Postdischarge outcomes of COVID-19 patients from South Asia: a prospective study

Visula Abeysuriya\textsuperscript{a},* Sujanith L. Seneviratne\textsuperscript{a,b}, Arjuna P. De Silva\textsuperscript{c}, Riaz Mowjood\textsuperscript{d}, Shazli Mowjood\textsuperscript{d}, Thushara de Silva\textsuperscript{d}, Prime\textsuperscript{e} de Me\textsuperscript{e}, Chandima de Me\textsuperscript{e}, R.S. Wijesinha\textsuperscript{a}, Amitha Fernando\textsuperscript{d}, Sanjay de Me\textsuperscript{g}, and Lal Chandrasena\textsuperscript{a}

\textsuperscript{a}Nawaloka Hospital Research and Education Foundation, Nawaloka Hospitals PLC, Colombo-02, Sri Lanka; \textsuperscript{b}Institute of Immunity and Transplantation, Royal Free Hospital and University College London, NW3 2PP, UK; \textsuperscript{c}Department of Medicine, Faculty of Medicine, University of Kelaniya, P.O Box 6, Sri Lanka; \textsuperscript{d}Department of Respiratory Disease, Nawaloka Hospitals PLC, Colombo-02, Sri Lanka; \textsuperscript{e}The Princess Alexandra Hospital, the Princess Alexandra Hospital NHS Trust, Hamstel Rd, Harlow CM20 1QX, UK; \textsuperscript{f}National Hospital, WV99+FHX, Colombo-07, Sri Lanka; \textsuperscript{g}Department of Haematology-Oncology, National University Cancer Institute, National University Health System Singapore, Singapore

*Corresponding author: Tel: +94 77 326 555 2; E-mail: visulasrilanka@hotmail.com

Received 21 October 2021; revised 26 March 2022; editorial decision 6 April 2022; accepted 8 April 2022

Background: Coronavirus disease 2019 (COVID-19) may cause clinical manifestations that last for weeks or months after hospital discharge. The manifestations are heterogeneous and vary in their frequency. Their multisystem nature requires a holistic approach to management. There are sparse data from the South Asian region on the outcomes of hospital-discharged COVID-19 patients. We assessed the posthospital discharge outcomes of a cohort of Sri Lankan COVID-19 patients and explored the factors that influenced these outcomes.

Methods: Data were prospectively collected from patients who were discharged following an admission to the Nawaloka Hospital, Sri Lanka with COVID-19 from March to June 2021. At discharge, their demographic, clinical and laboratory findings were recorded. The patients were categorised as having mild, moderate and severe COVID-19, based on the Sri Lanka Ministry of Health COVID-19 guidelines. Following discharge, information on health status, complications and outcomes was collected through clinic visits and preplanned telephone interviews. A validated (in Sri Lanka) version of the Short Form 36 health survey questionnaire (SF-36) was used to assess multi-item dimensions health status of the patients at 1, 2 and 3 mo postdischarge.

Results: We collected data on 203 patients (male, n=111 [54.7%]). The level of vaccination was significantly associated with disease severity (p<0.001). Early recovery was seen in the mild group compared with the moderate and severe groups. At 3 mo, on average 98% of mild and 90% of moderate/severe patients had recovered. Based on the SF-36, physical functioning dimensions, role limitation due to physical and emotional health, energy/ fatigue, emotional well-being, social functioning, pain and general health were significantly different in the moderate/severe vs mild COVID-19 groups at 1, 2 and 3 mo postdischarge (p<0.05). Twenty-three patients developed complications, of which the most common were myocardial infarction with heart failure (n=6/23; 26.1%), cerebrovascular accident (n=6/23; 26.1%) and respiratory tract infections (n=3/23; 13.01%) and there were six deaths.

Conclusions: In our cohort, receiving two doses of the COVID-19 vaccine was associated with reduced disease severity. Those with mild disease recovered faster than those with moderate/severe disease. At 3 mo posthospital discharge, >90% had recovered.

Keywords: COVID-19, outcome, SARS-CoV-2, SF-36, vaccination

Introduction

Coronavirus disease 2019 (COVID-19), due to the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus, has affected >230 million people worldwide and has led to adverse health and economic impacts.\textsuperscript{1,2} In addition to several novel treatment strategies proposed for its treatment, vaccination is an important preventive strategy for the reduction of
morbidity and mortality in COVID-19. A range of symptoms may persist following acute COVID-19 and the effective management of these may put further pressure on already stretched healthcare systems. The short- and long-term outcomes in such patients and the patterns of recovery postacute COVID-19 may vary in different regions of the world. Delineation of such patterns would allow countries to put into place optimal plans for such patients and to more efficiently allocate limited health resources. The multisystem nature of the manifestations would require a holistic approach to management and this may prove to be a challenge in many low- and middle-income countries.

