

PREDICTORS OF POST-COVID SYNDROME AMONG ADULT PATIENTS WITH COVID -19 INFECTION IN IBADAN, NIGERIA

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Abstract

Background: While most individuals recover from acute Coronavirus disease (COVID-19), a subset experiences persistent symptoms, referred to as post-COVID-19 Syndrome (PCS). Understanding the clinical spectrum and determinants of PCS is essential to provide evidence-based long-term care for COVID-19 survivors. This study aimed to describe the clinical spectrum and predictors of PCS among hospitalized and non-hospitalized COVID-19 patients in Ibadan, Nigeria.

Methods: A retrospective cross-sectional study involved 536 adult individuals who tested positive for SARS-CoV-2 via polymerase chain reaction (PCR) in Ibadan, Nigeria. Data, including demographics, symptoms, comorbidities, and quality of life, were collected using a semi-structured questionnaire and analyzed with descriptive statistics. Pearson's Chi-square and logistic regression were used to assess associations and predictors of PCS.

Results: Among the 536 participants, 98 (18.3%) had PCS. Of these, 67 (68.4%) reported mild symptoms, while 31 (31.6%) experienced severe symptoms. Common symptoms included fatigue/malaise (36.7%), headache (19.4%), cough (17.3%), and sore throat (13.3%). Comorbidities, initial COVID-19 severity, vaccination status pre-infection, treatment location, oxygen supplementation, and ICU care were associated with PCS. Logistic regression revealed that having received a pre-COVID-19 vaccination decreased the odds of PCS by 62.4% (aOR=0.376; 95% CI [0.205, 0.692]). Individuals that experienced PCS had lower quality of life scores (Mean EQ VAS score: 85.8) compared to those without PCS (89.7), with impacts across mobility, self-care, daily activities, pain/discomfort, and anxiety/depression domains in EQ-5D analysis.

Conclusion: PCS affects a significant proportion of COVID-19 survivors in Ibadan, Nigeria. Pre-COVID-19 vaccination was associated with a reduced risk of PCS. Understanding the clinical and demographic factors predicting PCS can aid in providing long-term care and support for affected individuals.

Keywords: Post COVID 19 syndromes; Clinical spectrum; Quality of life; Ibadan; Nigeria.

Introduction

The event of Coronavirus outbreak devastated the global population, causing lots of destruction to lives and economies. The virus was identified as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), commonly referred to as COVID-19, with outcomes ranging from asymptomatic cases to severe and, in some instances, fatal outcomes¹. According to the Center for Disease Control (CDC), between 2019 and 2023, the world witnessed approximately 800 million confirmed cases, leading to 7 million reported deaths². While the global burden of COVID-19 has reduced significantly³, the aftermath has a profound impact on those who experienced it. There have been reports of persistent and prolonged symptoms after acute COVID-19 and this was termed "Post-COVID syndrome"⁴.

The World Health Organization (WHO) defines it as "the continuation or development of new symptoms three months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least two months with no other explanation"⁵. The Centre for Disease Control (CDC) characterized the syndrome as signs and symptoms that continue or develop four weeks or more after the initial phase of infection of COVID-19 infection. These symptoms may be multi-systemic; and present with a relapsing-remitting

pattern and progression or worsening over time, with the possibility of severe or life-threatening events even months after infection⁶. These varied definitions collectively describe Post-COVID Syndrome as a spectrum of persistent health problems experienced after the acute phase of COVID-19, varying in duration from a few weeks to over a year, affecting individuals irrespective of their hospitalization status^{7,8}. The prevalence of Post-COVID Syndrome varies significantly in different countries and across continents⁹. Studies in China found a prevalence as high as 90.4%¹⁰, while a prevalence of 7.3% was reported among a random sample of 3042 United States (US) adults¹¹. A retrospective study in an outpatient clinic in Lagos, Nigeria found a prevalence of 40.9%¹². However, there is a global reduction in incidences¹³.

