

Patient-Reported Outcome Measures, 1 Year After COVID-19: A Cohort Study of Symptomatic, Laboratory-Confirmed Cases in South Trinidad, 2020–2021

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Abstract

Aim: The study aims to describe patient-reported long-term health effects, 1 year post-acute COVID-19 infection, and predictors, according to illness severity.

Methods: A cohort of adults who were symptomatic with laboratory-confirmed COVID-19 infection between March 2020–May 2021 were followed up for ≥12 months to evaluate persistent, newly occurring, or worsening symptoms. Multivariable-adjusted linear and logistic regression models estimated the odds ratios, β coefficients, and 95% CIs for associations between disease severity and long-term health consequences.

Results: Seventy-five percent (324/431) of eligible participants were enrolled. The median age was 41 years (interquartile range: 34–52), with 51.23% being men, and 33.02% having comorbidities. One year later, 60.00% reported ≥1 persistent symptom; the most common were dyspnoea (52.16%), fatigue (42.59%), and muscle weakness (31.48%); 13.60% reported symptoms of anxiety or depression, as measured by the Patient Health Questionnaire-4 (PHQ-4). In the unadjusted analysis, participants with moderate/severe illness had a significantly increased risk of developing fatigue or muscle weakness (p=0.043), anxiety/depression (p<0.001), breathlessness (p<0.001), and reduced health-related quality of life (p<0.001). When adjusted for age, gender, and comorbidities, their risk of developing fatigue or muscle weakness, anxiety/depression, and breathlessness was nullified, except for health-related



quality of life. Overall, the mean (SD) health index value score was 0.931 (0.13), comparable to the national norms of 0.950. For those with moderate/severe illness, the mean (SD) was 0.894 (0.16), with a statistically significant decrease compared to mild illness (p<0.001).

Conclusion: After 1 year of post-acute COVID-19 infection, a significant proportion of survivors have persistent symptoms. The health index value for those with moderate/ severe illness was below the population norms. Therefore, interventions should be prioritised for their long-term recovery.

Key Points

- 1. Long-term symptoms after COVID-19 affect a significant proportion of survivors globally, with implications for healthcare systems in both high- and low-resource settings.
- 2. This retrospective cohort study followed 324 patients who were symptomatic with COVID-19 in South-West Trinidad for 1 year to assess post-COVID symptoms, breathlessness, quality of life, and mental health.
- 3. Moderate/severe illness predicted poorer long-term outcomes, highlighting the need for integrated, multidisciplinary follow-up and expanded long COVID services in community and primary care settings.

INTRODUCTION

The COVID-19 pandemic has led to a global prevalence of more than 7.80% confirmed cases with over 0.08% deaths.1 In Trinidad and Tobago (TT), since 12 March 2020, there have been prevalences of over 11.90% confirmed cases, 11.40% recovered cases, and 0.30% deaths.²

Post-COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset, with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include, but are not limited to, fatigue, shortness of breath, and cognitive dysfunction, and generally have an impact on everyday functioning. Symptoms might be of new onset following initial recovery from an acute COVID-19 episode, or persist from the initial illness. Symptoms might also fluctuate or relapse over time.3 There has been a notable impact on the physical, cognitive, mental, and social health status of patients, regardless of the severity of the illness.4-7

Published studies have focused predominantly on previously hospitalised patients with severe COVID-19, reporting symptoms up to 6 months post-discharge.8-10

Globally, data have been published regarding the 1-year health consequences of post-COVID-19 infection.9,11-13 However, a review of published literature shows that few studies have been conducted in TT or the Englishspeaking Caribbean. This study sought to determine the difference in health-related quality of life (HRQoL), symptoms, anxiety/ depression, and degree of breathlessness experienced 1 year after being diagnosed with COVID-19 according to the severity of illness, and to determine the predictors/ factors associated with these main outcomes. It captured COVID-19 survivors who resided in the community of South-West Trinidad, not only those who were hospitalised, but also those who presented to a health facility for testing and were managed in home quarantine by primary care physicians in the community. From this study, the long-term burden of COVID-19 may be better understood in TT.

METHODS

Literature Search Strategy and Review

Several databases such as PubMed. MEDLINE, and Scopus were searched up to March 2021 without any language restrictions. The search terms used were 'COVID-19', 'Coronavirus disease 2019',



'2019-nCoV', 'SARS-Cov-2', 'post-acute COVID-19 syndrome, 'post-COVID-19', 'post-acute seguelae of COVID-19', or 'long COVID', and 'one-year health consequences', '12-month health consequences', 'longterm health consequences, or 'long-term' sequelae'. Early in the pandemic, studies reported that hospital-discharged COVID-19 survivors might have reduced quality of life due to persistent symptoms. However, representation may have been limited due to a short follow-up duration (up to about 6 months post-discharge), low response rates (as many patients could not be contacted post-discharge), and the use of single study centres. As the pandemic progressed, 1-year post-COVID-19 studies were published, and relevant findings were compared to the authors' findings. However, the long-term health consequences, particularly for outpatients and their associated factors, remain unknown.