Information on the varied postacute and long-term effects of COVID-19 is currently gathered in several settings. Early reports suggest there may be prominent residual effects of the infection with a resultant decline in quality of life. In addition, thromboembolic events have been noted to occur post-COVID-19, and may contribute to both morbidity and mortality. As of yet, the outcomes and disease patterns post-COVID-19 are poorly defined and studied among South Asian patients. There are hardly any data on outcomes of discharged COVID-19 patients in this region. Our objective was to assess multidimensional postdischarge outcomes of a cohort of hospitalised COVID-19 patients and to determine the factors that affect these outcomes.

Materials and Methods

Study design

A prospective study was conducted on adults who were discharged following hospitalisation for COVID-19. The patients were hospitalised at Nawaloka Hospital, Sri Lanka, from March to June 2021.

Study population

We included 203 patients (aged >18 y) with SARS-CoV-2 infection confirmed by RT-PCR from a nasopharyngeal swab (AccuPower SARS-CoV-2 RT-PCR kit; Bioneer, South Korea). Positive test results were reanalysed with RealStar SARS-CoV-2 RT-PCR Kit 1.0 (Altona diagnostics, Germany) for confirmation. The flowchart of patient recruitment and follow-up is shown in Supplementary Figure 1.

We used a validated (in Sri Lanka) version of the Short Form 36 health survey questionnaire (SF-36) to assess multi-item dimensions health status of the hospital-discharged COVID-19 patients at 1, 2 and 3 mo following discharge. The eight dimensions of the SF-36 were physical functioning, role limitation due to physical health, role limitation due to emotional health, energy/fatigue, emotional well-being, social functioning, pain and general health. Additional information on health status, complications and outcomes was obtained through clinic visits and preplanned telephone interviews. Patients were categorised as having mild, moderate and severe COVID-19 based on the national guidelines, “Provisional clinical practice guidelines on COVID-19 suspected and confirmed cases” of the Ministry of Health, Sri Lanka.

Data collection

Demographic, laboratory and health survey data

Demographic, clinical and laboratory information was obtained by a trained study team member from the patient and their medical records. The SF-36 was completed when the patients attended a COVID-19 clinic and at preplanned telephone interviews.

Data analysis

Continuous variables were described using mean and standard deviation values. Continuous data were compared using one-way and repeated modal ANOVA and categorical data were compared using the χ² test. p<0.05 was considered statistically significant. Data were analysed using Statistical Package for Social Sciences 16 (SPSS 16.0, Chicago, IL, USA) and STATA version 12 (TX, USA).

Results

Table 1 shows the demographic characteristics and vaccine status (at the time of hospital admission) in the study population. COVID-19 disease severity was significantly associated with the level of COVID-19 vaccination. Of 29 patients who had received both vaccine doses, 2 (6.8%) got severe COVID-19. In those who had still not received a vaccine dose or had received a single dose, 26.5% (n=18) and 25.4% (n=27) had severe COVID-19, respectively. Among the fully vaccinated group, the highest cyclic threshold value (mean [SD]) upon admission (at a median of 3 d) was 24.6±3.5 d and the shortest length of hospital stay was 11.9±2.2 d.

Table 2 shows a comparison of the different dimensions of the SF-36 scores between mild, moderate and severe COVID-19 patients at 1, 2 and 3 mo following hospital discharge. There was a significant difference in the following SF-36 dimensions: physical functioning, role limitation due to physical health, role limitation due to emotional health, energy/fatigue, emotional well-being, social functioning, pain and general health between those who had mild and moderate/severe COVID-19 and this was noted at each time point (p<0.05). Earlier recovery was achieved by those with mild disease compared with those in the moderate/severe groups.

Table 3 shows the observed complications in the patients, subgrouped according to COVID-19 severity and vaccination status. In total, 23 complications were observed during a 3-mo postdischarge interval. These were myocardial infarction with heart failure (n=6/23; 26.1%), cerebrovascular accident (n=6/23; 26.1%), respiratory tract infections (RTIs) (n=3/23; 13.01%), pulmonary embolism (n=2/23; 8.7%), acute kidney injury (n=1/23; 4.3%), intracranial haemorrhage (n=2/23; 8.7%), gastrointestinal bleeding (n=2/23; 8.7%) and deep vein thrombosis (n=1/23; 4.3%). There were six deaths and all occurred in
those who developed a complication. Among the three patients who had a lower RTI, one patient each had Aspergillosis species, Acinetobacter species and methicillin-resistant Staphylococcus aureus lung infections. Table 4 shows the characteristics of the post-COVID-19 patients who developed complications (n=23). The length of hospital stay was significantly longer among post-COVID-19 patients with complications who died compared with those who recovered. Mean cycle threshold value on median day 3 (i.e. upon admission) was significantly lower in those with post-COVID-19 complications who died in comparison with those who recovered. Low vaccination coverage was found in those who died.

