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Neurological, Cognitive, and Systemic Manifestations of Post-COVID Syndrome: A Cross-Sectional Study in a Caucasian Cohort

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ABSTRACT

BACKGROUND. Post-COVID syndrome is increasingly recognized as a heterogeneous clinical condition characterized by persistent neurological, cognitive, and systemic symptoms. While individual manifestations have been widely reported, the overall clinical phenotype and symptom distribution remain insufficiently characterized, particularly in specific regional populations.

OBJECTIVES. To characterize the neurological, cognitive, and systemic manifestations of post-COVID syndrome in a Caucasian cohort and to evaluate their association with acute COVID-19 severity.

METHODS. This cross-sectional study included 360 individuals with prior SARS-CoV-2 infection and persistent post-COVID symptoms. Demographic, clinical, and disease-related variables were collected, including disease severity, hospitalization status, and comorbidities. Neurological, cognitive, and systemic symptoms were assessed using patient-reported outcomes and clinical evaluation. Neuropsychological status was evaluated using validated instruments, including PHQ-9, BDI, STAI, and MoCA. Statistical analyses were performed to describe symptom distribution and to assess differences across disease severity groups.

RESULTS. Neurological and systemic symptoms were highly prevalent, with anosmia (78.9%) and ageusia (59.4%) representing the most common manifestations. Cognitive symptoms were also frequent, including memory complaints (45.8%) and executive dysfunction (30.8%). Fatigue was reported in 42.8% of participants. Symptom burden varied according to disease severity, with significantly higher prevalence of cognitive impairment, fatigue, and neuropathic symptoms observed in patients with severe acute COVID-19 ($p < 0.05$). In contrast, sensory symptoms such as anosmia and ageusia were distributed relatively evenly across severity groups. Neurological and systemic symptoms demonstrated substantial heterogeneity across the study population.

CONCLUSIONS. A heterogeneous clinical phenotype with a high prevalence of sensory, cognitive, and systemic symptoms characterizes Post-COVID syndrome. Disease severity is associated with increased burden of cognitive and systemic manifestations, while sensory dysfunction appears independent of severity. These findings highlight the importance of comprehensive clinical assessment and support the need for multidisciplinary management strategies in post-COVID populations.

KEYWORDS. Ageusia; Anosmia; Caucasian population; Clinical phenotype; Cognitive impairment; Cross-sectional study; Disease severity; Fatigue; Long COVID; Neurological symptoms; Neuropsychology; Post-COVID syndrome.

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BACKGROUND

Post-COVID syndrome, also referred to as long COVID, has emerged as a persistent clinical condition affecting a substantial proportion of individuals following acute SARS-CoV-2 infection.[1] While respiratory manifestations dominate the acute phase, increasing attention has been directed toward long-term neurological and neuropsychological sequelae that significantly impact patients' quality of life and functional capacity.[2] These manifestations include a broad spectrum of symptoms, ranging from sensory disturbances and headaches to cognitive impairment, fatigue, and affective disorders.[3]

The clinical presentation of post-COVID neurological involvement is notably heterogeneous. Patients may report isolated symptoms such as anosmia or headache. In contrast, others experience complex symptom clusters involving cognitive dysfunction, including memory impairment, reduced attention, and executive dysfunction, often described as "brain fog." In parallel, psychological disturbances such as anxiety and depressive symptoms are

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frequently observed, further complicating the clinical picture. Importantly, these manifestations are not limited to individuals with severe acute disease and may occur even after mild infection, suggesting that post-COVID syndrome represents a multifactorial and systemic condition rather than a direct consequence of disease severity alone.[4,5]

Despite the growing body of literature, the majority of studies have focused on isolated domains, such as cognitive impairment or psychiatric outcomes, without systematically characterizing the full spectrum of neurological and systemic symptoms within a unified clinical framework. As a result, the real-world phenotypic variability of post-COVID syndrome remains insufficiently defined, particularly in specific populations.[6] Understanding the distribution and co-occurrence of symptoms is essential for improving clinical recognition, patient stratification, and management strategies.[7,8]

