Review Article

Behavioural health issues in post coronavirus disease (COVID) syndrome and suicide risk: a narrative review

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Background and Objective: Post coronavirus disease (COVID) syndrome includes a wide range of signs and symptoms among which symptoms ascribable to behavioural health issues are as high as 30% for different sub-domains. Recognizing the etiologic role played by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is still a matter of debate, since many psychosocial and interactional factors connected to the pandemic dynamics are affecting behavioral health globally. Suicide risk in people who experienced coronavirus disease 2019 (COVID-19) has been investigated by a relative paucity of studies. Objective of this narrative review is seeking to summarize published evidence on behavioural health issues and suicide risk in post-COVID syndrome, alongside investigating the potential involvement of neuroinflammation.

Methods: This narrative review attempts on summarizing evidence published between 25th December 2019 and 1st June 2022 about behavioural health issues and suicide risk in post-COVID syndrome, and the possible role of neuroinflammation. This work was produced identifying the research question, search methods to define relevant studies, study selection, and summarising data and reporting results. A search was run on PubMed using appropriate mesh terms, only publications in English were included.

Key Content and Findings: Hyperinflammation is considered a central actor in COVID-19 and neuroinflammatory damage is thought to be a putative pattern of pathogenesis of neuronal and behavioural health issues connected to increased suicide ideation and behaviour. A prolonged inflammatory status is thought to play a role in driving behavioural health issues in post-COVID syndrome patients. Based on reported data, the risk of behavioral health issues in post-COVID syndrome is comparable to or slightly higher than that in non-post-COVID syndrome cases. This variation spans similar rates to a 10–30% increase across different subdomains. The role of direct viral damage and social factors in the context of public health strategies is discussed.

Conclusions: More endeavors are needed to gain a deeper understanding of the actual influence of virological and neuro-inflammatory factors on behavioural health disorders associated with post-COVID syndrome. Additionally, emphasis should be placed on public health strategies dedicated to preventing and supporting individuals facing these challenges.

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Introduction

Background

Despite massive vaccination campaigns and antiviral drugs approval, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is still spreading throughout the world (1). While new virus variants are emerging there are also new clinical concerns about long term coronavirus disease 2019 (COVID-19) related complications. Generally speaking, the definition of 'long COVID' has been initially proposed to identify signs and symptoms that continue or develop after acute COVID-19 (2). Two different clinical conditions were considered: ongoing symptomatic COVID-19 (from 4 to 12 weeks) and post-COVID-19 syndrome (12 weeks or more) (2). Much uncertainty and discussion existed about this topic. The England National Institute for Health Excellence (NICE) guidelines defines post COVID-19 syndrome the "signs and symptoms that develop during or after an acute infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis" (2). Later on, a Delphi WHO consensus updated the clinical case definition as follows: "post-COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset, with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include, but are not limited to, fatigue, shortness of breath, and cognitive dysfunction, and generally have an impact on everyday functioning" (3).

In this context the clinical presentation can be insidious and signs and symptoms can be protean. More than 50 clinical features were associated with post COVID-19 syndrome, the most common were neuropsychiatric signs and symptoms such as fatigue (58%), headache (44%) and attention disorder (27%) (4). Others features includes respiratory symptoms, cardiovascular and neurological complications, hair loss and many other variable manifestations (4).

Rationale and knowledge gaps

Worldwide an increased risk of behavioural health issues, such as depression, has been highlighted in various scientific works and observational studies (5) during COVID-19 pandemic. This trend has not been confirmed in all published studies (6) and discordant literature has been published on the topic (7). On one hand, psychosocial factors, such as the economic crisis, the impact of "infodemia" (8), and experiences of social isolation and loneliness (9), have been observed to influence the mental health of the general population; on the other hand, it has been proposed that people infected by Sars-CoV-2 may have a higher risk of developing behavioral health complications and consequently being at higher suicidal risk (10). Many factors may have contributed to this, such as post-traumatic stress disease, but it has also been proposed a direct or indirect effect of neuro-inflammation due to COVID-19 (11). Previous literature described evidences of long-lasting neuropsychiatric consequences after viral infections (12), and indeed a possible role of COVID-19 as a trigger of neuropsychiatric impairment is under investigation. In fact, post-COVID syndrome patients, with symptoms spanning psychiatric, neurological, and physical issues, may face an increased risk of suicidal tendencies. This risk extends to COVID-19 survivors without post-COVID syndrome.

