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Long COVID symptom trajectories according to post-COVID-19 vaccination status: a prospective longitudinal study

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Running head: Long COVID symptoms and vaccination status

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ABSTRACT

Long COVID remains a substantial public health challenge, and the relationship between post-COVID-19 vaccination and symptom persistence remains uncertain. This prospective longitudinal study evaluated long COVID symptom trajectories according to post-COVID-19 vaccination status. Adult patients who were unvaccinated at the time of COVID-19 diagnosis were followed at 1, 3, 6, and 9 months and categorized according to vaccination status. Symptom Tool (ST) and Impact Tool (IT) scores and SARS-CoV-2 IgG antibody levels were assessed longitudinally. A total of 59 patients (mean age 43.1±14.1 years; 45.8% male) were included, of whom eight were vaccinated. The most frequently reported symptoms were memory problems, fatigue, brain fog, word-finding difficulties, and excessive sweating. Baseline characteristics were broadly comparable between groups. ST and IT scores decreased significantly over time in the overall cohort; however, no statistically significant association between vaccination status and symptom trajectories was identified. SARS-CoV-2 IgG antibody levels were higher among vaccinated participants but were not associated with symptom burden. Given the small sample size and substantial group imbalance, the study is underpowered and the findings should be interpreted cautiously. Larger prospective studies are needed to better clarify the relationship between post-COVID-19 vaccination and long COVID outcomes.

INTRODUCTION

Since its emergence in 2019, severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2), the causative agent of Coronavirus Disease 2019 (COVID-19), has resulted in over 700 million confirmed infections and millions of deaths globally. While the acute phase of the disease typically resolves within two to four weeks in most individuals, a significant proportion of patients report persistent symptoms beyond the

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acute phase—a clinical condition widely referred to as “long COVID” (1,2). Common symptoms include fatigue, cognitive impairment, dyspnea and chest pain, which may last for months (3,4). The pathogenesis of long COVID remains incompletely understood but is believed to be multifactorial, involving viral persistence, immune dysregulation, autoimmunity, endothelial dysfunction, and latent viral reactivation (5,6). Given the heterogeneity of clinical presentations and the lack of standardized therapeutic strategies, long COVID poses a significant challenge to healthcare systems.

Vaccination has been the cornerstone of global efforts to control the pandemic, with substantial evidence supporting the efficacy of SARS-CoV-2 vaccines in preventing severe disease, hospitalization, and death (7). However, the role of vaccination in modulating the risk and trajectory of long COVID, particularly in individuals who were unvaccinated at the time of infection, is an area of ongoing research and clinical interest. Preliminary studies suggest that vaccination may reduce the incidence and severity of long COVID, potentially through mechanisms such as accelerated viral clearance, prevention of reinfection, or immunological reprogramming (8,9). Protection against SARS-CoV-2 is primarily mediated by a neutralizing antibody (Nab) response. Nab titers achieved with inactivated virus vaccines are lower than those achieved with mRNA vaccines (10).

Furthermore, the longitudinal monitoring of SARS-CoV-2-specific antibodies offers a window into the host immune response and its relationship with clinical outcomes. Several studies have indicated that higher and sustained antibody titers may correlate with improved viral control and reduced symptom burden in both acute and post-acute phases of infection (11). However, the association between antibody dynamics and long COVID

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symptoms, particularly in individuals vaccinated after COVID-19 remains to be clearly elucidated.

In this prospective study, we aim to evaluate the clinical impact of SARS-CoV-2 vaccination on the symptoms of long COVID in individuals who were unvaccinated at the time of infection. By conducting serial measurements of SARS-CoV-2 antibody levels and correlating them with symptom trajectories over time, we seek to better understand the potential immunological mechanisms underpinning recovery or persistence of long COVID. These findings may inform future vaccination strategies and provide a foundation for personalized management approaches in post-COVID-19 care.

MATERIALS AND METHODS

Study design, setting: This prospective longitudinal observational study was conducted at Istanbul Faculty of Medicine Hospital between January 2022 and December 2023. The study was designed and reported in accordance with the STROBE guidelines.

Participants: Adult patients (18 years and older) with a confirmed diagnosis of SARS-CoV-2 infection by polymerase chain reaction (PCR) who had not received any prior SARS-CoV-2 vaccination at the time of diagnosis were eligible. Patients with hematological or solid organ malignancies, solid organ transplantation, or those requiring intensive care unit (ICU) admission during COVID-19 were excluded. Participants were invited for their first visit one month after diagnosis and were followed at 1, 3, 6, and 9 months after diagnosis. The research group was planned to consist of 100 patients who were vaccinated with the BioNTech® or CoronaVac®. The control group was designed to comprise 100 patients who were not vaccinated. The distribution of patients included in the study and control groups was planned to be similar in terms of age, gender, and comorbidity. During the period in which the study was conducted, there was a successful

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programme for the vaccination of the population against SARS-CoV-2 in our country. However, only a small proportion of participants agreed to receive vaccination during follow-up despite repeated counseling. This patient group consisted of people who were already hesitant about vaccination. So, obtaining informed consent from patients to include them in the study was more difficult than expected. As a result, the final sample size remained below the planned target. Only participants who completed all follow-up visits were included in the final analysis.

