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Burden of respiratory morbidity amongst survivors of COVID-19 infection in Lagos, Southwest Nigeria

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Abstract

Background: COVID-19 disease is associated with long-term effects in some survivors. There exists dearth of information about the burden of respiratory morbidity among COVID-19 survivors in Nigeria. This study was designed to identify the common respiratory symptoms of long COVID-19 to educate and increase index of suspicion of healthcare practitioners caring for such patient for optimal care.

Material and methods: This is a cross-sectional survey that took place at the adult pulmonology clinic of Lagos State University Teaching Hospital Ikeja. The individuals who were treated for PCR confirmed COVID-19 infection referred for unresolved symptoms 4 weeks following discharge that consented were recruited. A proforma was used to obtain information on socio-demographic characteristics, medical history, and comorbidities. The degree of dyspnea was assessed using MRC(Medical Research Council) dyspnea scale while the functional capacity of patients was assessed using Six-minute walk test (6mwt). The analysis of the data collected was done using descriptive statistics, and chi-square was used to test for association.

Results: Ninety-four subjects participated. The mean age of participants was 49.48±17.8 years, with male: female ratio of 1:1.1. The median duration of admission due to COVID-19 infection was 10.0 (7.0-15.8) days. The common symptoms were fatigue (85.1%), loss of smell (71.3%), dyspnea 53(56.4%), and Cough (62.8%). Dyspnea was present in 62.8% using the MRC dyspnea scale, while the 6-minutes walk test showed inadequate functional capacity in 61.7%, and both showed significant association. (X^2=18.606, P=0.001*)

Conclusion: Respiratory morbidity remains a significant post covid condition. There is a need to raise awareness amongst healthcare workers, particularly within the primary healthcare setting for early identification and referral of COVID-19 survivors with prolonged respiratory symptoms to pulmonology clinics for optimal care. There is also a need for further research on predictors of post COVID syndrome and treatment modalities.

Key words: post covid syndrome, Long covid, post covid disease

Introduction

Infection with SARS COV2 virus causing COVID-19 disease is associated with long-term effects in some survivors [1]. These clinical conditions have been referred to in the literature as long COVID, long haul COVID, post-acute sequelae of SARS-CoV-2 infection (PASC), long-term effects of COVID, and chronic COVID [1]. Post-COVID-19 Syndrome includes persistent symptoms related to residual inflammation, organ damage, non-specific effects from the hospitalization or prolonged ventilation (post-intensive care syndrome), social isolation, or impact on pre-existing clinical condition [1]. The multi-systemic clinical sequelae associated with COVID-19 are similar to post-acute viral syndromes described in survivors of other virulent coronavirus epidemics previously [2]. These symptoms include fatigue, dyspnea, cough, chest pain, sleep abnormalities, and mood disorders [3-5].

As of September 2022, the global pandemic caused by coronavirus disease 2019 (COVID-19) has affected more than 605, 000 000 people and caused more than 6,400 000 deaths in over 215 countries or regions worldwide [3,6]. There were a large number of patients

who had been cured and discharged from the hospitals all over the world. Presently, about 265,000 people have been treated for COVID-19 infection in Nigeria [6-8]. In Lagos State, 103,957 cases have been treated so far with 814 currently on admission and 102,372 discharged.

The clinical profile, treatment and prognosis of COVID-19 infection have been extensively studied. As a result, we are now more able to effectively optimize the treatment of patients with acute infection and prognosticate the outcome compared with the beginning of the pandemic. However, the prevalence, nature, duration and risk factors of sequelae in COVID-19 survivors have not been extensively reported in Nigeria. There exists dearth of information about the clinical sequelae, particularly pertaining to burden of respiratory morbidity among COVID-19 survivors in Nigeria. To bridge this gap, this study was thus designed to describe the clinical sequelae of COVID-19 infections amongst a group of COVID-19 survivors in Lagos, Southwest Nigeria to educate and increase index of suspicion of healthcare practitioners about the common respiratory symptoms of long COVID-19 for optimal care of survivors with delayed recovery. This study identified various respiratory manifestations as well as other systemic symptoms following acute infection with sarscov2. The implication of this is the need for follow-up of COVID survivors by a multidisciplinary team including pulmonologists for early identification of prolonged symptoms that could predict pulmonary morbidity which may be addressed or salvaged to improve the quality of life of such patients.

