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Research Article



A Survey on Respiratory and Neurological Symptoms in Alzheimer's, Schizophrenia, Bipolar, and Migraine Patients Following COVID-19 Infection

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Abstract

Background: The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 2019 led to the global coronavirus disease 2019 (COVID-19) pandemic with a wide range of clinical symptoms. Neurological complications have been a significant concern, with diverse symptoms and potential neuroinvasive mechanisms. The pandemic has also impacted individuals with mental health conditions, such as migraines, bipolar disorder (BD), and schizophrenia, highlighting the complex interconnections between physical and mental health during these challenging times.

Objectives: This retrospective report from the Iranian Network for Research in Viral Diseases (INRVD) study aimed to investigate the multifaceted interactions between COVID-19, neurological complications, and mental health disorders (e.g., migraines, BD, and schizophrenia) to better understand their collective impact on individuals' health and well-being.

Methods: This study involved 63 individuals who tested positive for COVID-19, including 32 females (50.8%) and 31 males (49.2%). The participants were categorized into different groups based on their underlying conditions: 7 individuals with schizophrenia, 8 with BD, 6 with migraines, 12 with Alzheimer's disease, and 30 with COVID-19 without any underlying neurologic disorder. This investigation was carried out in 12 hospitals supervised by the INRVD between March 2020 and May 2021. The study used frequencies and percentages to describe the data and employed chi-square tests, including the contingency coefficient, to explore associations between COVID-19 symptoms and disease groups.

Results: The analysis of clinical manifestations revealed distinctive patterns. Cough was the most prevalent symptom across the entire sample, affecting over 79% of participants. Fever followed as the second most common symptom, with approximately 62% of individuals reporting it. Fatigue ranked third, impacting 57% of the subjects. In contrast, vomiting was the least frequently reported symptom, with an incidence of only 14.3%. In terms of specific conditions, a notable discrepancy was observed in the prevalence of headaches. Although present in 71.4% of individuals with schizophrenia, this symptom was reported by only 50% of those with BD, followed by 66.7% with migraines and 83.3% with Alzheimer's. The patients without neurologic disorders exhibited a lower incidence of neurological manifestations, with only 23.3% reporting headaches.

Conclusions: This study provides insights into the clinical manifestations of COVID-19 in individuals with distinct underlying conditions. The prevalence and presentation of symptoms varied significantly across the different groups, and neurological symptoms exhibited a higher prevalence in this patient group than those without any underlying neurologic disorders. This study aimed for a more comprehensive understanding of the probable intricate interplay between COVID-19, underlying health conditions, and clinical manifestations. Understanding these differences is crucial for tailoring effective clinical interventions.

Keywords: SARS-CoV-2, COVID-19, Neurologic Disorder, Bipolar, Alzheimer, Schizophrenia

1. Background

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in late 2019 sparked a global

health crisis of unprecedented proportions, giving rise to the coronavirus disease 2019 (COVID-19) pandemic (1). Initially identified in the city of Wuhan, China, COVID-19

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swiftly spread across international borders, prompting widespread concern and stringent containment measures (1).

Common symptoms associated with SARS-CoV-2 infection encompass a range of respiratory and systemic manifestations (2). Patients afflicted by the virus often present with symptoms such as cough, shortness of breath, fever, fatigue, and headache (Figure 1) (2). Additionally, some individuals have reported gastrointestinal symptoms or anosmia (loss of smell) (2). It is essential to acknowledge that the severity of COVID-19 can vary significantly, spanning from mild cases akin to the common flu to severe illness and, tragically, fatalities (2).

In the realm of infectious diseases, COVID-19 has been classified as a self-limiting affliction, with most individuals experiencing mild symptoms typically recovering within one to two weeks (3). However, the outcomes of SARS-CoV-2 infection can be diverse, culminating in five different scenarios: Asymptomatic infection, mild to moderate cases, severe cases, critical cases, and death (4). Recent research even suggests that children under the age of 20 years might exhibit a relatively high proportion of asymptomatic infections (5).

As the COVID-19 pandemic unfolded, each country grappled with the virus's unique impact, leading to distinct statistics and outcomes. Notably, the United States, at a certain point, documented the highest number of COVID-19 cases, deaths, and overall mortality rate in the Americas and globally (6). The United States reported a staggering 103,436,829 confirmed cases and 1,138,309 deaths, corresponding to a mortality rate of 1.09%. On the other hand, China reported 99,319,332 confirmed cases and 121 781 deaths, resulting in a considerably lower mortality rate of 0.12% (6). These statistics underscore the variability in COVID-19's severity and mortality rates across different regions and nations.

However, the impact of SARS-CoV-2 extends beyond the realm of respiratory illnesses, as it has been implicated in a spectrum of neurological disorders (NDs), posing an additional layer of complexity to the pandemic's toll on public health (Figure 2) (7). Neurological disorders, characterized by various cognitive, motor, and sensory impairments, are already recognized as a significant public health challenge (8). These conditions often result from complex interactions between genetic predisposition and environmental factors (9).

