainly accounts for the presence of that complication in patients. Besides, in some surviving patients, the persistence of partial recovery or tissue remodeling associated with pulmonary fibrosis that may persist for a long time, and a disturbance of respiratory T cell responses. These alterations could be responsible for persistent tissue damage and impaired lung function would also contribute [18]. The persistence of coughs and dyspnea (two of the most frequently reported symptoms in our intensive care unit survivor population up to the 12th month), seems to confirm these pathophysiological hypotheses. In Nigeria, the three symptoms were also the common, so were they in other parts of the world [10, 12, 13,19].

Neurocognitive or neuropsychological symptoms such as headaches, anosmia, difficulty concentrating, sleep disorders are also described during long COVID [9, 11, 20]. Anosmia and ageusia, already infrequent in the cohort during hospitalization, were no longer found in the 3rd month. The onset and persistence of anxiety up to the 12th month were recorded in post-hospitalization by other authors, in similar proportions (7.3%) [21]. This persistent anxiety could be a consequence of the mortality related to this pathology (« death anxiety »), as well as health and social restrictions during the hospitalization of these patients [22]. Hence the importance of long-term psychological follow-up is real [23].

The socio-demographic characteristics of the participants in this study are similar to other reports on long COVID, including the media age of 46 years and male predominance [21,24, 25]. The latter is due to the prevalence of men hospitalized for severe COVID in Gabon [26, 27]. No relationship was established between the gender and the frequency of long COVID. In most studies, women are more at risk than men, particularly in terms of frequency of symptoms such as fatigue, anxiety and depression [10, 13, 21, 28]. The absence of a relationship between the presence of post-COVID symptoms and age, the presence of comorbidities, alcohol and tobacco consumption, the severity of the infection in its acute phase, and the length of hospitalization is common. Indeed, Perisse in France and Kinge in South Africa also made the same observation [20, 29]. Our population sample size the prevalence of young adults (the majority of whom did not have comorbidities), and the fact that all patients had severe COVID, may explain these different results from those reported by many authors [7, 13, 25, 30, 31]. Indeed, associations between persistent symptoms in patients and pre-existing hypertension, chronic lung disease, obesity, or asthma recorded [25, 30, 31]. Surprisingly, diabetics were less likely to have long COVID compared to non-diabetics. Yet, diabetes was identified as a risk factor for severity and death in Gabon (data from COPIL Coronavirus 2021). The same trend was observed Saudi Arabia [13]. The fact that the most frequently described symptoms of long COVID are neuropsychological and

therefore not directly related to the symptoms of COVID-19 and the comorbidity of patients, may partly explain this finding.

Nevertheless, it is worth noting that the persistence of symptoms beyond 3 months was more common among people over 60 years of age, health workers, smokers, asthmatics, and patients with respiratory assistance during hospitalization. It is therefore important to continue collecting information to distinguish groups that are likely to have long COVID, to systematically implement regular post-hospitalization monitoring, which will improve their recovery and let them resume their daily activities more quickly.

This study has some limitations: the small size of the sample and the fact data were used from a single health structure. However, the CHUL has the largest litter capacity, and its intensive care unit was the reference service for the management of severe COVID cases. Additionally, the effect of vaccination was not evaluated, although it seems to protect and decrease the intensity of post-COVID symptoms [32]. The study began before the vaccination rollout in Gabon and the prevalence of vaccinated patients in intensive care was less than 1% at that time. Finally, the study only involved patients with severe forms. Those with simple or asymptomatic forms, followed in ambulatory care, currently represent more than 80% confirmed cases in Gabon. Given that they also concerned with long COVID, it is essential to complete the current data by including those groups.

Nevertheless, this cohort study included patients with a confirmed PCR diagnosis, and it was conducted for 12 months, while most of publications cover a shorter period. It was carried out in Central Africa, where little data exists on long COVID. Therefore, it provides essential information to understand the profile of long COVID in sub-Saharan Africa, where the consequences of COVID-19 appear to be different in terms of prevalence.

4. Conclusion: The prevalence of long COVID is high among patients hospitalized for severe forms in Libreville. Most symptoms improve after 6 months. Anxiety and sleep disorders are common in post-COVID conditions. As COVID has become and endemic disease, it is imperative to continue generating information for the patients, practitioners and psychologists to learn more about its chronic form, and for appropriate prevention and monitoring measures to be adopted in Gabon.