Material and methods

This study took place at Lagos State University Teaching Hospital (LASUTH), a 600-bed tertiary center with a 20-bed isolation center for attending to active COVID-19 patients. The teaching hospital was not a COVID-19 treatment center during the first wave and post-COVID-19 disease was largely unrecognized. The Covid-19 management was coordinated by the family and community physicians as well as internist consultation on request. The service was supported by a specialist pulmonology clinic that in addition receives referrals from other public and private centers managing COVID-19 in Lagos. The clinic is manned by three pulmonologists in the service of Lagos State. Most patients were referred on account of persistent respiratory symptoms and abnormal imaging following COVID-19 disease management. However, following the relaxation of lockdown, the respiratory unit clinic experienced increased referral at the outpatient and in-patient of cases of COVID-19 pneumonia with residual symptoms and abnormal imaging.

We recruited patients with PCR confirmed COVID-19 managed at LASUTH isolation center or any of the isolation centers in Lagos State referred to our respiratory clinic on account of symptoms lasting more than four weeks after discharge or with abnormal imaging who consented to participate in the study.

We excluded symptomatic patients with positive COVID-19 PCR, individuals with no proven evidence of positive PCR but with abnormal imaging and also dyspnea associated (like COPD, and severe heart failure) illnesses prior to COVID-19 infection.

Ethical approval was gotten from Lagos State University Teaching Hospital Ethics and Review Committee. Written informed consent was obtained from individual participants.

The calculated sample size was 92 using the Cochran formula ($N = Z^2pq/d^2$ where, N = sample size, Z = standard normal deviation, usually set at 1.96, which corresponds to the 95% confidence interval, p = mean prevalence of adults at high risk of Covid 19 in Nigeria = 40 % [9], q = (1 — p), and d = degree of accuracy desired, usually set at 0.10) [10]. A proforma comprising of two sections was used to obtain needed information. Section A dealt with the socio-demographic characteristics (age, sex, occupation, duration of diagnosis, symptoms etc), medical history, comorbidities and MRC dyspnea scale.

MRC dyspnea scale

The MRC dyspnoea scale is a simple questionnaire that allows patients to indicate the extent to which their breathlessness affects their mobility. It is used to measure dyspnea in various conditions like COPD, bronchial asthma, restrictive disease, pulmonary fibrosis, occupational lung disease, and various heart conditions such as heart failure. It comprises of five statements that measure the degree of disability that breathlessness poses on day-to-day activities on a scale from 0 to 4: 0, no breathlessness except on strenuous exercise; 1, shortness of breath when hurrying on the level or walking up a slight hill; 2, walks slower than people of same age on the level because of breathlessness or has to stop to catch breath when walking at their own pace on the level; 3, stops for breath after walking ~100 m or after few minutes on the level; and 4, too breathless to leave the house, or breathless when dressing or undressing [11,12]. The questionnaire was administered by the researcher. The score is the number that best fits the patient's level of dyspnea with activity [11,12].

Six minutes walk test

The six-minute walk test (6mwt) aids in assessing the functional capacity of patients with cardiopulmonary disease [13,14]. The patients were instructed to walk as far as possible on a straight track of 100 feet in length. Patients were advised to walk on their own pace and pause to rest, if needed, but should resume walking as soon as they were able. The timer for the test continued throughout the 6 minutes period even during the times patients paused to rest. The total distance walked (six-minute walk distance) was obtained. The scoring involved figuring out the distance that a person has covered by multiplying the number of lengths by the distance of the track. The score range for healthy adults was set at 400–700 m. The higher a person's score, the better their exercise tolerance. A low score correlates with lower function. The estimation of arterial oxygen saturation by pulse oximetry was collected pre-test, at intervals during the test and at the end of test [13,14].

