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A PROSPECTIVE COHORT STUDY FOR COMPREHENSIVE ASSESSMENT OF RESPIRATORY MORBIDITY OF COVID-19 AMONG SARS-COV2 SURVIVORS

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Abstract

Introduction: COVID-19, caused by the novel coronavirus SARS-CoV-2, was first identified in December 2019 in Wuhan, China. It rapidly evolved into a global health crisis, challenging modern healthcare systems and public health policies. Long COVID, also known as Post-Acute Sequelae of SARS-CoV-2 infection (PASC), refers to a range of symptoms and health complications that persist for weeks or months after the acute phase of COVID-19 has resolved. The World Health Organization (WHO) defines Long COVID as symptoms that last for at least two months and occur three months after infection. These symptoms can significantly impact the quality of life, with some patients experiencing lasting issues long after recovery from the initial infection. This study was done with the aim to investigate the impact of extended morbidity of covid-19 among SARS CoV-2 survivors.

Material and method: The study is conducted at the Department of Respiratory Medicine, National Institute of Medical Science and Research, Jaipur, Rajasthan. We observed 235 patients in 18 months period.

Result: A total of 235 participants were included in this prospective cohort study assessing respiratory morbidity among SARS-CoV-2 survivors. Of the study population, 136 (57.9%) were male, and 99 (42.1%) were female. The mean age of the participants was 59.49 years, with a standard deviation of ±16.99 years

Conclusion: Given the complexity of the long-term impact of COVID-19, further research is critical to fully understand the mechanisms behind these lingering symptoms and immune responses. Longitudinal studies exploring immune system regulation, including the role of IgG and other immune markers, in SARS-CoV-2 survivors are necessary to identify potential therapeutic targets. Moreover, a deeper understanding of how severe illness and comorbidities influence long-term respiratory
health is essential to developing strategies for better management and recovery of affected individuals. Ultimately, such research will contribute to improving clinical management strategies and enhancing quality of life for COVID-19 survivor.

Keywords: SARS-CoV-2, Covid-19, Lung

Introduction

COVID-19, caused by the novel coronavirus SARS-CoV-2, was first identified in December 2019 in Wuhan, China. It rapidly evolved into a global health crisis, challenging modern healthcare systems and public health policies. The virus's highly contagious nature, with a basic reproduction number (R0) estimated between 2 and 3 during early outbreaks, contributed to its swift spread [1]. The WHO declared COVID-19 a pandemic on March 11, 2020, highlighting its international reach and severe implications.

Global mortality from COVID-19 exceeds 7 million as of November 2024, with significant disparities between high-income and low-income countries. Early in the pandemic, mortality was highest among older adults and individuals with underlying conditions, such as diabetes and cardiovascular disease [1]. Vaccination campaigns have since mitigated mortality, although inequitable vaccine distribution left many regions vulnerable [2].

Beyond acute illness, COVID-19 has imposed a long-term health burden on survivors. Hospitalization rates during major surges strained healthcare systems, delaying care for other conditions. A subset of survivor's experiences Long COVID, a condition characterized by symptoms such as fatigue, dyspnea, and cognitive dysfunction lasting months beyond the acute phase. Studies estimate that 10–30% of those infected may develop persistent symptoms, underscoring the importance of long-term health monitoring [3].

The clinical manifestation of COVID-19 varies widely, ranging from asymptomatic infection to life-threatening conditions. The majority of individuals infected with SARS-CoV-2 present with mild symptoms, such as fever, cough, fatigue, and sore throat, which resolve within a few days to a week. However, approximately 20% of patients progress to severe disease, which can manifest as pneumonia, ARDS, and, in some cases, multi-organ failure [4]. Emerging evidence also suggests that a portion of individuals who recover from acute COVID-19 continue to experience symptoms well beyond the acute phase. This condition, known as Long COVID or post-acute sequelae of SARS-CoV-2 infection (PASC), includes a wide range of symptoms such as fatigue, shortness of breath, cognitive dysfunction, and chronic pain. These symptoms can last for months, significantly impairing quality of life and highlighting the need for further research into the mechanisms behind these long-term effects [5].