Table 1. Demographic characteristics of the study population and the association with vaccine status

| Variable                                      | All (n=203) N (%) | Non vaccination (n=106) N (%) | Only first dose of vaccination (n=68) N (%) | First and second doses of vaccination (n = 29) N (%) | p     |
|-----------------------------------------------|-------------------|-------------------------------|-----------------------------------------------|---------------------------------------------------|-------|
| Age (y)                                       |                   |                               |                                               |                                                   |       |
| <30                                          | 12 (5.9)          | 8 (7.5)                       | 2 (2.9)                                       | 2 (2.9)                                           | $\chi^2_1=10.61$ | p=0.002       |
| 31 to 40                                      | 20 (9.9)          | 14 (13.2)                     | 3 (4.4)                                       | 3 (10.3)                                          |       |
| 41 to 50                                      | 44 (21.7)         | 18 (17.0)                     | 16 (23.5)                                     | 10 (34.5)                                         |       |
| 51 to 60                                      | 40 (19.7)         | 21 (19.8)                     | 13 (19.1)                                     | 6 (20.7)                                          |       |
| >60                                          | 87 (42.9)         | 45 (42.5)                     | 34 (50.0)                                     | 8 (27.6)                                          |       |
| Gender                                        |                   |                               |                                               |                                                   |       |
| Male                                         | 111 (54.7)        | 62 (58.5)                     | 36 (52.9)                                     | 13 (14.8)                                         | $\chi^2_1=1.84$ | p=0.399       |
| Female                                       | 92 (45.3)         | 44 (41.5)                     | 32 (47.1)                                     | 16 (55.2)                                         |       |
| Marital status                                |                   |                               |                                               |                                                   |       |
| Married                                      | 152 (74.9)        | 74 (69.8)                     | 57 (83.6)                                     | 21 (79.4)                                         | $\chi^2_1=7.383$ | p=0.084       |
| Never married                                 | 40 (19.7)         | 23 (21.7)                     | 10 (14.7)                                     | 7 (24.1)                                          |       |
| Divorced                                      | 7 (3.4)           | 6 (5.7)                       | 0                                             | 1 (3.4)                                           |       |
| Widow                                         | 4 (2.0)           | 3 (2.8)                       | 1 (1.5)                                       | 0                                                 |       |
| Educational level                             |                   |                               |                                               |                                                   |       |
| School education only                         | 146 (71.9)        | 76 (71.7)                     | 51 (75)                                       | 19 (65.5)                                         | $\chi^2_1=4.069$ | p=0.667       |
| Higher education                              | 57 (28.1)         | 30 (28.3)                     | 17 (25)                                       | 10 (34.5)                                         |       |
| Employment status\(^1\)                      |                   |                               |                                               |                                                   |       |
| Public employees                              | 50 (24.6)         | 24 (22.6)                     | 15 (22.1)                                     | 11 (37.9)                                         | $\chi^2_1=8.593$ | p=0.019       |
| Private employees                             | 77 (37.9)         | 43 (40.6)                     | 24 (35.3)                                     | 10 (34.5)                                         |       |
| Employers                                    | 56 (27.6)         | 25 (23.6)                     | 25 (36.8)                                     | 6 (20.7)                                          |       |
| Own account workers                           | 20 (9.9)          | 14 (13.2)                     | 4 (5.9)                                       | 2 (6.9)                                           |       |
| Monthly income (SLR)\(^2\)                   |                   |                               |                                               |                                                   |       |
| <51 862                                       | 14 (6.9)          | 11 (10.4)                     | 3 (4.4)                                       | 0                                                 | $\chi^2_1=8.22$ | p=0.004       |
| 51 863 to 81 371                              | 131 (64.5)        | 60 (56.6)                     | 49 (72.1)                                     | 22 (75.9)                                         |       |
| >81 372                                       | 58 (28.5)         | 35 (33.3)                     | 16 (23.5)                                     | 7 (24.1)                                          |       |
| Severity\(^3\)                                |                   |                               |                                               |                                                   |       |
| Mild                                         | 75 (36.9)         | 29 (27.4)                     | 24 (35.3)                                     | 23 (79.3)                                         | $\chi^2_1=23.59$ | p=0.001       |
| Moderate                                     | 80 (39.4)         | 50 (47.2)                     | 26 (38.2)                                     | 4 (13.8)                                          |       |
| Severe                                       | 48 (23.6)         | 27 (25.4)                     | 18(26.5)                                      | 2(6.8)                                            |       |
| Cyclic threshold value on median day 3 (upon admission) | 21.36±3.5  | 21.18±3.6\(^a\)             | 20.75±3.03\(^a\)                              | 24.45±3.45\(^b\)                                 | $F_{2,200}=6.686$ | p=0.001       |
| Mean±SD\(^a\)                                | 13.23±2.22        | 13.45±2.08                    | 13.44±2.26                                    | 11.89±2.22                                        |       |
| Abbreviation: SLR, Sri Lankan rupee.\(^1\)Department of Census and Statistics, Sri Lanka, 2018.\(^2\)Based on income quintiles of Household Income and Expenditure Survey, Sri Lanka, 2016.\(^3\)Provisional clinical practice guidelines on COVID-19 suspected and confirmed cases - Ministry of Health, Sri Lanka, 2020.\(^a\)One-way ANOVA and post-hoc test (Tukey).\(^b\)Means having a superscript with the same letter are similar.
Table 2. Comparison of dimensions of SF-36 scores between mild and moderate/severe COVID-19 patients following hospital discharge at 1, 2 and 3 mo