The intriguing connection between SARS-CoV-2 and NDs becomes apparent when we delve into the neurological phenomena associated with COVID-19. Studies have reported neurological symptoms in a substantial percentage of pediatric COVID-19 patients, including headaches (10). Among children diagnosed with multisystem inflammatory syndrome in children (MIS-C), neurological symptoms, such as altered mental status and encephalopathy, have been observed (11, 12). Furthermore, severe neurological complications, including seizures, coma, encephalitis, demyelinating disorders, and aseptic meningitis, have been documented in a subset of pediatric MIS-C cases (13). Even infants and toddlers with COVID-19 have exhibited encephalopathy-like symptoms (14). However, neurological manifestations are not limited to pediatric cases; they have also been noted in adults during the acute phase of COVID-19. These manifestations encompass a wide array of symptoms, including headache, altered mental status, seizures, and stroke (15). Intriguingly, a proportion of infected individuals develop post-infectious viral syndromes characterized by diverse neuropsychiatric symptoms (15).

To understand the mechanisms underlying these neurological complications, it is essential to explore how SARS-CoV-2 might potentially infiltrate the central nervous system (CNS). The virus's structure, encased within a nucleocapsid and surrounded by a nuclear envelope, offers insight into its potential neuroinvasive capabilities (16). Severe acute respiratory syndrome coronavirus 2 can enter the CNS through multiple routes, including the general circulation, nasal cavity, and cribriform plate (16, 17). Once inside, the virus can interact with angiotensin-converting enzyme 2 (ACE2) receptors on neurons, glia, endothelial cells, and other neural components, potentially causing neuronal damage and disrupting the blood-brain barrier (BBB) (16, 17). Such disruptions in the BBB might lead to cerebral edema, compromising vital respiratory functions (16).

Although the BBB is designed to prevent pathogen infiltration, neurotropic viruses have devised various strategies to breach this barrier (18). The hematogenous route, involving viremia and subsequent transcytosis or infection of endothelial cells, is one common pathway (19). Additionally, viruses can exploit infected monocytes as a "Trojan Horse" mechanism or enter the CNS through the coordination of motor or sensory nerves (19). Olfactory sensory neurons also serve as potential routes for many viruses to access the CNS (20).

Neurological complications following COVID-19 encompass a broad spectrum of symptoms, including headaches, ataxia, seizures, loss of taste and smell, vision impairment, and nerve pain (21). Furthermore, severe complications, such as polyneuritis, Guillain-Barré syndrome (GBS), meningitis, encephalitis, encephalopathy, cerebral hemorrhage, and infarction have been observed in some cases (21). This dynamic interplay between age and symptomatology adds an extra



Figure 1. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) typical respiratory symptoms including runny nose, cough, sore throat, breath shortness, and difficulty in breathing (created with BioRender.com)

layer of complexity to our understanding of COVID-19's neurological effects.

Psychological stressors have long been recognized as potential triggers for migraine episodes in pediatric patients (22, 23). The overwhelming emotional challenges, especially in educational environments, can lead to heightened central nervous system responses, increasing the risk of headaches and migraines (24). The COVID-19 pandemic has introduced new dimensions to the study of migraines. Research conducted during the pandemic reported fewer migraine attacks and lower pain levels among subjects with migraines, in addition to moderate levels of depression (25). The aforementioned findings underscore the intricate relationship between psychological stress, migraines, and the broader impact of the pandemic on individuals' physical and mental well-being.

Moreover, the pandemic has cast a profound shadow on individuals with severe mental illnesses (SMIs), including bipolar disorders (BDs) (26). Lockdowns and social distancing regulations have disrupted social support systems, increased loneliness, and disrupted circadian rhythms (27, 28). For those already living with BD and related conditions, the burden of these downstream consequences has been particularly significant. Bipolar disorder, in particular, is a well-established risk factor for suicidality, and the pandemic's socioeconomic impact might have exacerbated this risk (29-31). The pandemic's far-reaching effects have also reshaped the landscape of care for individuals, leading to dramatic changes in telepsychiatry legislation (32).

Furthermore, the interplay between COVID-19 and schizophrenia, another prevalent mental health condition, cannot be ignored. Coronavirus disease 2019's greater impact on older individuals and those with comorbidities holds substantial implications for schizophrenia patients, given their higher rates of comorbid conditions, including diabetes and pulmonary



Figure 2. Illustration of rare and common neurological manifestations in coronavirus disease 2019 (COVID-19) patients (created with BioRender.com).

diseases (33). These patients are also more likely to smoke, further complicating their respiratory health (33). In general, schizophrenia patients are more susceptible to a higher risk of acute organ dysfunction and death upon admission and in the intensive care unit (ICU) (34).

2. Objectives

The present study aimed to investigate patients who have tested positive for COVID-19, alongside those diagnosed with BD, migraine, Alzheimer's, and schizophrenia, to explore the intricate intersections of these conditions and their potential impact on individuals' health and well-being.

3. Methods

3.1. Data Collection and Extraction

3.1.1. Demographic Data

The study encompassed a total of 63 participants with varying diagnoses: 7 individuals with schizophrenia, 8 with BD, 6 with migraine, and 12 with Alzheimer's. Additionally, there was a group consisting of 30 subjects without an underlying neurological disorder but with a positive real-time polymerase chain reaction (PCR) test for SARS-CoV-2. All relevant information from patients' files was extracted.

