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The Role of Laboratory Teams and Biomarkers in the Diagnosis and Management of Psychological Disorders Associated with Long COVID: A Comprehensive Review

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Abstract

Background: The COVID-19 pandemic has profoundly impacted global health, with a significant number of survivors experiencing persistent symptoms, termed "long COVID" (LC). Understanding the role of biomarkers and laboratory teams in diagnosing and managing psychological disorders associated with LC is crucial for improving patient outcomes.

Methods: This review synthesizes existing literature on the epidemiology, laboratory findings, and biomarkers related to long COVID. We analyzed data from numerous studies focusing on the prevalence of psychological symptoms among LC patients, the laboratory markers indicative of systemic inflammation, and the immunological profiles that might underlie these symptoms.

Results: Long COVID affects approximately 10% of individuals post-infection, with a higher prevalence among hospitalized patients. Key laboratory findings include elevated levels of inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), and D-dimer, which are associated with both physical and psychological symptoms. Immunological dysregulation, characterized by alterations in T and B cell populations, has also been observed in LC patients. These findings suggest a multifaceted pathology that may contribute to the psychological burden experienced by survivors.

Conclusion: The intersection of biomarkers, psychological disorders, and long COVID underscores the need for interdisciplinary approaches in patient care. Laboratory teams play a vital role in identifying biomarkers that can inform treatment strategies and guide clinical decisions. Future research should focus on the development of standardized diagnostic criteria and effective therapeutic interventions to address the long-term effects of COVID-19 on mental health.

Keywords: Long COVID, biomarkers, psychological disorders, laboratory teams, immunological dysregulation.

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1. Introduction

The World Health Organization (WHO) designated COVID-19 as a pandemic about three years ago, 11 March 2020. As of 7 June 2023, there have been about 767,750,853 confirmed cases of COVID-19, leading to 6,941,095 fatalities [1,2]. Notwithstanding the significant direct and indirect mortality and the substantial social and economic repercussions of COVID-19, the severity of SARS-CoV-2 infections seems to be progressively diminishing at the individual patient level [3]. The accumulated knowledge of COVID-19 pathogenesis and clinical experience has enhanced patient care, while rising collective immunity from natural infection or vaccination and the evolving characteristics of SARS-CoV-2 variants may have contributed to this phenomenon [4,5]. The prevalence of the Omicron variety may be seen as a significant milestone in the pandemic, owing to the comparatively milder characteristics of the infections it causes relative to previous strains [6]. The prevailing Omicron XBB.1.5 subvariant also seems to adhere to this pattern [7,8].

As the death rate of SARS-CoV-2 infection remains consistently low, the focus has turned to survivors who have persistent symptoms after seemingly achieving clinical recovery [9]. The enduring clinical symptoms after successful infection clearance are encapsulated by the term "long-COVID (LC)," which encompasses a diverse array of heterogeneous morbid diseases after confirmed SARS-CoV-2 infection. Although these disorders are infrequently life-threatening, they significantly impair a patient's quality of life, and, coupled with the high prevalence of LC, contribute substantially to the overall healthcare and societal repercussions of the pandemic [10-12]. Modest estimates indicate that LC impacts at least 10% of infected persons, equating to around 76 million cases worldwide [13,14].

2. Epidemiology of Long COVID and Associated Risk Factors

The precise prevalence of LC is difficult to ascertain owing to the non-specificity of its clinical presentations, the absence of further screening, and the lack of diagnostic markers, possibly leading to under-reporting [15-20]. Moreover, these findings are complicated by the lack of a comparator control group devoid of recent SARS-CoV-2 infection, rendering an accurate assessment of COVID-attributable symptoms impracticable. Modest estimates indicate that around 10% of non-hospitalized survivors endure lasting symptoms, however, the prevalence is significantly elevated among hospitalized individuals, with over 70% reporting at least one corresponding clinical manifestation [21-27]. The figures alone may not accurately represent the actual healthcare and social burden of LC unless the high prevalence of SARS-CoV-2 infection and the prolonged length of post-infectious symptoms, frequently lasting several months, are included. This likely leads to a significantly elevated overall genuine prevalence of LC-associated severe symptoms in the general population [28,29].

