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Attributes and Factors Associated with Long COVID in Patients
Hospitalized for Acute COVID-19:
A Retrospective Cohort Study

A Manuscript Submitted to the Department of Internal Medicine, College of Health Sciences, School of Medicine, Addis Ababa University as a Partial Fulfillment of the Requirements for a Specialty Certificate in Internal Medicine

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April 2024

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Acknowledgment

I would like to thank the Internal Medicine Department of College of Health Sciences, Addis Ababa University for giving me the opportunity to do this research. I would also like to extend my gratitude to my advisors, Dr. Dawit Kebede and Dr. Wondwossen Amogne, for their invaluable guidance while doing this research. My heartfelt gratitude goes out to Mr. Eyob Kebede, who helped me tremendously during the data analysis process. Last but not least, I would like to thank Nurse Bethlehem Mesfin, Dr. Natnael Fitsum, and Dr. Musse Gebeyehu from Hallelujah Hospital for providing me with much-needed support and information to complete this proposal.

List of Acronyms

AAU - Addis Ababa University

BMI – Body Mass Index

CDC - Centers for Disease Control

COVID-19 - Corona Virus Disease of 2019

DLCO - Diffusion Capacity of the Lungs for Carbon Monoxide

EMR - Electronic Medical Record

ICU - Intensive Care Unit

MERS - Middle East Respiratory Syndrome

MV – Mechanical Ventilation

NIV – Noninvasive Ventilation

PICS - Post-Intensive Care Syndrome

SARS - Severe Acute Respiratory Syndrome

WHO - World Health Organization

Abstract

Background: It is now recognized that many patients have persistent symptoms after recovery from acute COVID-19 infection, an infection caused by the coronavirus SARS-CoV-2. This constellation of symptoms, commonly known in the literature as 'Long COVID' or 'Post COVID-19 Condition', may manifest with a wide range of physical and cognitive/psychological symptoms. Although the mechanisms are still poorly understood, much effort has been made in the scientific community to characterize this condition better. However, there is a lack of data on the frequency, risk factors, and severity of Long COVID in Africa.

Objective: To assess the prevalence, attributes, and factors associated with Long COVID in patients hospitalized for acute COVID 19

Method: This was a retrospective chart review (Electronic Medical Records [EMR]) of patients who were discharged after hospitalization for acute COVID-19 infection from Hallelujah General Hospital (one of the first private hospitals where patients were treated for COVID-19). The hospital's database was searched for patients who were hospitalized for acute COVID-19 infection from March 2020 to December 2022. Two hundred and forty-seven participants who underwent follow-up beginning four weeks after symptom onset were assessed for Long COVID. A structured questionnaire was used to collect data about their sociodemographic, clinical, laboratory, and imaging information during their admission and follow-up. The data was entered into SPSS version 29 for analysis. The relationship between the independent and dependent variables was explored through binary logistic regression.

Results: The mean age of the participants was 58.5 (± 13.9) years, and 160 (64.8%) were males. One hundred seventy-eight (72.1%) participants had at least one persisting symptom 4 weeks post symptom onset, at a median follow up time of 35 (IQR 32-40) days. The most frequently reported symptoms were fatigue (41.7%), shortness of breath (31.2%), cough (27.1%), and sleep disturbances (15%). Duration of symptoms more than 7 days before admission [aOR = 1.97; CI_{95%} = 1.04 to 3.75; P=0.038] and length of stay more than 10 days in the hospital [aOR = 2.62; CI_{95%} = 1.20 to 5.72; P=0.016] were found to be significantly associated with Long COVID on multivariate analysis.

Conclusion: There is a high prevalence of Long COVID among patients hospitalized for acute COVID-19. Those who had longer duration of symptoms before admission and a longer stay in the hospital appear to have a higher risk.

Keywords: COVID-19, Long COVID, Post COVID-19, Ethiopia, Cohort

1. Introduction

1.1 Background of the Study

Since the global COVID-19 pandemic started in 2020, caused by the coronavirus SARS-CoV-2, there have been more than 650 million confirmed cases globally and more than 6 million deaths [1]. This resulted in many people recovering from this disease, but the full consequences of the infection after recovery from acute illness were not initially recognized well by the scientific community. After the term “Long COVID” was first used by a patient early in the pandemic, recognition of the condition grew over a few months, mainly through patient-led efforts [2]. Since then, various other terms have been developed to describe a range of residual symptoms experienced by patients, such as ‘post-acute sequelae of COVID-19’, ‘post-acute sequelae of SARS-CoV-2 infection’, ‘chronic COVID syndrome’, ‘long-haul COVID’, and ‘post-COVID-19’ [3].

Various groups have tried to define and categorize the range of symptoms experienced by COVID-19 patients during the acute and prolonged phases of the illness. The definitions share the following features for Post COVID conditions proposed by the CDC and WHO; (1) signs and symptoms that develop in an individual with confirmed SARS-Cov-2 infection, (2) these continue four weeks or more after the initial infection, (3) multisystemic symptoms, (4) symptoms may be relapsing and remitting or progressing over time, (5) not explained by an alternative diagnosis [4,5].