Study Design: Sampling Methods and Sample Size

This retrospective cohort study was set in the community of South-West Trinidad. Multiple persons per household were included once they met the inclusion criteria. The inclusion criteria comprised patients who were symptomatic with laboratoryconfirmed COVID-19 for a minimum period of 1 year prior to the study; were ≥18 years of age during the study period (baseline: 12 March 2020-31 May 2021; ≥1-year follow-up: 26 July 2021-31 May 2022); resided within the study setting; spoke English; had no pre-existing conditions affecting the outcomes of interest (for example, cardiorespiratory conditions that cause shortness of breath, thyroid, and autoimmune diseases that may cause fatigue); were not reinfected with COVID-19 at the time of interview; were not pregnant at baseline or at follow-up; were capable of providing informed consent; and were alive and contactable at follow-up. This study included participants who presented to a health facility for testing. Some were hospitalised, while some were managed in home quarantine by primary care physicians in the community via telehealth.

The study excluded adults without laboratory-confirmed COVID-19;

asymptomatic laboratory-confirmed COVID-19 cases; persons who were reinfected with COVID-19 at follow-up; pregnant women with acute COVID-19 infection or those who were pregnant at follow-up; children and adolescents <18 years; non-residents of the South-West Trinidad community; non-English speaking; individuals with a history of pre-existing conditions that may affect outcomes of interest; individuals with diminished autonomy who were incapable of providing informed consent; individuals who died before 1-year follow-up; those who did not consent to participate; those who could not be contacted: and those who were not tested at a health care facility.

A sample of 324 participants was enrolled in the study. Based on a comparison of two proportions, a 30% prevalence of persistent symptoms for mild disease, and a 55% prevalence of persistent symptoms for moderate/severe disease was noted. This was calculated using a Type 1 error margin of 0.05, at a 95% CI, with a power of 80%.

Convenience sampling was done. If an eligible person could not be contacted or did not consent, the next eligible person on the list of participants was chosen.

Bias Reduction

Measures were taken to reduce sources of bias. To reduce non-response bias, the data collection tool was pre-tested to identify possible sources of bias in the length or content of the questionnaire, and to minimise the non-response rate. To mitigate recall bias, especially as participants might have had difficulty remembering certain baseline information, interviewers used prompts to aid memory recall during data collection. No sources of bias were identified through the use of the virtual canvases employed in the study.

Data Collection Tool

The 'COVID-19 Data Collection Tool' is shown in <u>Supplementary Figure 1</u>. The first section, containing baseline information, was collected during the



patient's nasopharyngeal swab. One year later, data on health-related outcomes were collected using the following questionnaires:

- Symptom Questionnaire: Participants were asked to report on newly occurring symptoms post-COVID-19 infection, which were persistent or worsening.⁸ Baseline data on participants' symptoms were unavailable for this study, so newly occurring symptoms post-COVID-19 infection, which were persistent or worsening, were assessed.
- Modified Medical Research Council (mMRC) dyspnoea scale: This is a fivecategory scale, which characterises the level of dyspnoea with physical activity. Higher scores correspond with increased dyspnoea.¹⁵ It quantifies the disability associated with breathlessness, by identifying if breathlessness occurs when it should not.
- EuroQol (EQ-5D-5L) questionnaire:
 This is a validated questionnaire to evaluate patient quality of life by assessing five factors: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each factor is divided into five levels that range from none to extreme problems.¹⁶
- EuroQol Visual Analog Scale (EQ-VAS): This is a patient's assessment of subjective assessment of generic health, ranging from 0–100, with higher scores representing better subjective health experience.¹⁶
- Patient Health Questionnaire-2 (PHQ-2):
 This is used for screening depression and measuring severity.¹⁷
- Generalized Anxiety Disorder Questionnaire-2 (GAD-2): This is a brief screening test for detecting generalised anxiety disorder.¹⁸
- Patient Health Questionnaire-4 (PHQ-4): This is a four-item patient health screening questionnaire for detecting depression and anxiety.¹⁹

Symptoms were recorded at the time of the survey, which was ≥1 year post-COVID-19 infection.

Data Collection Methods

Ethical approval was granted by the University of the West Indies, St. Augustine, TT; and the South-West Regional Health Authority (SWRHA), San Fernando, TT. Permission was given by the Medical Director, Primary Health Care, to access the SWRHA COVID-19 surveillance database from 12 March 2020–31 May 2021. This was compiled by the epidemiology unit at SWRHA, which would have included guarantined patients.

This database was used to recruit eligible study participants who consented to participate. A pilot study was first conducted with 20 participants to pretest the data collection tool.

Informed consent was obtained from the participants. Virtual interviews (Zoom video conferencing [Zoom Communications, San Jose, California, USA] and telephone) were conducted due to safety concerns during the COVID-19 pandemic. Participants were offered the options and allowed to choose the platform they were most comfortable with. None of the study participants received assistance from relatives in answering any of the questions. Permission to use the ED-5D-5L questionnaire and the EQ-VAS was granted by the EuroQol Research Foundation. Instructions were given to each participant to indicate how good or bad his/her health was on the scale. Primary outcomes measured include fatigue or muscle weakness, anxiety or depression, degree of breathlessness (mMRC score), and health-related quality of life (health index value). Those who had persistent symptoms were offered a referral to the 'long COVID' clinic at the San Fernando Teaching Hospital (SFTH), TT.

Statistical Analysis

Baseline characteristics and 1-year health consequences of participants with symptomatic, laboratory-confirmed COVID-19 were presented. Normally



distributed continuous variables were expressed as means (SDs) and non-normally distributed as medians (interquartile ranges). Categorical variables were presented as absolute values (N) with percentages (%). Participants were categorised into two groups according to their illness severity at acute infection.