Post-COVID Syndrome encompasses a wide range of persistent multi systemic symptoms, including the immune, respiratory, cardiovascular, gastrointestinal, neuropsychological, musculoskeletal systems¹⁴. Commonly documented symptoms include dyspepsia, fatigue, post-exertional malaise, brain fog, cough, chest pain, headache, palpitations, arthralgia, fatigue, paraesthesia, abdominal pain, diarrhea, insomnia, fever, pain, skin rash, menstrual cycle irregularities, muscle weakness, and other manifestations^{12,15}. The severity of these symptoms varies, from

mild to severe, with some cases resulting in fatal outcomes. In 2022, the CDC confirmed the death of over 3,500 patients in the United States due to persistent COVID-19 symptoms¹⁶. According to the US Household Pulse Survey, 78.5% of persons with PCC had some degree of activity limitations, while 23.1% had significant activity limitations¹⁷. Beyond physical symptoms, other non-physical complications have been observed in individuals with Post-COVID Syndrome, including depression, anxiety, sleep disturbances, and impaired daily function^{18,19}. These complications significantly impact their overall quality of life²⁰. A prospective study conducted on COVID-19 survivors in Korea, identified symptoms like difficulty in concentration, cognitive dysfunction, amnesia, depression, fatigue, and anxiety²¹. A study by the British Medical Association (BMA) revealed that 1 in 5 doctors suffered from PCS and were unable to work subjecting them to career loss, and loss of income²². Post-COVID-19 Syndrome has been associated with several risk factors such as female gender and advancing age²³, severity of the acute COVID-19 infection, and the presence of comorbidities such as hypertension, asthma, renal disease, chronic obstructive pulmonary disease, diabetes, immunosuppression, and ischemic heart disease^{21,24}. Vaccination against COVID-19 has been shown to reduce the likelihood of developing Post-COVID Syndrome, as unvaccinated individuals are more susceptible²⁵. The burden of Post-COVID Syndrome leads to an increased demand on the country's fragile healthcare systems²⁶. Therefore, it is imperative to characterise the symptoms and predictors of Post COVID Syndrome among COVID-19 survivors in Nigeria to provide long-term, evidence-based care for patients who recover from the infection. Therefore, this study aimed to describe the clinical spectrum and predictors of post-COVID-19 syndrome among hospitalized and non-hospitalised patients with COVID-19 infection.

in Ibadan, Nigeria.

Method and Materials

Study Design and Setting

A retrospective cross-sectional telephone interview study was conducted amongst adults who tested positive to SARS-CoV-2 polymerase chain reaction testing (PCR) in Ibadan, Oyo State, Nigeria. Patients four weeks post SARS-CoV-2 infection were randomly selected and interviewed via telephone calls.

Study Population

The study population included adult males and females aged 18 years and older who had COVID-19 infection confirmed through PCR assay using nasopharyngeal swabs. Eligible respondents were selected from the clinical data registry of the Oyo State Emergency Operations Center (EOC), Ibadan between June and December 2021 using systematic random sampling.

Operational Definition of Variables

Post-COVID-19 syndrome was defined as persistent and delayed symptoms or long-term complications of SARS-CoV-2 infection beyond four weeks from the time of positive RT-PCR SARS-CoV-2 test and that the symptoms could not be attributed to an alternative

diagnosis.

Estimated Sample Size

The estimated sample size was calculated using the Leslie Kish formula for cross-sectional studies by taking p as 40.9% (the prevalence of post-COVID-19 syndrome in Lagos, Nigeria¹², 5% level of significance, and 0.05% confidence interval.

Sampling procedure

Systematic random sampling was used to randomize the participants. From the EOC registers, approximately 1297 adults were seen within the six-month period at the Centre. To calculate the sampling interval (k), the adult population was divided by the sample size that is $1297/536=2.41$ approximated to 2. A computer-generated table of random numbers was used to select the first adult (r) from numbers one to six from the register. The k generated was 2. Thereafter, patients subsequently recruited were $r+2$, $r+4$, and so on until the sample size was completed.