1.2 Statement of the Problem

Due to the large number of people infected with COVID-19, it is important to evaluate the burden of its complications. Since its recognition, various studies have tried to characterize the prevalence and attributes of Long-COVID. Some of the largest global studies on this condition have reported a prevalence ranging from 6.2%-45% [3,6,7]. The high range of prevalences reported could be due to the difference in definitions, methods, and populations used in the studies.

It is essential to identify patients affected by this condition better, understand how often patients develop it and pinpoint its risk factors, so that the consequences it leads to can be adequately addressed. Data from good quality studies can be used to provide clinical guidance to healthcare providers, and aid in making relevant plans and policies to tackle the problem at a large scale.

The African continent has reported the lowest number of COVID-19 infections from all the continents. Despite that, the pandemic in all sectors has impacted it the most, since it is home to many developing nations [8]. Similarly, Long COVID is expected to affect various aspects of life on the continent. So far, only a few studies have been published on the prevalence, clinical presentations, and determinants of Long COVID in Africa, and this study aims to fill that knowledge gap.

1.3 Significance of the Study

To date, this study is the first to report the prevalence, clinical presentations, and factors associated with Long COVID in Ethiopia, where there are nearly half a million confirmed cases [1], and East Africa. It explores the number of people affected by this condition, symptoms in various systems, and its associated factors. There is a global interest in gaining an increased understanding of Long COVID. It will add valuable input to the existing research by filling the knowledge gap in underserved regions like Africa.

2. Literature Review

Continuing symptoms after recovery from an acute viral illness is not new. This was noted as well in the previous coronavirus pandemics, namely the severe acute respiratory syndrome (SARS) and the Middle East Respiratory Syndrome (MERS) [9, 10]. A meta-analysis of 28 studies found complications such as impaired diffusion capacity for carbon monoxide and reduced exercise capacity in SARS and MERS survivors up to 6 months after discharge [9]. Another study of 369 SARS survivors reported the presence of psychiatric morbidities and chronic fatigue in up to 40% of patients at a 4-year follow-up [10]. This could indicate an underlying common pathophysiologic mechanism for the continuing symptoms in these patients. In addition, new or worsening cognitive, psychiatric, or physical function after critical illness is a recognized condition known as Post-Intensive Care Syndrome (PICS) [11].

Since recognizing long-term symptoms after a person is infected with COVID-19, the scientific community worldwide has researched to understand the problem better. Hundreds of cross-sectional studies were done in the early stages, mainly in North America, Europe, and Asia [12-19]. These were followed by a few others in Africa [20-22]. More recently, large meta-analyses have been done that help us unify the results of these smaller studies, although almost all of them are limited in making firm conclusions due to the heterogeneity of the studies included (in terms of case definitions, follow up duration, and study designs) [3,7, 23-29].

Of these, the most recent is a meta-analysis published in January 2023 that included 194 studies and 735,006 participants. It reported that at a mean follow-up duration of 126 days, 45% of the patients continued to experience at least one ongoing symptom [3]. Another large meta-analysis of 54 studies and two medical record databases of 1.2 million individuals found that 6.2% of patients who had symptomatic COVID-19 had at least 1 of 3 symptom clusters 3 months after the infection (cognitive problems, fatigue with bodily pain or mood swings, respiratory symptoms) [7]. This vast difference in prevalence is also reflected in the numbers presented in other studies, with prevalence estimates of 6.2% - 80%. [3, 7, 23-29]

This significant difference in reported prevalences makes determining the actual number of people affected by Long COVID difficult. It mainly arises from varying case definitions, follow-up times, core outcomes, data collection methods (self-report, in-person and telephone examinations, electronic medical records), symptom assessment tools (self-report vs. standard scales), and adjustment for health

status before COVID-19. In order to solve this problem, some authors have put forward a few methodological recommendations for future studies of persistent COVID-19 symptoms [26].

Fatigue is a dominant symptom of Long COVID, with prevalence estimates ranging from 3.7% to 58% in various studies [3, 7, 23-29]. Other common symptoms include respiratory problems such as shortness of breath, abnormal lung imaging or DLCO findings, and concentration, memory and sleep issues. [3, 7, 25-27]. Decreased quality of life is also reported in many patients [25]. In addition, it is worth noting that symptoms can be present in any system, such as hematologic, cardiovascular, renal, endocrine, gastrointestinal and hepatobiliary, and dermatologic [29,33]. In order to harmonize future research findings on the post-COVID-19 condition, a WHO definition and a set of core outcomes that map symptom classification are put in place, and will be used in this research [4,30].

Respiratory symptoms are common including dyspnea, cough, chest discomfort, as well as abnormal imaging and reduced pulmonary diffusing capacity [7,23,24,25,27]. The prevalence of dyspnea is reported in various studies ranging from 7.7% to 41.7% [26]. This variation is explained by self-report vs. the Modified Medical Research Council Dyspnea Scale, with higher numbers obtained when patients self-report the symptom. Abnormal imaging is also another persistent finding after recovery from COVID-19 (34% prevalence in one meta-analysis of 15 studies) [23]. Some common features include ground-glass opacity, evidence of fibrosis, consolidation, and reticulation [24,25]. Although these changes may persist for up to 90 days after discharge in two-thirds of the patients [23], improvement or radiologic resolution is observed when compared to initial CT findings in some studies [25].