For this study, patients who met the Ministry of Health (MOH), TT, and hospital admission criteria for COVID-19 home-quarantined patients (Kavita Dharamraj, data on file; Supplementary Figure 2) were considered moderately/severely ill, while those who did not were considered mildly ill. An individual with mild illness exhibited one or more of the following symptoms: fever (measured ≥38 °C or reported), cough, runny nose (coryza), sore throat, shortness of breath (dyspnoea), body pains, joint pains, and loss of taste and/ or smell. Individuals who presented with severe acute respiratory illness, exhibited acute respiratory infection with a history of fever or measured fever of ≥38 °C and cough, with symptom onset within the last 10 days at the time of presentation, and those who were admitted to the hospital, were included the moderate/severe illness category.²⁰

Comparisons of baseline characteristics, symptoms, degree of breathlessness and HRQoL, anxiety, and depression were made between mild and moderate/ severe groups. For this study, cut-points for positive screens for depression, PHQ-2 score ≥ 3 , 7 anxiety, GAD-2 ≥ 3 anxiety/ depression, 18 PHQ-4 score ≥ 6 9 were used. The Student's t-test was used for parametric data, and the Mann-Whitney U test was used for non-parametric data.

Multivariable adjusted logistic regression models were used to estimate the odds ratios (OR) and 95% CI for the association between illness severity and categorical outcomes (fatigue or muscle weakness, degree of breathlessness, and anxiety/depression), stratified by ICU admission. ICU admissions were highlighted to provide insight into patients who were severely ill, as moderately/severely ill patients were represented as one category in this study. Major criteria for

ICU admission include those who require invasive mechanical ventilation or septic shock with the need for vasopressors.

For the association between illness severity and continuous outcomes (health index value), multivariable adjusted linear regression models were used to estimate β values and 95% Cls. Adjustments were made for the effects of the predictor variables including age, gender, comorbidities, previous history of anxiety/depression, and PHQ-4 score, using regression models. A two-sided p value ≤0.05 was considered statistically significant. There were no missing data. Statistical analysis was done using Stata Version 16 (StataCorp, College Station, Texas, USA) and Microsoft Excel 2019 (Microsoft Corporation, Redmond, Washington, USA).

RESULTS

Baseline Socio-Demographics

Seventy-five percent of eligible participants were enrolled in this study (Figure 1). Selected characteristics of individuals who were symptomatic and tested positive for COVID-19 (n=324), from South Trinidad, and met the inclusion criteria, stratified by illness severity, are summarised in Table 1. In this study, 50% of the participants (n=162) experienced mild illness, while 50% experienced moderate/severe illness. The median age of the population was 41 years (interquartile range: 34–52). More men (51.23%; n=166) were included in this study compared to women (48.77%). A greater percentage of men (58.02%) had mild illness, while a greater percentage of women (55.56%) had moderate/severe illness. Eleven percent (n=18) of the participants with moderate/severe illness were healthcare workers. Being a healthcare worker (p=0.070) and age (p=0.15) had no statistically significant association with illness severity.

A χ^2 test was used to compare categorical variables in Table 1.



	Total	Mild	Moderate/Severe	p value	
Demographics	n (%) 324 (100)	n (%) 162 (50)	n (%) 162 (50)		
Age, median (IQR)	41 (34–52)	41 (31–52)	42 (36–52)	p=0.150	
Age group (years)					
18-30	56 (17.28)	36 (22.22)	20 (12.35)		
31–40	94 (29.01)	44 (27.16)	50 (30.86)		
41–50	83 (25.62)	38 (23.46)	45 (27.78)	p=0.227	
51–60	60 (18.52)	29 (17.90)	31 (19.14)		
61–80	31 (9.57)	15 (9.26)	16 (9.88)		
Gender					
Male	166 (51.23)	94 (58.02)	72 (44.44)	0.044	
Female	158 (48.77)	68 (41.98)	90 (55.56)	p=0.011	
Healthcare worker					
• Yes	27 (8.33)	9 (5.56)	18 (11.11)	0.070	
• No	297 (91.67)	153 (94.44)	144 (88.89)	p=0.070	
No comorbidities	217 (66.98)	119 (73.46)	98 (60.49)		
Comorbidities	107 (33.02)	43 (26.54)	64 (39.51)	p=0.013	
Hypertension					
• Yes	73 (22.53)	30 (18.52)	43 (26.54)	0.004	
• No	251 (77.47)	132 (81.48)	119 (73.46)	p=0.084	
Type 2 diabetes					
• Yes	53 (16.36)	20 (12.35)	33 (20.37)	0.050	
• No	271 (83.64)	142 (87.65)	129 (79.63)	p=0.050	
Asthma					
• Yes	15 (4.63)	6 (3.70)	9 (5.56)	0.400	
• No	309 (95.37)	156 (96.30)	153 (94.44)	p=0.428	
Ischaemic heart disease					
• Yes	5 (1.54)	0 (0.0)	5 (3.09)	. 0004	
• No	319 (98.46)	162 (100.0)	157 (96.91)	p=0.024	
Cerebrovascular disease					
• Yes	2 (0.62)	0 (0.0)	2 (1.23)	n_01EC	
• No	322 (99.38)	0 (0.0)	160 (98.77)	p=0.156	

Table 1: Baseline characteristics of symptomatic COVID-19 cases, South Trinidad (Continued).