Objective

The aim of this work is to summarize the evidences published up to 1st of June 2022 about the possible behavioural health issues, particularly suicidal ideation (SI) and suicidal behaviours (SB), in post COVID syndrome and the potential role of neuroinflammation in possibly driving such behaviours. We present this article in accordance with the Narrative Review reporting checklist (available at https://jphe.amegroups.com/article/view/10.21037/jphe-23-13/rc).

Table 1 Search strategy summary

Items	Specification
Date of search	01 June 2022
Databases and other sources searched	PubMed
Search terms used	(((“Post-COVID syndrome”) OR (“long COVID”) OR (“persistent COVID”)) AND ((“Suicide”) OR (“Psychiatric disease”) OR (“Psychiatric sequelae”) OR (“Neuropsychiatric complications”))); (((“Post-COVID syndrome”) OR (“long COVID”) OR (“persistent COVID”)) AND ((“neuroinflammation”) OR (“hyperinflammation”)))
Timeframe	25th December 2019–1st June 2022
Inclusion and exclusion criteria	(I) Article included are in English language only (II) Article type: we included original articles, systematic review, and review (III) Case reports and case series were excluded
Selection process	Articles were screened according to the eligibility criteria and revised independently by M.C., F.T., B.R., F.M., G.S. and L.B.. References of included original studies were also screened and selected independently and consensus obtained homogenously

COVID, coronavirus disease.

Methods

This narrative review was produced identifying the research question, search methods for define relevant studies, study selection, summarising data, and reporting the results (*Table 1*). The main research aim was to summarize current evidence on suicide risk in post-COVID syndrome, and the possible role played by neuroinflammation. A search was run in 1st June 2022 on PubMed using the terms (((“Post-COVID syndrome”) OR (“long COVID”) OR (“persistent COVID”)) AND ((“Suicide”) OR (“Psychiatric disease”) OR (“Psychiatric sequelae”) OR (“Neuropsychiatric complications”))), resulting in 14 articles. We also ran another search on the same database using the terms: (((“Post-COVID syndrome”) OR (“long COVID”) OR (“persistent COVID”)) AND ((“neuroinflammation”) OR (“hyperinflammation”))), resulting in 32 articles. Results were limited to the time-frame 25th December 2019–15th May 2022. Studies were filtered for original articles, systematic review, and review. Case reports and case series were excluded. Articles in languages other than English were excluded. Finally, quality assessment of full-text studies was performed. Articles were screened according to the eligibility criteria and revised independently by M.C., F.T., B.R., F.M., G.S. and L.B. References of included original studies were also screened and selected independently. We reviewed the summary of all articles searched, and ultimately used data from 33 full articles to compile this narrative review. Furthermore, throughout the editorial process of this narrative review, we incorporated suggestions from the Editorial team and reviewers, which included papers that might not have been identified through the initial searches. After thorough and collaborative evaluation, we have included additional data from these suggestions for the purpose of discussion. We included papers that described evidence on suicide risk in post-COVID syndrome, and evidence on neuroinflammation. Results are reported in the following paragraphs.

Results

Suicide and post COVID-19 syndrome

Studies have been performed to examine the impact of the COVID-19 pandemic on the behavioral health of the general population, and we retrieved data concerning the behavioral health sequelae in this setting and more specifically for what pertains to the post-COVID syndrome, and the relationship with increased suicidal risk.