Exposure (vaccination status): All participants were unvaccinated at baseline. During follow-up, participants were asked whether they wished to receive SARS-CoV-2 vaccination. Those who accepted vaccination were advised to initiate vaccination after the 1-month visit and complete the vaccination schedule before the 3-month visit. Vaccine type (mRNA or inactivated vaccine) was recorded at the 3-month visit. Participants who received vaccination during follow-up were classified as the vaccinated group, while those who remained unvaccinated constituted the control group.

Outcome measures: According to the Centre for Disease Control and Prevention (CDC), the definition of long COVID is the persistence or emergence of physical or cognitive symptoms (12) in the period following the initial four weeks of infection. The participants of the study were evaluated in accordance with the aforementioned definition and subsequently included in the study. Symptoms and their impact were assessed using previously described scoring tools (13).

-Symptom tool (ST): Presence of 53 predefined symptoms was recorded at each visit (1st, 3rd, 6th and 9th months). Each symptom was scored as 1 point, yielding a total score range of 0–53 (13).

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Fatigue, difficulty in sleeping, changing mood / impact on morale, body aches, fever and chills, hot flushes, sleeping more, sweats, loss of appetite, heat / cold intolerance, weight loss, dyspnea, tachycardia / palpitations / arrythmia, chest pressure, sharp sudden pain / chest burns, costal pain, cough, headache, brain fog / difficulty concentrating, word finding problems, memory problems, dizziness / malaise, change / loss of smell, paresthesia, change / loss of taste, balance disorder, tremor, hypoesthesia, abdominal pain, diarrhea, nausea / vomiting, tinnitus, congested / runny nose, sore tongue / dysphagia, ear pain, clogged ears, blurry vision, dry eyes, phono/photophobia, muscle aches, neck/ back and low back pain, bone and joint pain, heavy legs / swelling of the legs, high or low blood pressure, circulatory problems (including bulging veins), spontaneous bruises, swollen lymph nodes, dry skin / peeling, hair loss, skin rash, discoloration / swelling of hands and feet, urinary problems, gynecological symptoms.

-Impact tool (IT): The impact of symptoms on daily functioning experienced by patients in the 1, 3, 6 and 9 months were evaluated across six domains (each scored 0–10), resulting in a total score range of 0–60 (13).

- Difficulties in performing basic activities (0-10)
- Difficulties in their professional lives (0-10)
- Difficulties in fulfilling their family roles (0-10)
- Difficulties in having social activities (0-10)
- Fear of missing out their lives and/or uncertainty about the future (0-10)
- Negative impact on relationships with care providers (0-10)

Data collection: At the 1-month visit, demographic characteristics (age, sex), comorbidities, medication use, and indicators of acute COVID-19 severity were recorded. Inclusion required persistent symptoms lasting at least four weeks, a ST score ≥1 and

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absence of an alternative diagnosis. Follow-up visits were conducted at 1, 3, 6, and 9 months after diagnosis. At each visit, ST and IT scores were recorded, and blood samples were collected for laboratory analyses. Blood counts, biochemical test results, and SARS-CoV-2 IgG antibody levels were assessed at each visit. Serum samples were stored at −80°C until analysis. Data regarding SARS-CoV-2 reinfection or subsequent viral exposure during the follow-up period were not systematically collected. During these visits, ongoing symptoms and their impacts were assessed and documented using scoring tools (13). These tools were based on prior literature. However, their validation in this specific population was limited. We also acknowledged that validated symptom tools (ST and IT) were applied in this population without prior formal validation. Only participants who completed all scheduled follow-up visits were included in the final analysis.