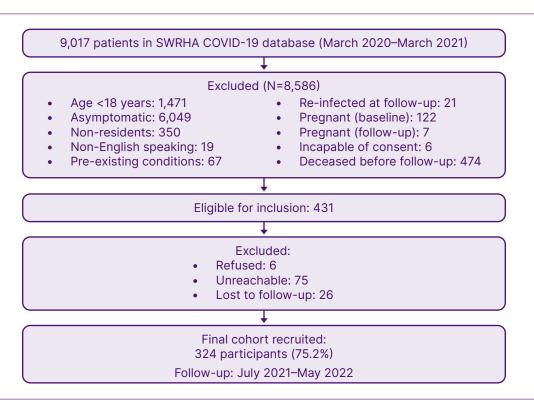
	Total	Mild	Moderate/Severe	p value
Chronic kidney disease				
• Yes	1 (0.31)	0 (0.00)	1 (0.62)	. 0.217
• No	323 (99.69)	0 (0.00)	161 (99.38)	p=0.317
Number of comorbidities				
• 0	217 (66.98)	118 (72.84)	99 (61.11)	
• 1–2	103 (31.79)	44 (27.16)	59 (36.42)	p=0.012
• ≥3	4 (1.23)	0 (0.00)	4 (2.47)	
State Quarantined				
Early phase hospitalisation	31 (9.57)	26 (16.05)	5 (3.09)	
Late-phase hospitalisation	74 (22.84)	11 (6.79)	63 (38.89)	p<0.001
No hospitalisation	219 (67.59)	125 (77.16)	94 (58.02)	

Data are n/N (%) or mean (SD), unless otherwise specified.

p values ≤0.05 are statistically significant and are bolded to highlight this.

IQR: interquartile range.

Figure 1: Flow chart of the recruitment of the study participants.



SWRHA: South-West Regional Health Authority.



Clinical Characteristics

Approximately, one-third of the study participants, 33.02% (107), had comorbidities. Approximately 40.0% of patients with moderate/severe illness had comorbidities, and 73.0% of patients with mild illness had no comorbidities. Patients with comorbidities were more likely to experience moderate/ severe illness compared to patients without comorbidities (p=0.013). Hypertension was the most common comorbidity (22.53%) seen among symptomatic patients with COVID-19, followed by Type 2 diabetes (T2D; 16.36%). People with T2D (p=0.050) and ischaemic heart disease (p=0.024) were more likely to have moderate/severe illness than those who did not have those conditions.

Notably, in the early phase of the pandemic, for the first 4 months, 12 March-20 July 2020, state quarantine was mandatory, once COVID-19 positive, regardless of the degree of illness. In this study, 9.57% of participants were under mandatory state quarantine during this time. From Phase II, 21 July 2020, the indication for hospitalisation was for only those who met the admission criteria, (Kavita Dharamraj, data on file) and 23.00% (n=74) of participants were hospitalised. There were 82.72% (n=268) individuals in home quarantine, with equal proportions, 82.72% (n=134), having both mild illness and moderate/severe illness.

Symptoms, Health-Related Quality of Life at 12-Month Follow-Up

Table 2 shows the lingering post-COVID-19 symptoms and HRQoL at a minimum follow-up period of 12 months, stratified by severity of illness. Sixty percent (n=195) of the participants had at least one of the following post-COVID-19 symptoms outlined in Table 2. Most COVID-19 survivors were troubled by fatigue 42.59% (n=138), muscle weakness 31.48% (n=102), and sleep difficulties 22.84% (n=74). Individuals who experienced moderate/severe illness were 3.5 times more likely to have at least one long-COVID symptom, as compared to those who had the milder illness (OR: 3.51; 95% CI: 2.19–5.61).

The mMRC scores were grouped into categories 0 and ≥1. A score 0 indicates

that the participant 'only gets breathless with strenuous exercise', and a score ≥1 indicates that at minimum the participant 'gets short of breath when hurrying on level ground or walking up a slight hill'. In the group with mild illness, 62.35% (n=101) scored 0, and among those with moderate/severe illness, 66.67% (n=108) scored ≥1. The risk of an mMRC score ≥1 was 3.3 times increased in participants with moderate/severe illness compared to those with mild illness (OR: 3.31; 95% CI: 2.1–5.22).

Using the EQ-5D-5L instrument, the health index value was derived for each participant. The mean (SD) score was 0.931 (0.13). Those with milder illness reported a slightly higher score, mean (SD) of 0.967 (0.07), as compared to those with moderate/severe illness, mean (SD) score of 0.894 (0.16). The mean (SD) EQ-VAS score was 79.06 (15.74). Those with mild illness reported a slightly higher score, mean (SD) of 84.04 (12.58), compared to those with moderate/severe illness, mean (SD) score of 74.09 (16.99). Using the cut-points for the screening tools (17–19) stated above for positive screens, 13.58% had anxiety/ depression, 13.89% had depression, and 16.98% had anxiety, with statistically significant differences (all p values < 0.001).

EQ-5D-5L responses from the study cohort

In Figure 2, 40.0% of respondents reported symptoms of anxiety/depression, 30.0% reported pain/discomfort, 22.0% had problems performing their usual activities, such as work, study, housework, family, or leisure activities, 11.0% had problems with mobility, and 4.0% had problems with self-care, 1-year post-COVID-19.

Predictors of Selected Outcome Measures

Table 3 A–D shows multivariate regression models for the four primary outcomes.

