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Article

COVID-19 vaccination and persistent post-COVID symptoms among primary health care users in a rural district of Albania: A cross-sectional study

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Abstract

Background: Long COVID remains a frequent consequence of SARS-CoV-2 infection, and vaccination may influence its occurrence and course. Evidence from primary health care in Southeastern Europe remains limited. We aimed to assess the association between COVID-19 vaccination status and persistent post-COVID symptoms among primary health care users. Methods: A cross-sectional study was conducted in March 2025 among 49 adult primary health care users in a predominantly rural area of northern Albania. A structured questionnaire recorded sociodemographic characteristics, COVID-19 and vaccination history, and persistent post-COVID symptoms. Groups were compared with Fisher's exact and Mann–Whitney U tests, and odds ratios (OR) were adjusted for sex with the Mantel–Haenszel method. Results: Mean age was 50.1 ± 19.7 years and 57.1% were women; 34.7% reported previous COVID-19 and 40.8% were vaccinated. Among the 17 previously infected participants, infection preceded vaccination in most vaccinated participants. Long COVID was reported by 40.0% of vaccinated and 85.7% of unvaccinated participants (p = 0.134). Vaccinated participants reported fewer persistent symptoms (0.9 ± 1.2 vs. 2.1 ± 1.2; p = 0.046) and fewer neurological symptoms (10.0% vs. 85.7%; p = 0.004; sex-adjusted OR 0.10, 95% CI 0.01–0.90). Conclusions: In our study, COVID-19 vaccination, received mostly after infection, was associated with a lower burden of persistent symptoms, particularly neurological symptoms. Larger longitudinal studies are needed to confirm these findings.

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Long COVID; post-COVID-19 condition; COVID-19 vaccination; primary health care; Albania

Introduction

Post-COVID-19 condition, or long COVID, is defined by the World Health Organization as symptoms that persist or appear after probable or confirmed SARS-CoV-2 infection, last for at least two months and cannot be explained by an alternative diagnosis (1). Among people with a previous infection, its global pooled prevalence has been estimated at 43%, with fatigue and memory problems among the most frequently reported of more than 200 symptoms affecting multiple organ systems (2,3). Female sex, smoking, obesity and comorbidities have been consistently identified as risk factors, whereas vaccination has been associated with a lower risk (4,5).

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Vaccination reduces the risk of long COVID when received before infection (6,7), and some studies suggest that vaccination after infection may also be followed by an improvement in persistent symptoms (8,9). In Albania, booster uptake has been low even among health care workers (10), while vaccination coverage in the general population has remained incomplete and vaccine effectiveness has been assessed among hospitalized patients (11). Data on long COVID among primary health care users, particularly in rural areas, are lacking. We aimed to assess the association between COVID-19 vaccination status and persistent post-COVID symptoms among primary health care users in northern Albania.

Methods

Study design and participants

A cross-sectional study was conducted in March 2025 in primary health care centres of a predominantly rural area of Shkodër region, northern Albania. Adult users attending the centres were included; at the final sampling stage, participants were selected consecutively. One participant was excluded because of missing data. The study was conducted in accordance with the Declaration of Helsinki. Participation was voluntary, written informed consent was obtained from all participants, and data were collected and analysed anonymously.

Questionnaire and definitions

An interviewer-administered structured questionnaire recorded sociodemographic characteristics, previous COVID-19 confirmed by a PCR or rapid antigen test, severity of the first infection, vaccination history (number of doses, vaccine type, timing of infection relative to vaccination) and persistent post-COVID symptoms with their consequences. Long COVID was defined as self-reported prolonged or recurrent symptoms after a test-confirmed COVID-19 episode. Neurological symptoms comprised memory problems, taste or smell changes or headache.

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) and categorical variables as frequencies and percentages. Associations with vaccination status were examined among previously infected participants (n = 17) with Fisher's exact test and the Mann–Whitney U test (exact p-values). Odds ratios (OR) with 95% confidence intervals (CI) were calculated with unvaccinated participants as the reference, crude and adjusted for sex (Mantel–Haenszel method). Statistical significance was set at $p < 0.05$. Analyses were performed in Python 3.13 using the pandas, SciPy and IBM SPSS Statistics, version 26 (IBM Corp., Armonk, NY, USA).

Results

In our study, 49 primary health care users were included, with a mean age of 50.1 ± 19.7 years; 57.1% were women. Previous COVID-19 was reported by 34.7% of participants, and 40.8% had been vaccinated, almost all with two or more doses (Table 1).

Table 1. Characteristics of participants (n = 49)

Variable	Value
Age, years, mean ± SD	50.1 ± 19.7
Women, n (%)	28 (57.1)
Years of schooling, mean ± SD	10.0 ± 3.9
Unemployed, n (%)	24 (49.0)
Previous COVID-19, n (%)	17 (34.7)
Long COVID[a], n (%)	10 (58.8)
Vaccinated, n (%)	20 (40.8)
Two or more doses[b], n (%)	19 (95.0)

Note. SD = standard deviation. [a] Among previously infected participants (n = 17). [b] Among vaccinated participants (n = 20).

