

Prevalence and socioeconomic determinants of post-acute sequelae of SARS-CoV-2 among individuals from a peri-urban township and an informal settlement in Johannesburg, South Africa

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Background. Individuals infected with SARS-CoV-2 who develop COVID-19 are susceptible to persistent symptoms and sequelae, referred to as post-acute sequelae of SARS-CoV-2 (PASC). The prevalence of PASC is estimated to range between 10% and 30%. However, there is a paucity of data from African countries.

Objectives. To investigate the prevalence and sociodemographic determinants of PASC in a peri-urban township and an informal settlement in South Africa (SA) during the COVID-19 pandemic.

Methods. A prospective cohort study was conducted among individuals residing in sampled households within the Soweto and Thembelihle Health and Demographic Surveillance System in Gauteng Province, SA. Between August 2021 and January 2022, all individuals from 214 sampled households were tested for SARS-CoV-2 and followed up for 6 months for symptoms. The prevalence of PASC, defined as persistence of symptoms through to at least 30 (PASC-30) and 90 (PASC-90) days, was evaluated, and determinants of PASC were identified using logistic regression models.

Results. There were 268 individuals with documented COVID-19 illness identified, of whom 65.3% ($n=175$) were female. The median age was 24 years. The overall prevalence of PASC-30 was 23.9% (95% confidence interval (CI) 19.2 - 29.3), including 24.6% (95% CI 19.7 - 30.3) and 12.5% (95% CI 3.5 - 36.0) in individuals who were unvaccinated or had received a COVID-19 vaccine, respectively ($p=0.283$). The overall prevalence of PASC-90 was 2.2% (95% CI 1.0 - 4.8). Factors associated with PASC-30 included living in an informal (39.2%, 105/268) v. formal settlement (60.6%, 163/268) (adjusted odds ratio (aOR) 4.1, 95% CI 2.1 - 8.3), although participants living in larger households (aOR 0.8, 95% CI 0.7 - 0.9, $p=0.011$) were less likely to report PASC-30 than those from smaller households. Age, gender, marital status, level of education, employment status, vaccination status and the presence of comorbidities were not significantly associated with PASC.

Conclusion. PASC-30 (23.9%) was prevalent at the population level in individuals with documented COVID-19, particularly among residents of informal settlements, while PASC-90 (2.2%) was low. Further exploration into PASC within informal settlements is imperative to comprehensively understand these findings.

Keywords: South Africa, Soweto, peri-urban, informal settlement, HDSS, PASC

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Infections by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), have posed a significant public health challenge since December 2019. After a COVID-19 infection, some people experience persistent symptoms for >30 days while still actively shedding the SARS-CoV-2 virus, a condition referred to as post-acute sequelae of SARS-CoV-2 (PASC).^[1] The symptoms of PASC could be of new onset after initial recovery from an acute COVID-19 episode, or persistence of symptoms following the initial illness, which may fluctuate or relapse over time.^[1] PASC, long-COVID,^[2] post-COVID-19 condition^[3] and post-COVID-19 syndrome^[4] are some of the terms used to describe persistent symptoms after a COVID-19 infection. While often used

interchangeably, the definitions of these terms have slight technical differences, mainly regarding how long symptoms must persist to meet each definition.^[5]

A meta-analysis covering the period from December 2020 to March 2022 reported PASC at least 4 weeks after acute COVID-19 in 43% (95% confidence interval (CI) 39 - 46) of individuals, ranging from 31% (95% CI 21 - 43) in North America to 51% (95% CI 37 - 65) in Asia.^[6] No studies were identified from Africa. A subsequent systematic review from December 2019 to January 2022, which included 194 studies and only two from Africa, reported a global prevalence of ongoing PASC at least 4 weeks post-acute-COVID-19 in 45% of COVID-19 survivors.^[7] A meta-analysis from

March 2020 to February 2023 including only African studies ($n=25$) reported a prevalence of PASC at least 3 months after onset of COVID-19 of 48.6% (95% CI 37.4 - 59.8).^[8] The over-representation of hospitalised and intensive care unit patients in the analysed African studies potentially limits generalisability of the findings at the population level.