Table 3A shows a multivariate logistic regression of differences in fatigue or muscle weakness by illness severity stratified by ICU admission. Among all study participants, in the unadjusted analysis, those with moderate/severe illness had a significantly increased risk of developing fatigue or



Table 2: Symptoms and health-related quality of life at follow-up according to severity of illness.

	Total	COVID-19 status at baseline (mild)	COVID-19 status at baseline (moderate/severe)	Unadjusted OR or β (95% CI)	p value
	n (%) 324 (100.0%)	n (%) 162 (50.0%)	n (%) 162 (50.0%)		
Time from baseline to follow-up (months) Mean (SD)	12.69 (1.21) 95% CI: (12.55–12.82)	12.68 (1.24) 95% CI: (12.49–12.87)	12.70 (1.19) 95% CI: (12.51–12.88)	β 0.01 (-0.17–0.19)	p=0.891
Median (IQR)	12 (12–13)	12 (12–13)	12 (12–13)		
Symptoms					
Any one of the following symptoms:	195 (60.19)	74 (45.68)	121 (74.69)	OR: 3.51 (2.19–5.61)	p<0.001
Fatigue	138 (42.59)	41 (25.31)	97 (59.88)	OR: 4.40 (2.74-7.07)	p<0.001
Muscle weakness	102 (31.48)	25 (15.43)	77 (47.53)	OR: 4.96 (2.93-8.40)	p<0.001
Sleep difficulties	74 (22.84)	22 (13.58)	52 (32.10)	OR: 3.01 (1.72-5.25)	p<0.001
Hair loss	56 (17.28)	17 (10.49)	39 (24.07)	OR: 2.70 (1.46-5.02)	p=0.001
Joint pains	44 (13.58)	11 (6.79)	33 (20.37)	OR: 3.51 (1.71-7.23)	p<0.001
Appetite disturbance	43 (13.27)	6 (3.70)	37 (22.84)	OR: 7.70 (3.15-18.82)	p<0.001
Headache	40 (12.35)	11 (6.79)	29 (17.90)	OR: 2.99 (1.44-6.22)	p=0.002
Taste disturbance	31 (9.57)	9 (5.56)	22 (13.58)	OR: 2.67 (1.19-5.99)	p=0.013
Smell disturbance	28 (8.64)	7 (4.32)	21 (12.96)	OR: 3.30 (1.36-7.99)	p=0.005
Dizziness	27 (8.33)	6 (3.70)	21 (12.96)	OR: 3.87 (1.52-9.87)	p=0.002
Chest pain	23 (7.10)	2 (1.23)	21 (12.96)	OR: 11.91 (2.74–51.71)	p<0.001
Palpitations	31 (9.57)	10 (6.17)	21 (12.96)	OR: 2.26 (1.03-4.97)	p=0.036
Body pains (myalgia)	18 (5.56)	0 (0.0)	18 (11.11)	OR: 1.00	NA
Nasal congestion	18 (5.56)	6 (3.70)	12 (7.41)	OR: 2.08 (0.76-5.68)	p=0.142
Skin rash	10 (3.09)	0 (0.0)	10 (6.17)	OR: 1.00	NA
Sore throat	9 (2.78)	2 (1.23)	7 (4.32)	OR: 3.61 (0.74-17.66)	p=0.082
Nausea	9 (2.78)	3 (1.85)	6 (3.70)	OR: 2.04 (0.50-8.29)	p=0.306
Low-grade fever	8 (2.47)	1 (0.62)	7 (4.32)	OR: 7.27 (0.88-59.78)	p=0.023
Difficulty to swallow	5 (1.54)	1 (0.62)	4 (2.47)	OR: 4.07 (0.45-36.87)	p=0.162
Diarrhoea	5 (1.54)	0 (0.0)	5 (3.09)	OR: 1.00	NA
mMRC score					
• 0	155 (47.84)	101 (62.35)	54 (33.33)		
• ≥1	169 (52.16)	61 (37.65)	108 (66.67)	OR: 3.31 (2.1–5.22)	p<0.001
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Table 2: Symptoms and health-related quality of life at follow-up according to severity of illness (Continued).

Health Index Value, Mean, (SD) (T&T values: 0.95)	0.93 (0.13) 95% CI: (0.92-0.94)	0.97 (0.07) 95% CI: (0.96-0.98)	0.89 (0.16) 95% CI: (0.87-0.92)	β: -8.65 (-12.195.10)	p<0.001
*Quality of Life, EQ-VAS score Mean, (SD)	79.06 (15.74) 95% CI: (77.34-80.78)	84.04 (12.58) 95% CI: (82.09-85.99)	74.09 (16.99) 95% CI: (71.45-76.72)	β: -0.04 (-0.060.03)	p<0.001
	Total n (%)	Mild n (%)	Moderate/ severe, n (%)	Mann-Whitney U test, z-value	p value
PHQ-4 score ≥6	44 (13.58)	8 (4.94)	36 (22.22)		p<0.001
PHQ-4 score <6	280 (86.42)	154 (95.06)	126 (77.78)	-4.534	
PHQ-2 score ≥3	45 (13.89)	8 (4.94)	37 (22.84)	4.054	0 001
PHQ-2 score<3	279 (86.11)	154 (95.06)	125 (77.16)	-4.651	p<0.001
GAD-2 score ≥3	55 (16.98)	13 (8.02)	42 (25.93)	4.005	n 10 001
GAD-2 score <3	269 (83.02)	149 (91.98)	120 (74.07)	-4.285	p<0.001

^{*}Quality of life was assessed using the EuroQol Visual Analog Scale, ranging from 0 (worst imaginable health) to 100 (best imaginable health).