3.1.2. Data Extraction

The study was conducted across 12 hospitals under the auspices of the Iranian Network for Research in Viral Diseases, including facilities such as Ali Asghar, Amin, Amiral Momenin, Imam Khomeini, Hajar, Khansari, Razi, Rouhani, Shariati, Sina, Vali Asr, and Yas Medical Center. Data collection spanned from March 2020 to May 2021, and patient information was retrieved from their medical records. Before participation, each patient provided informed consent, and the study protocol received approval from the Ethics Committees of Tehran University of Medical Sciences, Tehran, Iran (IR.TUMS.VCR.REC. 1399.599).

3.1.3. Statistical Methods

In this study, frequencies and percentages were used to describe different aspects of the data. The Chi-squared test was applied for independence, and the contingency coefficient, a chi-squared-based test for association, was employed to investigate the existence of any association between COVID-19 symptoms and different disease groups. All computations were performed using the IBM SPSS statistical package (version 27).

4. Results

This study examined a cohort of 63 COVID-19-infected patients, comprising 32 females (50.8%) and 31 males (49.2%). Among the individuals, 7 cases (11.1%) had schizophrenia, along with 8 cases (12.7%) with BD. Additionally, 6 patients (9.5%) reported migraine and 12 subjects (19%) were diagnosed with Alzheimer's disease. A group of patients without an underlying neurological disorder, consisting of 30 subjects (47.6%), had none of the aforementioned conditions but tested positive for SARS-CoV-2. Notably, the gender distribution did not show significant differences across the five subgroups (chi-square test value = 4.628, P = 0.328).

Table 1 shows the symptoms of COVID-19 observed in both the entire sample and within each subgroup. Across the entire sample, cough was the most prevalent symptom, affecting over 79% of the subjects. Fever ranked as the second most common symptom, experienced by approximately 62% of individuals. Fatigue followed closely as the third most reported symptom, affecting 57% of the subjects. Conversely, vomiting was the least frequently reported symptom, occurring in only 14.3% of cases.

Table 2 shows the findings regarding the potential correlation between experiencing COVID-19 symptoms and different subgroups. The contingency coefficient for headaches was calculated as 0.447, with a P-value less

than 0.05, indicating a significant association between subgroup membership and experiencing headaches. Notably, patients without an underlying disorder exhibited a notably lower proportion of individuals reporting headaches than the other four groups, as indicated in Table 1. Furthermore, statistically significant associations were observed for breath shortness (P = 0.032), dizziness (P < 0.001), and sleep problems (P = 0.030), with contingency coefficients suggesting notable links between experiencing these symptoms and subgroup membership. This finding suggests that individuals in various subgroups, including those experiencing breath shortness, sleep problems, dizziness, and headaches, were significantly more likely to report these symptoms in the context of COVID-19 infection. Associated symptoms stratified by neurological comorbidities are shown in Figure 3, and neurologic and respiratory symptoms of each group are shown in Figures 4 and 5. Neurologic symptoms might be due to underlying neurological disorders in Alzheimer's, BD, migraine, and schizophrenia; nevertheless, respiratory symptoms are attributed to COVID-19. However, there might be an elevated risk of these symptoms following SARS-CoV-2 infection.

5. Discussion

This study examined a sample comprising 7 individuals with schizophrenia, 8 cases of BD, 6 individuals with migraines, and 12 cases of Alzheimer's disease. The findings revealed that cough had the highest prevalence at 79% among clinical symptoms, followed by fever at 62% and fatigue at 57%. Additionally, neurological symptoms, such as headaches, were prevalent in 56.25% of the cases, and sleep problems affected 46.87%, both showing significant occurrence rates.

Coronavirus disease 2019, caused by the novel coronavirus, can exhibit diverse neurological symptoms, including headaches, loss of taste and smell, confusion, and, in severe cases, strokes and encephalitis. Understanding and monitoring these symptoms is crucial for comprehensive patient care. In a study focused on neurological symptoms among a cohort of 891 individuals, the findings showed that headaches were prevalent in 63.9% of cases, sleep disturbances affected 51.3%, hyposmia/anosmia was observed in 46%, and dizziness occurred in 45.4%, establishing them as the predominant neurological symptoms in the studied population. The aforementioned results indicate differences from the present study, which reported lower rates of headaches and sleep disturbances but higher rates of dizziness in comparison (35).