| Dimensions of SF-36         | 1 mo posthospital discharge (n=186) | 2 mo posthospital discharge (n=175) | 3 mo posthospital discharge (n=168) |
|-----------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
|                             | Mild (mean±SD)                       | Moderate (mean±SD)                  | Severe (mean±SD)                    |
|                             | (n=75)                              | (n=80)                              | (n=31)*                             |
| Physical functioning        | 88.3±2.3a                           | 63.9±3.4b                           | 61.9±8.8b                           |
| Role limitation due to     | 13.6±2.1a                           | 70.1±4.5c                           | 74.4±1.5c                           |
| physical health             |                                    |                                    |                                    |
| Role limitation due to     | 11.3±4.6a                           | 70.3±3.2b                           | 72.5±8.5b                           |
| emotional health            |                                    |                                    |                                    |
| Energy/fatigue              | 81.3±6.1a                           | 54.1±5.2b                           | 52.2±8.4b                           |
| Emotional well-being        | 84.5±4.3a                           | 57.2±4.3b                           | 54.3±4.7b                           |
| Social functioning          | 87.3±2.1a                           | 61.2±4.6b                           | 58.5±19c                            |
| Pain                        | 12.1±3.1a                           | 80.1±6.1b                           | 83.7±2.1c                           |
| General health              | 87.8±2.0a                           | 60.2±4.8b                           | 56.9±19c                            |

1, 4 and 7 Mean values of patients who had mild COVID-19 symptoms on first, second and third months were compared with repeated measure ANOVA (between groups): F(2,68)=29.13, p<0.001.
2, 5 and 8 Mean values of patients who had moderate COVID-19 symptoms on first, second and third months were compared with repeated measure ANOVA (between groups): F(2,74)=32.23, p<0.001.
3, 6 and 9 Mean values of patients who had severe COVID-19 symptoms on first, second and third months were compared with repeated measure ANOVA (between groups): F(2,23)=32.23, p<0.001.

The mean SF36 scores of mild, moderate and severe groups in each month were compared with one-way ANOVA. There was a statistical significant difference (p<0.05) for all the dimensions within groups in each month.

a, b and c Significant categories within the month based on post-hoc tests (Tukey).
*3 patients died and 14 patients were lost to follow-up within 1 mo.
**3 patients died and 3 patients were lost to follow-up within 1–2 mo of discharge.
***1 patient lost to follow-up within 3 mo of discharge.
5 lost to follow-up.
551 lost to follow-up.
555 lost to follow-up.
Table 3. Outcomes based on severity of disease and the association with vaccine status

| Disease status | Post discharge 1 mo N (%) | Type of complication and outcome | Post discharge 1-2 mo N (%) | Type of complication and outcome | Post discharge 2-3 mo N (%) |
|----------------|---------------------------|---------------------------------|-----------------------------|---------------------------------|-----------------------------|
| Mild COVID-19  | 0                         | N/A                             | 0                           | N/A                             | 0                           |
| (n=75)         |                           |                                 |                             |                                 |                             |
| Non-vaccinated | 0                         |                                 | 0                           | N/A                             | 0                           |
| 1st dose only  | 0                         |                                 | 0                           | N/A                             | 0                           |
| Both doses     |                           |                                 |                             |                                 |                             |
| Moderate COVID-19 | 3 (3.75)\(^1,2,3\) | 1 MI & HF – recovered           | 0                           | N/A                             | 0                           |
| (n=80)         |                           |                                 |                             |                                 |                             |
| Non-vaccinated | 0                         | 2 MI & HF – recovered            | 0                           | N/A                             | 0                           |
| 1st dose only  | 0                         | 3 MI & HF – recovered            | 0                           | N/A                             | 0                           |
| Both doses     |                           | 4 PE – died                      | 0                           | N/A                             | 0                           |
| Severe COVID-19 | 10                        | 1 MI & HF – recovered            | 5 (10.4)\(^1\) to \(^5\) | 1 CVA – recovered               | 0                           |
| (n=48)         |                           |                                 |                             |                                 |                             |
| Non-vaccinated | 20 (8.1)\(^1\) to \(^10\) | 2 MI & HF – died                 | 1 (2.1)\(^1\)              |                                 | 2 CVA – recovered            |
| 1st dose only  | 3 (6.3)\(^11,12,13\)     | 3 MI & HF – recovered            |                             |                                 | with L/side body weakness   |
| Both doses     | 0                         | 4 CVA – recovered with L/side body weakness |                             |                                 | 2 CVA – recovered            |
|                |                           | 5 CVA – recovered with R/side body weakness |                             |                                 | with L/side body weakness   |
|                |                           | 6 CVA – recovered with R/side body weakness |                             |                                 | with L/side body weakness   |
|                |                           | **7 RTI - fungal infection with sepsis - died** |                             |                                 | with L/side body weakness   |
|                |                           | with sepsis - recovered** |                             |                                 | 3 CVA – recovered            |
|                |                           | with lung fibrosis               |                             |                                 | with L/side body weakness   |
|                |                           | 9 RTI - bacterial infection with sepsis-recovered*** |                             |                                 | with L/side body weakness   |
|                |                           | with lung fibrosis               |                             |                                 | 4 ICH - died                 |
|                |                           | 10 PE – recovered                |                             |                                 | 5 ICH - died                 |
|                |                           | 11 AKI - recovered               |                             |                                 | following                   |
|                |                           | 12 GI bleeding – gastric ulcer – recovered |                             |                                 | LRTI with sepsis            |
|                |                           | 13 GI bleeding – gastric ulcer – recovered |                             |                                 | 6 DVT lower                  |
|                |                           |                                 |                             |                                 | limb sepsis                 |
|                |                           |                                 |                             |                                 | and died                    |