Data Collection

A semi-structured questionnaire developed from literature and reviewed by experts was developed. The questionnaire was pretested, and the interviewer administered. Data was collected on demography and a symptom checklist was used to document symptoms experienced during acute COVID-19 infection, and persistent COVID-19-like symptoms. Questions included comorbidities and the quality of life was assessed using the EQ-5D validated questionnaire²⁰.

The EQ-5D is a standardised measure of health status developed by the EuroQol Group in Europe but has been validated amongst the African population. It is a quick and easy to use instrument comprising five categories as follows: mobility, self-care, usual activities (e.g., work, study, housework, family, or leisure activities), pain/discomfort, and anxiety/depression. EQ visual analogue scale (EQ VAS) is a self-rated quantitative measure of health outcome as adjudged by the individual respondents.

Statistical Analysis

Demographic information, medical history and persistence of symptoms was analysed using descriptive statistics. Continuous variables were presented as mean $\pm$ sd and categorical variables were presented as numbers (percentage, %). Categorical variables were analyzed using Fisher's exact test or chi-square test to compare the differences between respondents with and without persistent symptoms and for comparison of age, severity group, and sex differences according to the persistent symptoms. Multivariate regression analysis was performed to determine the association between demographic information, comorbidities and the presence or absence of persistent COVID-19 symptoms. P values of < 0.05 were considered statistically significant.

Ethical Considerations

Ethical approval of the study was obtained from Oyo State Ministry of Health Institutional Review Board, with registration number AD 13/479/44231B. Appropriate permissions were also obtained from the Oyo State Ministry of Health Emergency Operations Center for Collation (EOC) before embarking on data collection. Participation was voluntary, and participants were free to opt out at any time

during the study. Oral consent was obtained from all participants at the beginning of the telephone interview, and the information volunteered was kept confidential as identifiers such as the respondents' name and other identifiers were not included in the questionnaires.

RESULTS

Table I: Socio-demographic and clinical characteristics of patients with covid-19 in Ibadan (n=536)

VARIABLES	FREQUENCY (N=536)	PERCENTAGE (%)
18 – 20	35	6.5
21 – 40	331	61.8
41 – 60	112	20.9
> 60	58	10.8
Gender		
Male	216	40.3
Female	320	59.7
Marital Status		
Single	209	39.0
Married	315	58.8
Separated/Divorced/Widowed	12	2.2
Education		
No education	7	1.3
Primary	9	1.7
Secondary	56	10.4
Tertiary	464	86.6
Employment Status		
Employed	402	75.0
Unemployed	134	25.0
Vaccinated against COVID		
Yes	412	76.9
No	124	23.1
Co-morbidities		
Hypertension	76	14.3
Diabetes	10	1.9
Respiratory Disease	20	3.7
Others [#]	46	8.6
No Co-morbidities	383	71.5
Symptoms during acute infection		
Mild	398	74.3
Moderate / Severe	138	25.7
Place of treatment		
Home isolation	444	82.8
District Hospitals	81	15.1
Tertiary Hospitals	11	2.1
Post COVID syndrome		
Yes	98	18.3
No	438	81.7
Symptoms Post COVID	FREQUENCY(N=98)	PERCENTAGE (%)
Mild	67	68.4
Moderate / Severe	31	31.6

Others[#] include HIV, cancer, sickle cell disease and chronic liver disease

Most respondents (61.8%) fell within the age range of 21 to 40 years, indicating a predominantly young adult population. The clinical characteristics of the respondents showed that a higher proportion (76.9%) had received COVID-19 vaccination before contracting COVID-19 infection, suggesting a high level of breakthrough infections. However, the majority (73.7%) reported experiencing mild symptoms, while 25.7% reported moderate to severe symptoms. Additionally, 82.8% of those who tested positive were managed at home, while 15.1% and 2.1% were managed in district and tertiary hospitals, respectively. Hypertension (14.2%) was the most common co-morbidity, with only 18.3% of the respondents experiencing post-COVID-19 syndrome. Among those with the

syndrome, 68.4% had mild symptoms, while the remaining 31.6% had moderate to severe symptoms.