Symptom	Schizophrenia (n = 7)	Bipolar (n = 8)	Migraine (n=6)	Alzheimer (n = 12)	Non-neurologic Disorder (n = 30)	Total (n = 63)
Cough	6 (85.7)	6 (75)	5 (83.3)	10 (83.3)	23 (76.7)	50 (79.4)
Fever	4 (57.1)	3 (37.5)	4 (66.7)	7 (58.3)	21 (70)	39 (61.9)
Fatigue	2 (28.6)	2 (25)	3 (50)	7 (58.3)	22 (73.3)	36 (57.1)
Headache	5 (71.4)	4 (50)	4 (66.7)	10 (83.3)	7 (23.3)	30 (47.6)
Anorexia	3 (42.9)	4 (50)	2 (33.3)	6 (50)	13 (43.3)	28 (44.4)
Breath shortness	2 (28.6)	4 (50)	5 (83.3)	7 (58.3)	7 (23.3)	25 (39.7)
Dizziness	4 (57.1)	2 (25)	5 (83.3)	10 (83.3)	4 (13.3)	25 (39.7)
Sore throat	3 (42.9)	3 (37.5)	2 (33.3)	4 (33.3)	11 (36.7)	23 (36.5)
Muscle pain	4 (57.1)	3 (37.5)	2 (33.3)	4 (33.3)	10 (33.3)	23 (36.5)
Lethargy	2 (28.6)	2 (25)	4 (66.7)	6 (50)	8 (26.7)	22 (34.9)
Rhinorrhea	2 (28.6)	2 (25)	1 (16.7)	2 (16.7)	12 (40)	19 (30.2)
Sleep problem	5 (71.4)	1 (12.5)	2 (33.3)	7 (58.3)	5 (16.7)	19 (30.2)
Nausea	3 (42.9)	2 (25)	1 (16.7)	3 (25)	5 (16.7)	14 (22.2)
Lack of taste	3 (42.9)	1(12.5)	0(0)	4 (33.3)	5 (16.7)	13 (20.6)
Lack of smell	1(14.3)	1(12.5)	0(0)	3 (25)	7 (23.3)	12 (19)
Diarrhea	2 (28.6)	2 (25)	1 (16.7)	2 (16.7)	4 (13.3)	11 (17.5)
Sneezing	1(14.3)	0(0)	0(0)	1(8.3)	9 (30)	11 (17.5)
Vomiting	1(14.3)	0(0)	1 (16.7)	2 (16.7)	5 (16.7)	9 (14.3)

1. 11

^a Values are expressed as No. (%).

Moreover, in an unrelated study focusing on neurological symptoms in 841 individuals diagnosed with COVID-19, it was discovered that 57.4% of these patients displayed neurological symptoms. Among these symptoms, myalgias were the most prevalent at 17.2%, followed by headaches at 14% and dizziness at 6.1%. These results starkly contrast with the results of the present study, where there were headache and dizziness occurrence rates of 56% and 65%, respectively, indicating a significant variation in the prevalence of neurological symptoms between the two studies (36).

Research indicates that individuals with pre-existing conditions, such as diabetes, cardiovascular disease, and chronic respiratory illnesses, have a higher risk of experiencing severe COVID-19 symptoms. These underlying health issues can worsen the virus's physiological processes, resulting in heightened inflammation, immune system dysfunction, and an increased probability of cytokine storms (37). In a study conducted to investigate clinical symptoms in individuals with diabetes, researchers discovered that the most frequently observed symptoms among these individuals were fever at 89.6%, cough at 77.1%, dyspnea at 68.8%, anorexia at 43.8%, and fatigue at 58.3%. It is noteworthy that the occurrence rates of fever, cough, and fatigue were similarly prevalent in the current study, classifying them as three common symptoms in both research endeavors (38).

Furthermore, in another study involving individuals with diabetes, researchers categorized them into three groups: Euglycemia, secondary hyperglycemia, and diabetic groups. In the first group, fever exhibited the highest prevalence at 86.3%, followed by cough at 56.8%, along with fatigue and shortness of breath. The second group displayed symptom prevalence similar to the first. However, in the third group, fever remained predominant, with an occurrence rate of 85.7%, followed by cough and fatigue at 57.1% in the second position and shortness of breath at 35.7% in the third position. These symptoms were the most frequent within these groups, and it is noteworthy that the present study also reported higher occurrence rates for these symptoms, albeit with varying prevalence percentages. For instance, in the present study, cough had a prevalence rate of 84%; nevertheless, fever and shortness of breath were prevalent at 56%, and fatigue had a rate of 43% (39).

Another study investigated the clinical symptoms of COVID-19 in individuals with documented cardiovascular



Figure 3. Associated symptoms stratified by neurological comorbidities; symptoms categorization by prevalence in patients with Alzheimer's disease, migraine, bipolar disorder, and schizophrenia.

disease. A comprehensive examination was carried out on a total of 184 participants, who were divided into two groups: severe and non-severe cases. In general, shortness of breath emerged as the predominant symptom, affecting 75.54% of the participants, followed by cough at 46.19%, chest pain at 42.39%, and fatigue at 26%. The aforementioned symptoms proved to be prevalent among this group of individuals, and the current study also identified a substantial occurrence rate of these symptoms (40).

Another research study was undertaken to investigate the impact of COVID-19 among individuals with chronic obstructive pulmonary disease (COPD), specifically focusing on this population. This investigation encompassed 1 069 participants who were categorized into two groups: those with COPD and those without. In the COPD group, the most prevalent symptom was shortness of breath at 81.1%, followed by cough at 71.7%, hypoxemia at 43.4%, and fever at 34%. Conversely, in the non-COPD group, cough was the dominant symptom at 70%, followed by fever at 49% and shortness of breath at 26%. A comparison between the aforementioned study and the present study reveals that the occurrence of fever and cough in the current study population surpassed that in both the COPD and non-COPD groups. However, the prevalence of shortness of breath in the current study population was lower than in the COPD group but higher than in the non-COPD group (41).