Laboratory analysis: The SARS-CoV-2 IgG quantitative antibody test was performed on patient serum samples at the Virology and Basic Immunology Department Laboratory of Istanbul University, Istanbul Faculty of Medicine. The chemiluminescent microparticle immunoassay (CMIA) method, on which the SARS-CoV-2 IgG II Quant kit (Abbott, USA) is based, was utilized. This method detects IgG antibodies developed against the S1/RBD domain of the SARS-CoV-2 spike protein. The test was performed on serum samples collected from patients with confirmed cases of the disease and stored in a -80°C refrigerator, in accordance with the manufacturer's recommendations, using the Architect i2000SR (Abbott, USA). According to the manufacturer data and independent validation study, the Abbott SARS-CoV-2 IgG II Quant assay demonstrates a sensitivity of approximately 98–100% and a specificity of approximately 99.6–99.9%, particularly ≥14 days after infection. The diagnostic sensitivity of the assay was known to increase with time from symptom onset, which was considered in the interpretation of

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antibody results (14,15). The results of the SARS-CoV-2 IgG quantitative test, whose analytical measurement range was set between 21 and 40000 by the manufacturer, were interpreted by a medical microbiology specialist according to the cutoff value of 50.0 AU/ml.

Data management and statistical analysis: Statistical analyses were performed using IBM SPSS Statistics for Windows, version 28.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean values with ranges, and categorical variables as frequencies and percentages. Between-group comparisons were performed using Student's t-test or the Mann–Whitney U test, depending on data distribution. Categorical variables were compared using the χ^2 test or Fisher's exact test. Longitudinal changes in ST and IT scores were analyzed using linear mixed-effects models, including time, vaccination status, and their interaction as fixed effects, and participant as a random effect to account for within-subject correlation. Due to the limited sample size, particularly the small number of vaccinated participants, adjustment for multiple confounding variables (including age, sex, comorbidities, and disease severity) was not performed to avoid model overfitting. Therefore, potential residual confounding should be considered when interpreting the results. A two-sided p-value <0.05 was considered statistically significant.

Ethical approval: The study was conducted in accordance with the Declaration of Helsinki and the International Council for Harmonisation Good Clinical Practice (ICH-GCP) guidelines. Ethical approval was obtained from the Istanbul Faculty of Medicine Clinical Research Ethics Committee (21.12.2021, No: 2021/2118). Written informed consent was obtained from all participants.

RESULTS

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A total of 59 patients were included in the study. Twenty-seven of the patients were male, 32 were female, and the mean age was 43.1 ± 14.1 years. 35.6% of patients had comorbidities with 13.6% having more than one. The most common comorbid conditions were hypertension and diabetes mellitus. The severity of the COVID-19 was mild in 41 (69.5%) patients, moderate in 8 (13.6%) patients, and severe in 10 (16.9%) patients. Sixteen patients (27.1%) were hospitalized with a mean length of stay of 10.6 days. Patients' ST scores (mean ± standard deviation) at 1, 3, 6 and 9 months were 8.66 ± 5.73, 5.98 ± 5.02, 2.85 ± 3.55 and 1.14 ± 1.55 respectively. Patients' IT scores (mean ± standard deviation) at 1., 3., 6. and 9. months were 7.10 ± 8.62, 3.95 ± 6.48, 1.81 ± 4.07 and 0.41 ± 1.70, respectively (Table 1). Eight patients received the full dose SARS-CoV-2 vaccine (3 CoronaVac®, 5 BioNTech®). As there were few vaccinated patients they were analyzed as a single vaccinated group. When the characteristics of the vaccinated and unvaccinated patients were evaluated, it was found that the two groups were similar in terms of demographics, comorbidities, characteristics during the SARS-CoV-2 infection. Longitudinal changes in SARS-CoV-2 IgG antibody levels were assessed in both vaccinated and unvaccinated participants (Table 1). Vaccinated participants consistently exhibited higher IgG antibody levels throughout follow-up, whereas antibody levels in the unvaccinated group declined between 1 and 6 months but increased at 9 months (1,682 ± 1,747 vs. 5,049 ± 9,978 AU/mL). Mean ST and IT scores decreased over time in both groups (p=0.001, p=0.047). (Figure 1). Although temporal patterns differed numerically between vaccinated and unvaccinated participants, no statistically significant interaction between vaccination status and time was observed (p=0.406, p=0.434) (Figure 2). In addition, CRP value measured at the 3-month was 13.3 mg/l in vaccinated patients, and 2.3 mg/l in unvaccinated patients (p=0.001). At 9-month, platelet

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counts were significantly higher in patients with long COVID (301562/µl) compared to those without long COVID (215120/µl) (p=0.021). The most common long COVID symptoms were memory problems, fatigue, brain fog, difficulty in finding words, and excessive sweating (Figure 3).

DISCUSSION

This prospective longitudinal study investigated the association between post-infection SARS-CoV-2 vaccination, long COVID symptom trajectories, and SARS-CoV-2 IgG antibody dynamics in a cohort of patients with persistent symptoms. Both vaccinated and unvaccinated participants demonstrated a decline in ST and IT scores over time. However, no statistically significant interaction between time and vaccination status was observed. Vaccinated participants exhibited higher SARS-CoV-2 IgG antibody titers, whereas no significant association was identified between antibody levels and long COVID symptom severity. Taken together, these findings suggest that symptom improvement over time occurred irrespective of vaccination status and may reflect the natural course of recovery following COVID-19.

