Original Article

# DOES THE SUFFERING END AFTER CURE FROM COVID?

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## Abstract

**Background:** Multisystem involvement of Covid-19 has been known since beginning of the pandemic. Multisystem after-effects or sequelae of covid-19 have been noted and the term 'long Covid' encompasses these signs and symptoms. This leads to prolonged morbidity which have not been adequately addressed by Covid guidelines.The primary aim of our study was to know the spectrum of different sequelae patients have endured after recovery from acute Covid-19 and study their impact on their quality of life.

**Methods:** It was a longitudinal observational study of a cohort of 146 patients who recovered from Covid-19 illness. Patients were enrolled within a week of their onset of Covid symptoms and were followed up monthly for a duration of 6 months with a detailed clinical and investigational pulmonary, cardiac, neurological and psychiatric assessment anda final follow-up after a year. Impact on quality of life was assessed using EQ-5D-3L questionnaire. Those lost to follow up were excluded from the analysis.

**Results:** 120/146 patients qualified for final analysis. Pulmonary sequelae (40%) were the majority among the patients, followed by psychiatric (25%), neurological (21.7%) and opportunistic infections (5.8%). 4/120 died within a year. 62/120 patients documented worsening in quality of life. Sequelae like pulmonary fibrosis, PTSD had the worst impact on the quality of life.95% severe, 54.5% moderate and 25% mild Covid patients reported deterioration in QoL score respectively.

**Conclusion:** Study indicates health related consequences from Covid-19 extend far beyond acute infection andmake significant impact on their quality of life, regardless of the severity of the disease.

**Keywords:** Covid, Sequelae, Multisystem, Quality of life, Impact

## INTRODUCTION:

The World Health Organization (WHO) declared Coronavirus Disease-19 (Covid-19, hereafter mentioned as only Covid) as a pandemic on March 11, 2020 owing to the widespread impact of its morbidity and mortality.[1] Although the respiratory system suffers the most from this disease, many of the body's major systems might get compromised by the virus. Numerous respiratory, circulatory, neurological, and musculoskeletal problems may continue even after Covid has been treated.[2] Depending on the severity of the illness, active Covid symptoms often last for 1 to 4 weeks. Most infections are mild or even asymptomatic, particularly in children and

adolescents, and as people age and have additional co-morbidities, their chances of developing severe illness and needing hospitalisation significantly rise.[3]

Globally, a small percentage of patients who suffered from Covid are exhibiting a variety of chronic persistent symptoms that may persist for several months. In addition to the acute phase morbidity and mortality, many Covid survivors experience post-Covid health issues and sequelae. [2, 4]

In addition to direct viral damage, the immune system, cytokine storm, adverse effects of the treatment, pre-existing co-morbidities or a combination of these; all leave a significant mark on the patient's life. In addition, psychological elements such as extended isolation, fear of death, worry about infecting family members, socioeconomic problems, and the stigma associated with the infection may have significant effects on mental health and wellbeing that causes an impact on quality of life.[5] The terminology "long-covid" is frequently used to refer to signs and symptoms that persist or new symptoms occurring after 4 weeks following acute Covid. It comprises of both persistent Covid symptoms and the "post Covid-19 syndrome". Post-Covid syndrome is the terms used for persons whose symptoms started/persisted for three months after the acute Covid and are not explained by a different diagnosis.[6]

The primary aim of the study was to evaluate the spectrum of different sequelae or after-effects that patients have endured after suffering from Covid in the first 6 months after recovery from the acute infection and the impact this disease had on their quality of life.

## MATERIALS AND METHODS:

This longitudinal observational study was conducted during October 2020 to July 2022, in a dedicated Covid hospital of a tertiary care centre in Pune, India. Approval from the institutional ethics committee was obtained before commencement of the study. Patients aged 18 years and above who were throat swab confirmed cases of Covid and had recovered from acute disease were enrolled in the study after obtaining their informed consent. A confirmed case of Covid was defined as a patient whose nasopharyngeal swab was positive for SARS-CoV-2 by RT-PCR (Quantitative real-time reverse transcription polymerase chain reaction) and recovery from acute disease was defined as time period after 4 weeks from onset of symptoms of Covid.[6] For analytical purpose, the enrolled subjects were classified in to categories based on the disease severity as per the guidelines set by Indian Council of Medical Research.[7] Pregnancy, language barrier, inability to perform the diagnostic tests or fill out questionnaire as required by the protocol etc. were excluded from the study.