DECLARATION OF INFORMED CONSENT:informed consent was obtained from all subject involved in the study.

REFERENCES

1. Katarina Hedin, Alike W. van der Velden, Malene Plejdrup Hansen, Anna B. Moberg, Anca Balan, Pascale Bruno, et al. Initial symptoms and three months follow-up after acute COVID-19 in outpatients: An international prospective cohort study. European Journal of General Practice, 2023 ; 2154074.
2. Soriano JB, Murthy S, Marshall JC, Relan P, & Diaz JV. Condition WCCDWG on PC 19. A clinical case definition of post-COVID-19 condition by a Delphi consensus. Lancet Infect Dis, 2022 ; 22 :e102-107.
3. Venkatesan P. NICE guideline on long COVID. Lancet Respir Med. 2021; 9 (2):129.
4. World health Organization : Coronavirus disease COVID 19, post COVID-19 condition : WHO, 19 December 2021.
5. Seeßle J, Waterboer T, Hippchen T, Simon J, Kirchner M, Lim A et al. Persistent Symptoms in Adult Patients 1 Year After Coronavirus Disease 2019 (COVID-19) : A Prospective Cohort Study. Clin Infect Dis. 2022 ; 74(7):1191-1198.
6. World health Organization : Coronavirus disease COVID 19, post COVID-19 condition : WHO, 13 September 2022.

7. Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al. Attributes and predictors of long COVID. Nature medicine, 2021 ; *27*(4), 626-631.
8. Groff D, Sun A., Ssentongo AE, Ba DM, Parsons N, Poudel GR, et al. Short-term and long-term rates of postacute sequelae of SARS-CoV-2 infection: a systematic review. *JAMA network open*, 2021 ; *4*(10), e2128568-e2128568.
9. Afroze F, Arafat SM, Ahmed CM, Alam B, Banu S, Islam MZ, et al. Features and risk factors of post-COVID-19 syndrome: findings from a longitudinal study in Bangladesh. Lancet Reg HealthSoutheast Asia. 2022 ; 23:100134.
10. Ogoina D, James HI, Ogoinja SZ. Post-Discharge Symptoms among Hospitalized COVID-19 Patients in Nigeria: A Single-Center Study. Am J Trop Med Hyg. 2021 ; 105(3):731-736.
11. Lombardo MDM, Foppiani A, Peretti GM, Mangiavini L, Battezzati A, Bertoli S, et al. Long-Term Coronavirus Disease 2019 Complications in Inpatients and Outpatients: A One-Year Follow-up Cohort Study. Open Forum Infect Dis. 2021;8(8):ofab384.
12. Ma Y, Deng J, Liu Q, Du M, Liu M, Liu J. Long-Term Consequences of COVID-19 at 6 Months and Above: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2022;19(11):6865.
13. Tleyjeh IM, Saddik B, AlSwaidan N, AlAnazi A, Ramakrishnan RK, Alhazmi D, et al. Prevalence and predictors of Post-Acute COVID-19 Syndrome (PACS) after hospital discharge: A cohort study with 4 months median follow-up. PLoS One. 2021;16(12):e0260568.
14. Chen C, Haupert SR, Zimmermann L, Shi X, Fritsche LG, & Mukherjee B. Global prevalence of post-coronavirus disease 2019 (COVID-19) condition or long COVID: a meta-analysis and systematic review. The Journal of infectiousdiseases. 2022 ; *226*(9), 1593-1607.
15. Hui DS, Wong KT, Ko FW, Tam LS, Chan DP, Woo J, et al. The 1-year impact of severe acute respiratory syndrome on pulmonary function, exercise capacity, and quality of life in a cohort of survivors. Chest. 2005;128(4):2247-61.
16. Michelen M, Manoharan L, Elkheir N, Cheng V, Dagens A, Hastie C, et al. Characterising long COVID: a living systematic review. BMJ Glob Health. 2021;6(9):e005427.
17. Hui DS, Young JJ, Bruno D, Pomara N. A review of the relationship between pro inflammatory cytokines and major depressive disorder. J. Affect Disord. 2014;169:15–20.
18. Cheon IS, Li C, Son YM, Goplen NP, Wu Y, Cassmann T, et al. Immune signatures underlying post-acute COVID-19 lung sequelae. Science Immunology, 2021 ; *6*(65), eabk1741.
19. Hung L, Lin M. Clear, consistent and credible messages are needed for promoting compliance with COVID-19 public health measures. EvidBasedNurs. 2022 ; 25(1):22.
20. Perisse A, De Cacqueray F, Delarbre D, Marsaa H, Bergmann C, Da Silva V, et al. Symptoms of Long-COVID 1-Year after a COVID-19 outbreak among sailors on a French aircraft carrier. Infect Dis Now. 2023;53(4):104673.
21. Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet. 2021;397(10270):220-232.
22. Andersen AJ, Mary-Krause M, Bustamante JJH, Héron M, El Aarbaoui T, Melchior M. Symptoms of anxiety/depression during the COVID-19 pandemic and associated lockdown in the community: longitudinal data from the TEMPO cohort in France. BMC Psychiatry. 2021 28;21(1):381.
23. Rivera-Izquierdo M, Láinez-Ramos-Bossini AJ, de Alba IGF, Ortiz-González-Serna R, Serrano-Ortiz Á, Fernández-Martínez NF, et al. Long COVID 12 months after discharge: persistent symptoms in patients hospitalised due to COVID-19 and