Statistical analysis

Continuous variables were described using mean with standard deviation (SD) or median while categorical variables were expressed as percentage. The correlation between MRC dyspnea scale with saturation levels of patients at rest and after a 6 minutes-walk test was assessed using spearman's test. The comparison between MRC dyspnea scale and adequacy of distance covered during 6 minutes-walk test was done using the Chi-square test. The conventional level of statistical significance of 0.05 was used for all the analyses. Statistical analyses was performed using SPSS Version 21.0.

Results

There were ninety four participants with mean age of 49.48±17.8, and male: female ratio of 1:1.1. The median duration of illness of the participants during the acute infection was 10.0(7.0-15.8). Seventy six (80.6%) of the participants have never smoked previously. Other socio-demographic characteristics is shown in Table 1. Common comorbidities

Table 1 Demographic and clinical characteristics of participants

Variable	Frequency (n=94)	Percentage
Age		
<40	39	41.5
41-60	25	26.6
>70	30	31.9
Mean±SD	49.48±17.8	
Gender		
Male	45	47.9
Female	49	52.1
Year of COVID diagnosis		
2020	41	43.6
2021	53	56.4
COVID variant		
Delta	9	9.6
Omicron	13	13.8
Unknown	72	76.6
Median duration of illness (Days)	10.0 (7.0-15.8)	
Comorbidities		
Hypertension	58	61.7
Diabetes	32	34.0
Obesity	16	17.0
Asthma	9	9.6
Heart failure	2	2.2
Renal failure	2	2.2
OSA	1	1.1
COPD	1	1.1
Connective tissue disease	1	1.1
Cancer	1	1.1
Sickle cell disease	1	1.1
Coronary heart disease	1	1.1
GERD	1	1.1
None	22	23.4
Smoking status		
Never	76	80.9
Previous smoker	11	11.7
Current smoker	7	7.4

The table shows the socio-demographic characteristics of the participants as well as the distribution of comorbidities.

amongst the participants are hypertension 58(61.7%), diabetes 31 (34.0%), and obesity 16(17.0%). Frequent respiratory symptoms experienced include fatigue 80(85.1 %), loss of smell/ taste 67(71.3%), dyspnea 53(56.4%), and Cough 59 (62.8%). Non–respiratory symptoms include headache 2(2.1%), GIT symptoms 5 (5.3%) and depression 5(5.3%) as shown in Figure 1.

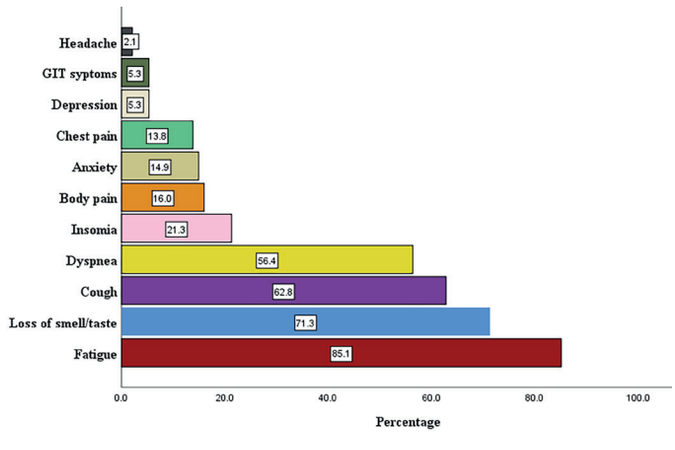

Figure 1 - Prevalence of respiratory symptoms post COVID
The figure is a histogram chart showing the distribution of post covid symptoms

Treatment received by patients include multivitamins 94 (100%) and Zinc 93 (98.9%) taken by all. Other treatment modalities used includes Ivermectin, dexamethasone, antipyretic and oxygen used by 71 (75.5%), 50(53.2%), 48 (51.1%) and (48.4%) respectively. This is shown in Table 2.