Concerning behavioral health impact, we can assert that a recent revision of the World Health Organization (13) defines some reference points: in the first year of the pandemic there was an increase in the prevalence of behavioral health disorders, in particular anxiety and depression, and mostly among the female gender, young people and those with previous health problems. On the other hand, different reports highlighted how emergency care for suicidal behaviour did not increase during the pandemic and showed high variability (14-17). Going deeply, and moving from acute mental health issues to post-

aute COVID care the picture becomes more diversified. According to a Chinese study, about 23% of patients that recovered from COVID and suffered post-COVID syndrome reported anxiety or depression at 6 months follow-up (18).

As it is known, suicidal behaviour is frequently associated with behavioural health issues such as depression, post-traumatic stress disorder (PTSD), anxiety and mood disorders (19). Studies on behavioural health issues and sequelae of SARS-CoV-1 and MERS-CoV found an increased incidence of cognitive and psychological issues (12). Amid the pandemic, attempts were undertaken to gauge the repercussions of lockdown by analysing data sourced from social media. Unique methods were deployed to delve into the self-reported viewpoints and real-life encounters of adolescents COVID survivors as they navigated through their COVID-19 illness. These personal narratives were willingly shared across different media channels and social media platforms during the extensive lockdown period in India (20). Interestingly, almost all enrolled survivors reported emotional and psychological distress, and association between thoughts of fear and end of life, depression and suicide were confirmed (20). Moreover, coming back to the relation between COVID-19, post-COVID syndrome and suicidal risk, recent data highlighted that individuals who had COVID were 46% more likely to experience SI during the post-acute phase, in comparison to those who did not have COVID, and a recent study indicated that certain post-COVID patients endure persistent suicidality (21). According to Sher *et al.* (22), SI and behaviour may be associated with a variety of features of acute or post-COVID syndromes; interestingly, an inflammatory damage to the brain among those individuals has been called out, raising the possibility of a neurobiological injury beyond psychiatric and physical pathological elements. However, this risk appears to be similar among COVID-19 survivors without post-COVID features. In a large systematic review involving 3,304 COVID-19 survivors sequelae were evaluated up to 30 or 60 days, and psychiatric symptoms like PTSD (31%), feeling depressed (20%), and suicidality (2%) had a higher prevalence (23). Length of hospital stays among COVID-19 patients positively correlated with higher rates of depression and anxiety. Major depressive episodes (MDE) and anxiety disorders, like generalized anxiety disorder or panic disorder, commonly occur post-COVID-19. Particularly, among patients with post-COVID syndrome respiratory complaints, anxiety disorders are frequent, similarly to what happens in other chronic respiratory conditions. In the COMEBAC cohort of 177 survivors assessed four months after hospitalization for acute COVID-19, respiratory complaints were associated with a sevenfold higher risk of anxiety disorders and a fourfold higher risk of MDE (24). Additional studies from electronic health records reported a 6.2% prevalence of abnormal breathing, associated with anxiety disorders or MDE, during the six months following acute COVID-19. This corresponded to a twofold higher co-occurrence of these lingering manifestations compared to a matched cohort of patients recovering from influenza (24). Also, difference have been highlighted with studies examining the psychiatric aftermath of SARS-COV-1 conducted 31–50 months post-infection; these revealed a substantial rise in mental health issues, reporting a 54.5% occurrence of PTSD, 39% for depression, 32.5% for panic disorder, and 15.6% for obsessive–compulsive disorder. This marked a significant escalation from the pre-infection prevalence of any psychiatric diagnoses, which was only 3% (21,22). This is slightly higher but similar from what has been reported in patients after COVID-19, presenting up to 28% for PTSD, 31% for depression, 42% for anxiety, 20% for obsessive–compulsive symptom (21,22). Generally speaking, different metanalysis assessed symptoms in post-acute COVID, also focusing on mental health issues; unfortunately, none of these are very specific to post-COVID syndrome as later defined (25). Evidence on the increase in suicidal thoughts and behaviours during pandemic is sparse, except in young people or other fragile populations, where a higher risk of SB appears more frequent, coupled with other disorders (14-17,19,26,27). In particular, contrary to what is reported elsewhere (14-17), a meta-analysis investigated suicide behaviour during the COVID-19 pandemic on 308 596 records, taking in to account international series. A consistent increase in suicidal thoughts, suicide attempts and self-harm compared with pre-pandemic studies was found (26). It's worth mentioning that children and adolescents are likely to experience elevated rates of depression and anxiety, both during and after the period of enforced isolation (28). Another additional explanation for this specific population is ascribable to findings showing that numbers of children affected by COVID-19-associated orphanhood and caregiver death almost doubled in 6 months compared with the amount after the first 14 months of the pandemic (29). In Korea, a cross-sectional Youth Risk Behavior Web-based Survey focusing on school-going adolescents revealed elevated rates of depression, SI,