146 patients were enrolled in the study. On the day of enrolment, each patient’s demographics, medical history, hospitalization details and treatment details were recorded. Enrolled patients were followed up every month for a period of 6 months telephonically and once in person for Pulmonary assessment (symptomatology, respiratory examination, chest imaging, pulse oximetry, six-minute walk test, spirometry), neurological assessment, cardiac assessment (ECG, echocardiography) and psychological assessment/screening. Psychiatric screening was done using M.I.N.I. version 5.0.0 questionnaire. Patients were followed up telephonically again at the end of one year of enrolment for understanding the final status of post Covid sequelae and overall well-being. For evaluation of impact on quality of life, patients were asked to fill the EuroQoL (EQ-5D-3L) questionnaire at the time of enrolment and at the end of 6 months of follow up. It comprised of five questions with three possible responses for each (1 being no problems, 2 being some problems and 3 being major or extreme problems) about mobility, self-care, usual/routine activities, pain & discomfort and anxiety or depression.

Data processing and analysis was conducted in SPSS 26.0.Categorical variables were expressed in frequencies and proportions. Normality of Continuous variables were tested by Kolmogorov Smirnov test. Mann-Whitney test and Kruskall Wallis test was applied to test the association between categorical variables and continuous variables. Wilcoxon signed rank test was used to assess the significance in the difference between pre and post COVID-19 quality of life. A p-value of less than 0.05 was statistically significant.

## RESULTS:

Out of the 146 enrolled subjects, 10 revoked consents during the follow up period and 16 were dropped out of the study due do various reasons such as lost to follow up due to relocation, death, etc. Data of remaining cohort of 120 patients was analysed. The mean age of the study patients was 41.7 years with a range of 20-83 years. Majority of the patients were however in the younger age group of 21-30 years (50.8%). 76/120 (63.3%) were males and 44/120 (34.7%) were females. A large proportion of the enrolled subjects were healthcare workers (43/120 i.e. 35.8%), followed by Service industry workers (23/120 i.e. 19.2%) and 24/120 (20%) were unemployed. 72/120 (62%) cases were hospitalized during their acute illness phase for treatment. 51/120 (43%) had moderate or severe disease. 19/120 (15.8%) patients in the study population received intensive care treatment. Mean duration of hospital stay for hospitalized patients was 17.5 days with a range of 1 to 50 days.

Various sequelae reported by the patients were categorized based on the organ system involved (Figure 1). 74/120 (62%) of enrolled patients suffered from some or other form of structural or functional post Covid sequelae. Pulmonary sequelae were the majority (48/120 i.e. 40%), followed by psychiatric (30/120 i.e. 25%), neurological (26/120 i.e. 21.7%) and opportunistic infections (7/120 i.e. 5.8%). Among the pulmonary sequelae, patients complained of prolonged symptomatology on follow up. Complaints such as prolonged dyspnoea and cough were reported by 32.5% (39/120) and 9.2% (11/120) participants respectively. 21.7% (26/120) cases had radiologically confirmed signs of pulmonary fibrosis. 2.5% (3/120) cases suffered from spontaneous pneumothorax during their follow up period and required management with tube thoracostomy.2/120 (1.6%) and 1/120 (0.8%) cases were diagnosed with pleural effusion and pulmonary thromboembolism respectively. Among the psychological sequelae, depression, generalized anxiety disorder, dysthymia and post traumatic stress disorder (PTSD) was reported among 2/120 (1.7%), 10/120 (8.3%), 13/120 (10.8%) and 8/120(6.7%) patients respectively during screening. Among the neurological sequelae, persistent headache, persistent ageusia, persistent anosmia and neuropathywas found in 7/120 (5.8%), 6/120(5%), 11/120 (9.2%)and 1/120 (0.8%) patients respectively.7/120 (5.8 %) patients were diagnosed with mucormycosis, either rhinocerebral, pulmonary or sino-orbital, the mean time of occurrence being approximately 3 weeks from the Covid recovery.