Table 2 Treatment modalities during Acute infection phase

Variable	Frequency (n=94)	Percentage
Pulmonary rehabilitation	16	17.0
Anticoagulant	16	17.0
Multivitamin	94	100.0
Zinc	93	98.9
Antipyretic	48	51.1
Ivermectin	71	75.5
Dexamethasone	50	53.2
Colchicine	16	17.0
Proning	19	20.2
CPAP	12	12.8
Oxygen administration	47	50.0

The table shows the distribution of various treatments received by the participants during acute infection.

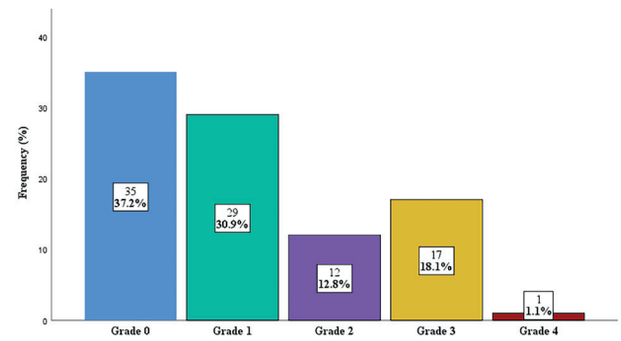

Figure 2 - MRC DYSPNEA scale among participants
The figure is a bar chart showing the number of participants with different grades of dyspnea.

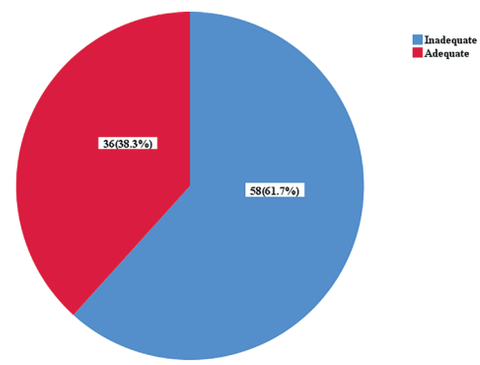

Figure 3 - 6-minutes walk test
The figure is a pie chart showing the adequacy of six minutes walk test among the participants (N = 94)

Table 3 Association between 6-meter walk test and MRC DYSPNEA scale among participants

	6-minutes walk test		χ^2	p-value
	Inadequate	Adequate		
MRC DYSPNEA scale			18.606	0.001*
Grade 0	12(34.3)	23(65.7)		
Grade 1	21(72.4)	8(27.6)		
Grade 2	10(83.3)	2(16.7)		
Grand 3	14(82.4)	3(17.6)		
Grade 4	1(100.0)	0(0.0)		

Dyspnea was present in 62.8% using the MRC dyspnea scale: Grade 1 was present in 30.9%, Grade 2 in 12.8%, Grade 3 in 18.1% while 1.1% had grade 4 as shown in Figure 2. The mean baseline saturation was 95.92±20.0 while the mean post 6 minutes walk test saturation was 94.55±29. The mean total distance covered during the test was 402.07±110.5. The functional capacity assessed using 6-minutes-walk test was adequate only in 36 (38.3%) of participants as shown Figure 3. There was negative correlation between MRC dyspnea scale with baseline saturation and end of test saturation (correlation coefficient: -0.733 and p <0.001, correlation coefficient: -0.765 and p< 0.001 respectively). Table 3 shows a significant association between functional capacity using 6-meter walk test and respiratory disability using MRC Dyspnea scale (x2=18.06, p=0.001), implying that with increase in proportion of patients with inadequate functional capacity there is increase in the grade of respiratory disability.

