

Inflammation and Long-Term Mental Health Outcomes in Post-COVID-19 Patients: A Follow-Up Study

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INTRODUCTION

COVID-19 has been associated with increased rates of depression, anxiety, and Post-Traumatic Syndrome Disorder (PTSD)^{1,2}. Systemic inflammation during acute infection has been proposed as a key biological mechanism^{3,4,5}, yet its relationship with long-term psychiatric outcomes remains unclear^{6,7,8}. This study examines psychiatric symptoms and their association with inflammatory markers and COVID-19 severity 24-36 months post-infection.

AIMS

- To evaluate the prevalence of psychiatric symptoms (depression, psychological distress, and PTSD symptoms) 24–36 months after COVID-19 infection.
- To examine the association between inflammatory markers (measured during the acute phase and at long-term follow-up) and psychiatric outcomes.
- To explore the relationship between COVID-19 severity and psychiatric symptoms.

METHODS

Study Design:
Multicentre observational cohort study

Sample:
N = 91
Males = 53 (58.2 %)
Age (mean ± SD): Males = 55.30 ± 8.9. Females = 53.13 ± 8.1



Inclusion criteria:

- Age 18-65 years.
- SARS-CoV2 infection confirmed by nasopharyngeal PCR.
- No prior psychiatry or neurological disorders.

Procedure:

Acute COVID-19 phase

Blood samples collected during acute infection.

Inflammatory markers and clinical data were obtained from medical records.

COVID-19 severity classified according to WHO criterio⁹.

Long-term follow-up

Participants recruited for follow-up assessment.

A new blood sample collected to measure inflammatory markers.

Clinical interview and psychiatric assessment performed.

Inflammatory markers:

- C-reactive protein (CRP)
- Neutrophil-to-lymphocyte ratio (NLR)
- Platelet count
- Systemic immune-inflammation index (SII)

Psychiatry assessment:

- Depressive symptoms: Beck Depression Inventory-II (BDI-II).
- Psychological distress: Symptom Checklist-90-R (SCL90). Global Severity Index (GSI).
- Post-traumatic stress symptoms: Davidson Trauma Scale (DTS).

*Validated cut-off scores were used to define clinically relevant symptoms.

RESULTS

1 Prevalence of psychiatric outcomes following COVID-19.

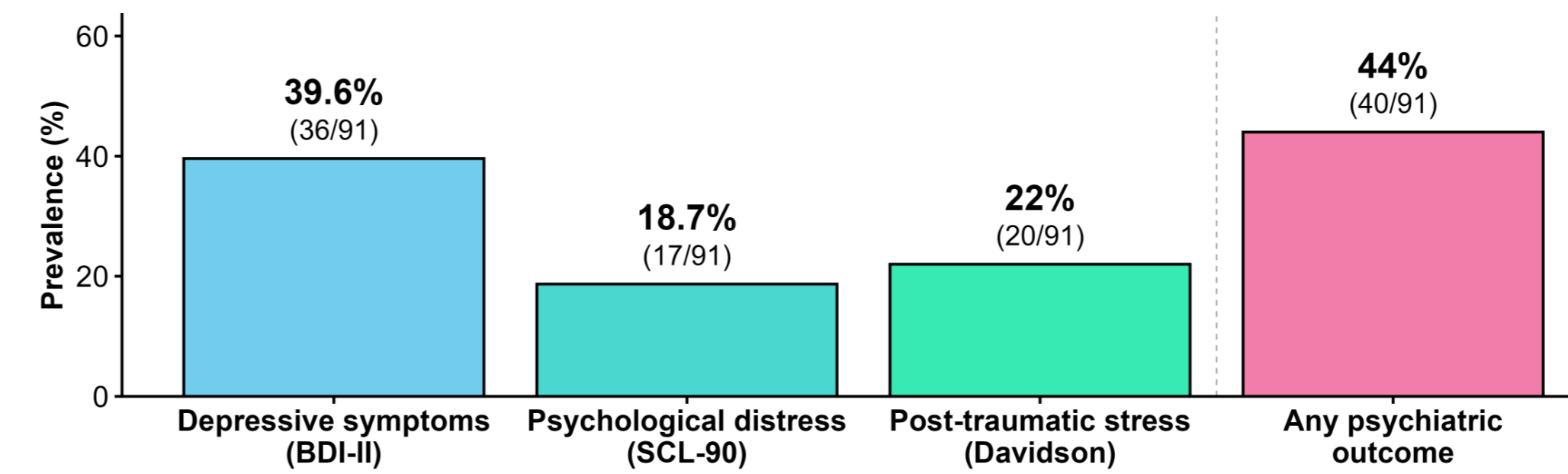


Figure 1. Psychiatric outcomes are presented individually. “Any psychiatric outcome” indicates the presence of at least one symptom domain. Values represent prevalence percentages with the corresponding number of cases (n/N).

