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Unveiling Long COVID burden in Hospital and Community Settings: findings from the PASCNET Study in Italy's pandemic epicentre

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Bando Cariplo - Networking and capacity building on PASC

PROGETTO
"The Post-Covid-19 Syndrome: network building and innovative management to address a new public health emergency"

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ABSTRACT

Background

Four years after the first wave of SARS-CoV-2 infection, a sizeable minority of survivors remain trapped in what patients themselves have labelled “long COVID”, a chronic, multisystem illness that persists well beyond the acute respiratory syndrome. In contemporary literature, the syndrome is called either post-acute sequelae of SARS-CoV-2 infection (PASC) or post-COVID-19 condition (PCC), yet the common thread is characterized by symptoms that linger, relapse, or newly emerge once the acute phase has resolved. The syndrome is not necessarily confined to critically ill subjects and both primary care and hospitalized patients with COVID-19 infection may be affected. Data on incidence and long term prevalence of PCC are still puzzling and different between studies and countries. Yet the problem requires a clear clinical definition of the syndrome and adapting health systems to support longitudinal, multidisciplinary care for chronic, post-viral conditions.

In Italy, existing COVID-19 follow-up studies have mainly focused on hospital-based samples. Few data describe the prevalence and clinical profiles of post-acute sequelae in the general population, especially in Lombardy, the epicentre of Italy’s earliest pandemic wave. The present PASCNET study addresses this gap by estimating the incidence of post-COVID-19 condition up to one year after an individual’s episode of COVID-19, alongside its current estimated prevalence, providing a projection on Lombardy’s adult population. The sample comprises both Hospitalized Patients (HP) and those managed in the community by their General Practitioners Patients (GPP), enabling a comprehensive assessment of long-term outcomes across a range of disease severities.

Materials and Methods

This retrospective–prospective observational study enrolled adults aged 18–70 years residing in Lombardy, Italy, who had a confirmed SARS-CoV-2 infection between 1 March 2020 and 31 December 2022. Two random samples were identified. The HP sample included patients whose primary reason for hospitalisation was COVID-19 (ICD-9CM codes 078.89, 043, 480.4, 518.9, or 519.7). They were hospitalized in one of six public hospitals (Azienda Socio Sanitaria Territoriale, ASST) and in one research institute (IRCCS) participating in the PASCNET consortium and resided in the territory of one of the participating ATS (Agenzie di Tutela della Salute) both at admission and at enrolment. The GPP sample included patients who tested positive for SARS-CoV-2, resided in the territory of one of the participating ATS at diagnosis and enrolment, and were never hospitalised for COVID-19. These individuals were registered with their general practitioner belonging to IML (Iniziativa Medica Lombarda) at the time of infection and were managed through the infection without hospitalisation.

The study visit occurred between January 16th, 2024 and December 23, 2024 (enrolment period). At this visit, in the enrolling hospital for HP and in the doctors’ office for GPP, retrospective data covering the first year after infection and prospective clinical data, with selected diagnostic tests, were collected.

Data were entered into a dedicated electronic database (DBMS) compliant with European data protection (GDPR) regulations. The study protocol received approval from the relevant Ethics Committees; all participants provided written informed consent.

Sample size was based on the width of the 95% CI, set between 0.04 to 0.07 depending on different scenarios for the cumulative incidence of PCC at 1 year, expected to range between 10% and 40%.

Incidence of PCC in the first year after infection and cumulative probability of recovering from PCC were estimated according to Kaplan–Meier and compared between the two cohorts with the log-rank test. A validation of the recently proposed NIH RECOVER-score to classify probable PASC was performed and a logistic model was fitted to assess its predictive value on PCC at 1 year. The results of the logistic model were used to predict the long-term prevalence of PCC based on the updated score at the study visit.

Results

Data were available on 1162 patients, 616 GPP and 546 HP. Their characteristics show a lower median age in GPP compared to HP (42.9 years, IQ range 32.7-54.6 vs 57.1 years, IQ range 49.7-62.9), a lower frequency of males (47.7% vs 66.1%); not surprisingly, absence of any comorbidity was seen in 72.3% of GPP and 26.1% of HP and the prevalence of frequent comorbidities was lower in GPP compared to HP cohort.

The pattern of symptoms at diagnosis of COVID-19 infection was characterised by a large prevalence (approximately 90% or more) of flu-like and respiratory problems in both cohorts; anosmia and/or ageusia occurred not so often in GPP compared to HP (25.5% vs 46.0%, p<0.0001); other quite frequent symptoms were those related to the musculoskeletal and neurological system, these latter more frequent in GPP (39.4% versus 29.9% in HP, p=0.0007); cardiovascular symptoms were less frequent in both cohorts (12.3% and 18.7% in GPP versus HP, p=0.0025).

During the first year post infection, and mainly within 6 months, 280 patients developed PCC, 57 and 223 in the GPP and HP cohort, and the estimated 1-year cumulative incidence of PCC was 9.1% (95% CI 7.1 – 11.7) and 39.9% (95% CI 35.9 – 44.1) in the GPP and HP cohort (p-value <0.0001), respectively. The prevalence of this condition lowered to 13 out of 616 (2.1%) GPP and to 173 out of 546 HP (31.7%) as the remaining patients resolved their syndrome by the end of the first year from PCC occurrence.

Prospective data collected at study visit after a minimum of 2.9 up to a maximum of 4.2 years from diagnosis of SARS-CoV-2 infection show a marked decrease in the frequency of each type of symptom in those patients who resolved their PCC condition compared to those who did not resolve it.

Symptoms collected in the study were adapted to the approach taken to calculate the NIH RECOVER-score to classify probable PASC on both cohorts based on the 1-year and the follow-up evaluation. At 1 year, in the GPP cohort, the median score for 57 patients with PCC was 4 (IQ range 2-10) as compared to 1 (IQ range 0-5) in 559 patients without PCC. In the HP cohort, the median score for 223 patients with PCC was 7 (IQ range 3-13) as compared to 0 (IQ range 0-5) in 323 patients without PCC. The score, updated at the follow-up visit for the 57 patients with PCC in the GPP cohort and for the 223 patients with PCC in the HP cohort, was higher for those who did not resolve PCC compared those who had resolved.

The logistic model showed that the score (continuous variable) significantly increases the odds of PCC at 1 year from infection (OR 1.16, 95% CI 1.13 – 1.20).

Conclusions

Long-term sequelae after SARS-CoV-2 infection have emerged as a major, heterogeneous public-health problem. Drawing on a multicentre follow-up of hospitalised and community-managed adults throughout Lombardy, the PASCNET study shows that post-COVID-19 syndrome remains substantial and multifaceted during the first year and extends through the four-year observation window. By capturing incidence, persistence, and clinical profiles of post-COVID-19 syndrome across pandemic waves and care settings, the PASCNET study offers an unprecedented look at how this condition evolves over time.