Long COVID, also known as Post-Acute Sequelae of SARS-CoV-2 infection (PASC), refers to a range of symptoms and health complications that persist for weeks or months after the acute phase of COVID-19 has resolved. The World Health Organization (WHO) defines Long COVID as symptoms that last for at least two months and occur three months after infection. These symptoms can significantly impact the quality of life, with some patients experiencing lasting issues long after recovery from the initial infection [6]. This study was done with the aim to investigate the impact of extended morbidity of covid-19 among SARS CoV-2 survivors.

Method and material

The study is designed as a longitudinal cohort study. This design facilitates the observation and analysis of long-term health outcomes and morbidity among COVID-19 survivors over an extended period. The participants are followed over time to track the persistence, recurrence, or emergence of health issues.

The study is conducted at the Department of Respiratory Medicine, National Institute of Medical Science and Research, Jaipur, Rajasthan. We observed 235 patients in 18 months period. We onserved values at baseline, at 3 months and then at 6 months. Patients aged >18 years with confirmed SARS-CoV-2 infection via PCR testing (Swab or sputum samples) and gave informed consent were included in this study. Patients with active pulmonary tuberculosis or other pulmonary infections, malignancies , sarcoidosis, chronic liver disease, chronic kidney disease or immunodeficiency disorder were excluded from this study. This location provides access to a diverse population of post-COVID patients seeking medical care. The study received clearance from the Institutional Scientific and Ethics Committee. Data were analyzed using SPSS Version 23 and Microsoft Excel.

Result

Table 1- Distribution of cases according to demographic data

Parameters	**Frequency (Percentage)**
Total Sample	235 (100.0%)
Gender	
Female	99 (42.1%)
Male	136 (57.9%)
Age, Mean ± SD	59.49 ± 16.99

A total of 235 participants were included in this prospective cohort study assessing respiratory morbidity among SARS-CoV-2 survivors. Of the study population, 136 (57.9%) were male, and 99 (42.1%) were female. The mean age of the participants was 59.49 years, with a standard deviation of ±16.99 years.

Table 2- distribution of cases according to chief complaints

	Baseline		**3 months followup**		**6 months followup**	
Chief Complaint	**Yes (Frequency %)**	**No (frequency %)**	**Yes (Frequency %)**	**No (Frequency %)**	**Yes (Frequency %)**	**No (Frequency %)**
Cough	109 (46.4%)	126 (53.6%)	71 (30.2%)	164 (69.8%)	109 (46.4%)	126 (53.6%)
Breathlessness	212 (90.2%)	23 (9.8%)	211 (89.8%)	24 (10.2%)	211 (89.8%)	24 (10.2%)
Fever	154 (65.5%)	81 (34.5%)	154 (65.5%)	81 (34.5%)	154 (65.5%)	81 (34.5%)
Fatigue	199 (84.7%)	36 (15.3%)	199 (84.7%)	36 (15.3%)	188 (74.7%)	47 (25.3%)
Diarrhoea	145 (61.7%)	90 (38.3%)	145 (61.7%)	90 (38.3%)	145 (61.7%)	90 (38.3%)
Arthralgia	190 (80.9%)	45 (19.1%)	190 (80.9%)	45 (19.1%)	178 (70.9%)	57 (29.1%)
Gastritis	135 (57.4%)	100 (42.6%)	135 (57.4%)	100 (42.6%)	135 (57.4%)	100 (42.6%)
Loss of Taste	203 (86.4%)	32 (13.6%)	204 (86.8%)	31 (13.2%)	194 (76.8%)	41 (23.2%)
Nausea/Vomiting	155 (66.0%)	80 (34.0%)	126 (53.6%)	109 (46.4%)	141 (60.0%)	94 (40.0%)
Headache	169 (71.9%)	66 (28.1%)	165 (70.2%)	70 (29.8%)	169 (71.9%)	66 (28.1%)

At baseline, the chief complaints of the participants were documented, with varying frequencies. Breathlessness was the most common complaint, reported by 212 participants (90.2%), followed by loss of taste (203 participants, 86.4%), and fatigue (199 participants, 84.7%). Arthralgia was reported by 190 participants (80.9%), while headache was noted in 169 participants (71.9%). Fever and nausea/vomiting were reported by 154 (65.5%) and 155 (66.0%) participants, respectively. Diarrhea was present in 145 participants (61.7%), and gastritis in 135 participants (57.4%). Cough was the least frequently reported symptom, affecting 109 participants (46.4%). These findings highlight the diverse range of symptoms experienced by SARS-CoV-2 survivors at baseline, with respiratory and systemic complaints being predominant.