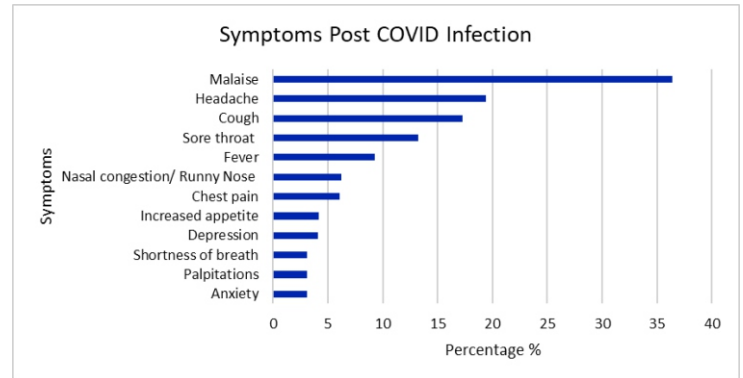


Figure 1: Persistent post-COVID-19 symptoms reported by patients with covid-19 in Ibadan

Figure 1 shows the persistent symptoms reported by the respondents post-COVID-19 infection. The most common symptoms reported were malaise (36.7%), headache (19.4%), cough (17.3%), and sore throat (13.3%).

Table II: Bivariate analysis of factors associated with post-covid syndrome in Ibadan, Nigeria

Variables	Post-COVID Syndrome			Statistical Indices
	No (%) n=98	Yes (%) n=438	Total (%) N=536	
Gender				
Male	176 (81.5)	40 (18.5)	216 (100.0)	$\chi^2 = 0.013$ p = 0.908
Female	262 (81.9)	58 (18.1)	320 (100.0)	
Marital Status				
Single	172 (82.3)	37 (17.7)	209 (100.0)	$\chi^2 = 0.384$ p = 0.825
Married	257 (81.6)	58 (18.4)	315 (100.0)	
Others	9 (75.0)	3 (25.0)	12 (100.0)	
Smoking History				
Current smoker	16 (88.9)	2 (11.1)	18 (100.0)	$\chi^2 = 0.741$ p = 0.690
Never smoked	413 (81.5)	94 (18.5)	507 (100.0)	
Stopped smoking	8 (80.0)	2 (20.0)	10 (100.0)	
Co-morbidities				
Hypertension	59 (77.6)	17 (22.4)	76 (100.0)	$\chi^2 = 14.452^*$ p = 0.006
Diabetes Mellitus	7 (70.0)	3 (30.0)	10 (100.0)	
Respiratory Diseases	14 (70.0)	6 (30.0)	20 (100.0)	
Others	30 (65.2)	16 (34.8)	46 (100.0)	
Nil	328 (85.6)	55 (14.4)	383 (100.0)	
Acute COVID-19 severity				
Mild	339 (85.8)	56 (14.2)	395 (100.0)	$\chi^2 = 18.014^*$ p = <0.001
Moderate/Severe	96 (69.6)	42 (30.4)	138 (100.0)	
Vaccination				
No	104 (83.9)	20 (16.1)	124 (100.0)	$\chi^2 = 0.501$ p = 0.479
Yes	334 (81.1)	78 (18.9)	412 (100.0)	
Vaccination before COVID infection (n=412)				
No	241 (88.0)	33 (12.0)	274 (100.0)	$\chi^2 = 25.289^*$ p = <0.001
Yes	93 (67.4)	45 (32.6)	138 (100.0)	
Treatment Place				
Home Isolation	379 (85.4)	65 (14.6)	444 (100.0)	$\chi^2 = 20.056^*$ p = <0.001
District Hospitals	52 (64.2)	29 (35.8)	81 (100.0)	
Tertiary Hospital	7 (63.6)	4 (36.4)	11 (100.0)	
Oxygen Supplementation				
No	431 (82.9)	89 (17.1)	520 (100.0)	$\chi^2 = 11.965^*$ p = 0.001
Yes	7 (43.8)	9 (56.3)	16 (100.0)	
ICU Care				
No	430 (82.5)	91 (17.5)	521 (100.0)	$\chi^2 = 6.527^*$ p = 0.011
Yes	8 (53.3)	7 (46.7)	15 (100.0)	

* p < 0.05

The factors significantly associated with post-COVID syndrome are Comorbidities, Severity of COVID-19 acute infection, Vaccination before COVID infection, Treatment place, Oxygen supplementation and ICU care as shown in Table II.