In addition, demographic and clinical factors such as age, sex, comorbidities, and severity of the acute infection may influence the manifestation and persistence of neurological symptoms.[9,10] However, the extent to which these factors shape the clinical phenotype of post-COVID syndrome remains incompletely understood, particularly in underrepresented regional populations. Studies focusing on Caucasian cohorts from the South Caucasus region are limited, despite potential differences in healthcare systems, genetic background, and socio-environmental factors that may influence disease expression.[11]

From a clinical perspective, identifying dominant symptom patterns and their associations with baseline characteristics has practical implications. A structured phenotypic approach may facilitate early recognition of high-risk patient groups, guide targeted neurological and psychological assessment, and support the development of multidisciplinary management strategies. Moreover, descriptive analyses of symptom burden and distribution provide an essential foundation for future mechanistic and longitudinal studies.

Therefore, the present study aimed to characterize the clinical phenotype of neurological, cognitive, and systemic manifestations in individuals with post-COVID syndrome in a Caucasian cohort.

METHODS

This cross-sectional study included 360 individuals with documented SARS-CoV-2 infection. Participants were recruited from outpatient and follow-up clinical settings between January 2021 and December 2024. Eligibility criteria comprised age ≥18 years, documented prior SARS-CoV-2 infection, and persistence of symptoms compatible with post-COVID syndrome for at least four weeks following the acute phase of infection. Individuals with a history of major neurological disorders, pre-existing severe psychiatric conditions, active malignancy, or incomplete clinical data were excluded from the study.

Clinical and demographic data were collected using standardized data collection forms. Variables included age, sex, ethnicity, geographic location, level of education, body mass index, smoking status, and the presence of comorbid conditions such as hypertension, diabetes mellitus, and cardiovascular disease. COVID-19–related variables included disease severity during the acute phase, categorized as mild, moderate, or severe, as well as hospitalization status, intensive care unit admission, oxygen therapy requirement, reinfection history, vaccination status, and time since infection in months.

Neurological, cognitive, and systemic manifestations were assessed based on patient-reported symptoms and clinical evaluation. Symptoms were categorized into neurological and sensory manifestations, cognitive complaints, systemic symptoms, and peripheral neurological features. In addition, recovery patterns related to smell and taste, use of sleep medication, and findings from neurological examination were recorded.

Neuropsychological assessment was performed using validated instruments, including the Patient Health Questionnaire-9 (PHQ-9), Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), and Montreal Cognitive Assessment (MoCA). These measures were analyzed as continuous variables to reflect the distribution of psychological and cognitive impairment within the cohort.

Statistical analyses were conducted using IBM SPSS Statistics, version 27.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on distribution,

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while categorical variables were presented as frequencies and percentages. Group comparisons were performed using the chi-square test for categorical variables and the Mann–Whitney U test or Kruskal–Wallis test for continuous variables. Subgroup analyses were conducted by disease severity and hospitalization status. A p-value <0.05 was considered statistically significant.

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the TSMU Ethical Committee (approval number TSMU/2019/2.22). All participants provided written informed consent before inclusion in the study.

RESULTS

A total of 360 participants were included in the analysis. The cohort's mean age was 47.6±19.0 years, with a slight predominance of male participants (55.0%). The study population comprised a Caucasian regional cohort, predominantly Georgian (75.8%), followed by Armenian (11.7%), Azerbaijani (7.5%), and Russian (5.0%) participants. The majority of individuals (66.4%) resided in urban areas, 27.5% in rural areas, and 6.1% in semi-urban areas. Educational attainment was generally high, with most participants holding bachelor's or master's degrees. The mean body mass index was 28.8±5.8 kg/m². Hypertension represented the most common recorded chronic medical condition and was identified in 36.1% of participants.

Regarding acute COVID-19, disease severity was mild in 57.8%, moderate in 15.6%, and severe in 26.7%. Hospitalization was required in 36.7% of patients, and 20.0% required admission to the intensive care unit. The median time since infection was 29 months [IQR 28.0–32.5]. A detailed overview of the demographic and clinical characteristics of the study population is presented in **TABLE 1**.