In South Africa (SA), the prevalence of PASC in individuals following mild COVID-19 was found to be 60% at 2 months, of whom 17.2% required medical treatment.^[9] Using data from the SA national hospital surveillance system, the prevalence of PASC was found to be 82.1% and 66.7% at 1 month and 3 months after discharge from hospital, respectively.^[10] We investigated the prevalence and sociodemographic determinants of PASC in a peri-urban township and an informal settlement in SA, to fill the gap in our understanding of PASC in such settings.

Methods

Study setting

The Wits Vaccines and Infectious Diseases Analytics (Wits-VIDA) research unit at the University of the Witwatersrand runs the Soweto and Thembelihle Health and Demographic Surveillance System (SaT-HDSS) in Gauteng Province, SA. The SaT-HDSS monitors the population in selected neighbourhoods of peri-urban Soweto townships and Thembelihle informal settlement, collecting data on population health and demographic events. Located on the southern outskirts of the City of Johannesburg, Soweto and Thembelihle represent two different types of development. Soweto was formally established during apartheid to house black African residents,^[11] while Thembelihle developed as an unplanned informal settlement on the residual land.^[12] The SaT-HDSS includes eight clusters in Soweto and three clusters in Thembelihle, with 91 969 and 18 878 individuals under surveillance, respectively. Most (98.5%) residents of the greater Soweto area are black Africans, with a median age of 27 years.^[13] The unemployment rate is 24%. In the SaT-HDSS, 84.3% of houses are formal dwellings made of brick/concrete, and 14.8% are informal shacks. Ninety-nine percent of households have access to piped water within a 500 m radius. The demographic distribution for Thembelihle is similar to that of Soweto; however, the median age is 24 years, and 23.9% of houses are informal shacks.^[13]

Study design

The SaT-HDSS cohort was used as the sampling frame to study COVID-19 household transmission dynamics. Sampled households were screened for COVID-19 from 13 August 2021 to 11 February 2022. Screening of all household members involved both nasopharyngeal swabs (NPS) and dried blood spot (DBS) tests. Households with ≥ 1 member who tested positive for COVID-19 were enrolled, followed up weekly for 1 month, and then monthly for the following 5 months. The follow-up involved collecting information on COVID-19 symptoms for the positive case, and testing other household members to determine whether there had been new cases within the household. Sampled households with no reported COVID-19 cases were followed up every 14 days until a COVID-19 case was identified, following which household members were followed up to determine the rate of household transmission. A comprehensive description of the cohort is provided in a forthcoming article. This study utilised data from confirmed cases, with follow-up to collect NPS and DBS specimens to characterise the cell-mediated immune response, along with recorded information on COVID-19 symptoms. We analysed for PASC at 30 days (PASC-30) and 90 days (PASC-90) after a positive SARS-CoV-2 test.

Measures

Information collected included basic demographic characteristics such as age, sex, education level, employment and marital status, and details of COVID-19 vaccination status. Participants who tested positive for COVID-19 through either NPS or DBS also self-reported whether they had experienced predefined COVID-19-related signs and symptoms that included stroke, fever, fatigue, cough, loss of appetite, malaise, muscle pain, sore throat, dyspnoea, nasal congestion, headache, diarrhoea, nausea and vomiting, and the duration of these within the preceding 14 days. In each subsequent follow-up, participants were asked to report whether they were experiencing any of the previously defined COVID-19-related signs and symptoms. COVID-19 vaccination status was also self-reported.

Statistical analysis

Statistical analysis was performed using R statistical software (R Foundation for Statistical Computing, Austria), version 4.3.1. Categorical variables were summarised using frequencies and proportions, and comparisons made using the χ^2 test. Continuous variables were summarised using medians and interquartile ranges. Differences between groups were reported using the Kruskal-Wallis H test. Logistic regression was applied to model binary outcomes. In all statistical tests, $p < 0.05$ was considered significant.