In our study, a decrease in ST and IT scores was in line with findings reported in the literature. One study reported that vaccination after COVID-19 could alleviate symptoms of long COVID; a 13–30% improvement in symptoms was reported after vaccination (9). A 2023 meta-analysis associated COVID-19 vaccination before COVID-19 with a reduced risk of long COVID, but vaccination did not cause symptomatic changes in most patients with long COVID (16). Another study showed that vaccination before COVID-19 significantly reduced the incidence of long COVID (17). The positive effects of vaccination have been demonstrated in numerous other studies, and one study even emphasized that it reduces the increased risk of cardiovascular and/or

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cerebrovascular complications and excess disease burden (18). Another study has shown that vaccination against COVID-19 is associated with a reduction in long COVID symptoms and heart damage, emphasizing the importance of fully vaccinating the entire population (19). The literature suggests that possible mechanisms for the reduction of long COVID symptoms include faster clearance of viral residues, immune system reprogramming, and suppression of potential autoimmune processes. However, the lack of a significant vaccine-symptom interaction in our study may be related to the limited sample size. The discrepancy between previous observational studies and the present findings may reflect differences in study design, patient selection, timing of vaccination, outcome definitions, and statistical power.

In the present study, no clear baseline difference in ST and IT scores between vaccinated and unvaccinated participants was observed. Therefore, differences in symptom trajectories over time should be interpreted with caution and cannot be attributed to baseline imbalance. Although baseline differences were not clearly observed in our data, the potential for selection bias remains inherent to the observational design, as vaccination status was not randomly assigned. Symptom improvement over time may also reflect the natural course of recovery following COVID-19.

The finding of significantly higher antibody levels at 3-month in vaccinated patients is an expected result and is consistent with the knowledge that vaccines induce a strong humoral response against SARS-CoV-2. However, in our study, no significant correlation was found between the increase in antibody levels and the reduction of long COVID symptoms. This finding is also consistent with current theories regarding the pathogenesis of long COVID. Proal and VanElzakker emphasize that not only the presence of viral residues but also T cell dysfunction, autoimmunity, microthrombi

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formation, and persistent inflammation play a significant role in long COVID (6). Su and colleagues demonstrated distinct immunological signatures (cytokine elevation, B cell dysfunction, and persistent inflammatory markers) in long COVID (5). Therefore, high antibody levels alone may not be sufficient to diminish long COVID symptoms. An unexpected increase in SARS-CoV-2 IgG antibody levels was also observed in the unvaccinated group at the 9-month follow-up. Although the present study was not designed to investigate the causes of longitudinal antibody dynamics, several biologically plausible explanations exist, including SARS-CoV-2 reinfection, exposure to circulating viral variants during the study period, or other sources of antigenic stimulation. Because reinfection data were not systematically collected during follow-up, these hypotheses could not be formally evaluated and should therefore be interpreted cautiously.

An additional finding was higher CRP levels in vaccinated individuals at 3. months. Given the small sample size and variability in post-acute recovery, this should be interpreted cautiously and may reflect transient inflammatory variation rather than a sustained biological difference. Larger longitudinal studies are needed to clarify its clinical relevance. It is noteworthy that platelet counts were significantly higher in patients with long COVID at the 9-month follow-up of the study. The increased platelet count may be related to the chronic endothelial activation and microthrombi hypothesis described in long COVID (6,20); however, larger and controlled studies are needed to determine whether this finding is causal.

The most significant limitation of this study is the small number of patients. The extremely small number of vaccinated participants (n=8) substantially limits statistical inference and prevents reliable comparison between groups. Due to the limited sample size, particularly in the vaccinated group, inclusion of multiple covariates in the statistical

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models was not feasible without risking overfitting and unstable estimates. Therefore, residual confounding remains a major limitation and cannot be excluded. Given the limited sample size and group imbalance, the study should be considered exploratory in nature, and findings should be interpreted with caution and considered hypothesis-generating rather than confirmatory. Other limitations include the reliance on subjective scores for symptom assessment and the potential influence of psychosocial factors on symptom perception. In addition, SARS-CoV-2 reinfection or subsequent viral exposure during follow-up was not systematically assessed. Consequently, the unexpected increase in IgG antibody levels observed in the unvaccinated group could not be further investigated, introducing uncertainty into the interpretation of both the longitudinal antibody findings and the interpretation of long COVID symptom trajectories.