TABLE 1. Baseline demographic and clinical characteristics

Variable	Value
Age in years (mean±SD)	47.6±19.0
Age groups n (%)	
18–30	67(18.6)
31–45	156(43.3)
46–60	61(16.9)
≥61	76(21.1)
Sex n (%)	
Female	162(45.0)
Male	198(55.0)
Ethnicity n (%)	
Georgian	273(75.8)
Armenian	42(11.7)
Azerbaijani	27(7.5)
Russian	18(5.0)
Geographic location n (%)	
Urban	239(66.4)
Rural	99(27.5)
Semi-urban	22(6.1)
Education level n (%)	
Secondary	71(19.7)
Bachelor's	127(35.3)
Master's	121(33.6)
Doctorate	41(11.4)
BMI (mean±SD)	28.8±5.8
Comorbidity burden n (%)	
None	232(64.4)
≥1 condition	128(35.6)
Hypertension	130(36.1)
Diabetes mellitus	44(12.2)
Smoking status n (%)	
Never	184(51.1)
Former	38(10.6)
Current	138(38.3)
COVID-19 severity n (%)	
Mild	208(57.8)
Moderate	56(15.6)
Severe	96(26.7)
Hospitalization n (%)	132(36.7)
ICU admission n (%)	72 (20.0)
Oxygen therapy n (%)	115(31.9)
Reinfection n (%)	69(19.2)
Time since infection months (median [IQR])	29.0[28.0-32.5]

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; IQR, Interquartile range.

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Neurological and systemic symptoms were highly prevalent and demonstrated considerable variability across the cohort. The most frequently reported manifestations were anosmia (78.9%) and ageusia (59.4%), followed by headache (46.7%) and fatigue (42.8%). Cognitive symptoms were also common, with memory complaints reported by 45.8% of participants, executive dysfunction by 30.8%, attention impairment by 21.7%, and brain fog by 22.8%. Peripheral neurological symptoms, including neuropathic complaints, were observed in 28.6% of cases. Less frequent symptoms included dizziness or balance disturbances and gastrointestinal complaints.

Regarding recovery patterns, 70.6% of participants reported complete recovery of smell and taste, while 29.4% reported only partial recovery. Neurological examination findings were normal in the majority of individuals (73.9%), whereas hyperreflexia, sensory deficits, and gait abnormalities were observed in smaller subsets. The full distribution of neurological, cognitive, and systemic symptoms is summarized in **TABLE 2**.

Symptom burden varied according to the severity of the acute phase of COVID-19. Patients with severe disease demonstrated a higher prevalence of cognitive complaints, including memory impairment and executive dysfunction, compared to those with mild disease. Similarly, fatigue and neuropathic symptoms were more frequently observed in the severe group. In contrast, sensory symptoms such as anosmia and ageusia were distributed more evenly across severity categories and showed no statistically significant differences.

Comparative analysis confirmed that the prevalence of memory complaints, executive dysfunction, fatigue, and neuropathic symptoms increased significantly with disease severity ($p < 0.05$). Hospitalization status was recorded in the clinical dataset; however, detailed subgroup analyses were beyond the scope of the present study. The distribution of key symptoms according to disease severity is presented in **TABLE 3**. This pattern is further illustrated in **FIGURE 1**.

TABLE 2. Neurological, cognitive, and systemic symptom profile

Symptom	n (%)
Core neurological symptoms	
Anosmia	284(78.9)
Ageusia	214(59.4)
Headache	168(46.7)
New-onset headache	90(25.0)
Dizziness/balance disturbance	58(16.1)
Cognitive symptoms	
Memory complaints	165(45.8)
Executive dysfunction	111(30.8)
Brain fog	82 (22.8)
Attention impairment	78(21.7)
Systemic symptoms	
Fatigue	154(42.8)
Muscle pain	87(24.2)
Gastrointestinal symptoms	57(15.8)
Post-exertional malaise	43(11.9)
Peripheral symptoms	
Neuropathic symptoms	103(28.6)
Recovery patterns	
Complete smell/taste recovery	254(70.6)
Partial recovery	106(29.4)
Sleep medication use	31(8.6)
Neurological examination	
Normal	266(73.9)
Hyperreflexia	52(14.4)
Sensory deficit	29(8.1)
Gait disturbance	13(3.6)