In another distinct study involving 47 individuals who were co-infected with both human immunodeficiency virus (HIV) and the SARS-CoV-2 virus, the results unveiled that fever was the most prevalent symptom at 87.23%, followed by cough at 48.93% and shortness of breath at 21.27%. Headaches were less common, with an incidence rate of 6.38%, highlighting a significant deviation from the findings in the present study (42). The aforementioned study centers on the repercussions faced by solid organ transplant recipients in the United States who have contracted COVID-19. The study delves into various aspects, including mortality rates, complications, and specialized treatments designed for this particular patient group. In this study cohort, cough and shortness of breath emerged as the most prevalent symptoms, with occurrence rates of 70%, followed by fever at 61% and fatigue at 37%. When contrasting these statistics with the outcomes of the present study, noticeable disparities between the findings of these two studies become apparent (42).

In a study conducted to explore the association



Neurologic symptoms of PATIENTS with and without neurologic disorder

Figure 4. Neurologic symptoms of patients with and without neurologic disorder



Respiratory symptoms of COVID-19 in patients with and without neurological disease

Figure 5. Respiratory symptoms of coronavirus disease 2019 (COVID-19) in patients with and without neurological disorder

Symptoms	Test Value ^a	P-Value
Cough	0095	0.966
Fever	0.215	0.550
Fatigue	0.354	0.060
Headache	0.447	0.003 ^b
Anorexia	0.095	0.966
Breath shortness	0.379	0.032 ^b
Dizziness	0.530	$< 0.001^{b}$
Sore throat	0.057	0.995
Muscle pain	0.152	0.827
Lethargy	0.277	0.254
Rhinorrhea	0.215	0.550
Sleep problem	0.382	0.030 ^b
Nausea	0.194	0.652
Lack of taste	0.283	0.243
Lack of smell	0.190	0.668
Diarrhea	0.141	0.865
Sneezing	0.316	0.137
Vomiting	0.155	0.817

 Table 2. Test for Existence of Any Association Between Coronavirus Disease 2019 (COVID-19) Symptoms and Subgroups

 $^{\rm a}$ Contingency coefficient (takes values in (0,1) interval; larger value corresponds to association).

^b Significant at 5%.

between obesity and the severity of COVID-19 cases at a specific hospital in Shenzhen, China, 383 patients were assessed and categorized into four groups: underweight, normal, overweight, and obese. Regarding clinical symptoms, fever followed by cough exhibited the highest prevalence across all groups. Fever was reported at 63.5%, 68.5%, 66.7%, and 87.8% in these respective groups; nevertheless, cough was documented at 31.3%, 33.5%, 43%, and 56.1%. By comparing the aforementioned findings to the findings of the present study, the current study revealed a lower incidence of fever, with the most significant difference observed in the obesity group and the least difference in the underweight group. Conversely, the present study showed a higher prevalence of cough than all four groups examined in the aforementioned study (43).

Another study delved into hospitalization rates and clinical characteristics observed in confirmed COVID-19 patients admitted to the hospital. Among the clinical symptoms, fever/chills had the highest prevalence at 54%, followed by poor feeding and vomiting at 31% and cough at 29.5%, respectively. It is noteworthy that these findings contrast with the results of the present study. For instance,

vomiting, which is one of the most common symptoms in the aforementioned study, has the lowest occurrence rate in the current study (44).

A meta-analysis investigated the prevalence, clinical characteristics, and outcomes of COVID-19 cases. In terms of clinical symptoms, headaches were the most prevalent at 67%, followed by fever at 55%, cough at 45%, and myalgia at 35%. These prevalence figures are notable when compared to the studies included in the present study. It is worth mentioning that although the occurrence of headaches and fever aligns with the present study, there is a significant contrast in the prevalence of cough, which is notably lower in the findings of the current study (45).

Considering the constraints inherent in the present study, such as the unavailability of COVID-19 infection records, limited cooperation from certain patients, and relatively small sample size from a statistical standpoint, it is advisable to embark on further research endeavors with more extensive and diverse samples. This approach will facilitate a more comprehensive understanding of the subject matter at hand.

In conclusion, this study examined a diverse sample, revealing prevalent symptoms among individuals with various conditions, including neurological manifestations. The neurological impact of coronavirus disease 2019 is significant, and understanding these symptoms is crucial for comprehensive patient care. However, it is crucial to emphasize that obtaining a more profound understanding of these symptoms necessitates access to the names of the medications prescribed to the patients, a limitation that the present study acknowledges. To enhance our understanding, further research with larger and more diverse samples is recommended, considering the limitations faced in this study, including the data.

5.1. Conclusions

The obtained findings of this study underscore the importance of recognizing the differential impact of the virus on individuals with schizophrenia, BD, migraine, and Alzheimer's disease compared to those without any neurologic disorder. Notably, the prevalence of specific symptoms, such as headaches, exhibited substantial variations across the groups. Cough emerged as the most prevalent symptom among COVID-19-infected individuals across all subgroups, with over 79% of participants reporting this manifestation. Conversely, vomiting exhibited the lowest occurrence, documented in only 14.3% of the cases. This finding emphasizes the necessity for tailored approaches in the clinical management of COVID-19 patients with diverse neurological backgrounds. Understanding these disparities allows for more precise diagnostic and therapeutic approaches. Furthermore, the elevated prevalence of certain symptoms in individuals with underlying neurological conditions highlights the heightened vulnerability of these groups to COVID-19 complications. This finding underscores the imperative of prioritizing preventive measures, early intervention, and specialized care for individuals with conditions such as schizophrenia, BD, migraine, and Alzheimer's disease during the ongoing pandemic. Ultimately, a comprehensive understanding of these interactions will not only enhance clinical outcomes but also inform public health strategies aimed at safeguarding vulnerable populations.