Data are n/N (%) or mean (SD), unless otherwise specified. p values ≤0.05 are statistically significant and are bolded to highlight this.

GAD-2: Generalized Anxiety Disorder Questionnaire-2; EQ-5D-5L: EuroQol five-dimension five-level questionnaire; IQR: interquartile range; mMRC: Modified Medical Research Council; NA: not applicable; OR: odds ratio; PHQ-2: Patient Health Questionnaire; PHQ-4: Patient Health Questionnaire; T&T: Trinidad and Tobago.

Figure 2: Distribution of the EuroQol five-dimension five-level questionnaire (EQ-5D-5L) responses by health domain.

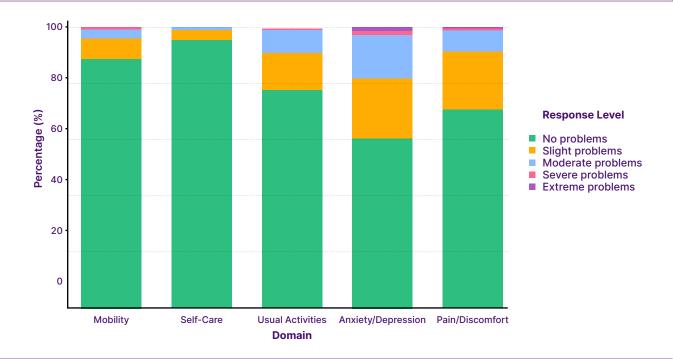


Table 3A: Multivariate logistic regression of difference in fatigue or muscle weakness by illness severity stratified by ICU admission.

	Illness Severity	Unadjusted OR (95% CI)	Adjusted OR (95% CI) p value
ICU Admission Status	(Reference group: Mild illness)	p value	Model 1: Adjusted for age (centred), gender, and comorbidities
All participants Moderate/		1.58 (1.01–2.47)	1.40 (0.814-2.40)
Severe		p=0.043	p=0.224
Non-ICU admission	Moderate/	1.49 (0.95-2.35)	1.42 (0.81-2.48)
	Severe	p=0.083	p=0.215

p values ≤0.05 are statistically significant and are bolded to highlight this. OR: odds ratio.

Table 3B: Multivariate logistic regression of difference in anxiety or depression symptoms by illness severity stratified by ICU admission.

	Illness Severity		Adjusted OR (95% CI) p value		
ICU Admission Status	(Reference group: Mild illness)	Unadjusted OR (95% CI) p value	Model 1: Adjusted for age (centred), gender, and comorbidities	Model 2: Adjusted for age (centred), gender, comorbidities, and previous history of anxiety or depression	
All participants	Moderate/ Severe	2.32 (1.47–3.66) p<0.001	1.49 (0.85–2.61) p=0.159	6.38 (2.28–17.84) p<0.001	
Non-ICU admission	Moderate/ Severe	2.25 (1.41–3.59) p=0.001	1.50 (0.84–2.67) p=0.173	6.55 (2.34–18.29) p<0.001	

p values \leq 0.05 are statistically significant and are bolded to highlight this. OR: odds ratio.

muscle weakness (OR: 1.58; 95% CI: 1.01–2.47; p=0.043). In model 1, when adjusted for age, gender, and comorbidities, there was no significant risk of developing fatigue or muscle weakness among all participants who had moderate/severe illness (OR: 1.40; 95% CI: 0.814–2.40; p=0.224). Table 3B shows the multivariate logistic regression of differences in anxiety or depression by illness severity stratified by ICU admission. In the crude model, among all participants, those with moderate/severe illness were 2.3 times more likely to experience anxiety/

depression 12 months post-COVID-19 infection, compared to the mild cases (OR: 2.32; 95% CI: 1.47–3.66; p<0.001). In model 1, when adjusted for age, gender, and comorbidities, there was no significant risk of experiencing anxiety/depression among all participants who had moderate/ severe illness (OR: 1.49; 95% CI: 0.85–2.61; p=0.159). When adjusted for a previous history of anxiety or depression, the risk of having anxiety/depression among all participants, 1-year post-COVID-19 infection, was 6.4 times higher among participants



	Illness Severity (Reference group: Mild illness)		Adjusted OR (95% CI) p value
ICU Admission Status		Unadjusted OR (95% CI) p value	Model 1: Adjusted for age (centred), gender, and comorbidities
All participants	All participants Moderate/Severe		1.58 (0.90–2.78) p=0.110
Non-ICU admission	Moderate/Severe	3.15 (1.98–5.01) p<0.001	1.43 (0.802–2.550) p=0.226

p values ≤0.05 are statistically significant and are bolded to highlight this.

mMRC: Modified Medical Research Council; OR: odds ratio.

Table 3D: Multivariate linear regression of change in health-related quality of life (Health Index Value) by illness severity stratified by ICU admission.