The assessment of post-COVID-19 vaccination effects on long COVID is methodologically challenging because vaccination status is self-selected rather than randomly assigned, resulting in potential confounding that cannot be fully eliminated through statistical adjustment. Although randomized controlled trials would provide the highest level of causal evidence, they are often infeasible in this context due to ethical and logistical constraints during mass vaccination programs, where withholding vaccination from eligible individuals is not acceptable. Consequently, current evidence is primarily derived from observational studies and should be interpreted within these inherent limitations (21, 22). Future research should prioritize multicenter prospective cohorts with standardized definitions of long COVID, detailed characterization of acute disease severity and baseline symptom burden, and adequate longitudinal follow-up in sufficiently large populations. To strengthen causal inference in the absence of randomization, advanced analytical frameworks such as propensity score methods,

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inverse probability weighting, and target trial emulation may be employed to reduce bias and improve interpretability. In this context, target trial emulation has emerged as a particularly valuable approach for leveraging real-world data to approximate randomized trial conditions and generate more robust evidence to inform clinical and public health decision-making (13).

Despite these limitations, the study has notable strengths. It provides prospective longitudinal follow-up over a 9-month period, incorporates serial quantitative antibody measurements, and evaluates both symptom burden and functional impact using structured scoring systems. The integration of clinical and immunological data offers a more comprehensive perspective on post-COVID recovery trajectories than symptom-based studies alone.

In conclusion, long COVID symptom burden decreased over time irrespective of vaccination status. No statistically significant association between vaccination status and symptom trajectories was identified, and no clear association was observed between SARS-CoV-2 IgG antibody levels and symptom trajectories. However, interpretation of these findings is limited by the small sample size, particularly the very low number of vaccinated participants, as well as the inability to adjust for important confounding factors. The study is underpowered, and non-significant findings should not be interpreted as evidence of no effect. Therefore, the results should be considered exploratory and hypothesis-generating, and causal inferences cannot be drawn. Further large-scale prospective studies with adequate adjustment for confounding and balanced comparison groups are needed to better clarify the relationship between post-COVID-19 vaccination and long COVID outcomes.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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FIGURE LEGENDS

Fig. 1- Longitudinal changes in (A) Symptom Tool (ST) scores and (B) Impact Tool (IT) scores in the overall study population (n=59) following COVID-19. ST and IT scores measured at 1, 3, 6, and 9 months following SARS-CoV-2 infection. Thin lines represented individual patient trajectories. Bold lines and markers indicated group mean values, with error bars representing standard deviation. A significant decrease over time was observed for both ST and IT scores (ST: $p<0.001$; IT: $p=0.047$).

Fig. 2- Comparison of longitudinal (A) Symptom Tool (ST) score and (B) Impact Tool (IT) score trajectories according to post-COVID-19 vaccination status. ST and IT scores measured at 1, 3, 6, and 9 months following SARS-CoV-2 infection. Each thin line represented an individual patient trajectory. Group mean values were shown with bold lines and markers, with error bars representing standard deviation. Solid lines indicated unvaccinated participants (n=51), while dashed lines indicated vaccinated participants (n=8, 3 CoronaVac®, 5 BioNTech®). No statistically significant interaction between time and vaccination status was observed (ST: $p=0.406$; IT: $p=0.434$).

Fig. 3- Distribution of common clinical symptoms among patients with long COVID. The proportion of patients reporting each symptom at 1, 3, 6, and 9 months following SARS-CoV-2 infection was shown. Each month was indicated by different bar colors. Symptoms were ordered by baseline (1-month) prevalence to facilitate comparison across time points. Values represented the percentage of patients reporting each symptom at the specified time point.

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Table 1- Demographical, clinical and laboratory characteristics of vaccinated and unvaccinated patients after COVID-19

	Total patients (n=59)[1)]	Vaccinated patients (n=8)[1)]	Unvaccinated patients (n=51)[1)]	*P-value*[2)]
Male gender	27 (45.8%)	6 (75%)	21 (41.2%)	0.126
Age	43.1 ± 14.1	44.8 ± 13.8	42.8 ± 14.3	0.714
Educational status				0.846
-Primary school	16 (27.1%)	3 (37.5%)	13 (25.4%)	
-High school	21 (35.6%)	2 (25%)	19 (37.2%)	
-University	19 (32.2%)	3 (37.5%)	16 (31.3%)	
Active working	29 (49.2%)	3 (37.5%)	26 (51%)	0.706
Disease severity				0.416
-Mild	41 (69.5%)	4 (50%)	37 (72.5%)	
-Moderate	8 (13.6%)	2 (25%)	6 (11.7%)	
-Severe	10 (16.9%)	2 (25%)	8 (15.6%)	
COVID-19 hospitalization	16 (27.1%)	3 (37.5%)	13 (25.4%)	0.670
Duration of COVID-19 hospitalization (day)	10.6 ± 5.6	12 ± 4	10.3 ± 6	0.669
Comorbidity	21 (35.6%)	2 (25%)	19 (37.2%)	0.699
-More than one	8 (13.6%)	0 (0)	8 (15.6%)	0.582
Favipiravir usage	5 (8.5%)	2 (25%)	3 (5.8%)	0.131
Corticosteroid usage	16 (27.1%)	3 (37.5%)	13 (25.4%)	0.407
Anakinra usage	7 (11.9%)	2 (25%)	5 (9.8%)	0.238