Pulmonary function tests such as spirometry, diffusion capacity, lung volumes and exercise tests are also included in some studies of Post-COVID-19 Conditions. The most common finding from these is reduced DLCO, with occurrence rates of up to 16.3% [24,25,27]. In one study, reduced DLCO <80% was associated with a high level of D-dimer at admission, suggesting this could be a potential biomarker to predict reduced DLCO in COVID-19 patients [24]. Other pulmonary function test abnormalities include restrictive patterns on spirometry and, less commonly, obstructive and mixed patterns [27,31,32].

Persistent laboratory abnormalities are found in some patients. These include D-dimer, N-terminal (NT)-pro hormone BNP (NT-proBNP), C-reactive protein (CRP), serum ferritin, procalcitonin, and interleukin-6 (IL-6), in decreasing frequency [23].

Potential risk factors for Long COVID have been proposed in the literature, since not all patients with acute COVID-19 infection develop persistent symptoms. Some of these include female sex [7,23,24,25,28,29], older age [24], hospital admission especially to the ICU [3,24,25,28], comorbidities such as asthma, hypertension, chronic lung conditions [24,29], need for oxygen during the acute phase of the illness [24]. On the other hand, other studies found no association existing with sex and age [3]. This difference could be explained by the heterogeneity of the studies, suggesting that more data is needed to make firm conclusions. Average follow-up time was also found to determine the prevalence of symptoms, with fewer patients having symptoms at 12 months compared to 3 months [7, 28].

Only a few studies have been done in Africa on Long COVID, namely in Egypt, Ghana, and South Africa [20-22]. Two of these are cross-sectional analyses, while the largest, enrolling 8309 patients, is a prospective cohort study that surveyed patients with laboratory-confirmed SARS-CoV-2 infection 1 and 3 months after hospital discharge [20]. The findings in two of these studies are consistent with those from other parts of the world: females are more affected, fatigue and respiratory symptoms are the commonest sequelae, and comorbidities such as hypertension and diabetes mellitus determine Long COVID [20,21]. Contrary to other studies, the study done in Egypt reported more Long COVID symptoms in non-hospitalized patients than hospitalized patients [22].

In Ethiopia, while there are a handful of studies assessing time to recovery of acute COVID-19 patients, all used a negative COVID-19 PCR test to define recovery and did not report on persistence of symptoms [35,36]. To this date, only one study has been done assessing Post-COVID-19 pulmonary complications among recovered COVID-19 patients [37]. In that study, 14.1% of the patients were found to have pulmonary complications at 3 months post hospital discharge. There are no other published studies reporting on Long COVID in other systems as well.

Overall, it is clear that insufficient data exists from Africa on Long COVID, and especially from Ethiopia. In addition, studies from the rest of the world used varying case definitions, core outcomes, and follow-up times, making a harmonized interpretation of data nearly impossible. Hence, more studies are needed that use the standard definition and core outcome set of Long COVID, and this study tries to fill that gap.

3. Objectives of the Study

General Objective

To assess the prevalence, attributes and factors associated with Long COVID in Patients Hospitalized for Acute COVID 19

Specific Objectives

To determine the clinical presentation (signs and symptoms) of patients with Long COVID

To describe the laboratory and imaging features of patients with Long COVID

To evaluate factors associated with Long COVID after hospitalization for acute COVID-19 infection

4. Research Methods

Study setting

The study was done at Hallelujah General Hospital, Addis Ababa, Ethiopia. It is one of the first private hospitals where patients with COVID-19 were treated as in-patients and out-patients. It has one full time pulmonologist, four internists, one infectious diseases specialist, two part-time pulmonary and critical care physicians, and other health care professionals. It has a 6 - 7 Intensive Care Unit (ICU) bed capacity. Its outpatient follow-up clinics are attended by an infectious diseases specialist as well as pulmonary and critical care specialists.

Study Period

The study period was October – November 2023

Study Design

Retrospective Cohort Study

Source Population

All patients who were hospitalized for acute COVID-19 at Hallelujah General Hospital in the specified period

Study Population

All patients on follow-up upon discharge after hospitalization for acute COVID-19, and had at least one follow up at least 4 weeks post symptom onset

Sample Size

The sample size was determined by using the formula for single population proportion considering a prevalence of 82.1%, from a study done in South Africa in a similar population [20]. The sample size was calculated by assuming a confidence interval of 95% and 5% margin of error.

$$n = Z^2 p(1 - p) / d^2$$

- Z - z-score -1.96
- d - margin of error - 0.05
- p - population proportion - 82.1%
- n - Sample size - 226

This was the minimum number of patients that was planned to be included in the study. However, in order to increase the power of the study, all eligible patients during the study period were included.

Study Variables

Dependent Variable - number of patients with one or more symptoms of Long COVID

Independent Variables - Age, Sex, Comorbidities (Asthma, Chronic Lung conditions, Hypertension, Diabetes), the severity of acute COVID-19 infection, duration of symptoms before admission, number of symptoms during acute COVID-19 infection, need for ICU and mechanical ventilation, length of stay in the hospital, complications during hospitalization, vaccination status

Inclusion and Exclusion Criteria

Inclusion criteria - age 18 or more, confirmed SARS-CoV-2 infection, hospitalized for acute COVID-19 during the study period

Exclusion criteria - lost to follow-up less than four weeks after discharge from hospital, incomplete documentation of condition during hospitalization

Operational Definitions

Long COVID - signs and symptoms that develop in an individual with confirmed SARS-Cov-2 infection that continue four weeks or more after the initial infection.