patients hospitalised due to other causes - a multicentre cohort study. *BMC medicine*, 2022 ; *20*(1), 92.
24. Liu T, Wu D, Yan W, Wang X, Zhang X, Ma K, et al. Twelve-Month Systemic Consequences of Coronavirus Disease 2019 (COVID-19) in Patients Discharged From Hospital: A Prospective Cohort Study in Wuhan, China. Clin Infect Dis. 2022;74(11):1953-1965.
25. Jassat W, Mudara C, Vika C, Welch R, Arendse T, Dryden M, et al. A cohort study of post-COVID-19 condition across the Beta, Delta, and Omicron waves in South Africa: 6-month follow-up of hospitalized and nonhospitalized participants. International Journal of InfectiousDiseases, 2023 ;*128*, 102-111.
26. Diallo M, Eyamamé D. COVID management at the Regional Hospital of Lambaréné (Gabon) from March 2020 to February 2021. Med Trop Sante Int. 2022 Aug 19;2(3):mtsi.v2i3.2022.268.
27. Igala M, Bivigou EA, Kombila UD, Ngomas JF, Mougougou A, Makao AI, et al. Complete Blood Count Parameters, C-Reactive Protein and the Severity of Coronavirus Disease. Clin Lab. 2021;67(12).
28. Menges D, Ballouz T, Anagnostopoulos A, Aschmann HE, Domenghino A, Fehr JS, &Puhan, M. A. Estimating the burden of post-COVID-19 syndrome in a population-based cohort study of SARS-CoV-2 infected individuals: Implications for healthcare service planning.*medRxiv*, 2021.
29. Wose Kinge C, Hanekom S, Lupton-Smith A, Akpan F, Mothibi E, Maotoe T, et al. Persistent Symptoms among Frontline Health Workers Post-Acute COVID-19 Infection. *International Journal of EnvironmentalResearch and Public Health*. 2022;19(10):5933.
30. Mehandru S, Merad M. Pathological sequelae of long-haul COVID. Nat Immunol. 2022;23(2):194-202.
31. Fabbri A, Voza A, Riccardi A, Vanni S, De Iaco F; Study & Research Center of the Italian Society of Emergency Medicine (SIMEU). Unfavorable Outcome and Long-Term Sequelae in Cases with Severe COVID-19. Viruses. 2023;15(2):485.
32. Richard SA, Pollett SD, Fries AC, Berjohn CM, Maves RC, Lalani T, et al. Epidemiology, Immunology, and Clinical Characteristics of Emerging Infectious Diseases With Pandemic Potential (EPICC) COVID-19 Cohort Study Group. Persistent COVID-19 Symptoms at 6 Months After Onset and the Role of Vaccination Before or After SARS-CoV-2 Infection. JAMA Netw Open. 2023 ; 6(1):e2251360.