			Adjusted β (95% CI) p value		
ICU Admission Status	Illness Severity (Reference group: Mild illness)	Unadjusted β (95% CI) p value	Model 1: Adjusted for age (centred), gender, and comorbidities	Model 2: Adjusted for age (centred), gender, comorbidities, and PHQ-4 score (centred)	
All participants	Moderate/Severe	-0.071 (-0.0970.044) p<0.001	-0.044 (-0.0760.01) p=0.006	-0.026 (-0.0300.022) p<0.001	
Non-ICU admission	Moderate/Severe	-0.058 (-0.0799–0.036) p<0.001	-0.027 (-0.050.0009) p=0.043	-0.021 (-0.024–-0.018) p<0.001	

p values ≤0.05 are statistically significant and are bolded to highlight this.

who were moderately/severely ill (OR: 6.38; 95% CI: 2.28–17.84; p<0.001). Illness severity predicting anxiety or depression was dependent on prior mental health history.

Table 3C shows the multivariate logistic regression of difference in degree of breathlessness (mMRC score) by illness severity stratified by ICU admission. In the unadjusted model, among all participants, those with moderate/severe illness were 3.31 times more likely to experience breathlessness 12 months post-COVID-19

infection (OR: 3.31; 95% CI: 2.10–5.22; p<0.001). In Model 1, when adjusted for age, gender, and comorbidities, there was no significant risk of experiencing breathlessness among all participants who had moderate/severe illness (OR: 1.58; 95% CI: 0.90–2.78; p=0.110).

Table 3D shows the multivariate linear regression of change in HRQoL (Health Index Value) by illness severity stratified by ICU admission. In the unadjusted analysis, among all study participants, those

with moderate/severe illness had a 0.071 decrease in health index value compared to those with mild illness (β : -0.071; 95% CI -0.097--0.044; p<0.001). When adjusted for age, gender, and comorbidities in Model 1, (β : -0.044; 95% CI: -0.076--0.01; p=0.006), and further adjusted for PHQ-4 score (β : -0.026; 95% CI: -0.030--0.022; p<0.001), statistically significant differences were noted.

DISCUSSION

Illness Severity at Baseline Illness severity criteria

Illness severity criteria were infrequently defined in the published literature, and most studies focused on cohorts of hospitalised patients. The local MOH and TT criteria (Kavita Dharamraj, data on file) were most suitable for this study. Examples of published illness severity criteria to assess outcomes included mild (86.8%), severe (3.5%), or critical (9.7%) COVID-19 severity by Yang et al.,21 under the 'COVID-19 Prevention and Control Plan (Sixth Edition)';²¹ ward (80.0%) versus ICU patients (20.0%) by Garrigues et al.;10 and non-hospitalised (37.6%) versus hospitalised (62.4%) patients by Lombardo et al.²² Standardised, clearly defined illness severity criteria would better impact future studies.

Socio-demographics

In the authors' study, more women survived moderate/severe illness. Most studies found gender to be independent of illness severity.^{21,23,24} However, Maestre-Muñiz et al.¹² also found that women were more likely to experience moderate/severe illness.

Comorbidities

Hypertension was the most common comorbidity seen, followed by T2D, consistent with national prevalences. ^{25,26} The authors found that individuals with comorbidities, particularly T2D and ischaemic heart disease, were more likely to experience moderate/severe illness, this is consistent with published studies by Maestre-Muñiz et al. ¹² and Lombardo et al. ²² Vulnerable groups should be encouraged to get vaccinated and boosted.

Outcomes 1 Year Later Symptomology

The findings from the authors' study showed that 60% were troubled by at least one lingering symptom, with 46% among them mildly ill and 75% with moderate/ severe illness. Long-term care and follow-up should be made available for these afflicted groups. Globally, a wide variation is seen in the prevalence of post-COVID-19 conditions (PCC). In China, Huang et al.13 reported that the proportion of hospital-discharged patients with at least one PCC decreased from 68% at 6 months to 49% at 12 months. After 1 year, in Italy, Comelli et al.11 found that 91.7% of hospital-discharged patients experienced at least one PCC. Similarly, Lombardo et al.²² reported a prevalence of 81%, regardless of the severity of the acute illness. In Moscow, Pazukhina et al.27 observed a lower prevalence of 34% among patients after hospital discharge. For mild-to-moderate COVID-19 cases, Boscolo-Rizzo et al.28 reported a 1-year PCC prevalence of 53%.

In the authors' study, after 1 year, the most frequently reported symptoms were dyspnoea, fatigue, muscle weakness, sleep difficulties, and hair loss, regardless of the illness severity in the acute phase. Compared to international studies, some of the authors' findings were similar at 1-year post-COVID-19. In China, Huang et al.¹³ most commonly report dyspnoea, fatigue, sleep difficulties, joint pain, and hair loss, among hospital-discharged patients. In Italy, Lombardo et al.²² found fatigue and weakness, muscle and joint pain, sleep disorders, respiratory disorders, and neurological and cognitive impairments prevalent regardless of the illness severity in the acute phase.

HRQoL

In the authors' study, overall, the health index value (0.931) was comparable to national norms,²⁹ but lower for persons with moderate/severe illness (0.894). The overall EQ-VAS score was 79.06%, lower than the score for TT (83.6%), and even lower for persons with moderate/severe illness (74.09%). For post-acute COVID-19, in a pooled prevalence of poor quality of life, EQ-VAS was 59% (95% CI: 42–75%).¹⁴ At 110 days post-hospitalisation, Garrigues et al.¹⁰ reported EQ-VAS score of 70.3%,



and an EQ-VAS index of 0.86.10 At 6 months post-hospitalisation, Huang et al.8 reported EQ-VAS score of 80% (70-90%).