2 Inflammatory markers across psychiatric outcomes

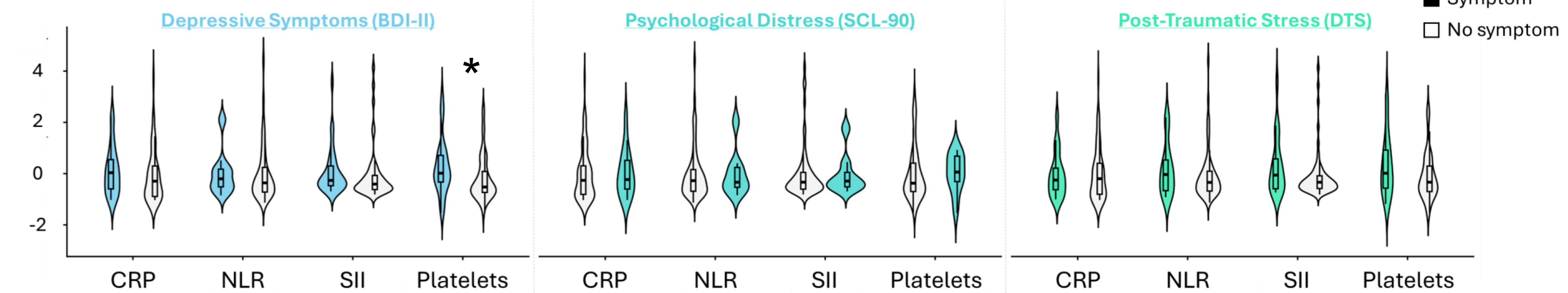


Figure 2. Standardized inflammatory marker levels (z-scores) during the acute COVID-19 phase are shown according to the presence or absence of psychiatric symptoms. Colored violins indicate symptoms and white violins no symptoms. Violin plots show distribution with median and interquartile range. Group differences were assessed using Mann–Whitney U tests. Significance: *p < 0.05. Only statistically significant comparisons are indicated. Follow-up inflammatory markers are not shown, as no significant differences were observed.

3 Psychiatric Outcomes by COVID Severity

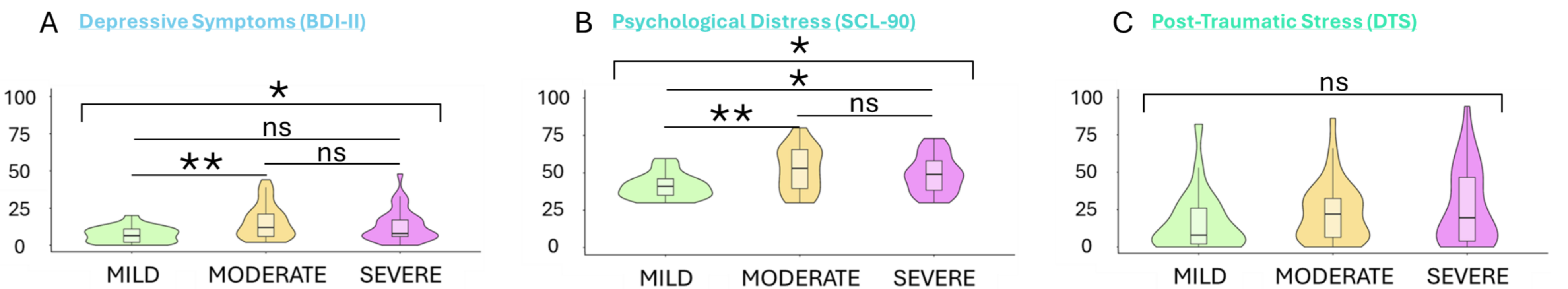


Figure 3. Comparison of psychiatric outcomes by COVID-19 severity. (A) Depressive symptoms (BDI-II), (B) Psychological distress (SCL-90R; GSI), (C) Post-traumatic stress (DTS). Violin plots show distribution with median and IQR. Group differences were assessed using Kruskal–Wallis tests, followed by Mann–Whitney U tests for pairwise comparisons. Significance: ns, *p < 0.05, **p < 0.01.

CONCLUSIONS

- ✓ Psychiatric symptoms were frequent after COVID-19, with nearly half of participants showing at least one outcome.
- ✓ Platelet levels differed between participants with and without depressive symptoms, while other markers showed no differences.
- ✓ Psychiatric symptoms varied according to COVID-19 severity for BDI-II and SCL-90, but not for DTS.

In our cohort, nearly half of participants reported psychiatric symptoms after COVID-19, with limited associations with acute-phase hematological inflammatory markers and higher levels in moderate and severe cases.

ACKNOWLEDGEMENTS:

- Instituto de Salud Carlos III (PI21/00059 to BR),
- Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR: 2021SGR01475 and 2021SGR01380 and SGR00832)