Complications (n=23): myocardial infarction with heart failure (MI & HF) (n=6/23; 26.1%), cerebrovascular accident (CVA) (n=6/23; 26.1%), respiratory tract infections (RTI) (n=3/23; 13.01%), pulmonary embolism (PE) (n=2/23; 8.7%), acute kidney injury (AKI) (n=1/23; 4.3%), intracranial haemorrhage (ICH) (n=2/23; 8.7%), gastrointestinal (GI) bleeding (n=2/23; 8.7%), deep vein thrombosis (DVT) and sepsis (n=1/23; 4.3%).

*Aspergillus species.
**Acinetobacter species.
***Methicillin-resistant Staphylococcus aureus.

Proportion of deaths from the complication after discharge: 6/23 (26.1%).
Bold words show the post COVID deaths.
1 to 13 Shows the outcome of post discharged severe COVID patient after one month.

Discussion

There is a scarcity of data from South Asia on the short- and long-term outcomes among COVID-19 patients following hospital discharge. We found cardiovascular complications predominated in our cohort during the first 3 mo posthospital discharge. Using the SF-36 to assess health status among the discharged COVID-19 patients, we found those with mild disease to have less adverse health effects compared with those with moderate or severe disease. Furthermore, early recovery was significantly more common in those with mild compared with moderate or severe cases. However, it was apparent that most of those with moderate or severe COVID-19 also recovered within the 3-mo period. We found non-receipt of a single dose of the COVID-19 vaccine to be significantly associated with severe COVID-19. Following hospital discharge, those who had mild
COVID-19 had fewer complications than those with moderate or severe disease. Three patients had lower RTIs (due to three different organisms) and two had lung fibrosis during the follow-up period. Studies from the West have found a sizeable proportion of patients to have lung fibrosis, interstitial lung diseases and pulmonary hypertension following COVID-19.\textsuperscript{21,22} Post-COVID-19 pulmonary fibrosis is a recognised sequel among survivors, where pulmonary architectural distortion and irreversible pulmonary dysfunction contributes to secondary lung infection.\textsuperscript{23} Furthermore, secondary lung infection may be associated with older age, male gender and smoking.\textsuperscript{24} A possible pathological mechanism of prolonged lung damage includes direct viral cytotoxic damage following binding to ACE2 receptors. This leads to dysregulation of the renin angiotensin aldosterone system, downregulation of ACE2 action and decreased cleavage of angiotensin I and angiotensin II. Tissue injury and remodelling, inflammation, vasoconstriction, increased microvascular permeability, endothelial cell damage leading to endothelitis, apoptosis and thrombo-inflammation, decreased fibrinolysis, increased thrombin production and complement activation may occur. These in turn lead to diffuse alveolar damage and secondary lung infection during post-COVID-19.\textsuperscript{25}

Our study did not find a significant association of vaccine status with age, gender, marital status, educational level, employment status or monthly income. However, some other studies have found older people, females and lower education groups to be at a higher risk of COVID-19 due to vaccine hesitancy and refusal.\textsuperscript{26} Married males living in urban areas, educated for ≤16 y and with low income were hesitant to be vaccinated against COVID-19.\textsuperscript{27,28} Studies also found misleading comments on television, a lack of health education on COVID-19, low income levels, residential area, employment status, family income and higher age to be associated with vaccine hesitancy.\textsuperscript{28,29} As lower vaccine hesitancy leads to better clinical outcomes, appropriate health education is important.

Our study found a high rate of recovery from the post-COVID-19 complications. Currently, it is unclear why some patients experience long-term symptoms after COVID-19. Potential causes for different outcomes include viral load as well as host-dependent factors such as genetic susceptibility or induction of anti-inflammatory cells.\textsuperscript{30} Increased age, female gender, disease severity and body mass index are known attributes and predictors of persistent COVID-19.\textsuperscript{31,32} Prior research has found lower chances of recovery among older COVID-19 patients or those who have underlying diseases such as coronary heart disease or cancer.\textsuperscript{32} We recommend that further large cohort studies should be conducted to identify possible factors contributing to recovery from post-COVID-19 complications.