suicide planning, and suicide attempts. These percentages reached as high as 26.5%, 12.2%, 3.7%, and 2.4%, respectively, when compared to the pre-pandemic period. The variables associated with these outcomes in the short-term analysis reflected socioeconomic vulnerabilities (30). In this specific population, data are limited and scattered. More broadly, information about the timespan after infection lacks a clear and consistent definition, and follow-up procedures vary among the presented studies. These studies do not specifically assess what is now recognized as the definition of post-COVID syndrome. As a fact, some of these data were generated before the definition was agreed upon, resulting in a lack of consistency, or time to follow-up ranged very broadly.

To delve more specifically into post-COVID syndrome, we further examined data, particularly focusing on this syndrome and its association with suicidality. For example, an Italian study enrolling more than one-thousand patients suffering from post-COVID syndrome investigated the relationship between post-COVID syndrome and suicidality (31). Through the utilization of the Mini International Neuropsychiatric Interview, it was discerned that individuals with a susceptibility to suicide manifested higher percentages of physical complaints both during and after their bout with COVID-19. Furthermore, they exhibited an increased prevalence of a psychiatric history, a familial background of psychiatric issues, and a higher likelihood of prior psychopharmacotherapy. Additionally, these individuals showed heightened levels of anxiety and mixed depressive symptoms. Notably, the escalation in physical complaints and psychopathology during the post-COVID syndrome was identified as a potential exacerbator of suicide risk. Effectively addressing physical complaints through treatment and incorporating psychotherapy emerged as pivotal strategies in mitigating the risk of suicide within this demographic (31). Another study among a random community-based sample of people in Texas, USA found out that post-COVID syndrome is correlated with higher levels of depression (13% increase), anxiety (28% increase), SI (10% increase), and PTSD (20% increase), along with decreased life satisfaction and daily functioning. Moreover, connections were uncovered demonstrating an association between Long COVID and PTSD, SI; in particular reduced life satisfaction were mediated by heightened daily functional challenges and the presence of common mental disorders (32).

Combining this data underscores the inconclusive nature of the debate, yet it certainly offers valuable insights into the behavioural health issues inherent in the unprecedented situations related to the pandemic and post-COVID syndrome.

Also, while processes underlying COVID-19 associated suicidality remains poorly elucidated, putative neuroinflammatory phenomena may explain at least partly this changing trend (11,17,21,25). We therefore explored the role of neuroinflammation in COVID, post-COVID syndrome and behavioural health issues.