Ethical considerations

This study received ethical approval from the University of the Witwatersrand's Human Research Ethics Committee (ref. no. 170216). Prior to participation, all adult household members provided written informed consent. For children aged < 16 years, written informed consent was obtained from parents or adult caregivers, and the children provided their informed assent.

Results

The study screened 1 783 participants for COVID-19. Participants who did not report their vaccination status ($n=595$; 33.4%) were removed from the analysis (Fig. 1). Of the remaining 1 188 participants, 920 (51.6%) did not report any COVID-19 symptoms, and were also excluded from the analysis. A total of 268 (15.0%) participants were included in the study.

The overall median (interquartile range) age was 24 (10 - 46) years, and 34.7% were male. Most eligible participants were from Soweto townships (60.8%), with the remainder from Thembelihle informal settlement (39.2%). Only 6.0% ($n=16$) were vaccinated: 62.5% with Pfizer and 37.5% with Johnson & Johnson (Table 1). Among the vaccinated, 87.5% were from Soweto and 12.5% were from Thembelihle. The prevalence of ≥ 1 of the following comorbidities was notably higher among vaccinated participants (62.5%, 10/16) than unvaccinated participants (21.8%, 55/252): hypertension, asthma, chronic liver disease, stroke, diabetes, HIV, tuberculosis, obesity, chronic lung disease, chronic heart disease, cancer and chronic obstructive pulmonary disease.

All 268 participants had reported ≥ 1 COVID-19 symptom during the study period. The most frequently reported symptoms among the participants were coughing (54.5%), nasal congestion (21.6%), headache (20.5%), fever (12.7%) and a sore throat (12.3%) (Fig. 2). Overall, 17.5% displayed > 1 symptom within the same visit, and 42.9% displayed multiple symptoms across their follow-up time.

Approximately 24% (95% CI 19.2 - 29.3) had PASC-30, with a higher prevalence in the unvaccinated group (24.6%, 95% CI 19.7 - 30.3) than the vaccinated group (12.5%, 95% CI 3.5 - 36.0, $p=0.283$). The overall prevalence of PASC-90 was 2.2% (95% CI 1.0 - 4.8), with 1.6% (95% CI 0.6 - 4.0) among unvaccinated participants,

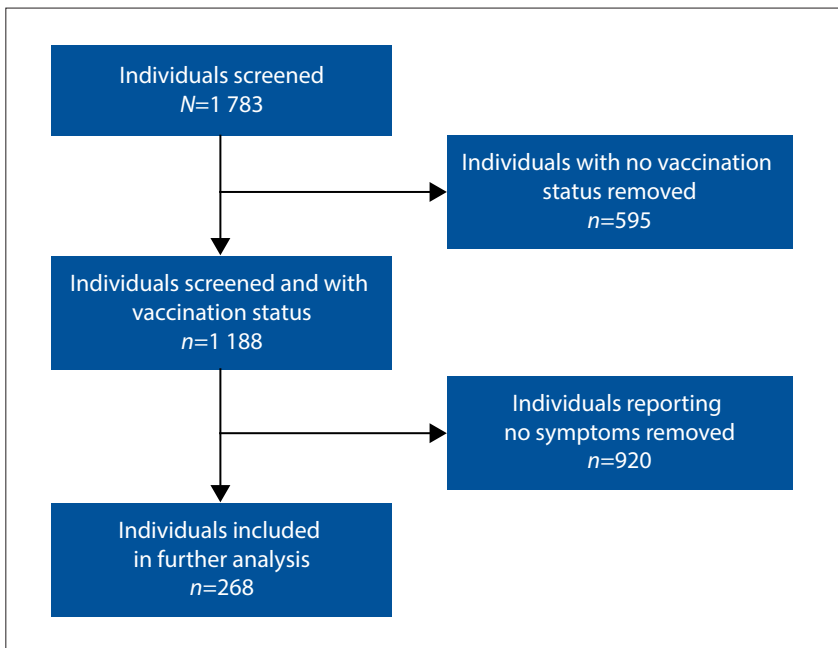


Fig. 1. Screening of individuals for analysis.