Table III shows all other variables were not significantly associated with multivariate analysis. It was found that, holding all other predictor variables constant, the odds of Post-COVID Syndrome occurring decreased by 62.4% (aOR= 0.376; 95% CI [0.205, 0.692]) for respondents who were vaccinated before COVID-19 infection when compared with those that were not previously vaccinated.

Table III: Multivariate analysis on Predictors of Post-COVID Syndrome in Ibadan, Nigeria

Variable	Adjusted Odds Ratio (aOR)	95% CI Lower- Upper
Vaccination before COVID		
No (ref)	0.376	0.205 - 0.692
Yes		
Co-morbidities		
Nil (ref)		
Hypertension	0.575	0.216 - 1.527
Diabetes	0.374	0.116 - 1.204
Mellitus	0.416	0.058 - 2.998
Respiratory	0.633	0.144 - 2.785
Disease		
Others		
COVID severity		
Mild (ref)		
Moderate/Severe	0.416	0.143 - 1.212
Treatment Place		
Home Isolation		
(ref)	1.378	0.215 - 8.820
State Isolation	2.055	0.327 - 12.934
Teaching		
Hospital		
Treatment Place		
Home Isolation		
(ref)	1.378	0.215 - 8.820
State Isolation	2.055	0.327 - 12.934
Teaching		
Hospital		
Oxygen		
Supplementation		
No	0.211	0.018 - 2.492
Yes (ref)		
ICU Care		
No		
Yes (ref)	5.137	0.364 - 72.513

Table IV: Association Between Post-Covid Syndrome and Quality of Life in Ibadan, Nigeria

EQ-5D Dimensions		Post-COVID syndrome		Total	Chi-squared	p-value
		Yes	No			
Mobility	No problem(%)	82 (83.7)	425 (97.0)	507 (94.6)	27.924	< 0.001
	Problem (%)	16 (16.3)	13 (3.0)	29 (5.4)		
Self-care	No problem (%)	85 (87.6)	433 (98.9)	518 (96.8)	32.550	< 0.001
	Problem (%)	12 (12.4)	5 (1.1)	17 (3.2)		
Usual activities	No problem (%)	76 (77.6)	422 (96.3)	498 (92.9)	42.952	< 0.001
	Problem (%)	22 (22.4)	16 (3.7)	38 (7.1)		
Pain/discomfort	No problem (%)	75 (76.5)	420 (95.9)	495 (92.4)	42.489	< 0.001
	Problem (%)	23 (23.5)	18 (4.1)	41 (7.6)		
Anxiety/depression	No problem (%)	64 (66.0)	395 (90.2)	459 (85.8)	38.170	< 0.001
	Problem	33 (34.0)	43 (9.8)	76		

Table IV indicates that developing PCS is significantly associated with having a problem on each of the 5 dimensions of health status measured by the EQ-5D ($p < 0.001$). Anxiety and depression domain is most affected; 34.0% and 16.3% of respondents with post-COVID-19 syndrome report problem with mobility as compared to 13% of respondents without post-COVID-19 syndrome. Mann-Whitney U test indicated that the quality of life as measured on the EQ Visual Analogue Scale (EQ VAS) was significantly lower in people who had post-COVID syndrome ($p = 0.001$).