Time zero - Date of symptom onset of acute COVID-19 infection

Chest CT findings*	Typical appearance (Peripheral, bilateral, GGO; multifocal GGO of rounded morphology, reverse halo sign or other signs of organizing pneumonia)
	Indeterminate appearance (Absence of typical features AND presence of multifocal, diffuse, perihilar or unilateral GGO lacking a specific distribution or few very small GGO with a non-rounded and non-peripheral distribution)
	Atypical findings (Absence of typical or indeterminate features AND presence of isolated lobar or segmental consolidation without GGO, discrete small nodules, lung cavitation, smooth interlobular septal thickening with pleural effusion)
	Negative for pneumonia (No CT features of pneumonia)

*based on Radiological Society of North America Categorization [34]

Data Collection and Analysis

Data was collected from Electronic Medical Records (EMR) for retrospective review. A structured questionnaire was developed to collect the data, based on WHO and CDC guidelines, established outcome sets of Long COVID, and information from previous research on the condition. The data was collected using Kobo toolbox, thoroughly cross-checked, and entered into the SPSS software for analysis. Statistical significance was considered at P < 0.05. Factors associated with Long COVID were determined by

unadjusted logistic regression and those with a P value of <0.25 were considered for multivariable analysis.

Ethical Considerations

Ethical approval was obtained from the Addis Ababa University, College of Health Sciences IRB and relevant authorities in Hallelujah General Hospital. Data was anonymized, and the confidentiality of the participants was maintained throughout the study.

5. Results

In-patient records at the internal medicine ward and ICU of Hallelujah General Hospital were searched for patients admitted with the diagnosis of acute COVID-19 infection. Of these, 323 were found to have at least one follow up visit after discharge. Those patients who had no follow up visit after at least ≥ 4 weeks since symptom onset were excluded from the study, and in-patient and follow up data was collected from the 247 eligible participants.

5.1 Socio-demographic characteristics

The mean age of the participants was 58.5 (± 13.9) years. One third of the participants were above the age of 65. Most of the patients were male with a male to female ratio of 1.8:1. One hundred and one (40.9%) participants were either overweight or obese.

Table 1. Sociodemographic characteristics of the participants

Age	Frequency (n)	Percentage (%)
18-34	7	2.8
35-49	65	26.3
50-64	89	36
≥ 65	86	34.8
Sex		
Male	160	64.8
Female	87	35.2
BMI		
Normal	28	11.3
Overweight	45	18.2
Obese	56	22.7
Not stated	118	47.8
Total	247	100

BMI: Body mass index

5.2 Characteristics of the patients during admission for acute COVID-19 infection

Infection was confirmed by COVID-19 PCR in 242 (98%) of the patients, while diagnosis was made clinically in the rest. Only one patient had a re-infection, whereas it was a first-time infection for 246 (99.6%) patients. Ten patients (4%) had received COVID-19 vaccination before their infection.

The median duration of viral shedding (time from the first positive COVID-19 PCR to the first negative test) was 14 days (IQR 11-17). Patients had five symptoms on average during their acute illness, and they experienced their symptoms for a median of 7 days before admission.

Table 2. Characteristics of the patients during admission

		Frequency (n)	Percentage (%)		
Severity of acute COVID-19 infection	Mild	5	2		
	Moderate	27	10.9		
	Severe	196	79.4		
	Critical	19	7.7		
Number of symptoms	<5	116	47		
	≥5	131	53		
Duration of symptoms before hospitalization	≤7 days	130	52.6		
	>7 days	117	47.4		
Symptoms	Cough	201	81.4		
	Fatigue	166	67.2		
	Fever	133	53.8		
	Dyspnea	115	46.6		
	Myalgia/arthralgia	85	34.4		
	Chills	47	19		
	Headache	58	23.5		
	Chest pain	25	10		
	Diarrhea	23	9.3		
	Nausea/vomiting	23	9.3		
	Anosmia	47	19		
	Ageusia	51	20.6		
	Loss of appetite	84	34.1		
	Laboratory abnormalities	Anemia	50	20.2	
		Leukocytosis	152	61.5	
Lymphopenia		212	85.8		
Raised aminotransferases		82	33.2		
Raised LDH		55	22.3		
Raised ESR		58	23.5		
Raised CRP		94	38.1		
Raised creatinine		34	13.8		
Imaging abnormalities	Chest x-ray		Chest CT		
		Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
	Typical	212	85.8	76	30.8
	Atypical	22	8.9	6	2.4
	Indeterminate	4	1.6	-	-
	No features of pneumonia	6	2.4	1	0.4
Not done	3	1.2	164	66.4	

Patients were admitted for a median of 13 days (IQR 10-15). One hundred seventy-seven (71.7%) of the patients were admitted to the hospital for more than 10 days. Twenty-two (8.9%) patients were admitted to the ICU during their stay. While 48 (19.4%) did not need any oxygen support, 13 (5.6%) patients

required a higher level of respiratory support i.e. noninvasive ventilation or mechanical ventilation. Eighteen (7.3%) patients received antiviral treatment (Remdesivir).