TABLE 3. Symptom prevalence according to COVID-19 severity

Symptom	Mild (%)	Moderate (%)	Severe (%)	p-value
Memory complaints	39.0	48.2	58.3	<0.05
Executive dysfunction	25.0	32.1	43.8	<0.05
Fatigue	36.5	44.6	55.2	<0.05
Neuropathic symptoms	22.6	30.4	41.7	<0.05
Anosmia	80.2	76.8	77.1	0.42
Ageusia	60.1	58.9	57.3	0.61

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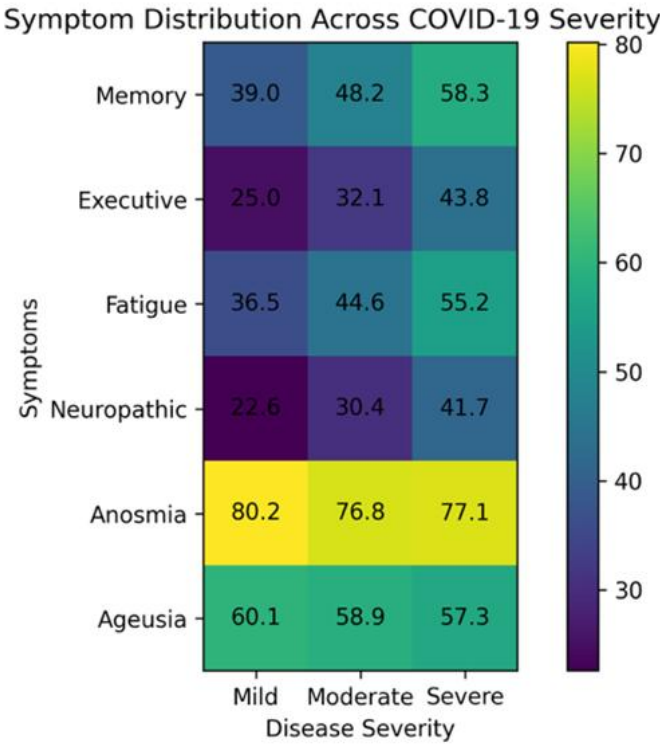
FIGURE 1. Heatmap illustrating the distribution of key neurological and systemic symptoms across COVID-19 severity groups



Neuropsychological assessment revealed a broad distribution of scores within the cohort.

DISCUSSION

The present study provides a comprehensive clinical characterization of neurological, cognitive, and systemic manifestations in post-COVID syndrome within a Caucasian cohort. The findings demonstrate a high prevalence of persistent symptoms, particularly sensory disturbances, cognitive complaints, and fatigue. Importantly, symptom distribution was heterogeneous, supporting the concept that post-COVID syndrome is a multidimensional clinical entity rather than a uniform condition.

One of the most consistent observations in this study was the high prevalence of sensory symptoms, particularly anosmia and ageusia, affecting more than half of the cohort. These findings are in line with previous reports indicating that olfactory and gustatory dysfunction are among the most common and persistent features of post-COVID syndrome, even in patients with initially mild disease. [12] Boscolo-Rizzo et al. reported similar patterns of persistence in smell and taste dysfunction, highlighting their clinical relevance as long-term sequelae of SARS-CoV-2 infection. [13,14] This consistency across studies supports the reliability of sensory dysfunction as a hallmark feature of post-COVID neurological involvement.