Table 1. Sample characteristics by vaccination status (N=268)

Characteristic	Unvaccinated, n (%) [*]	Vaccinated, n (%) [*]
Settlement		
Soweto (township)	149 (59.1)	14 (87.5)
Thembelihle (informal settlement)	103 (40.9)	2 (12.5)
Age group, years		
0 - 14	98 (38.9)	0
15 - 24	42 (16.7)	1 (6.2)
25 - 39	47 (18.6)	4 (25.0)
40 - 59	44 (17.5)	3 (18.8)
≥60	21 (8.3)	8 (50.0)
Sex		
Male	90 (35.7)	3 (18.8)
Female	162 (64.3)	13 (81.2)
Marital status		
Married or living with a partner	30 (11.9)	4 (25.0)
Single	222 (88.1)	12 (75.0)
Education level		
No schooling	53 (21.0)	0
Primary school	100 (39.7)	5 (31.2)
Secondary school	60 (23.8)	8 (50.0)
Matric or post-matric qualification	39 (15.5)	3 (18.8)
Employment status		
Employed	28 (11.1)	2 (12.5)
Not employed	224 (88.9)	14 (87.5)
Number of household members, n (median (IQR))	5 (4 - 7)	6 (4 - 6)
Comorbidities, n		
0	197 (78.2)	6 (37.5)
1	42 (16.7)	3 (18.7)
≥2	13 (5.1)	7 (43.8)
Total, n	252	16

IQR = interquartile range.
^{*}Unless otherwise indicated.

and remained unchanged at 12.5% among vaccinated participants. The prevalence of PASC-30 in Soweto (14.1%, 95% CI 9.6 - 20.3) was significantly lower than in Thembelihle (39.1%, 95% CI 30.3 - 48.6). The prevalence of PASC-90 in Soweto (0.6%, 95% CI 0.1 - 3.4) was still lower than in Thembelihle (4.8%, 95% CI 2.1 - 10.7), although the difference was not significant.

The prevalence of fatigue was significantly higher among those with PASC-30 (Table 2). Based on the same definition, the prevalences of coughing and headache were significantly lower among those with PASC-30. The prevalence of sore throat and headache were significantly higher among those with PASC-90.

A univariable analysis for PASC-30 shows that participants from Thembelihle were nearly four times (unadjusted odds ratio (uOR) 3.9, 95% CI 2.2 - 7.1, $p < 0.001$) more likely to have PASC relative to those from Soweto (Appendix Table S3). Based on the same definition, participants aged 15 - 24 years (uOR 0.3, 95% CI 0.1 - 0.8, $p = 0.022$), those with secondary schooling (uOR 0.4, 95% CI 0.2 - 0.9, $p = 0.026$) and those in larger households (uOR 0.8, 95% CI 0.7 - 0.9, $p = 0.002$) were significantly less likely to have PASC. A multivariable analysis for PASC-30 showed that participants from Thembelihle were significantly more likely to display PASC than those from Soweto (adjusted OR (aOR) 4.1, 95% CI 2.1 - 8.3, $p < 0.001$). Participants in larger households were significantly less likely to report symptoms that suggest PASC than those in smaller households (aOR 0.8, 95% CI 0.7 - 0.9, $p = 0.011$).

A univariable analysis for PASC-90 showed that vaccinated participants were nearly nine times (uOR 8.9, 95% CI 1.2 - 49.6, $p = 0.016$) more likely to have PASC than those not vaccinated. Participants with one (uOR 14.4, 95% CI 1.8 - 296.0, $p = 0.022$) and at least two (uOR 22.4, 95% CI 2.1 - 497.0, $p = 0.013$) comorbidities had a significantly higher likelihood of experiencing PASC-90 than those with no comorbidities. Participants who were not married (uOR 0.1, 96% CI 0.0 - 0.8, $p = 0.017$) were less likely to have PASC-90 than those who were married or living with a partner. A multivariable analysis for PASC-90 was not undertaken owing to the limited number of participants experiencing PASC.