Table 3. Treatment received by the patients

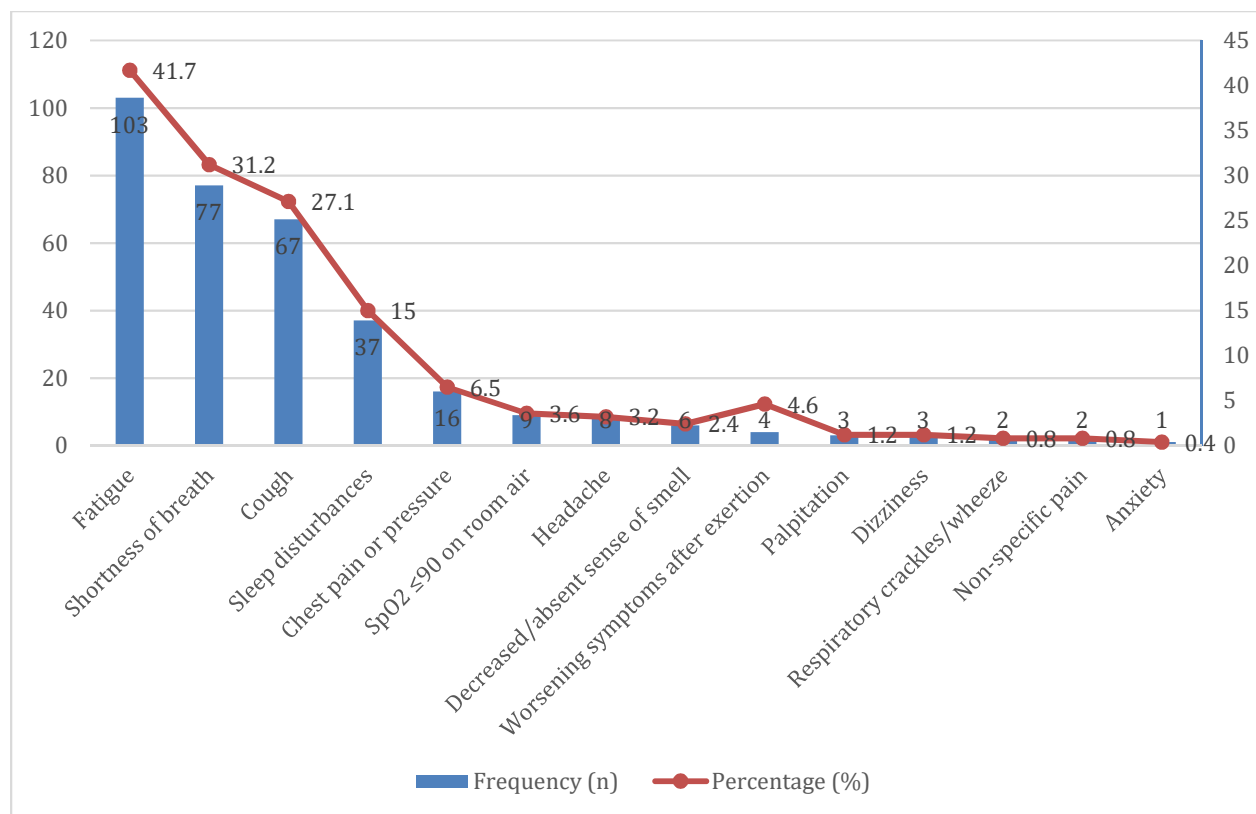
		Frequency (n)	Percentage (%)
Maximum level of respiratory support	None	48	19.4
	Intranasal oxygen	166	67.2
	Facemask oxygen	19	7.7
	Noninvasive ventilation	8	3.2
	Mechanical ventilation	5	2.4
Total		247	100
Treatment received	Steroids	226	91.5
	Antibiotics	245	99.2
	Prophylactic anticoagulation	68	27.5
	Therapeutic anticoagulation	169	68.4
	Antiviral (Remdesivir)	18	7.3

One hundred and forty-eight (59.9%) patients had at least one comorbidity. The most common of these include diabetes mellitus (34%), hypertension (33.6%), and dyslipidemia (10.1%). Twenty-two (8.9%) patients had 2 or more complications during admission, while 123 (49.8%) patients had no complications at all. The most common complication was secondary bacterial infection, experienced by 97 (39.3%) of the patients. For a complete list of comorbidities and complications in the patients, see Appendix.

5.3 Follow up characteristics

Among the patients who had follow up at least 4 weeks after onset of symptoms, the median timing of first follow up was 35 (IQR 32-40) days, and that of the last follow up was 43 (IQR 34-65) days. Data on clinical findings as well as laboratory and imaging abnormalities recorded during the first follow up 4 weeks after symptom onset was collected, to look for any persisting abnormalities. One hundred seventy-eight (72.1%) patients had at least one persisting symptom 4 weeks post symptom onset. Patients had 2 symptoms on average, the most frequently reported symptoms being fatigue (41.7%), shortness of breath (31.2%), cough (27.1%), and sleep disturbances (15%). During their last follow up (at a median of 43 days), 62.5% of the patients had persistent symptoms.