Neuroinflammation, COVID-19, post-COVID syndrome and behavioural health issues

The central nervous system (CNS) has long been considered a "sanctuary organ" for its peculiar barriers. However, despite its specific immune and circulatory system that may mimick a sort of "golden cage", data point out to the fact that many viral agents may make their way to the CNS through different routes, including haematogenous, or carried by leukocytes, or through the choroid plexus crossing and other neuronal retrograde routes. Therefore, the resulting pathological or physiological interactions are very complex both at the immune, metabolomic and proteomic level; although no selective advantage from neuronal invasion results for the pathogen nor the host, the direct damaging resulting effect or the immune-dysfunction that are both provoked by these interactions may engender high morbidity (33). More specifically, the role of microglial activation appears to be key, as the highly diversified residing mononuclear phagocytes of the brain play a pivotal role in the cytokine/chemokine balance and internal homeostasis (34), and their uncontrolled activation is indicative of neuropathology and is considered a marker of brain injury and neuroinflammatory events, as demonstrated for other acute or chronic viral infections (35,36). Coronaviruses (CoVs) are respiratory viruses with neurotropic potential. An early hypothesis explaining the phenotypic presentation of SARS-CoV-2 infection suggested a systemic inflammatory condition known as a "cytokine storm". This involved disruptions in pathways and imbalances in levels of IL-1, IL-6, IL-12, IL-18, CCL2, CCL5, GM-CSF, TNF-α, and IFN-γ (37). Moreover, conjectures have been raised regarding the exact role of ACE2 as the cellular entry receptor for the SARS-CoV2 and its role for pathology development and clinical complications. The receptor is extensively present in various tissues, including the brain. SARS-CoV-2's direct infection of exposed parenchyma can

lead to dysregulated inflammation in peripheral tissues and potential neurological complications. The hyper-inflammatory syndrome in SARS-CoV-2 infection is driven by various effector cells, with a crucial subset originating from the innate immune system in both peripheral and CNS (38). As anticipated, the mononuclear phagocyte system is involved in this mechanism. Elevated circulating inflammatory markers, namely IL-1, IL-6, IL-8, and TNF-α, are observed in individuals with severe COVID-19 disease, primarily produced by macrophages and monocytes (33-37). Other markers have been proposed to identify patients at higher risk, but no conclusive data exist for this differentiation regarding the CNS (39). Data from other studies proposed a role for mast-cell in this inflammatory syndrome. Mast cells can release important mediators like histamine, carboxypeptidase A3, chymase, tryptase, and serotonin. These molecules are higher in sera of COVID-19 patients and are positively correlated with other hyperinflammatory markers (40-42). Interestingly, this signature is absent in other well-studied models of infection, such H1N1 virus (43). On the other hand, mast cell in COVID-19 patients seems to potentially lead to the cytokine storm due to a specific trigger by histamine. As a matter of fact, histamine is able to induce the production of IL-1, IL-6, IL-8 and several inflammation cytokines and chemokines. In post-mortem histological studies of COVID-19 patients, intense microgliosis and nodules in various brain regions and perivascular spaces have been observed (44). Histological analyses indicate that microgliosis is linked to the expression of inflammatory markers that are also dysregulated in peripheral blood, suggesting the activation of resident microglial cells. Another feature that has been identified in these studies is astrocyte reactivity. That particular feature of astrogliosis was identified through the detection of high level of S100b in the brain samples and in the sera of moderate to severe COVID-19 patients; also, that same marker positively correlated with other inflammatory ones (44). All these data are mostly coming from acute COVID-19, while data for long COVID-19 are more difficult to study. Still, authors from different countries attempted to better describe the interrelationship between neuroinflammation, post-COVID syndrome and behavioural health issues. In particular, the precise mechanisms behind the symptoms observed in post-COVID syndrome remain largely unclear. However, various theories implicate both the nervous system and systemic factors, including the persistence of SARS-CoV-2 viral presence and its potential invasion into the nervous system, abnormal immune responses, autoimmune reactions, coagulation disorders, and dysfunction of the endothelium. SARS-CoV-2 infection has the capacity to disrupt both innate and adaptive immunity, leading to phenomena such as the expansion of monocytes, T-cell exhaustion, and prolonged release of cytokines. These disruptions may contribute to neuroinflammatory responses, activation of microglia, abnormalities in white matter, and alterations in microvascular structures and endotheliopathy (45,46). Moreover, Interferon-Stimulated Genes (ISGs) are crucial for innate immunity defence against SARS-COV-2, inhibiting viral replication by hindering viral entry and trafficking into the cell nucleus. They also impede transcription and translation processes, degrade viral nucleic acids, and obstruct the formation of viral particles. Patients experiencing post-COVID syndrome exhibited prolonged elevation in the levels of type I interferon (IFN-β) and type III interferon (IFNλ1), persisting for at least eight months post-infection, indicating that inflammation may resolve slowly or defectively in post COVID syndrome patients (47). In addition to that, the literature on neuroinflammation suggests that there are issues in long Covid that may be influenced by the activation of microglia. When microglia are activated, they release cytokines and chemokines, initiating an inflammatory signalling process. Normally, this activation and resulting inflammation are brief, serving to address immune system challenges. However, if microglia activation is impaired, it can lead to prolonged expression of inflammatory cytokines. This cytokine activation is known to impact dopamine levels, inhibiting reward motivation and causing anhedonia. Consequently, this can affect an individual's ability to perform their usual roles, both professionally and personally. The impact of neuroinflammation on mood is significant, and there is a greater vulnerability to long COVID in individuals with comorbidity disorders such as depression and anxiety. Various studies have demonstrated a connection between inflammation and depression, as cytokines directly affect brain regions involved in emotion regulation. Therefore, the links between anxiety, depression, and long COVID may be reflective of a shared neuroinflammatory connection between these conditions (45).