Impact on quality of life assessed using the EuroQoL questionnaire found statistically significant change in quality-of-life (QoL) score, as mentioned in table 1. Total of 62/120 patients (51.66%) in the study population had documented deterioration in quality of life during follow-up. The overall mean QoL score in the study was 5.99 (SD=1.19) with baseline being 5. Individually, mobility domain had the maximum score (mean=1.31, max=3) followed by anxiety and depression(mean=1.28, max=3) (Figure 2).Approximately 39/41 (95%) severe, 6/11 (55.4%) moderate and 17/68 (25%) mild Covid cases in the study reported worsening in the quality of life score compared to at the start of the study. Comparison of quality-of-life score with severity of disease is shown in table 2.

## DISCUSSION:

About 30% of Covid patients who were followed for up to 9 months after the illness experienced ongoing symptoms, according to one study.[8] Long Covid, post-acute Covid-19 syndrome (PACS), or post-acute sequelae of Covid-19 (PASC) are the diagnoses given to these patients.[9] Existing data suggests that those with severe acute Covid are being diagnosed with post-acute sequelae, but so are patients with mild symptoms or even asymptomatic cases.[8] In our study as well, both severe as well as mild cases were diagnosed with post-acute sequelae.

On follow-up, majority patients were compliant with the protocol. During the span of one year follow-up of these cases, 4/120 (3.3%) had died. Cause of death in these cases was either attributed to the post-covid status or their underlying comorbidities.

Pulmonary sequelae, being the majority, included both structural sequelae such as pulmonary fibrosis, pneumothorax as well as functional/symptomatologic sequelae. Even though prolonged dyspnoea was the most

common sequela, 36/120 (30%) of these cases didn't have any structural lung abnormality which suggests others factors at play causing dyspnoea such as psychogenic causes, post viral weakness, etc. Pulmonary fibrosis may be attributed to post ARDS recovery whereas increased alveolar pressure and alveolar damage in severe Covid leading to subsequent rupture and leakage of air may explain post-covid pneumothorax/pneumomediastinum.[10 – 12] Opportunistic infections like Mucormycosis was noted in 7/120 (5.8%) of our study participants, and was observed in patients with uncontrolled diabetes during their Covid illness.

In our study, there was significant decline in the Quality of Life in all domains after Covid. Tabacof et al. found significant impact on patients' QoL in all the 5 domains after Covid which was in accordance with our study.[13] Interestingly, 17/68 (25%) of the mild covid patients in our study also reported deterioration in quality of life based on the scoring questionnaire. This highlights the fact that Covid can have a significant impact on quality of life of patients suffering from any grade of severity of the disease. Overall quality of life as well as in separate domains such as in mobility, self-care, usual activities, anxiety/depression was found to be significantly worse in patients with severe Covid. 47/63 (74.2%) of the patients who reported decline in quality of life had history of hospitalization for their Covid treatment. Hospitalized patients showed greater impact in domains like mobility (43/63 i.e. 67.56%) and anxiety/depression (57/63 i.e. 90.4%) compared to those who were not hospitalized. This can be attributed to the higher severity of disease leading to pulmonary sequelae as well as the psychological impact of hospitalization, financial burden or fear of death. Additionally, patients who developed sequelae like pulmonary fibrosis and PTSD had far worse decline in quality of life compared to those with other structural/functional sequelae. Similar studies done in other parts of the world also have reported significant impact on physical as well as psychological heath of the survivors.[14, 15]

Our study indicates that health related consequences from Covid extend far beyond an acute viral infection. Post Covid sequalae extend from minor persistent symptoms to life altering complications and can happen post severe as well as mild disease and can significantly affect the quality of life of these patients. A thorough systematic post Covid follow-up is therefore warranted in all patients for appropriate physical and psychological rehabilitation.