Figure 1. Symptoms reported during follow up visits



The following lab abnormalities were present in the patients 4 weeks after their symptom onset.

Table 4. Laboratory abnormalities during follow up

Laboratory finding	Frequency (n)	Percentage (%)
Lymphopenia	44	17.8
Leukocytosis	36	14.6
Raised ESR	28	11.3
Raised CRP	21	8.5
Anemia	20	8.1
Raised creatinine	14	5.7
Raised aminotransferase levels	9	3.6
Raised LDH	6	2.4

During their follow up, 68 (27.5%) patients had chest x-ray done, out of whom 12 (17.6%) had normal readings. The most common abnormality was fibrosis, detected in 29 (42.6%) of the patients, followed by ground-glass opacities in 27 (39.7%) patients. Other abnormalities included reticulations, consolidation, and pleural effusion. Only one patient had chest CT done, and it showed residual fibrotic bands with acute pulmonary thromboembolism.

5.4 Factors associated with Long COVID in patients hospitalized for acute COVID-19 infection

While patients with age ≥ 70 were found to have 2.2 times increased odds of having Long COVID on bivariate analysis [CI_{95%} = 1.06, 4.72], this was not true when controlling for the other variables. Other factors such as viral shedding more than 2 weeks, duration of symptoms >7 days before admission, length of stay >10 days in the hospital, and staying an extra day in the hospital were found to confer risk of Long COVID on bivariate analysis. However, only duration of symptoms >7 days before admission [aOR = 1.97; CI_{95%} = 1.04 to 3.75] and length of stay >10 days in the hospital [aOR = 2.62; CI_{95%} = 1.2 to 5.72] were found to be significantly associated with the outcome on multivariate analysis.

Table 5. Factors associated with Long COVID

		COR with 95% CI	p-value	AOR with 95% CI	p-value
Age	18-69	1			
	70 or above	2.241 (1.062, 4.728)	0.034	2.064 (0.855, 4.984)	0.107
Sex	Male	1			
	Female	1.123 (0.624, 2.019)	0.699		
Weight	Normal	1			
	Overweight/obese	1.701 (0.676, 4.282)	0.259		
Duration of viral shedding	<2 weeks	1			
	>2 weeks	1.859 (1.002, 3.448)	0.049	1.366 (0.673, 2.773)	0.387
Vaccination	No	1			
	Yes	0.567 (0.155, 2.074)	0.391		
Severity*	Mild/moderate	1			
	Severe	1.310 (0.593, 2.893)	0.505		
	Critical	4.452 (0.867, 22.878)	0.074		
Number of symptoms	<5	1			
	5 or more	1.572 (0.898, 2.749)	0.113	1.433 (0.756, 2.718)	0.270
Duration of symptoms before admission	<7	1			
	>7	2.051 (1.153, 3.65)	0.015	1.971 (1.037, 3.748)	0.038

Comorbidities	Not present	1			
	1 comorbidity	0.671 (0.375, 1.201)	0.179	0.570 (0.294, 1.106)	0.097
	Chronic respiratory illness	0.759 (0.273, 2.109)	0.597		
	Diabetes	1.043 (0.579, 1.878)	0.889		
	Hypertension	1.342 (0.734, 2.455)	0.340		
	CKD	1.172 (0.308, 4.462)	0.816		
	Chronic cardiac illness	0.692 (0.245, 1.949)	0.485		
	Duration of admission	≤10 days	1		
>10 days		2.908 (1.608, 5.259)	<0.001	2.621 (1.200, 5.727)	0.016
Odds for each additional day in the hospital		1.083 (1.013, 1.158)	0.019	0.986 (0.920, 1.056)	0.681
ICU admission	No	1			
	Yes	4.241 (0.964, 18.654)	0.056	1.840 (0.182, 18.631)	0.605
Level of respiratory support	None	1			
	Intranasal oxygen, facemask	1.132 (0.569, 2.254)	0.724		
	NIV/MV	5.909 (0.707, 49.404)	0.101	2.138 (0.091, 50.528)	0.638
Complications during treatment	No	1			
	Yes (Any complication)	1.311 (0.750, 2.291)	0.341		
	2 or more complications	2.629 (0.752, 9.185)	0.13	1.821 (0.286, 11.587)	0.526
	Odds for each additional complication	1.408 (0.927, 2.140)	0.109	0.869 (0.448, 1.687)	0.679

*Severity omitted from multivariate analysis because of high degree of correlation with ICU admission.

Abbreviations: NIV – noninvasive ventilation, MV – mechanical ventilation

6. Discussion

In this study, the prevalence of persistent symptoms in patients hospitalized for acute COVID-19 was assessed at ≥ 4 weeks post-symptom onset, according to the WHO definition of Long COVID. Standard definitions suggested by previous meta-analyses for time zero, Long COVID outcome set, and imaging abnormalities were applied.

The findings showed that among 247 patients included in the study, 178 (72.1%) had one or more symptoms of Long COVID at a median follow-up time of 35 days (IQR 32-40). This number is within the range of results from several studies, with prevalence estimates varying from 6.2 to 80% [3,7, 23-29]. While this wide range is due to multiple factors, one of the most important is the varying definition of Long COVID used in the studies. We get a slightly narrower estimate of 20 to 80% when we look at those studies that used a similar time cut-off to define Long COVID to this study.