Discussion

COVID-19 patients from selected households from the Soweto townships and Thembelihle informal settlement, SA, who were affected by COVID-19 exhibited a diverse range of symptoms lasting for at least

1 month, particularly among those who were unvaccinated. However, the frequency of these symptoms diminished by 3 months. The overall prevalence of PASC-30 or PASC-90 observed in this study was lower than pooled global estimates^[6] and pooled estimates from African samples.^[8] In SA, the prevalence of post-COVID-19 condition at 6-month follow-up was reported as 19% among non-hospitalised patients,^[14] which was close to our findings.

The most persistent COVID-19-related respiratory symptoms were coughing and nasal congestion. Headache was the most persistent symptom related to the nervous system, and fatigue was most persistent among general symptoms. These symptoms were also persistent among long-COVID^[8] or post-COVID-19 condition^[14] patients in other SA settings.^[8,14] The cumulative prevalence of coughing and headaches was significantly lower in the PASC-30 group. A likely explanation is that these symptoms were common in the initial 30 days of infection, but only a small number of people who experienced them went on to develop PASC-30. Therefore, the lower prevalence is likely because they were less persistent in the group that ultimately met the PASC-30 criteria. The prevalence of dyspnoea was lower than observed elsewhere^[6,8,15] – this may be because this was the subjective perception of participants in our study compared with others^[14] that used the modified Medical Research Council Dyspnea scale.^[16] The lower prevalence of dyspnoea could be a result of the severity of the initial infection. A previous study also found that a small number of construction workers denied having symptoms of dyspnoea that contradicted findings from their clinical examination.^[17]

Among the unvaccinated, women experienced COVID-19 symptoms for a longer duration than men; this was similar to results from mostly high-income countries,^[18] as well as an SA study.^[10] It has been argued that men have poorer health-seeking behaviour than women, and as a

result are less likely to report persistent symptoms.^[10] The same article also suggested that men face a higher risk of death during the acute phase of COVID-19 than women, whereas the surviving women are more likely to encounter long-term health challenges.

A multivariable analysis shows that participants from Thembelihle were more likely to report symptoms that suggest PASC at 1 month than those from Soweto. It was anticipated that residents of informal settlements would face a higher risk of COVID-19 owing to the lack of adequate basic services and social amenities necessary to adhere to recommended transmission prevention measures.^[19] It is possible that factors such as overcrowding may have contributed to increased transmission rates, while socioeconomic factors such as poverty may have heightened susceptibility to severe COVID-19, which both increase the likelihood of individuals developing long-term COVID-19 complications. The multivariable analysis also showed that participants living in larger households were significantly less likely to report symptoms that suggest PASC than those in smaller households. Despite our anticipation that individuals in larger households might exhibit prolonged COVID-19 symptoms, consistent with observations elsewhere,^[20,21] our study did not reveal such an association. Notably, other studies have also reported no significant link between household size and PASC among individuals with probable or confirmed SARS-CoV-2 infection,^[22,23] although the reasons for this discrepancy in our study remain unclear. We found no difference in persistent COVID-19 symptoms between vaccinated and unvaccinated participants after adjusting for other variables. This is in line with findings from another study conducted in SA,^[14] which argues that it is probably because of using self-reported vaccination status, which lacks objectivity, and the lack of information to differentiate between partial and complete vaccination.