Studies performed in other regions have found varying time periods (from 3 to 9 mo) for recovery from COVID-19 following

| Variable                                      | All (n=23) | Recovered (n=17) | Died (n=6) | p    |
|-----------------------------------------------|------------|------------------|------------|------|
| Age in y (mean±SD)                            | 61.2±5.4   | 60.2±6.7         | 62.4±7.5   | 0.51*|
| Gender: male, n (%)                           | 14 (60.8)  | 9 (64.3)         | 5 (35.7)   | 0.23**|
| Comorbidities, n (%)                          |            |                  |            |      |
| None                                          | 8 (34.7)   | 5 (62.5)         | 3 (37.5)   | 0.33**|
| Diabetes                                      | 4 (17.4)   | 3 (75.0)         | 1 (25.0)   | 0.18**|
| Hypertension                                  | 4 (17.4)   | 4 (100)          | 0          | N/A  |
| Dyslipidaemia                                  | 6 (26.1)   | 5 (83.3)         | 1 (16.7)   | 0.03**|
| Ischaemic heart disease                       | 2 (8.7)    | 2 (100)          | 0          | N/A  |
| Chronic kidney disease                        | 2 (8.7)    | 2 (50.0)         | 0          | N/A  |
| Asthma/COPD                                    | 2 (8.7)    | 1 (50.0)         | 1 (50.0)   | N/A  |
| Malignancy                                     | 1 (4.3)    | 1 (100)          | 0          | N/A  |
| Length of hospital stay, d (mean±SD)          | 15.21±2.1  | 14.3±2.3         | 16.7±2.5   | 0.04*|
| Vaccination status                            |            |                  |            |      |
| None                                          | 13 (56.6)  | 9 (69.2)         | 4 (30.8)   | 0.04**|
| 1st dose                                      | 8 (34.7)   | 6 (75.0)         | 2 (25.0)   | 0.04**|
| 2nd dose                                      | 2 (8.6)    | 2 (100)          | 0          | N/A  |
| Cyclic threshold value on median day 3 (upon admission) (mean±SD) | 19.4±4.5  | 20.1±2.6         | 17.3±3.1   | 0.04*|

Abbreviations: COPD, chronic obstructive pulmonary disease; N/A, not applicable.
*p value obtained through independent sample t-test.
**p value obtained through comparison of proportions.
hospital discharge. In an Australian study, 80, 90 and 93% recovered by 1, 2 and 3 mo, respectively. On the other hand, in an Italian study of 143 hospital-discharged COVID-19 patients (at a mean of 60 d), 12.6, 32 and 55% were completely free of symptoms, had 1–2 or ≥3 symptoms, respectively. None had fever or features of an acute illness, while the main manifestations were fatigue (53%), dyspnoea (43%), joint pain (27%) and chest pain (22%). Two-fifths reported a poorer quality of life.

Thus there appears to be a variation of outcomes among posthospital-discharged COVID-19 patients in different regions of the world. A few studies have identified factors that are associated with higher rates of complications post-COVID-19, including female gender, respiratory distress during the hospital stay, lethargy and long disease duration. Genetic factors may also play a role and need to be better defined. Other studies have reported cardiovascular complications—myocardial injury, thromboembolic events, arrhythmia and heart failure—following COVID-19. Multiple mechanisms may contribute to this including cytokine (such as IL-6) mediated inflammation, direct viral invasion of cardiomyocytes leading to unopposed effects of angiotensin II, increased metabolic demand, immune activation or microvascular dysfunction. Furthermore, a study conducted in Israel found an increase in STEMI hospitalisations correlated with the end of the first wave of the COVID-19 pandemic. Research has found a strong association between being in the post-COVID-19 period and acute myocardial infarction (AMI). The increased risk of AMI in individuals post-COVID-19 is likely related to dysregulated inflammatory responses and hypercoagulability. Such pathophysiological mechanisms may also be aggravated by other biological, environmental and psychosocial factors. Some of the potential mechanisms for post-COVID-19-related heart involvement includes direct injury via binding to ACE-2 on cardiac myocytes, the massive cytokine storm, an imbalance in subtypes of T-helper cells and increased apoptosis of cardiac myocytes due to hypoxia-induced excessive intracellular calcium accumulation. Among post-COVID-19 patients who developed complications, low vaccine coverage, higher viral loads (low Ct values) and prolonged hospital stay were key factors associated with death. Further studies on initial viral load and post-COVID-19 outcomes need to be carried out in larger cohorts to provide better insights into this aspect.

Study limitations

Our study has some limitations. First, the study was conducted at a single centre and would need to be assessed in multiple centres using larger sample sizes. However, the observed post-COVID-19 effects give an insight into this aspect in a South Asian cohort. Second, the study did not assess the reasons behind the observed vaccine hesitancy in some. We suggest that these factors be considered in future studies. Third, the study sample was from a private hospital in Sri Lanka. As a result, higher proportions of the sampled population reside in urban areas and have higher levels of education. An over-representation of such individuals may lead to an underestimation of vaccine hesitancy.

Conclusion

In our cohort, receiving two doses of the COVID-19 vaccine was associated with reduced disease severity. Those with mild disease recovered faster than those having moderate/severe disease. Over 90% recovery was observed at 3 mo following hospital discharge in this group of COVID-19 patients.

Supplementary data

Supplementary data are available at Transactions online.