In a prospective cohort study in South Africa by M. Dryden et al that evaluated patients at 1 month and 3 months after hospitalization, 80.2% of them had one or more persistent symptoms at 1 month [20]. Similarly, 80% of the patients had one or more long-term symptoms at follow-up days ranging from 14 to 110 days in a meta-analysis of 47,910 patients [23]. These results are similar to the findings in our study. On the other hand, other studies have reported much lower estimates. For instance, a meta-analysis on the global prevalence of Long COVID found a prevalence of 37% at 30 days. However, this study included participants who were not hospitalized during their acute infection [27].

This study does not directly indicate the risk that any patient may experience persistent symptoms after contracting COVID-19, because the prevalence estimate only includes patients who were hospitalized and had follow-up visits at the time point mentioned above. Patients who recovered fully and did not need a follow-up visit at ≥ 4 weeks, or who did not have symptoms severe enough to necessitate hospitalization, are not included in this study and its conclusions do not apply to them.

Fatigue is the most common symptom reported in this study, with 41.7% of the patients experiencing it. This is consistent with most other studies [3,7,23-29]. Other common symptoms include shortness of breath, cough, and sleep issues, all of which were also found in this study with frequencies of 31.2%, 27.1%, and 15% respectively. In a study from Ethiopia on post-COVID-19 pulmonary complications done by Abebaw B. et al, 17.8% of the participants had respiratory complaints at 3 months from hospital discharge [37]. The most common of these included cough (7.7%) and shortness of breath (14.1%). The differences in the prevalence with this study could be due to the later date of follow up used. In addition, 5.7% of the patients had SpO₂ <90%, which was comparable to the finding in our study of 3.6%.

Participants in this study had some persistent laboratory abnormalities including lymphopenia (17.8%), leukocytosis (14.6%), raised ESR (11.3%) and raised CRP (8.5%). In the above-mentioned study from Ethiopia, 7.9% of the participants had lymphopenia at 3 months. This lower estimate could again be due to a longer time of follow-up in the study. Similar to our finding, raised CRP was found in 8% of patients

included in the meta-analysis discussed above [23]. Other commonly reported laboratory abnormalities such as elevated D-dimer, ferritin, and NT-proBNP levels could not be assessed in this study.

Another feature that was present in our study participants is persistent imaging abnormalities. Fibrosis and ground-glass opacity were the most frequent findings on chest x-ray, being reported in 42.6% and 39.7% of the patients for whom chest x-ray was done respectively, consistent with data from other research worldwide [23-25]. Since imaging during follow up was done as indicated based on clinical symptoms, a higher number of imaging abnormalities is to be expected had all patients (including asymptomatic ones) been imaged.

Two factors were found to be significantly associated with Long COVID; these are duration of symptoms before admission and length of hospital stay. Those with symptom duration >7 days before admission were found to have 1.97 times increased odds of having Long COVID, as compared to those whose symptoms had a shorter course before being admitted (aOR = 1.97, CI_{95%} = 1.037, 3.748). While the relationship between delayed diagnosis of COVID-19 and severity of acute illness have been explored in various studies, none were found that looked for an association with Long COVID. The presence of longer duration of symptoms before admission could reflect a delay in diagnosis, leading to delayed administration of treatment. This could have downhill effects on recovery.

Patients who stayed in the hospital more than 10 days were found to have 2.62 times increased odds of Long COVID, as compared to those who stayed or ≤10 days (aOR = 2.62, CI_{95%} = 1.200, 5.727). A multitude of factors can potentially contribute to an extended stay in the hospital, including severity of the illness, requiring oxygen support, comorbidities, and complications during treatment such as a secondary bacterial pneumonia. The association between length of stay and Long COVID could reflect a combination of these factors.

Neither age nor sex were found to be significantly associated with having Long COVID in this study. Previous studies have yielded conflicting results regarding these factors, some reporting significant association with older age [24, 28, 37], as well as female sex [7, 23-25, 28, 29], and others reporting none [3]. In this study, while those patients with age ≥70 were found to have 2.2 times increased odds of Long COVID on bivariate analysis, this was not true when controlling for confounders on multivariate analysis. This could suggest age alone may not confer risk for Long COVID.

Above normal BMI (overweight/obesity) was not found to be significantly associated with Long COVID in this study. This was also true in a prospective cohort study from South Africa, which did not find obesity to be an important predictor of Long COVID [20]. On the other hand, other studies from Switzerland and the USA found obese patients to have increased odds of Long COVID [28]. Since obesity increases the risk of severe illness in the acute phase of COVID-19 (according to various meta-analyses and cohort studies [38]), a potential association with persistent symptoms in obese patients should be further investigated before conclusions can be made.

Other potential risk factors that were not found to have significant association with Long COVID in this study include ICU admission, having one or more comorbidities (such as diabetes mellitus, chronic lung

conditions), need for oxygen or respiratory support during the acute phase of the illness, and increased number of symptoms on initial presentation. In other studies, one or more of these factors were reported to have an impact on Long COVID, however, the relevance of these factors was not consistent across the investigations [3,24,25,28,29].