Figure 1: Pie-chart depicting the multi-system sequelae post Covid-19 recovery

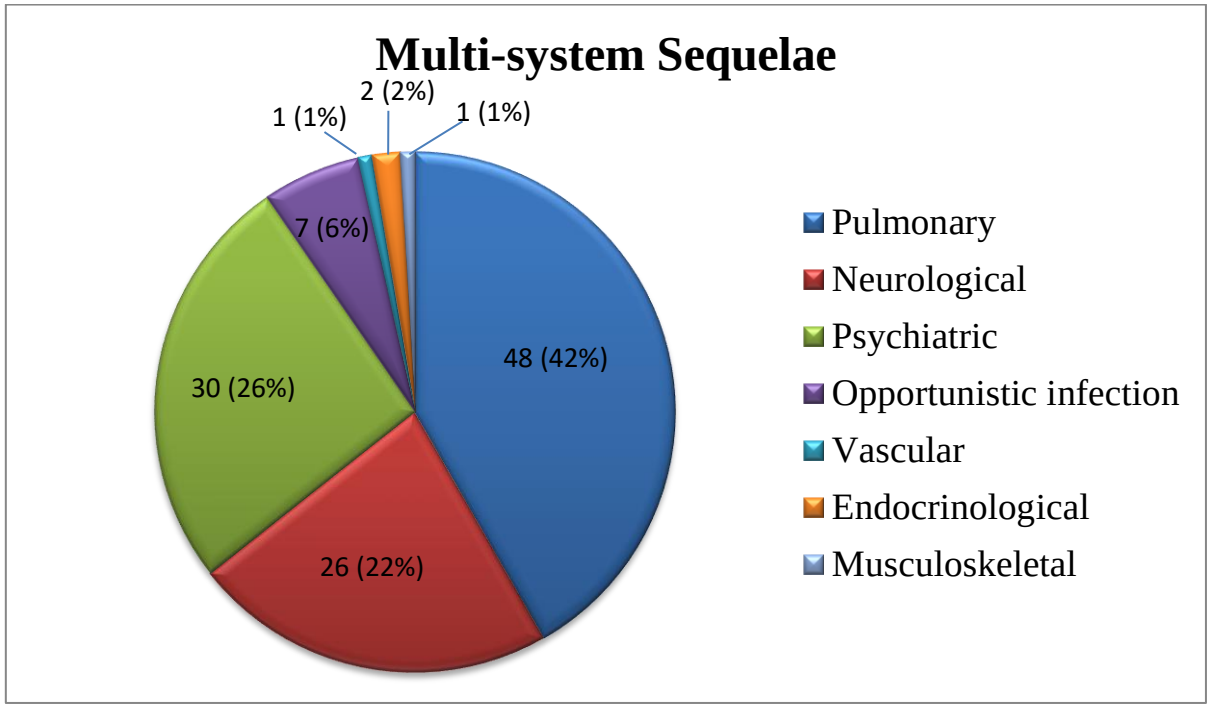

Figure 2: Covid survivor responses to the EuroQol (EQ-5D-3L) questionnaire

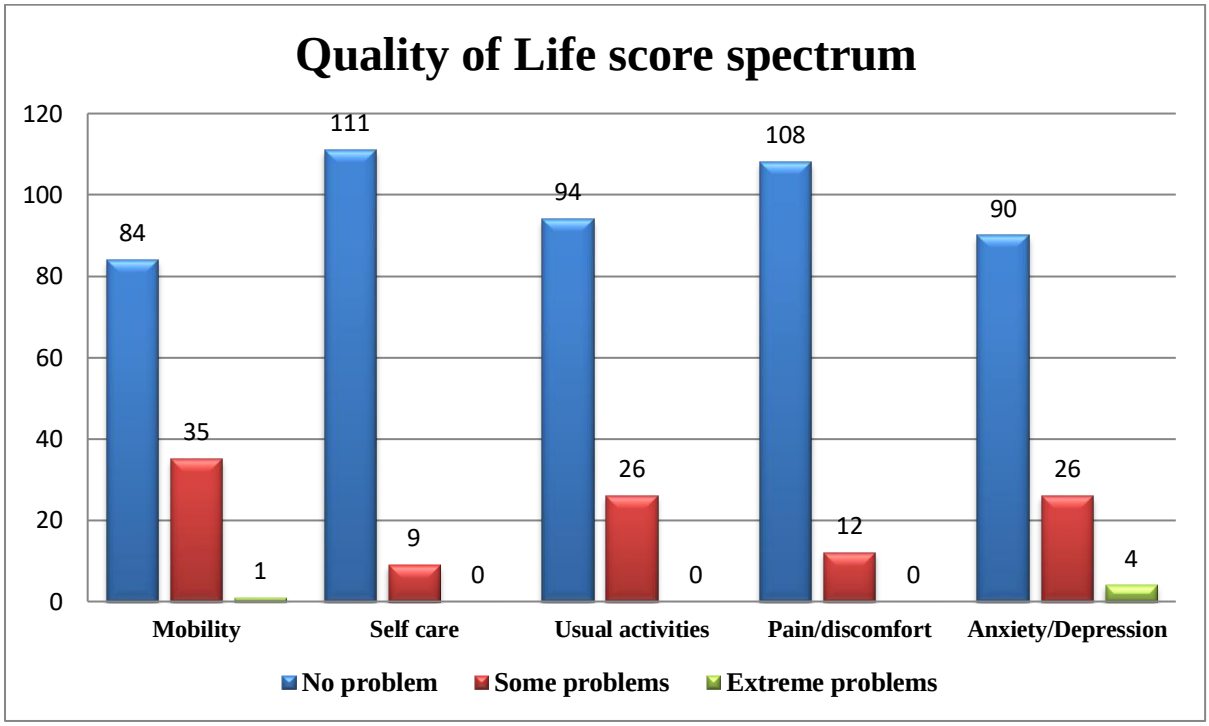


Table 1: Table depicting statistical evaluation of EuroQol questionnaire responses.

| | **Pre-COVID19** | | | | **Post-COVID19 (follow-up)** | | | | **p value*** |
|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Median | IQR | Mean | SD | Median | IQR | |
| Mobility | 1 | 0 | 1 | 1,1 | 1.31 | 0.48 | 1 | 1,2 | **<0.001** |
| Self-care | 1 | 0 | 1 | 1,1 | 1.08 | 0.26 | 1 | 1,1 | **0.003** |
| Usual Activities | 1 | 0 | 1 | 1,1 | 1.22 | 0.41 | 1 | 1,1 | **<0.001** |
| Pain/ discomfort | 1 | 0 | 1 | 1,1 | 1.11 | 0.31 | 1 | 1,1 | **<0.001** |
| Anxiety/ Depression | 1 | 0 | 1 | 1,1 | 1.28 | 0.52 | 1 | 1,1.75 | **<0.001** |
| Total | 5 | 0 | 5 | 5,5 | 5.99 | 1.19 | 6 | 5,7 | **<0.001** |

Table 2: Table depicting relationship of QoL score with severity of disease.