At the 3-month follow-up, the prevalence of chief complaints remained high among the participants, though some symptoms showed changes in frequency. Breathlessness continued to be the most prevalent complaint, affecting 211 participants (89.8%), followed by fatigue (199 participants, 84.7%) and loss of taste (204 participants, 86.8%). Arthralgia persisted in 190 participants (80.9%), and headache was reported by 165 participants (70.2%). Fever remained common, with 154 participants (65.5%) still reporting it, while 145 participants (61.7%) reported diarrhea, and 135 participants (57.4%) experienced gastritis. Cough decreased significantly, affecting only 71 participants (30.2%), while nausea/vomiting was reported by 126 participants (53.6%). These results suggest that while certain symptoms, particularly breathlessness and fatigue, persisted, others, such as cough, showed notable improvement over the three-month period.

At the 6-month follow-up, the frequency of chief complaints among the participants showed some changes compared to earlier time points. Breathlessness remained the most common complaint, affecting 211 participants (89.8%). Fatigue was reported by 188 participants (74.7%), while loss of taste was reported by 194 participants (76.8%). Arthralgia persisted in 178 participants (70.9%), and headache continued to affect 169 participants (71.9%). Fever was still present in 154 participants (65.5%), and diarrhea was reported by 145 participants (61.7%). Gastritis remained common, affecting 135 participants (57.4%). Cough had increased again, affecting 109 participants (46.4%), while nausea/vomiting was noted in 141 participants (60.0%). These results indicate that while certain symptoms such as breathlessness, fatigue, and loss of taste continued to affect a significant proportion of survivors, other symptoms, such as arthralgia and nausea/vomiting, had slightly decreased in prevalence compared to previous follow.

Table 3- Distribution of cases according to Spirometry findings

	Baseline	**3 months followup**	**6 month follow up**
Parameters	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
FEV1	68.77 ± 7.34	68.66 ± 7.58	69.54 ± 8.18
FVC	80.75 ± 6.11	81.03 ± 6.18	80.98 ± 5.74
FEV1/FVC	0.855 ± 0.092	0.851 ± 0.098	0.860 ± 0.093

At the 3-month follow-up, the spirometry parameters showed minimal changes compared to baseline. The mean forced expiratory volume in 1 second (FEV1) was 68.66 ± 7.58, indicating a slight decrease from baseline but still consistent with moderate obstructive lung impairment. The mean forced vital capacity (FVC) increased marginally to 81.03 ± 6.18, suggesting a slight improvement in lung volume. The FEV1/FVC ratio remained close to baseline at 0.851 ± 0.098, further supporting the presence of mild obstructive lung dysfunction. These spirometry results indicate that respiratory function in SARS-CoV-2 survivors remained relatively stable but did not show significant variation.
At the 6-month follow-up, the spirometry parameters showed slight improvements compared to the previous follow-up. The mean forced expiratory volume in 1 second (FEV1) increased to 69.54± 8.18, indicating a slight recovery in lung function. The mean forced vital capacity (FVC) remained stable at 80.98 ± 5.74, which is similar to the 3-month follow-up results. The FEV1/FVC ratio improved slightly to 0.860 ± 0.093, approaching the normal range, suggesting a minor resolution of obstructive lung dysfunction. These results indicate that while some recovery in lung function occurred over the 6-month period, it was modest, with participants still showing mild impairment in their respiratory capacity.