Footnotes

Authors' Contribution: A.L and A.A: Methodology, investigation, validation, and writing the original draft; S.S: Statistical analysis, and tables; A.Q.N: Figures, and investigation; B.H and R.S: Investigation; A.S: Conceptualization, supervision, review, and editing.

Conflict of Interests: The authors declare that there is no conflict of interest.

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References

- Oran DP, Topol EJ. Prevalence of Asymptomatic SARS-CoV-2 Infection : A Narrative Review. Ann Intern Med. 2020;**173**(5):362-7. [PubMed ID: 32491919]. [PubMed Central ID: PMC7281624]. https://doi.org/10.7326/M20-3012.
- Pan L, Mu M, Yang P, Sun Y, Wang R, Yan J, et al. Clinical Characteristics of COVID-19 Patients With Digestive Symptoms in Hubei, China: A Descriptive, Cross-Sectional, Multicenter Study. *Am J Gastroenterol.* 2020;**115**(5):766–73. [PubMed ID: 32287140]. [PubMed Central ID: PMC7172492]. https://doi.org/10.14309/ajg.0000000000000620.
- Jin Y, Yang H, Ji W, Wu W, Chen S, Zhang W, et al. Virology, Epidemiology, Pathogenesis, and Control of COVID-19. *Viruses*. 2020;12(4). [PubMed ID: 32230900]. [PubMed Central ID: PMC7232198]. https://doi.org/10.3390/v12040372.
- The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) - China, 2020. China CDC Wkly. 2020;2(8):113–22. [PubMed ID: 34594836]. [PubMed Central ID: PMC8392929].

- Han D, Li R, Han Y, Zhang R, Li J. COVID-19: Insight into the asymptomatic SARS-COV-2 infection and transmission. *Int J Biol Sci.* 2020;16(15):2803-11. [PubMed ID: 33061797]. [PubMed Central ID: PMC7545704]. https://doi.org/10.7150/ijbs.48991.
- 6. WHO COVID-19 Dashboard 2020. World Health Organization; 2023. Available from: https://covid19.who.int/.
- Lovrei L, Maver A, Zadel M, Peterli B. The Role of Epigenetics in Neurodegenerative Diseases. *IntechOpen*. 2013:345–65. https://doi.org/ 10.5772/54744.
- G. B. D. Multiple Sclerosis Collaborators. Global, regional, and national burden of multiple sclerosis 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol*. 2019;**18**(3):269–85. [PubMed ID: 30679040]. [PubMed Central ID: PMC6372756]. https://doi.org/10.1016/S1474-4422(18)30443-5.
- Brown RC, Lockwood AH, Sonawane BR. Neurodegenerative diseases: an overview of environmental risk factors. *Environ Health Perspect*. 2005;**113**(9):1250–6. [PubMed ID: 16140637]. [PubMed Central ID: PMC1280411]. https://doi.org/10.1289/ehp.7567.
- Jorden MA, Rudman SL, Villarino E, Hoferka S, Patel MT; CDC Covid-Response Team, et al. Evidence for Limited Early Spread of COVID-19 Within the United States, January-February 2020. MMWR Morb Mortal Wkly Rep. 2020;69(22):680–4. [PubMed ID: 32497028]. [PubMed Central ID: PMC7315848]. https://doi.org/10.15585/mmwr.mm6922e1.
- Cheung EW, Zachariah P, Gorelik M, Boneparth A, Kernie SG, Orange JS, et al. Multisystem Inflammatory Syndrome Related to COVID-19 in Previously Healthy Children and Adolescents in New York City. *JAMA*. 2020;**324**(3):294–6. [PubMed ID: 32511676]. [PubMed Central ID: PMC7281352]. https://doi.org/10.1001/jama.2020.10374.
- Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, Rowlands J, et al. Multisystem Inflammatory Syndrome in Children in New York State. N Engl J Med. 2020;383(4):347-58. [PubMed ID: 32598830]. [PubMed Central ID: PMC7346766]. https://doi.org/10.1056/NEJMoa2021756.
- Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. N Engl J Med. 2020;383(4):334–46. [PubMed ID: 32598831]. [PubMed Central ID: PMC7346765]. https://doi.org/10.1056/NEJMoa2021680.
- Lin JE, Asfour A, Sewell TB, Hooe B, Pryce P, Earley C, et al. Neurological issues in children with COVID-19. *Neurosci Lett.* 2021;743:135567. [PubMed ID: 33352286]. [PubMed Central ID: PMC7831718]. https://doi. org/10.1016/j.neulet.2020.135567.
- Balcom EF, Nath A, Power C. Acute and chronic neurological disorders in COVID-19: potential mechanisms of disease. *Brain.* 2021;144(12):3576–88. [PubMed ID: 34398188]. [PubMed Central ID: PMC8719840]. https://doi.org/10.1093/brain/awab302.
- Fiani B, Covarrubias C, Desai A, Sekhon M, Jarrah R. A Contemporary Review of Neurological Sequelae of COVID-19. *Front Neurol.* 2020;11:640. [PubMed ID: 32655489]. [PubMed Central ID: PMC7324652]. https://doi.org/10.3389/fneur.2020.00640.
- Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 Virus Targeting the CNS: Tissue Distribution, Host-Virus Interaction, and Proposed Neurotropic Mechanisms. ACS Chem Neurosci. 2020;11(7):995-8. [PubMed ID: 32167747]. https://doi.org/10.1021/ acschemneuro.0c00122.
- McGavern DB, Kang SS. Illuminating viral infections in the nervous system. Nat Rev Immunol. 2011;11(5):318–29. [PubMed ID: 21508982]. [PubMed Central ID: PMC5001841]. https://doi.org/10.1038/nri2971.
- Swanson P2, McGavern DB. Viral diseases of the central nervous system. *Curr Opin Virol*. 2015;**11**:44–54. [PubMed ID: 25681709]. [PubMed Central ID: PMC4456224]. https://doi.org/10.1016/j.coviro. 2014.12.009.
- Koyuncu OO, Hogue IB, Enquist LW. Virus infections in the nervous system. *Cell Host Microbe*. 2013;13(4):379–93. [PubMed ID: 23601101]. [PubMed Central ID: PMC3647473]. https://doi.org/10.1016/j.chom. 2013.03.010.