Discussion

Post-COVID-19 syndrome is now a clinical condition well recognized and includes new or worsening abnormalities in physical, cognitive and psychiatric domains after critical illness [15]. This study described the burden of respiratory morbidity as a clinical sequelae of COVID-19 infection amongst a group of COVID-19 survivors in Lagos, Southwest Nigeria. Our results are consistent with the findings by Yong et al who noted in a literature review of possible pathophysiology, risk factors, and treatments in long COVID that the common symptoms of long COVID reported in many studies include fatigue and dyspnoea that last for months after acute COVID-19 [16]. The study reported other persistent symptoms that include cognitive impairments, chest pains, joint pains, palpitations, myalgia, smell with taste dysfunctions, cough, headache, and gastrointestinal and cardiac issues [16].

The possible pathophysiologic explanation for the long COVID includes long-term tissue damage, pathological inflammation, immune dysregulation, and autoimmunity [16].

Raveendran et al in another review mentioned fatigue, cough, chest tightness, breathlessness, palpitations, and myalgia as symptoms reported in long COVID [17]. The implication of this is that patients with treatment for COVID could have prolonged symptoms which may be quite disturbing or debilitating after the acute infection. Hence, there is a need for follow up of such patients.

The common comorbidities reported in our study include hypertension, diabetes and obesity and these were similar to the findings in a prospective cohort study of COVID-19 survivors in Moscow where pre-existing hypertension was associated with post COVID-19 conditions at 12 months [18]. This is also similar to the findings in another cross-sectional study of COVID-19 survivors using hospital based where the main determinants of the persistent post-COVID-19 symptoms included hypertension, and chronic pulmonary disorders [19]. Conversely, Carvalho-Schneider et al reported that the presence of initial symptoms during acute infection(chest pain, dyspnoea, fever, anosmia, ageusia), gender or number of comorbidities did not predict post-COVID syndrome in a descriptive study where 150 patients with noncritical COVID-19 confirmed by real-time reverse transcriptase PCR at Tours University Hospital were followed up to two months post discharge [20]. This may suggest that there are still inconsistency in specific risk factors for developing and determining the severity of Long COVID. Hence, there is a need for more research on this subject.

Our findings revealed varying respiratory disabilities using MRC dyspnea scale and 6 minutes walk test in about two third of patients and this is similar to the findings of Ceurci Claudio et al who characterized pulmonary function and disability status of Covid survivors in a crossectional observational study and reported severe respiratory disability, and difficulty to perform 6-MWT with poor results in majority of the participants [21]. Similarly, Anastasio et al evaluated COVID survivors in Europe and reported that lung damage during COVID-19 correlates to the reduction of pulmonary function 4 months after acute infection [22]. However, Xiaojun in a prospective, cohort study in China among patients admitted to hospital for severe COVID-19 who did not require mechanical ventilation who were prospectively followed up at 3 months, 6 months, 9 months, and 12 months after discharge reported improved dyspnoea scores and exercise capacity over time [23]. Although, in a subgroup of patients at 12 months they still found evidence of persistent physiological and radiographic changes [23].

Our study is limited by our inability to carry out spirometry and further assess lung physiology. Inclusion of these data may have helped us to ascertain whether there is a correlation between altered physiology, physical performance, and reported persistent symptoms. The use of recall to assess presence of persistent symptoms may be subjected to recall bias.

Conclusion

Long COVID-19 is another public health crisis following the COVID-19 pandemic. Respiratory morbidity remains a significant post covid condition. There is a need to raise awareness amongst healthcare workers, particularly within the primary healthcare setting for early identification and referral of COVID-19 survivors with prolonged respiratory symptoms to pulmonology clinics for optimal care. There is also a need for further research on predictors of post COVID syndrome and treatment modalities.

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