Table 4- Distribution of cases according to Immunoglobin G

	Baseline	**3 month followup**	**6 month followup**
Parameter	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
Serum IgG	386.19 ± 79.66	386.19 ± 79.66	371.60 ± 90.81

At the 3-month follow-up, the mean serum immunoglobulin G (IgG) marker level remained stable at 386.19 ± 79.66. This consistent level of the IgG marker suggests that the immunological response observed at baseline persisted over the three months post-infection, indicating no significant changes in the inflammatory or allergic response within the study population. The stability of the IgG marker highlights the immune system's sustained activity during this period, reflecting potential ongoing immunological engagement in SARS-CoV-2 survivors.
At the 6-month follow-up, the mean serum immunoglobulin G (IgG) marker level slightly decreased to 371.60 ± 90.81. This modest reduction suggests a gradual resolution of the immune response associated with SARS-CoV-2 infection over time. Although IgG marker levels remained elevated compared to normal reference values, the decline indicates a trend toward normalization of the

immune system's activity. However, the persistent elevation above baseline suggests that some degree of immune system dysregulation may still be present in SARS-CoV-2 survivors at the 6-month mark.

Table 5- Distribution of cases according to radiological findings

Radiological findings	Baseline Frequency (%)	3 Months Frequency (%)	6 Months Frequency (%)
Consolidation	44 (18.7%)	44 (18.7%)	34 (14.5%)
Consolidation + Honeycombing	15 (6.4%)	15 (6.4%)	14 (6.0%)
GGO	40 (17.0%)	40 (17.0%)	28 (11.9%)
GGO + Honeycombing	13 (5.5%)	13 (5.5%)	10 (4.3%)
GGO + Consolidation	18 (7.7%)	18 (7.7%)	14 (6.0%)
GGOS	18 (7.7%)	18 (7.7%)	13 (5.5%)
Interlobular Septa Thickening + GGO	8 (3.4%)	8 (3.4%)	5 (2.1%)
Interlobular Septal Thickening + GGOS	5 (2.1%)	5 (2.1%)	3 (1.3%)
Normal	74 (31.5%)	74 (31.5%)	114 (48.5%)

At the 3-month follow-up, the radiological findings remained largely consistent with baseline results. Consolidation was observed in 44 participants (18.7%), while consolidation with honeycombing appeared in 15 participants (6.4%). Ground-glass opacities (GGO) were present in 40 participants (17.0%), and 13 participants (5.5%) exhibited both GGO and honeycombing. GGO combined with consolidation was seen in 18 participants (7.7%), and 18 participants (7.7%) had ground-glass opacities with septal thickening (GGOS). Interlobular septa thickening along with GGO was present in 8 participants (3.4%), while interlobular septal thickening combined with GGOS was found in 5 participants (2.1%). Normal radiological findings were seen in 74 participants (31.5%). These findings indicate that the radiological patterns of pulmonary involvement in SARS-CoV-2 survivors remained stable over the 3-month period, with a significant proportion of participants still showing ground-glass opacities and consolidation.

At the 6-month follow-up, there was a noticeable improvement in radiological findings compared to earlier time points. Consolidation was observed in 34 participants (14.5%), a decrease from both baseline and 3-month follow-up. Consolidation with honeycombing was seen in 14 participants (6.0%), and ground-glass opacities (GGO) were present in 28 participants (11.9%). GGO combined with honeycombing appeared in 10 participants (4.3%), and GGO with consolidation was noted in 14 participants (6.0%). Ground-glass opacities with septal thickening (GGOS) were observed in 13 participants (5.5%). Interlobular septa thickening with GGO was found in 5 participants (2.1%), and interlobular septal thickening combined with GGOS was seen in 3 participants (1.3%). Normal radiological findings were observed in 114 participants (48.5%),

which marks a significant increase in the proportion of participants with normal imaging. These results indicate substantial improvement in radiological findings over the 6-month period, with a notable reduction in the severity and frequency of pulmonary abnormalities, especially consolidation and GGO.

Discussion

The present study aimed to assess the respiratory morbidity among SARS-CoV-2 survivors over a 6-month follow-up period, focusing on clinical parameters, spirometry, immunoglobulin G (IgG) levels, and radiological findings. The findings highlight persistent symptoms, notably breathlessness and fatigue, while immunoglobulin G (IgG) levels did not exhibit significant changes over time. This section discusses the implications of these findings and provides context based on the literature.