Among the 17 previously infected participants, infection preceded vaccination in at least eight of the ten vaccinated participants. Long COVID was reported by 40.0% of vaccinated and 85.7% of unvaccinated participants (p = 0.134); this difference weakened after adjustment for sex (OR 0.30), as women predominated among the unvaccinated (85.7% vs. 30.0%). Vaccinated participants reported fewer persistent symptoms (0.9 ± 1.2 vs. 2.1 ± 1.2; p = 0.046) and fewer neurological symptoms (10.0% vs. 85.7%; p = 0.004), an association that remained after adjustment for sex (OR 0.10, 95% CI 0.01–0.90). Memory or taste/smell disturbances occurred only among unvaccinated participants (p = 0.015). Among the 10 participants with long COVID, the consequences of symptoms did not differ significantly by vaccination status (Table 2).

Table 2. Persistent post-COVID symptoms by vaccination status among previously infected participants (n = 17)

Variable	Vaccinated (n = 10)	Unvaccinated (n = 7)	p	Crude OR (95% CI)	Adjusted OR[c] (95% CI)
Women, n (%)	3 (30.0)	6 (85.7)	0.050[b]		
Long COVID, n (%)	4 (40.0)	6 (85.7)	0.134[b]	0.11 (0.01–1.31)	0.30 (0.04–2.41)
Persistent symptoms, mean ± SD	0.9 ± 1.2	2.1 ± 1.2	0.046[a]		
Joint or muscle pain, n (%)	4 (40.0)	4 (57.1)	0.637[b]		
Chronic fatigue, n (%)	2 (20.0)	4 (57.1)	0.162[b]		
Neurological symptoms, n (%)	1 (10.0)	6 (85.7)	0.004[b]	0.02 (0.001–0.36)	0.10 (0.01–0.90)
Memory or taste/smell disturbance, n (%)	0 (0.0)	4 (57.1)	0.015[b]		

Note. SD = standard deviation; OR = odds ratio; CI = confidence interval. Reference: unvaccinated participants. [a] Mann–Whitney U test (exact p-value); [b] Fisher's exact test; [c] adjusted for sex (Mantel–Haenszel method). Neurological symptoms: memory problems, taste or smell changes or headache.

Discussion

In our study, vaccinated primary health care users with a previous infection reported fewer persistent symptoms and markedly fewer neurological symptoms than unvaccinated users,

whereas the lower frequency of long COVID among vaccinated participants was not statistically significant and was partly explained by sex. Because most vaccinated participants were infected before vaccination, these findings concern the course of persistent symptoms rather than protection against their onset.

Previous studies, summarised in a recent review, have linked vaccination with a lower risk and symptom burden of long COVID, although the effect depends on the timing of vaccination relative to infection (12). For vaccination after infection, as in most of our participants, a French target trial emulation among patients with long COVID found that a first vaccine dose reduced the number of symptoms, doubled the rate of remission and lessened the impact of symptoms on daily life (13). A meta-analysis, however, found that most patients with ongoing long COVID reported no change after vaccination, whereas about one in five reported an improvement (14), suggesting that the benefit of vaccination after infection is moderate. The attenuation of the association after adjustment for sex agrees with the higher risk of long COVID among women, who had threefold higher odds of persistent symptoms in an Italian cohort (15). As in that cohort, musculoskeletal pain and fatigue were among the most frequent symptoms in our study.

The clearest difference concerned neurological symptoms, particularly memory problems and taste or smell changes. Cognitive deficit is among the most persistent sequelae of SARS-CoV-2 infection, with an excess risk still present two years after infection in a large cohort (16). Vaccination after infection may contribute to the resolution of such symptoms (13); however, the risk of long COVID also differs by variant and was lower with omicron than with delta (17). Because the period of infection and the circulating variants could not be assessed, differences in the timing of infection between vaccinated and unvaccinated participants may also have contributed.

Our study has several limitations. The small infected subgroup (n = 17) limited statistical power. Uncertain vaccination timing, differences in time since infection and viral variants, and sex-related healthcare-seeking or vaccine hesitancy may have introduced residual confounding or selection bias. Symptoms and infection history were self-reported and subject to recall bias. Participants with persistent symptoms may have been less willing to be vaccinated, which could inflate the observed association. The study was conducted in one rural area, and the findings may not apply to other settings. Nevertheless, it provides first data on persistent post-COVID symptoms among primary health care users in a rural area of Albania.

Conclusions

In our study, COVID-19 vaccination, received mostly after infection, was associated with fewer persistent symptoms, particularly neurological symptoms, among primary health care users with previous infection. Primary health care should combine vaccination counselling with systematic assessment of persistent post-COVID symptoms. Larger longitudinal studies are needed to confirm these findings.

Declarations

Conflict of interest: The authors declare no conflict of interest.

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