Authors’ contributions: VA, SLS, SDM, APS, RM, TS, AF, CDM and LC conceptualised the study; VA, RSW, SM and PDM collected the data; VA, SLS, SDM, and RM analysed the data; VA, SLS, SDM and RM wrote the manuscript; VA, LC, CDM, SA, AF and SDM conducted a critical review and editing of the manuscript. All the authors read and approved the final version of the manuscript. VA, SLS and SDM are guarantors of the paper.

Acknowledgements: We acknowledge the assistance given by the Director/General Manager and the management of the Nawaloka Hospital PLC, Colombo, Sri Lanka. We also thank the staff of the Medical Records Office and Computer Division unit of Nawaloka Hospital, Colombo. Finally, we thank all patients and next-of-kin for providing the necessary information required for the study.

Funding: No funding source was available.

Competing interests: None.

Ethical approval: Ethical approval for this study was obtained from the ethical committee of Nawaloka Hospital, Colombo, Sri Lanka.

Data availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Nalbandian A, Sehgal K, Gupta A, et al. Post-acute COVID-19 syndrome. Nat Med. 2021;27(4):601–15.
2. Seneviratne SL, Yassawadene P, Hettiarachchi D, et al. The Delta variant of SARS-CoV-2: the current global scourge. Sri Lankan Family Physician. 2021;36:17–25.
3. Seneviratne SL, Jayarajah U, Abeyesuriya V, et al. COVID-19 vaccine landscape. J Ceylon College Physicians. 2020;51(2):120.
4. Seneviratne S, Nilofaa R, De Zoysa I, et al. Remdesivir and COVID-19. Int J Adv Res. 2020;8(4):565–7.
5. Seneviratne SL, Abeyesuriya V, De Mel S, et al. Favipiravir in Covid-19. JIPSAT. 2020;19:143–5.
6. Mendelson M, Nel J, Blumberg L, et al. Long-COVID: An evolving problem with an extensive impact. S Afr Med J. 2020;111(1):10–2.
7. Kariyawasam JC, Jayarajah UJ, Riza R, et al. Gastrointestinal manifestations in COVID-19. Trans R Soc Trop Med Hyg. 2021;12:1362–88.
8. Rahman A, Nilofaa R, De Zoysa IM, et al. Neurological manifestations in COVID-19: A narrative review. SAGE Open Med. 2020;8:205031212095792.
9. Rahman A, Nilaoa R, Jayarajah U, et al. Hematological abnormalities in COVID-19: a narrative review. Am J Trop Med Hyg. 2021;104(4):1188–201.

10. Jayasekara D, Seneviratne SL, Jayasekara A, et al. Atypical presentations of COVID-19. Adv Infect Dis. 2020;10(3):136–42.

11. Abeysuriya V, Seneviratne SL, de Silva AP, et al. Combination of cycle threshold time, absolute lymphocyte count and neutrophil:lymphocyte ratio is predictive of hypoxia in patients with SARS-CoV-2 infection. Trans R Soc Trop Med Hyg. 2021. [Online ahead of print].

12. Gupta A, Madhavan MV, Sehgal K, et al. Extrapulmonary manifestations of COVID-19. Nat Med. 2020;26(7):1017–32.

13. Tenforde MW, Kim SS, Lindsell CJ, et al. Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network — United States, March–June 2020. MMWR Morb Mortal Wkly Rep. 2020;69(30):993–8.

14. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis. 2020;20(5):533–4.

15. Iba T, Connors JM, Spyropoulos AC, et al. Ethnic differences in thromboprophylaxis for COVID-19 patients: Should they be considered? Int J Hematol. 2021;113(3):330–6.

16. AccuPower ® SARS-CoV-2 Real-Time RT-PCR Kit. 2020.

17. RealStar® SARS-CoV-2 RT-PCR Kit – Altona-Diagnostics EN. 2020.

18. Lansokara N, Wickramasinghe AR, Seneviratne HR. Feeling the blues of infertility in a South Asian context: Psychological well-being and associated factors among Sri Lankan women with primary infertility. Women Health. 2011;51(4):383–99.

19. Dissabandara L, Loxton N, Dias S, et al. Psychometric properties of three personality inventories translated to Sinhalese. Sl J Psychiatry. 2011;2:13–7.

20. Ministry of Health - Sri Lanka. Provisional Clinical Practice Guidelines on COVID-19 Suspected and Confirmed Cases. Sri Lanka: Ministry of Health; 2020.

21. Atabati E, Dehghani-Samani A, Mortazavi-moghadam SG. Association of COVID-19 and other viral infections with interstitial lung diseases, pulmonary fibrosis, and pulmonary hypertension: A narrative review. Can J Respir Ther. 2020;56:70–8.

22. Solomon JJ, Heyman B, Ko JP, et al. CT of post-acute lung complications of COVID-19. Radiology. 2021;2:211396.

23. Ojo A, Bologun S, Williams O, et al. Pulmonary fibrosis in COVID-19 survivors: predictive factors and risk reduction strategies. hindawi.com [accessed 9 September 2021].

24. Ali RMM, Gokhiniy MBI. Post-COVID-19 pneumonia lung fibrosis: a worrisome sequela in surviving patients. Egyptian J Radiol Nucl Med. 2021;52(1):101.