The results of this study showed a persistent symptom burden in SARS-CoV-2 survivors, with breathlessness remaining the most commonly reported complaint throughout the 6-month follow- up. Fatigue also continued to affect the majority of participants (84.7% at baseline, 74.7% at 6 months). These findings align with prior research, which has reported prolonged symptoms in COVID-19 survivors, particularly breathlessness and fatigue (7,8). Interestingly, gastrointestinal symptoms such as diarrhea, nausea/vomiting, and gastritis showed no significant change at 3 and 6 months. However, diarrhea exhibited a stable prevalence (61.7% at baseline and 61.7% at 3 months), which is consistent with findings in the literature that gastrointestinal symptoms are common and persistent in post-acute COVID-19 syndrome (9).

One of the most notable changes in the symptom profile was the reduction in cough. While 46.4% of participants experienced cough at baseline, this decreased to 30.2% at the 3-month follow-up, and increased again to 46.4% at the 6-month follow-up. This fluctuation might reflect the natural progression of respiratory recovery, where certain symptoms may improve only to reappear in later stages (10). The changing prevalence of symptoms, including headache and loss of taste, suggests that these symptoms might fluctuate, indicating an incomplete recovery of some aspects of the post-COVID syndrome (11).

Spirometry results revealed moderate obstructive lung impairment at baseline, with a slight improvement observed over time. At baseline, the mean FEV1 (68.77 ± 7.34) suggested a degree of lung function impairment, which remained consistent at 3 months (68.66 ± 7.58) and showed slight recovery at 6 months (69.54 ± 8.18). These findings are in line with other studies reporting persistent respiratory dysfunction in COVID-19 survivors (12,13). The FEV1/FVC ratio remained close to the lower limit of normal at each time point, indicating mild obstructive lung dysfunction,
which was still present after 6 months. Previous studies have shown that while some recovery in lung function is expected over time, mild residual impairment is common (14). Elevated IgG marker levels may indicate a prolonged immune response following SARS-CoV-2 infection, but the lack of significant variation over time suggests that the immune response does not substantially resolve within the initial 6 months post-infection. Similar trends have been reported in other studies, where immune dysregulation, including elevated IgG marker levels, was observed in post-COVID patients (15). This indicates that the IgG marker remains elevated in many SARS-CoV-2 survivors, likely reflecting ongoing immune activation or hypersensitivity responses associated with viral recovery (16).

Radiological findings showed considerable improvement in the severity and frequency of pulmonary abnormalities over the 6-month period. At baseline, ground-glass opacities (GGO) and consolidation were common, seen in 17.0% and 18.7% of participants, respectively. However, at the 6-month follow-up, these patterns significantly decreased, and normal radiological findings increased to 48.5% (compared to 31.5% at baseline). This trend of radiological improvement supports previous reports of partial recovery of lung function and resolution of radiological abnormalities in many COVID-19 survivors (17,18).

Despite the significant improvement in radiological findings, some participants still exhibited persistent changes, such as consolidation and GGO, indicating ongoing pulmonary dysfunction. These results are in line with other studies showing that while most patients experience a degree of recovery, a subset continues to have residual abnormalities on imaging (19). It is worth noting that the observed radiological improvement does not always correlate with symptom resolution, as some participants continued to report breathlessness and fatigue despite improvements in their chest imaging.

This study provides valuable insights into the long-term effects of SARS-CoV-2 on respiratory health. While symptoms such as breathlessness, fatigue, and gastrointestinal disturbances remained prevalent

throughout the 6-month follow-up period, changes in immune markers, particularly IgG, were not significant. This suggests that although respiratory and systemic symptoms improve in some aspects, IgG-mediated immune responses persist, and residual lung dysfunction may continue for many survivors. Further research is needed to explore the long-term effects of COVID-19 on immune system regulation and respiratory health, particularly in individuals with more severe illness or underlying comorbidities.

Conclusion

Given the complexity of the long-term impact of COVID-19, further research is critical to fully understand the mechanisms behind these lingering symptoms and immune responses. Longitudinal studies exploring immune system regulation, including the role of IgG and other immune markers, in SARS-CoV-2 survivors are necessary to identify potential therapeutic targets. Moreover, a deeper understanding of how severe illness and comorbidities influence long-term respiratory health is essential to developing strategies for better management and recovery of affected individuals. Ultimately, such research will contribute to improving clinical management strategies and enhancing quality of life for COVID-19 survivor.

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