Moreover, various studies indicate a significant overlap in both symptomatology and pathophysiology between encephalomyelitis/chronic fatigue syndrome (ME/CFS) and post-COVID syndrome. Notably, neuroinflammation is identified as a key component in both conditions. Proteomic analyses of immune cells from ME/CFS and post-COVID syndrome patients reveal the presence of mitochondrial

protein imbalance with similar profiles (48,49). Furthermore, combinatorial analysis uncovers numerous shared genes highly associated with at least one of the long COVID sub-populations, suggesting a predisposition for these conditions (50).

Finally, some authors have suggested non-invasive methods and biomarkers for evaluating patients with post-COVID syndrome (51). These include imaging and easy to perform methods. These approaches not only support the hypothesis of a neuroinflammatory condition in post-COVID syndrome but also underscore the potential role of non-invasive tests for studying and monitoring these patients (52,53). Similarly, neurophysiological tests, reminiscent of those used in myalgic ME/CFS, have been proposed (54). However, the exact place of these tools in clinical management is still a subject of debate.

Lastly, it is well known that suicide per se has a complex multifactorial aetiology that has been postulated to be the result of dynamic interplays between psychological stressors and neurobiological risks, and there is no consensus regarding the exact role of each factor in the resulting outcome. Environmental stressor agents and arising hopelessness might constitute the major triggering events for most suicidal acts, while underlying neurobiological aberrations might concur in suicide vulnerability indirectly. Multiple autoptic studies of persons that committed suicide have provided important insights on putative neurobiological genesis of this psychiatric condition, and advanced imaging studies have provided additional insights (55). The elevation of various biomarkers of inflammation and its association with suicidal risk has been described in the literature, although no causation can be extrapolated (56). Additional data for this association comes from genetic analyses of suicidal subjects: higher risk for SA was associated with elevated IL-6, IL-8, and TNF-α. Moreover, serum IL-6, TNF-α, and CRP have been found to be abnormally elevated in depressed suicide attempters (55). Also, IL-6 was found to be elevated in the cerebrospinal fluid of suicide attempters and correlated with a history of violent suicidal acts and depression scores. This inflammatory cytokine expression in the CSF also correlated with suicidal risk in patients with depressive symptoms (10,11). Elevated frequencies of blood monocytes and granulocytes have also been linked with increased suicide risk (10,11). Similarly, macrophage infiltration into the brain parenchyma of depressed suicides has been noted by elevated expression of CD45, Iba1 as well as a classical macrophage chemoattractant, CCL2 (10,11). Astrocytic hypertrophy has also been observed in the anterior cingulate, thalamus, and caudate regions of depressed suicidal subjects. Furthermore, astrogliosis and microgliosis were observed in selected brain regions of suicide victims, suggesting widespread neuroinflammation might not be necessary to precipitate an increased risk for suicide (10,11). Despite these data, internal variability, epigenetic and other contextual factors should be controlled for in the search of an inflammatory phenotype in these subjects. Importantly, acute phase proteins and chemokynes do vary rather rapidly and intercepting relevant measurement to describe appropriate phenotypes is reasonably complicated.