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At least one symptom at 3-month	34/42 (81%)	6/7 (85.7%)	28/35 (80%)	1
SARS-CoV-2 IgG (AU/ml) (1-month)	3066 ± 3945	5019 ± 6492	2760 ± 3383	0.127
SARS-CoV-2 IgG (AU/ml) (3-month)	4305 ± 8722	13584 ± 18113	2449 ± 3545	0.023
SARS-CoV-2 IgG (AU/ml) (6-month)	3177 ± 7845	14137 ± 22403	1682 ± 1747	0.277
SARS-CoV-2 IgG (AU/ml) (9-month)	6241 ± 10348	13394 ± 11621	5049 ± 9978	0.108
1-month ST	8.66 ± 5.73	9.00 ± 5.01	8.61 ± 5.88	0.681
3-month ST	5.98 ± 5.02	3.71 ± 2.81	6.43 ± 5.27	0.191
6-month ST	2.85 ± 3.55	5.33 ± 6.65	2.52 ± 3.05	0.483
9-month ST	1.14 ± 1.55	2.00 ± 2.44	0.94 ± 1.30	0.456
1-month IT	7.10 ± 8.62	7.00 ± 8.12	7.12 ± 8.77	0.881
3-month IT	3.95 ± 6.48	1.57 ± 2.37	4.43 ± 6.94	0.465
6-month IT	1.81 ± 4.07	4.00 ± 6.92	1.52 ± 3.70	0.550
9-month IT	0.41 ± 1.70	2.00 ± 4.00	0.06 ± 0.23	0.201

[1)]: For categorical variables, n(%); for continuous variables, mean ± standard deviation (SD) values were given.

[2)]: *P*-values < 0.05 were considered statistically significant.

ST=Symptom Tool, IT=Impact Tool

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Fig.1- A.

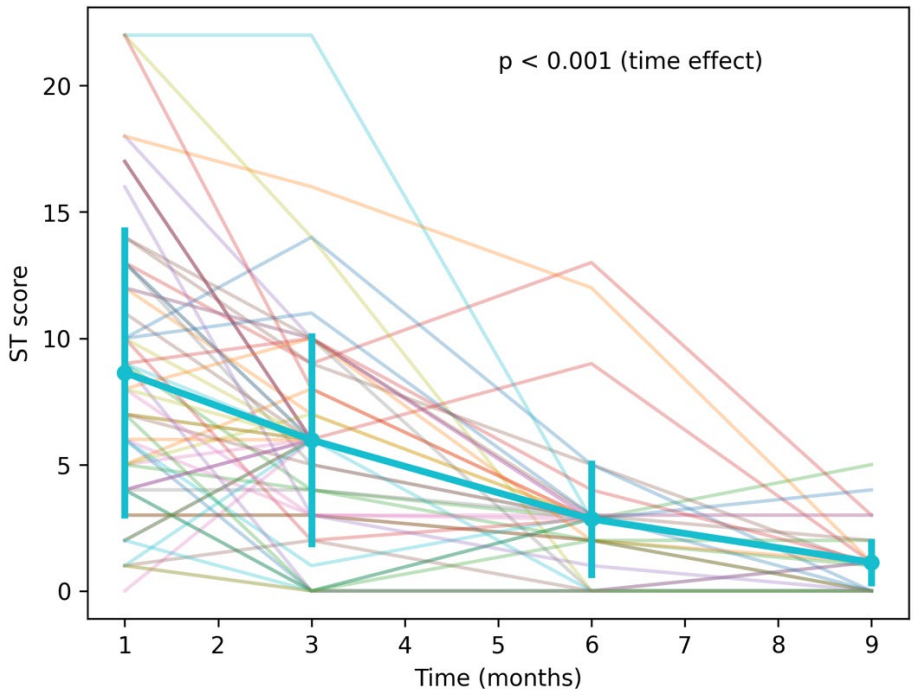
p < 0.001 (time effect)
ST score
Time (months)
0
5
10
15
20
1
2
3
4
5
6
7
8
9

Fig.1- B.