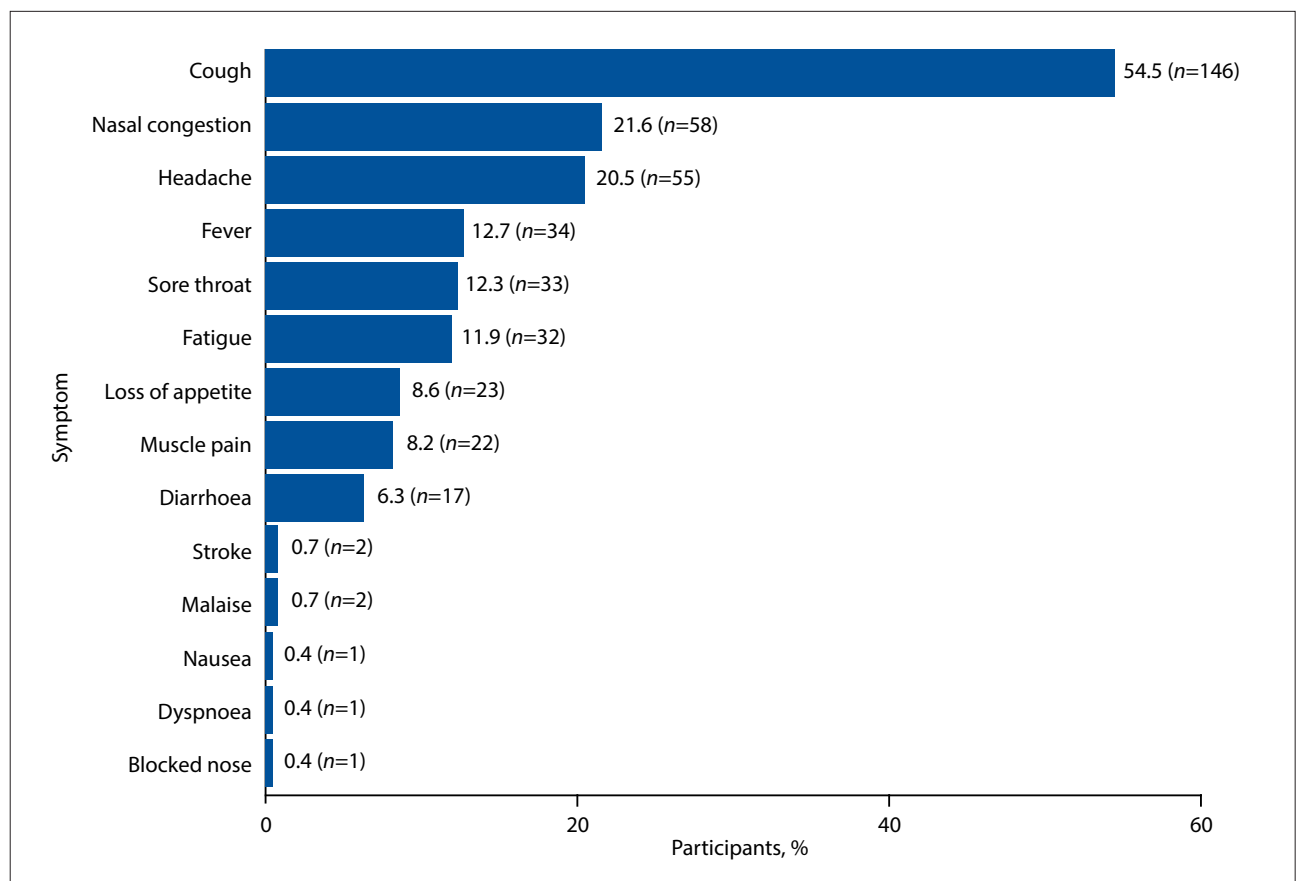


Fig. 2. Percentage of each symptom in relation to the total number of participants where it was reported at least once.

Table 2. Prevalence of COVID-19 symptoms by PASC status defined at 1 month and 3 months