Moreover, although LC is regarded as a spectrum of mostly benign illnesses primarily affecting the quality of life rather than mortality, it cannot be conclusively ruled out that the symptoms within this spectrum may contribute to a portion of excess deaths related to COVID-19. From 1 January 2020 to 30 June 2022, a total of 3,544 death certificates in the United States identified LC as an underlying or contributing cause of death [30]. Despite constituting under 0.3% of COVID-related fatalities, this statistic certainly underrepresents the true numbers owing to insufficient reporting, particularly among certain ethnic communities. Nonetheless, existing research does not provide conclusive confirmation that LC directly causes mortality, and its association with increased COVID-related fatalities remains speculative. In the above-described instances, LC may have been present as one of many concurrent comorbidities.

The development of novel variations and the subsequent evolution of individual infections, together with the pandemic as a whole, are followed by a change in the epidemiological characteristics of LC [31,32]. Regarding the Omicron variant, its subvariants, which are presently predominant globally, are associated with persistent symptoms post-infection that are likely less severe and of shorter duration than those caused by earlier wild-type, Alpha, Beta, and Delta variants, and exhibit lower overall relative prevalence compared to non-infected controls. A recent pooled study of two population-based cohorts indicates that the risk of lung cancer is reduced post-infection with the Omicron strain and subsequent immunization [33,34]. The frequency and severity of Multisystem Inflammatory Syndrome in Children (MIS-C) decreased

during the Omicron wave of the pandemic relative to previous waves [35]. The current ambiguity surrounding this observation stems from whether it is chiefly a result of the modified natural progression of infection due to the Omicron variant or is merely influenced by the effects of rising vaccine coverage, as well as the growing incidence of reinfections and breakthrough infections during the Omicron period [36-39].

While the majority of epidemiological data have been derived from adult populations, children and adolescents are much more prone to develop chronic symptoms associated with long-term COVID after confirmed SARS-CoV-2 infection, in comparison to age-matched non-infected controls [40,41]. Uninfected control juvenile populations exhibit several LC-compatible symptoms at a much greater frequency than adult controls [42], complicating direct comparisons of LC prevalence between children/adolescents and adults. Significantly, post-COVID neurodevelopmental effects may also be seen in babies born to women infected during pregnancy during the first year of life [43]. Additionally, specific pathogenetic characteristics (e.g., inflammatory, immunological, related to endothelial dysfunction) and various clinical manifestations of LC may coincide with those of the Multisystem Inflammatory Syndrome in Children (MIS-C), initially identified in pediatric populations shortly after infection [44]. Based on the case description of MIS-C [45], it is evident that a subset of afflicted individuals also qualifies as LC, particularly under the "ongoing symptomatic COVID-19" group. Disregarding semantics, this may have consequences for a deeper knowledge of LC and the pathophysiology of MIS-C, which remains mostly obscure, while also informing prospective treatment strategies for both disorders. However, a putative pathogenic link between the two disorders cannot be corroborated with the existing evidence and remains conjectural.

In addition to the previously described effects of various viral variations, certain patient-level risk factors have been shown to increase the risk for LC. A recent meta-analysis of 41 studies indicates that among COVID-19 survivors, older age (Odds Ratio (OR): 1.21), female sex (OR: 1.56), elevated Body Mass Index (BMI) (OR: 1.15), smoking (OR: 1.10), the presence of physical and mental comorbidities (OR: 2.48), and hospitalization or admission to the ICU (OR: 2.38) are correlated with an increased risk of Long COVID (LC) [46]. Extended hospital stays, Black or Hispanic ethnicity, and poor socioeconomic position are associated with an elevated risk. In pediatric and young adult cohorts, factors such as age under 5 years, age over 10 years, female gender, Black or Hispanic ethnicity, the existence of chronic comorbidities, acute-phase hospitalization, infection with a pre-Omicron variant, and prolonged exposure to ambient air pollution (e.g., particulate matter ≤ 2.5 μm) have been identified as risk factors [49-51]. Specifically, children with LC had a higher propensity for having experienced attention deficit hyperactivity disorder, chronic urticaria, or allergic rhinitis before SARS-CoV-2 infection [52].