In addition to sensory disturbances, cognitive symptoms were highly prevalent, with nearly half of the participants reporting memory impairment and a substantial proportion demonstrating executive dysfunction and attention deficits. [15] These findings are consistent with emerging evidence suggesting that cognitive impairment is a central component of post-COVID syndrome. A recent meta-analysis by Premraj et al. described a high frequency of cognitive and neuropsychiatric manifestations in post-COVID populations, reinforcing the concept that cognitive dysfunction is not an isolated phenomenon but part of a broader neuropsychological spectrum. [10,16]

A key finding of the present study is the association between disease severity and symptom burden. Patients with severe acute COVID-19 demonstrated a significantly higher prevalence of cognitive complaints, fatigue, and neuropathic symptoms compared to those with mild disease. This pattern suggests a dose–response relationship, in which greater systemic involvement during the acute phase is associated with a higher risk of long-term neurological sequelae. These findings are consistent with previous observations that severe infection is associated with increased risk of persistent neurological complications, potentially reflecting greater systemic stress, inflammatory burden, and organ involvement during the acute phase.

In contrast, sensory symptoms such as anosmia and ageusia were distributed relatively evenly across severity groups, suggesting that these manifestations may be less dependent on systemic disease severity and more related to localized mechanisms, such as viral effects on olfactory pathways. This distinction between severity-dependent and severity-independent symptoms highlights the heterogeneity of post-COVID neurological involvement and suggests that different pathophysiological mechanisms may underlie specific symptom domains.

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From a clinical perspective, the high prevalence of fatigue and cognitive complaints is particularly relevant, as these symptoms are closely associated with reduced functional capacity and quality of life. Although the present study did not focus on mechanistic pathways, the observed co-occurrence of cognitive and systemic symptoms suggests that these manifestations may cluster within specific clinical phenotypes. The identification of such patterns may facilitate improved patient stratification and targeted management strategies in clinical practice.

The findings of this study also underscore the importance of comprehensive clinical assessment in patients with post-COVID syndrome. The wide distribution of symptoms across neurological, cognitive, and systemic domains suggests that a multidisciplinary approach is required, integrating neurological evaluation, cognitive screening, and psychological assessment. Early identification of high-risk patients, particularly those with severe acute disease or multiple persistent symptoms, may improve long-term outcomes through timely intervention and rehabilitation strategies.

This study has several limitations that should be acknowledged. First, the cross-sectional design limits the ability to assess temporal dynamics or causal relationships between variables. Second, symptom assessment relied in part on patient-reported outcomes, which may be subject to reporting bias. Third, although the cohort was relatively large and well-characterized, it represents a specific regional population, which may limit generalizability to other populations. Nevertheless, the study provides valuable insights into the clinical phenotype of post-COVID syndrome in an underrepresented Caucasian cohort.

In summary, the present study demonstrates that a broad and heterogeneous spectrum of neurological, cognitive, and systemic manifestations characterizes post-COVID syndrome. Sensory dysfunction, cognitive impairment, and fatigue represent the most prominent features, while disease severity appears to influence the burden of cognitive and systemic symptoms. These findings contribute to a better understanding of the clinical phenotype of post-COVID syndrome and provide a foundation for future longitudinal and mechanistic studies.

The relatively long median interval since infection reflects the prolonged recruitment period and should be considered when interpreting patterns of symptom persistence.

The present findings should be interpreted primarily as a descriptive characterization of symptom distribution among individuals with persistent post-COVID manifestations, rather than as a formal phenotypic classification of post-COVID syndrome.

Several limitations should be considered. First, because participants were recruited from outpatient and follow-up settings and all had persistent symptoms, the cohort is not representative of all individuals recovering from COVID-19. Therefore, the reported frequencies should not be interpreted as general population prevalence. Second, the long median interval since infection may introduce recall bias and may reflect differences related to viral variants, reinfections, and vaccination status. Third, unadjusted comparisons may be influenced by age, sex, BMI, comorbidities, and hospitalization status.

CONCLUSIONS

Post-COVID syndrome is associated with a high prevalence of persistent neurological and cognitive symptoms, with substantial heterogeneity across patients. Sensory disturbances, cognitive impairment, and fatigue represent the dominant clinical features. Disease severity is associated with increased symptom burden, particularly in cognitive and systemic domains. These findings highlight the importance of structured clinical assessment and support the need for multidisciplinary management approaches in post-COVID populations.

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