Conclusion and Recommendations

There was a high prevalence of Long COVID among adult patients who were followed after hospital discharge and at least 4 weeks following symptom onset. The most reported symptoms were fatigue, shortness of breath, and cough. Duration of symptoms before hospitalization and length of stay in the hospital were found to have a significant association with the outcome. Prospective studies are needed that assess patients' persistent symptoms for a longer duration of follow-up, and with standard tools to measure the severity of symptoms.

7. Limitations

There are several limitations to this study. Since it was done in a single center, generalizing the results to the general population is challenging. In addition, owing to the retrospective design of the study, information that was not recorded in the charts may be missed. For example, information on the severity of each symptom, the prevalence of the symptoms before COVID-19 infection, and how long each symptom lasts would have been valuable. Moreover, issues that may not be addressed during a routine clinic visit, such as quality of life, could not be assessed.

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9. Appendix

Appendix I: Questionnaire

Questionnaire number ____

Section 1: Socio-demographic Characteristics

1. Age
2. Sex 0. Male 1. Female
3. BMI 0. Underweight 1. Normal weight 2. Overweight 3. Obese

Section 2: Acute COVID-19

1. Infection confirmed by COVID-19 PCR or RDT? 0. No 1. Yes
2. Infection status 0. Primary infection 1. Re-infection ____
3. Vaccination Status. 0. Unvaccinated 1. Vaccinated ____
4. Severity of acute COVID-19 infection. 0. Mild ____ 1. Moderate ____ 2. Severe ____ 3. Critical ____
5. Symptoms during acute-COVID 19 infection (tick all that apply)

Symptom	0. No 1. Yes
Cough	
Fever	
Myalgias	
Headache	
Dyspnea (new or worsening over baseline)	
Sore throat	
Diarrhea	
Nausea/vomiting	
Anosmia or other smell abnormalities	
Ageusia or other taste abnormalities	
Rhinorrhea and/or nasal congestion	
Chills/rigors	

Fatigue	
Confusion	
Chest pain or pressure	
Other (mention)	

6. Number of symptoms 1__ 2 ___ 3 ___ 4 ___ 5 or more ___
7. Duration of symptoms before admission
8. Laboratory abnormalities during acute COVID 19 infection

Lab Feature	0. No 1. Yes
Lymphopenia	
Leukocytosis	
Elevated aminotransferase levels	
Elevated LDH	
Elevated ESR	
Elevated CRP	
Elevated ferritin	
Elevated D-dimer	
Abnormal coagulation tests	
Elevated Creatinine	
Other	

9. Imaging abnormalities during acute COVID-19 infection

Chest X-ray findings		
Chest CT findings	Typical appearance	
	Indeterminate appearance	

	Atypical findings	
	Negative for pneumonia	

10. Pre-existing comorbidities (tick all that apply)

Comorbidities	0. No 1. Yes
Hypertension	
Diabetes Mellitus	
Asthma	
Other chronic lung condition	
HIV infection	
Smoking (current and former)	
Cancer	
Cerebrovascular disease	
Chronic liver disease	
Chronic kidney disease	
Heart conditions (heart failure, coronary artery disease, cardiomyopathies)	
Pregnancy	
Mental health disorders	
Use of corticosteroids or other immunosuppressive condition	
Other (state any other chronic condition)	

11. Date of hospitalization -

12. Date of discharge -

13. Place of admission. 0. Ward ___ 1. ICU ___

14. Length of stay in days. Ward ___ ICU ___ Total ___

15. Level of respiratory support received

Level of support	0. No 1. Yes
Intranasal oxygen	
Facemask oxygen	
High flow nasal cannula	
Non-invasive ventilation	
Mechanical ventilation	

16. Other treatment received

Treatment	0. No 1. Yes
Antibiotics	
Prophylactic anticoagulation	
Therapeutic anticoagulation	
Steroids	
Anti-viral agents (Mention specific drug)	
Immunomodulators (E.g. Tocilizumab) (Mention specific drug)	
Other treatment received	

17. Complications during acute COVID-19 hospitalization

Complication	0. No 1. Yes
ARDS	
Secondary infections	
Cardiovascular complications (shock, myocardial injury, arrhythmias, heart failure)	
Thromboembolic complications (VTE, stroke, limb ischemia)	
Neurologic complications (encephalopathy, seizure, movement disorders)	
Other	

Section 3: Follow-up

1. Duration of follow-up in days ____
2. Features on follow-up

Follow up number	Number of days from time 0	Symptoms reported	Laboratory abnormalities	Imaging abnormalities	Lung function test abnormalities
1					
2					
3					
4					

Appendix II: Supplementary tables

Table S1. Comorbidities of the patients

	Frequency (n)	Percentage (%)
Hypertension	83	33.6
Diabetes	84	34
Dyslipidemia	25	10.1
Asthma	13	5.3
COPD	3	1.2
HIV	5	2
Cerebrovascular disease	5	2
Chronic kidney disease	12	4.9
Cardiac illness	17	6.9
Thyroid disorders	7	2.8
Others	29	11.7

Table S2. Complications during admission

	Frequency (n)	Percentage (%)
ARDS	18	7.3
Secondary bacterial infections	97	39.3
Cardiovascular complications	2	0.8
Thromboembolic complications	17	6.9
Neurologic complications	1	0.4
Others	17	6.9