- Wang HY, Li XL, Yan ZR, Sun XP, Han J, Zhang BW. Potential neurological symptoms of COVID-19. *Ther Adv Neurol Disord*. 2020;13:1756286420917830. [PubMed ID: 32284735]. [PubMed Central ID: PMC7119227]. https://doi.org/10.1177/1756286420917830.
- Balottin U, Chiappedi M, Rossi M, Termine C, Nappi G. Childhood and adolescent migraine: a neuropsychiatric disorder? *Med Hypotheses.* 2011;**76**(6):778-81. [PubMed ID: 21356578]. https: //doi.org/10.1016/j.mehy.2011.02.016.
- Connelly M, Bickel J. An electronic daily diary process study of stress and health behavior triggers of primary headaches in children. J Pediatr Psychol. 2011;36(8):852–62. [PubMed ID: 21441572]. https://doi. org/10.1093/jpepsy/jsr017.
- Ashina S, Bendtsen L, Ashina M. Pathophysiology of tension-type headache. *Curr Pain Headache Rep.* 2005;9(6):415-22. [PubMed ID: 16282042]. https://doi.org/10.1007/s11916-005-0021-8.
- Parodi IC, Poeta MG, Assini A, Schirinzi E, Del Sette P. Impact of quarantine due to COVID infection on migraine: a survey in Genova, Italy. *Neurol Sci.* 2020;41(8):2025-7. [PubMed ID: 32613542]. [PubMed Central ID: PMC7329264]. https://doi.org/10.1007/s10072-020-04543-x.
- Fornaro M, De Prisco M, Billeci M, Ermini E, Young AH, Lafer B, et al. Implications of the COVID-19 pandemic for people with bipolar disorders: A scoping review. J Affect Disord. 2021;295:740-51. [PubMed ID: 34517248]. [PubMed Central ID: PMC8416293]. https://doi. org/10.1016/j.jad.2021.08.091.
- Murray G, Gottlieb J, Swartz HA. Maintaining Daily Routines to Stabilize Mood: Theory, Data, and Potential Intervention for Circadian Consequences of COVID-19. *Can J Psychiatry*. 2021;66(1):9–13. [PubMed ID: 32909832]. [PubMed Central ID: PMC7890582]. https://doi.org/10.1177/0706743720957825.
- Xue S, Husain MI, Ortiz A, Husain MO, Daskalakis ZJ, Mulsant BH. COVID-19: Implications for bipolar disorder clinical care and research. SAGE Open Med. 2020;8:2050312120981180. [PubMed ID: 33403113]. [PubMed Central ID: PMC7739076]. https://doi.org/10.1177/2050312120981178.
- Dong M, Lu L, Zhang L, Zhang Q, Ungvari GS, Ng CH, et al. Prevalence of suicide attempts in bipolar disorder: a systematic review and meta-analysis of observational studies. *Epidemiol Psychiatr Sci.* 2019;29. e63. [PubMed ID: 31648654]. [PubMed Central ID: PMC8061290]. https://doi.org/10.1017/S2045796019000593.
- Banerjee D, Kosagisharaf JR, Sathyanarayana Rao TS. 'The dual pandemic' of suicide and COVID-19: A biopsychosocial narrative of risks and prevention. *Psychiatry Res.* 2021;**295**:113577. [PubMed ID: 33229123]. [PubMed Central ID: PMC7672361]. https://doi.org/10.1016/j.psychres.2020.113577.
- Phiri P, Ramakrishnan R, Rathod S, Elliot K, Thayanandan T, Sandle N, et al. An evaluation of the mental health impact of SARS-CoV-2 on patients, general public and healthcare professionals: A systematic review and meta-analysis. *EClinicalMedicine*. 2021;**34**:100806. [PubMed ID: 33842872]. [PubMed Central ID: PMC8022621]. https://doi.org/10.1016/j.eclinm.2021.100806.
- Kinoshita S, Cortright K, Crawford A, Mizuno Y, Yoshida K, Hilty D, et al. Changes in telepsychiatry regulations during the COVID-19 pandemic: 17 countries and regions' approaches to an evolving healthcare landscape. *Psychol Med*. 2022;**52**(13):2606-13. [PubMed ID: 33243311]. [PubMed Central ID: PMC7750654]. https://doi.org/10.1017/S0033291720004584.
- Fonseca L, Diniz E, Mendonca G, Malinowski F, Mari J, Gadelha A. Schizophrenia and COVID-19: risks and recommendations. *Braz J Psychiatry*. 2020;42(3):236–8. [PubMed ID: 32294689]. [PubMed Central ID: PMC7236151]. https://doi.org/10.1590/1516-4446-2020-0010.