Discussion

Post-COVID-19 syndrome following acute COVID infection is an emerging disorder that must be understood. Hence, this study aimed to assess the clinical spectrum and predictors of post-COVID-19 syndrome among hospitalized and non-hospitalized adults in Ibadan between June and December 2021. According to our findings, 18.3% of the respondents experienced post-COVID-19 syndrome, with a third of them reporting severe symptoms. The clinical spectrum of post COVID 19 is wide, ranging from mild to severe cases, with several symptoms persisting from the acute COVID phase to the post COVID phase. Symptoms such as fatigue, headache, cough, and sore throat were commonly reported. Factors identified as potential predictors of post COVID 19 includes co-morbidities, the severity of COVID-19 infection, vaccination status before COVID-19 infection, the place of treatment, oxygen supplementation and receiving care in intensive care unit. However, only vaccination status before COVID was a significant predictor of post-COVID-19 syndrome. Additionally, this study found a decrease in the quality of life among patients with post-COVID-19 syndrome.

Our study revealed that one in five respondents who tested positive to SARS-CoV-2, experienced post-COVID-19 syndrome. Notably, this prevalence was lower than the 40.9% observed in a COVID 19 outpatient clinic in Lagos, Nigeria ¹². Another prospective study conducted among COVID 19 patients in Saudi Arabia reported the prevalence of post-COVID 19 syndrome as 29.7% ²⁷. Some of the symptoms observed during the acute phase of COVID-19 infection such as fatigue, headache, and cough persisted beyond the acute phase of COVID 19. Fatigue was found to be the most common post COVID symptoms reported. Similarly, Bell et al. reported fatigue as the most common symptom in a non-hospitalized cohort ²⁸.

Mental health symptoms such as depression and anxiety had an increased incidence during the post COVID phase. This finding was corroborated by a systematic review conducted by Zakia et al. It revealed that individuals recovering from COVID-19 are at risk of mental health illnesses such as depression, anxiety, poor sleep qualities, somatic symptoms, cognitive deficits and post-traumatic stress disorder ²⁹. The result of this study showed that the presence of comorbidities and the severity of COVID-19 infection was significantly associated with post-COVID-19 syndrome. Similarly, previous studies in Ghana, showed that those with comorbidities, especially hypertension and diabetes mellitus, stayed longer in the hospital during acute COVID treatment and had four times the odds of post-COVID-19 syndrome ³⁰. Though previous studies have reported a preponderance for the female gender to develop post-COVID-19 syndrome ³¹, there was no statically significant predilection across genders in our study.

Furthermore, prior vaccination before acute COVID-19 infection predicted a lower likelihood of developing post-COVID-19 syndrome among the study population. Similar finding was observed by Mizrahi et al., in assessing the clinical sequelae of long COVID in patients with mild disease. They found that vaccinated patients with a breakthrough SARS-CoV-2 infection had a lower risk of dyspnea compared to unvaccinated infected patients ³².

The result of our study revealed that the quality of life of respondents with post-COVID-19 syndrome reduced in five different domains. This may be due to the persistent physical and mental health distress experienced post-COVID-19 infection and this is consistent with the findings from other studies ³³⁻³⁶.

Strengths and limitations of this research

The strength of this research is that it is one of the few studies to provide insights into the clinical spectrum and the predictors of post-COVID-19 syndrome among hospitalized and non-hospitalized COVID-19 patients in Nigeria. However, the cross-sectional design of the study, limited the ability to investigate the causal relationships. Recall bias is a possibility in this self reported survey and participants could have given socially acceptable responses only.

Conclusion

Post COVID was characterized by physical symptoms of fatigue, headache, and cough. Depressive and anxiety symptoms were also

commonly reported. Understanding the spectrum of the post-COVID syndrome is essential for instituting longitudinal care after acute COVID-19 infection to manage appropriately the long-term sequel among COVID-19 survivors. Findings from this study could form the baseline data needed for longitudinal multicenter prospective studies by multidisciplinary healthcare professionals to monitor the sequel of Post COVID Syndrome among people of African Descent and beyond.

Declaration

Availability of data and materials: All relevant data are available upon reasonable request.

Competing interests: The authors declare that they have no known competing interests.

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Author's Contribution: TI conceived and designed the study. A.I.O, O.T.O, A.A.O contributed to the conception and design of the study. TI and O.T.O, performed statistical analysis, and drafted the initial manuscript. TI and A.I.O revised the manuscript. All authors approved the final version of the manuscript.

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