EQ-5D-5L Responses and Mental Health Outcomes

Most of the authors' participants fully recovered. However, a significant proportion had problems affecting HRQoL, which could have a negative economic impact.9 When the authors' findings were compared to a meta-analysis done by Malik et al.,4 using the EQ-5D-5L instrument, they observed a lower prevalence of mobility (11% versus 36%), self-care (4% versus 8%), usual activities (22% versus 30%), and pain/discomfort (30% versus 42%), but a higher prevalence of anxiety/ depression symptoms (40% versus 38%).4

In the authors' study, at 12-month follow-up, 14.0% of the respondents screened positive for either anxiety or depression. No similar studies were found for the comparison of anxiety/depression using the PHQ-4, PHQ-2, and GAD-2 questionnaires. Anxiety and depression can fit the definition of post-COVID-19 conditions if they meet the WHO criteria for post-COVID-19 condition. The tools assessed symptoms that the patient experienced in the preceding 14 days. Therefore, the presence of anxiety or depressive symptoms does not necessarily confirm a post-COVID-19 condition. However, the proportions detected remain significant for appropriate interventions.

Key Predictors

Age, gender, and comorbidities were confounders of the predicted primary outcomes, except for HRQoL. Illness severity predicting anxiety/depression was dependent on prior mental health history. HRQoL was worse in those with moderate/severe COVID-19 compared to mild disease, 1 year later, even after adjustment for demographics and PHQ-4 score. It is possible that factors other than age, gender, comorbidities, and PHQ-4 score were responsible for the participants' decreased quality of life, such as socioeconomic challenges. Baseline factors such as income level and living partners could be explored in future studies.

Through studying long-term sequelae after acute COVID-19, an evidence-based multidisciplinary team approach could be developed to care for these patients.⁵ Care should include optimisation for underlying comorbidities, physiotherapy, occupational therapy, and psychological support.6 In South Trinidad, at 12-month follow-up, patients with persistent symptoms were referred to the 'long COVID' clinic at the San Fernando Teaching Hospital. An intern, a cardiologist, and a psychiatrist form the multidisciplinary team. Further evaluation, rehabilitation, and appropriate care are offered to these patients.

Strengths

A review of published studies suggests that this type of study has not yet been undertaken in the Caribbean. The study's large sample size (n=324), with sufficient power to show associations between comparison groups, randomised cohort selection, and long follow-up duration, provides a good foundation for future related studies. The questionnaire allowed the investigation of many areas of the participant's health status. Standardised pre-tested data collection instruments were used. The response rate was good, providing a reliable estimation of the proportion of patients with COVID-19 who came to a health facility.

When people were invited to participate in the study, the response rate was quite high, over 99%. So, the study was not limited by people being more interested in participating if they had more significant health sequelae from COVID-19. Hence, the study results were generalisable.

Limitations

One major limitation of this study is that there is no measurement of baseline health-related quality of life or pre-infection symptom prevalence, so there is no proper baseline to compare to.

There was no control group, so comparisons could not be made with those who were not infected with COVID-19, as validation of absence COVID-19 in matched controls was beyond the scope of this study.



In this study, only symptomatic cases at baseline were included. However, a control group, such as an asymptomatic group, would have been useful for comparing the outcomes with symptomatic groups. This could be considered for future studies.

SARS-CoV-2 variants during the study period (ancestral versus others), which had different symptom profiles and severity, were not considered in this study.

Even though the tools were aimed to be very comprehensive, some symptoms may not have been captured. Establishing a structured, validated questionnaire that encompasses the full clinical spectrum of long COVID-19 would enhance the replicability of clinical studies.²⁹ It was assumed that the laboratory-confirmed COVID-19 cases were true positives and that individuals were not re-infected after the first time. Data related to the variants and post-COVID-19 symptoms were beyond the scope of this study.

Questionnaires were limited to patient-reported outcomes, via virtual interviews. This study's results may not be generalisable to all COVID-19-positive cases in TT, as there were equal proportions of mild and moderate/severe cases. It is possible that mild cases were under-reported, as more moderate/severe cases may have sought medical attention at health facilities, and therefore, were captured by the surveillance teams. Elderly patients may have had difficulty recalling some of the baseline information.

As the tools used to assess anxiety/ depression assessed symptoms that the patients experienced in the preceding 14 days, anxiety or depressive symptoms may not have represented a post-COVID condition.

CONCLUSION

Significant proportions of COVID-19 survivors have post-COVID symptoms after 1 year. The health index value of all participants was below the population norms, and even lower among those with moderate/severe illness. Interventions should be prioritised for those with the highest burden of persistent symptoms to aid their recovery. Further longitudinal observational national studies and clinical trials are needed to understand the long-term burden of COVID-19 in TT.

RECOMMENDATIONS

In TT, long-term surveillance programmes and long-term COVID clinics should aid long-haulers. An integrated approach of multidisciplinary teams with medical, psychological, and rehabilitation services, with appropriate follow-up, should be available for patients. 30,31 However, the effectiveness of these clinics would need to be evaluated. Public health and social policies need to be implemented to aid survivors, especially those who have had severe disease, for example, disability grants and flexible working hours. Trials of biologics for those with severe long-COVID symptoms could be done, similar to the posthospitalisation COVID-19 (PHOSP-COVID) study in the UK.31

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