Nevertheless, post-mortem finding coupled with complex social qualitative factors that are beyond the objective of this review may further elucidate the issue. Differential access to care and societal inequalities have been shown to play a decisive role in leading COVID-19 affected patients to one good outcome over another potentially fatal.

Debates surround the implementation of suicide prevention measures for post-COVID syndrome. The heightened risk of mental health issues sequelae related to COVID-19 appears to be most significant during the initial peak of the pandemic but diminishes over the ensuing years (25,57,58). The variations in outcomes may be attributed to factors such as different variants, the severity of infections, vaccination rates, and underlying social factors. Nevertheless, effectively tackling mental health issues stemming from COVID-19 necessitates well-thought-out treatment strategies. In light of the current absence of specific evidence-backed interventions, the suggested approach mirrors that utilized for addressing mental health issues sequelae resulting from other severe medical conditions. Adopting a stepped care model involves implementing a gradual hierarchy of mental health services that are customized to individual needs, accompanied by ongoing monitoring of mental health and cognitive concerns.

Strengths and limitations

The present study acknowledges a limitation in comprehensively assessing the diverse factors influencing suicide risk post-COVID infection. The highly variable nature of these factors, spanning different populations, countries, illness histories, economic statuses, mental health backgrounds, and familial dynamics, among others, poses a challenge in conducting an exhaustive evaluation within the scope of this study. The study recognizes the inherent heterogeneity of this population as a constraint in providing

a detailed analysis of each influencing factor. Additionally, in the early stages, the majority of studies investigating the impact of the pandemic on mental health employed online data collection methods to assess self-reported common indicators like mood, anxiety, or overall psychological distress. Pooled prevalence estimates of clinically significant high levels of depression and anxiety symptoms during the COVID-19 pandemic vary widely, posing challenges in interpretation due to substantial methodological and sample heterogeneity.

The strengths of this review stem from our insightful analysis within the framework of unique public health circumstances, emphasizing an infectious disease perspective. Additionally, our inclusion of data on neuronal alterations, particularly concerning neuroinflammation in both acute and post-COVID-19 syndrome, contributes to the robustness of this review. Limitations are inherent to the data we tried to retrieve from the literature, to their variability, and on the fact that this is not a systematic review assessing a single very specific research question. Moreover, due to these limitations, we could not assess how long do patients remain potentially suicidal after COVID infection, since we could not find relevant data on this topic, nor for the same reason we could assess the specific weight of virological variants on such issues. Data coming from more in-depth analysis of both virological and non-virological factors, and studies assessing temporal relationship between infection and SB may elucidate these matters.

Conclusions

Recent data link behavioral health disorders with COVID-19. Despite growing needs, mental health services remain underdeveloped. Suicidal risk rises, particularly in fragile populations exposed to COVID-19 morbidity. Understanding the complex biological processes involved may offer new insights into neuropsychiatric diseases. Urgent strategies are required to address behavioral health disorders in the post-acute phase. Collective efforts from the scientific community, governments, and public health authorities are crucial in addressing this Public Mental Health emergency.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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