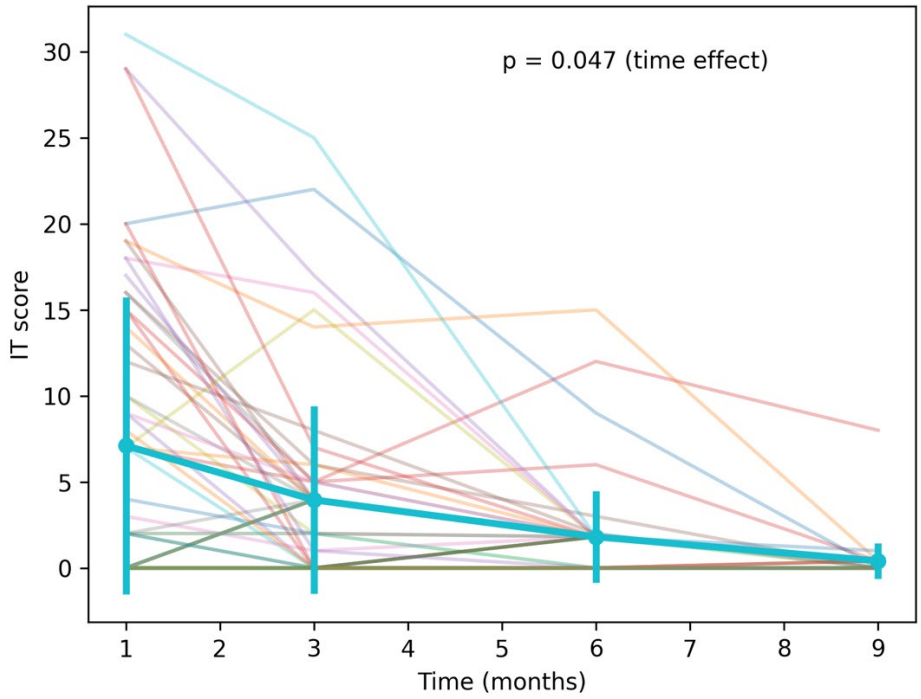
p = 0.047 (time effect)
IT score
Time (months)
0
5
10
15
20
25
30
1
2
3
4
5
6
7
8
9

Fig.2- A.

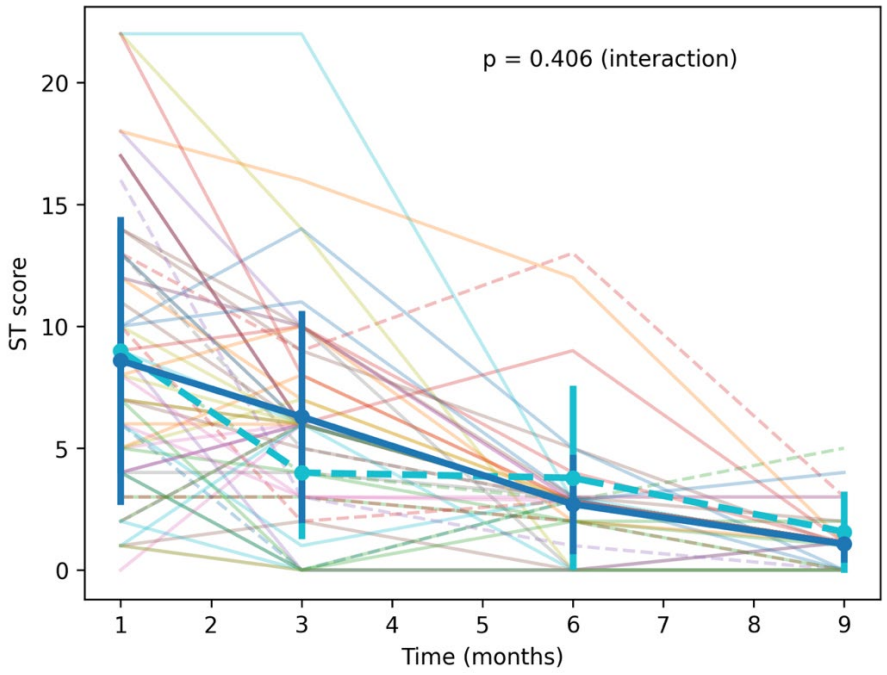

Fig.2- B.