25. Elizalde González JJ. Pulmón post-COVID. Medicina Crítica. 2020;34(6):318–9.

26. Samo AA, Sayed RB, Valecho J, et al. Demographic factors associated with acceptance, hesitancy, and refusal of COVID-19 vaccine among residents of Sukkur during lockdown: A cross sectional study from Pakistan. Hum Vaccin Immunother. 2022;021:1–5.

27. Ali M, Hossain A. What is the extent of COVID-19 vaccine hesitancy in Bangladesh? A cross-sectional rapid national survey. BMJ Open. 2021;11:e050303.

28. Al-Mohaithef M, Padhi BK, Ennaceur SA. Demographics of COVID19 vaccine hesitancy during the second wave of COVID-19 pandemic: A cross-sectional web-based survey in Saudi Arabia. medrxiv.org [accessed 2 September 2021].

29. Marzo RR, Sami W, Alam MZ, et al. Hesitancy in COVID-19 vaccine uptake and its associated factors among the general adult population: a cross-sectional study in six Southeast Asian countries. Trop Med Health. 2022;50(1):4.

30. Seeßle J, Waterboer T, Hippchen T, et al. Persistent symptoms in adult patients 1 year after coronavirus disease 2019 (COVID-19): a prospective cohort study. Clin Infect Dis. 2021;7:1191–8.

31. Salamanna F, Veronesi F, Martini L, et al. Post-COVID-19 syndrome: the persistent symptoms at the post-viral stage of the disease. A systematic review of the current data. Front Med. 2021;8:392.

32. Oskomaiya B, Erinozo O, Wright KO, et al. ‘Long COVID’ persistent COVID-19 symptoms in survivors managed in Lagos State, Nigeria. BMC Infect Dis. 2021;21(1):302–7.

33. Zandkarimi E. Factors affecting the recovery of Kurdistan province COVID-19 patients: A cross-sectional study from March to June 2020. Epidemiol Methods. 2021;10(s1):1–6.

34. Zayet S, Zahra H, Royer PY, et al. Post-COVID-19 syndrome: nine months after SARS-CoV-2 infection in a cohort of 354 patients: data from the first wave of COVID-19 in Nord Franche-Comté Hospital, France. Microorganisms. 2021;9(18):1719–23.

35. Otte MS, Bork ML, Zimmermann PH, et al. Persisting olfactory dysfunction improves in patients 6 months after COVID-19 disease. Acta Oto-laryngol. 2021;141(6):626–9.

36. Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet. 2021;397(10270):220–32.

37. Goertz YM, Van Herck M, Debrelissine JM, et al. Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome? ERJ Open Res. 2020;6(4):00542–2020.

38. van den Borst B. Recovery after Covid-19. Lancet Regional Health - Western Pacific. 2021;12:1–4.

39. Carfi A, Bernabei R, Landi F. Persistent symptoms in patients after acute COVID-19. JAMA. 2020;324(6):603–5.

40. Mahmud R, Rahman MM, Rassel MA, et al. Post-COVID-19 syndrome among symptomatic COVID-19 patients: A prospective cohort study in a tertiary care center of Bangladesh. PLoS One. 2021;16(4):e0249644.

41. Hou Y, Zhao J, Martin W, et al. New insights into genetic susceptibility of COVID-19: An ACE2 and TMPRSS2 polymorphism analysis. BMC Med. 2020;18(1):216.

42. Genome-wide association study of severe Covid-19 with respiratory failure. N Engl J Med. 2020;383(16):1522–34.

43. Lee CCE, Ali K, Connell D, et al. COVID-19-associated cardiovascular complications. Diseases. 2021;9(3):47.

44. Rubin EJ, Longo DL, Baden LR. Interleukin-6 receptor inhibition in Covid19 — cooling the inflammatory soup. N Engl J Med. 2021;384(16):1564–5.

45. Liu PP, Blet A, Smyth D, et al. The science underlying COVID-19. Circulation. 2020;142(1):68–78.

46. Campbell CM, Kahwash R. Will complement inhibition be the new target in treating COVID-19-related systemic thrombosis? Circulation. 2020;141(22):1739–41.

47. Chen L, Li X, Chen M, et al. The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2. Cardiovasc Res. 2020;116:1097–100.

48. Faridman A, Oren D, Berkovitch A, et al. Post COVID-19 acute myocardial infarction rebound. Can J Cardiol. 2020;36(11):1832.e15–6.
49. Clerkin KJ, Fried JA, Raikhelkar J, et al. COVID-19 and cardiovascular disease. Circulation. 2020;141(20):1648–55.

50. Gorini F, Chatzianagnostou K, Mazzone A, et al. “Acute Myocardial Infarction in the Time of COVID-19”: a review of biological, environmental, and psychosocial contributors. Int J Environ Res Public Health. 2020;17(20):1–17.

51. Naz A, Billah M. COVID-19 and coronary heart disease. Encyclopedia. 2021;1(2):340–9.

52. Oudit GY, Kassiri Z, Jiang C, et al. SARS-coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS. Eur J Clin Invest. 2009;39(7):618–25.