Characteristic	PASC-30, % (95% CI), n			PASC-90, % (95% CI), n		
	Yes	No	p-value	Yes	No	p-value
Overall	23.9 (19.2 - 29.3), 64	76.1 (70.67 - 80.83), 204	<0.001	2.2 (1.03 - 4.80), 6	97.8 (95.2 - 98.97), 262	<0.001
Respiratory						
Blocked nose	0.6 (0.03 - 3.9), 1	0 (0 - 2), 0	0.400	0 (0 - 21), 0	0.3 (0.01 - 1.7), 1	0.900
Cough	35 (27 - 42), 56	47 (41, 54), 110	0.011	47 (25 - 71), 9	42 (37 - 47), 157	0.600
Dyspnoea	0.6 (0.03 - 3.9), 1	0 (0 - 2.0), 0	0.400	0 (0 - 21), 0	0.3 (0.01 - 1.7), 1	0.900
Nasal congestion	15 (10 - 22), 25	16 (12 - 21), 37	0.900	5.3 (0.28 - 28), 1	16 (13 - 20), 61	0.300
Sore throat	11 (6.9 - 17), 18	7.3 (4.5 - 12), 17	0.200	26 (10 - 51), 5	8.0 (5.5 - 11), 30	0.019
Digestive						
Diarrhoea	6.2 (3.2 - 11), 10	3.0 (1.3 - 6.4), 7	0.130	0 (0 - 21), 0	4.5 (2.7 - 7.3), 17	0.900
Loss of appetite	4.9 (2.3 - 9.8), 8	6.9 (4.1 - 11), 16	0.400	5.3 (0.28 - 28), 1	6.1 (4 - 9.2), 23	0.900
Nausea	0.6 (0.03 - 3.9), 1	0 (0 - 2), 0	0.400	0 (0 - 21), 0	0.3 (0.01 - 1.7), 1	0.900
Nervous system						
Headache	10 (6.4 - 17), 17	18 (13 - 23), 41	0.048	32 (14 - 57), 6	14 (11 - 18), 52	0.045
Stroke	0.6 (0.03 - 3.9), 1	0.4 (0.02 - 2.8), 1	0.900	0 (0 - 21), 0	0.5 (0.09 - 2.1), 2	0.900
General						
Fatigue	16 (11 - 23), 26	3.9 (1.9 - 7.5), 9	0.000	0 (0 - 21), 0	9.3 (6.7 - 13), 35	0.400
Fever	6.8 (3.6 - 12), 11	10 (6.9 - 15), 24	0.200	16 (4.2 - 40), 3	8.5 (6 - 12), 32	0.200
Malaise	0 (0 - 2.9), 0	0.9 (0.15 - 3.4), 2	0.500	0 (0 - 21), 0	0.5 (0.09 - 2.1), 2	0.900
Muscle pain	6.8 (3.6 - 12), 11	5.2 (2.8 - 9.1), 12	0.500	0 (0 - 21), 0	6.1 (4 - 9.2), 23	0.600
Total, n*	162	232		19	375	

*Includes number of repeat visits where symptoms were observed.
PASC = post-acute sequelae of SARS-CoV-2.

Study limitations

The reported duration of COVID-19 symptoms was the time difference between date of symptom onset and date of last fieldwork reporting. It is possible that some individuals could have started showing symptoms earlier than the date assumed by the participants, and the symptoms could have ended some days after the last visit date. Therefore, the duration reported is potentially a conservative estimate of the actual duration of symptoms. With a sample size of 268, the study was only adequately powered to detect a significant difference in overall prevalence of PASC, specifically within the range of $\leq 16\%$. However, it was not adequately powered for subgroup analysis, which would have required a minimum sample size of 114 per group, assuming a minimum population-level prevalence of 10%. Commonly reported symptoms after acute COVID-19 such as palpitations, memory disturbances, difficulty in concentration, dizziness and chest pain were also not reported. The subjective assessment of dyspnoea rather than a grading scale limited our interpretation of the lower prevalence that was observed. With only a small number of participants having PASC-90 ($n=6$, 2.2%), further study of PASC that persisted beyond 3 months was not possible.

Conclusion

PASC-30 (23.9%) was prevalent at the population level in individuals with documented COVID-19, particularly among residents of informal settlements, while PASC-90 (2.2%) was low. The significant association between living in an informal settlement and PASC-30 highlights the unique challenges and manifestations of the condition in these settings. Further exploration into PASC within informal settlements is essential to comprehensively understand these findings. Such future studies may help to identify risk factors and formulate approaches for sustained care.

Data availability. Data are available from the authors upon reasonable request.

Declaration. None.

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Author contributions. TM developed the first draft of the manuscript. PM conceptualised the research project. SAM conceptualised the research project and acquired funding. All authors contributed to, reviewed and approved the final manuscript.

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Conflicts of interest. None.

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