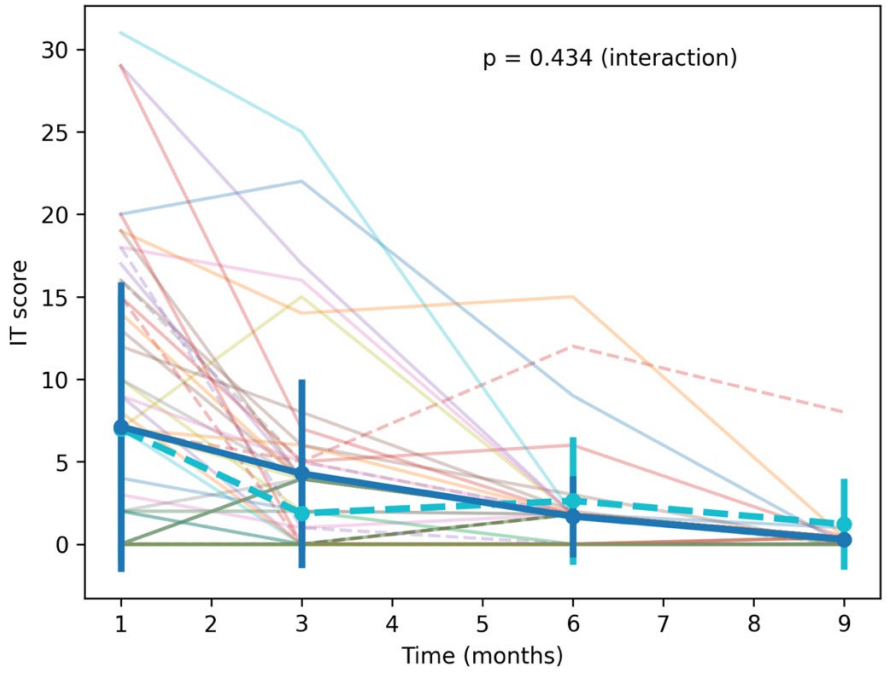

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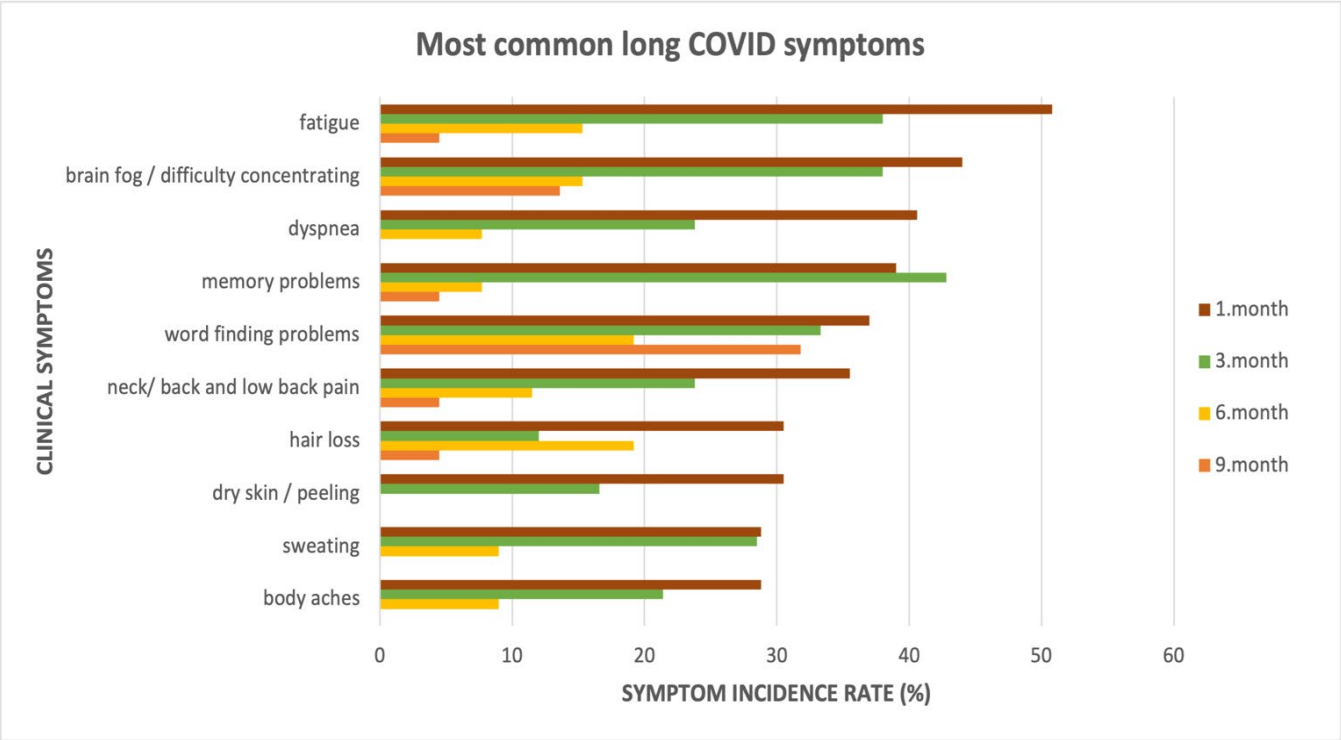
Fig.3



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