- 34. Shen HN, Lu CL, Yang HH. Increased risks of acute organ dysfunction and mortality in intensive care unit patients with schizophrenia: a nationwide population-based study. *Psychosom Med.* 2011;73(7):620-6. [PubMed ID: 21862830]. https: //doi.org/10.1097/PSY.0b013e3182280016.
- Nejad JH, Allahyari F, Hosseinzadeh R, Heiat M, Ranjbar R. Neurological symptoms of COVID-19 infection; a cross-sectional study on hospitalized COVID-19 patients in Iran. *Clin Neurol Neurosurg.* 2021;**210**:106985. [PubMed ID: 34700274]. [PubMed Central ID: PMC8502683]. https://doi.org/10.1016/j.clineuro.2021.106985.
- Romero-Sanchez CM, Diaz-Maroto I, Fernandez-Diaz E, Sanchez-Larsen A, Layos-Romero A, Garcia-Garcia J, et al. Neurologic manifestations in hospitalized patients with COVID-19: The ALBACOVID registry. *Neurology*. 2020;**95**(8):e1060–70. [PubMed ID: 32482845]. [PubMed Central ID: PMC7668545]. https://doi.org/10.1212/WNL.000000000009937.
- Bohn MK, Hall A, Sepiashvili L, Jung B, Steele S, Adeli K. Pathophysiology of COVID-19: Mechanisms Underlying Disease Severity and Progression. *Physiology (Bethesda)*. 2020;**35**(5):288–301. [PubMed ID: 32783610]. [PubMed Central ID: PMC7426542]. https://doi.org/10.1152/physiol.00019.2020.
- Yan Y, Yang Y, Wang F, Ren H, Zhang S, Shi X, et al. Clinical characteristics and outcomes of patients with severe covid-19 with diabetes. *BMJ Open Diabetes Res Care*. 2020;8(1). [PubMed ID: 32345579]. [PubMed Central ID: PMC7222577]. https://doi.org/10.1136/bmjdrc-2020-001343.
- Zhou W, Ye S, Wang W, Li S, Hu Q. Clinical Features of COVID-19 Patients with Diabetes and Secondary Hyperglycemia. *J Diabetes* Res. 2020;2020:3918723. [PubMed ID: 33062712]. [PubMed Central ID: PMC7545437]. https://doi.org/10.1155/2020/3918723.
- 40. Yazdi A, Alvandi M, Shaghaghi Z, Hashemi SH, Inanloo SO, Hashemi S, et al. Coronavirus Disease in Cardiovascular Patients: Clinical Characteristics and Final Prognosis. Avicenna Journal of Clinical Microbiology and Infection. 2023;10(1):20–6. https://doi.org/10.34172/ajcmi.2023.3421.
- Turan O, Arpinar Yigitbas B, Turan PA, Mirici A. Clinical characteristics and outcomes of hospitalized COVID-19 patients with COPD. *Expert Rev Respir Med.* 2021;**15**(8):1069–76. [PubMed ID: 33944643]. [PubMed Central ID: PMC8127171]. https://doi.org/10.1080/17476348.2021. 1923484.
- Gervasoni C, Meraviglia P, Riva A, Giacomelli A, Oreni L, Minisci D, et al. Clinical Features and Outcomes of Patients With Human Immunodeficiency Virus With COVID-19. *Clin Infect Dis.* 2020;**71**(16):2276-8. [PubMed ID: 32407467]. [PubMed Central ID: PMC7239244]. https://doi.org/10.1093/cid/ciaa579.
- Cai Q, Chen F, Wang T, Luo F, Liu X, Wu Q, et al. Obesity and COVID-19 Severity in a Designated Hospital in Shenzhen, China. *Diabetes Care*. 2020;43(7):1392-8. [PubMed ID: 32409502]. https://doi. org/10.2337/dc20-0576.
- 44. Kim L, Whitaker M, O'Halloran A, Kambhampati A, Chai SJ, Reingold A, et al. Hospitalization Rates and Characteristics of Children Aged <18 Years Hospitalized with Laboratory-Confirmed COVID-19 COVID-NET, 14 States, March 1-July 25, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(32):1081–8. [PubMed ID: 32790664]. [PubMed Central ID: PMC7440125]. https://doi.org/10.15585/mmwr.mm6932e3.</p>
- Badal S, Thapa Bajgain K, Badal S, Thapa R, Bajgain BB, Santana MJ. Prevalence, clinical characteristics, and outcomes of pediatric COVID-19: A systematic review and meta-analysis. J Clin Virol. 2021;135:104715. [PubMed ID: 33348220]. [PubMed Central ID: PMC7723460]. https://doi.org/10.1016/j.jcv.2020.104715.