| **Ranks** | | | | |
|---|---|---|---|---|
| Severity | | N | Mean Rank | p value* |
| **QoL1 (mobility)** | Mild | 68 | 47.75 | **<0.001** |
| | Moderate | 11 | 64.14 | |
| | Severe | 41 | 80.67 | |
| | Total | 120 | | |

| | | | | |
|---|---|---|---|---|
| **QoL 2 (Self-care)** | Mild | 68 | 56.88 | **0.002** |
| | Moderate | 11 | 56.00 | |
| | Severe | 41 | 67.71 | |
| | Total | 120 | | |
| **QoL 3(Usual Activities)** | Mild | 68 | 50.15 | **<0.001** |
| | Moderate | 11 | 74.77 | |
| | Severe | 41 | 73.84 | |
| | Total | 120 | | |
| **QoL 4 (Pain/discomfort)** | Mild | 68 | 58.41 | 0.069 |
| | Moderate | 11 | 54.00 | |
| | Severe | 41 | 65.71 | |
| | Total | 120 | | |
| **QoL 5 (Anxiety/depression)** | Mild | 68 | 55.10 | **0.009** |
| | Moderate | 11 | 56.05 | |
| | Severe | 41 | 70.65 | |
| | Total | 120 | | |
| **QoL (total)** | Mild | 68 | 42.79 | **<0.001** |
| | Moderate | 11 | 62.95 | |
| | Severe | 41 | 89.22 | |
| | Total | 120 | | |

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