Concerning the effects of previous immunization, although the results from existing research are not certain, the risk of LC post-infection in vaccinated persons is probably lower than in those who are unvaccinated [36]. An analysis of a random sample of adults in the United Kingdom indicated a 41% reduction in the incidence of LC after infection among those who had received two vaccine doses (either mRNA-based, adenovirus vector or a combination), in comparison to those who were unvaccinated [53]. Data from the national healthcare database of the US Department of Veterans Affairs indicated a relatively modest risk decrease of 15% [54]. When concentrating on the avoidance of certain symptoms, such as cognitive impairment or myalgia, the resultant benefits may be more pronounced [55]. The impact of vaccination on individuals diagnosed with LC is inconsistent; 61.9% report no change, 16.7% experience improvement, and 21.4% report worsening symptoms. This indicates that active immunization post-native infection may not be universally applicable as a secondary prevention strategy for affected individuals [56]. A recent meta-analysis has shown no significant difference in the clinical presentation and severity of COVID-19 between original infections and reinfections. Nevertheless, data regarding the risk of lung complications after reinfection in both vaccinated and unvaccinated persons is limited, while current research suggests an elevated risk for lung complications after recurrent infections [57,58].

3. Laboratory Results and Biomarkers in Long COVID-19

The principal laboratory findings and biomarkers in acute severe COVID-19 include indicators of systemic inflammation, such as proinflammatory cytokines, chemokines, and complement proteins, alongside markers of endothelial damage and coagulation pathways, which encompass platelet activation and neutrophil extracellular trap formation. The cardinal laboratory characteristics with prognostic significance include lymphopenia, whether isolated or concurrent with an elevated absolute neutrophil count; heightened levels of C-reactive protein (CRP), interleukin (IL)-6, and IL-2R; as well as increased concentrations of lactate dehydrogenase (LDH), D-dimer, ferritin, hepatic function markers, and troponins [59,60]. In addition to elevated D-dimer levels, other indicators of coagulation abnormalities, including prolonged PT and aPTT, severe thrombocytopenia, and increased fibrin degradation products, may signify life-threatening disseminated intravascular coagulation (DIC), necessitating heightened vigilance and immediate intervention [61-63]. All these indicators correlate with an elevated risk of disease progression, including acute myocardial infarction, venous thromboembolism, and acute ischemic stroke [60]. Conversely, venous thromboembolic diseases, including deep vein thrombosis and pulmonary embolism, are not fundamental traits of liver cirrhosis.

Given the complex character of LC, it is essential to note that no tests exist for its diagnosis. Similarly, clinical characteristics, laboratory results, and biomarkers may not be reliably ascribed to LC. Consequently, the diagnostic assessment must be individualized while simultaneously ensuring the patient that LC is a clinical phenomenon characterized by a wide range of presentations. Clinicians may sometimes link symptoms associated with POTS or ME/CFS to mental health conditions, such as anxiety or depression, a priori. COVID-19 has been identified as a potential catalyst for anxiety or depression symptoms and may even result in post-traumatic stress disorder in certain instances [64,65]. While certain symptoms within the LC spectrum may indicate psychiatric manifestations, clinician attention is essential to prevent the misdiagnosis of significant underlying diseases that might influence the outcome of mental disorders. The first diagnostic evaluation must consider that ongoing clinical symptoms are part of the LC spectrum rather than indicative of an underlying illness. In addition to standard hematologic, biochemical, coagulation, and inflammatory markers, such as CRP and serum ferritin, the diagnostic strategy may include cardiac markers, hormonal and vitamin indicators, glycemic parameters like glucose or hemoglobin A1c, and the assessment of autoantibodies. These fundamental tests often provide findings within the normal reference range for individuals with LC; nevertheless, some inflammatory biomarkers may remain elevated for an extended duration [11].

The imaging diagnostic methodology is crucial for assessing pulmonary fibrosis resolution by repeated chest CT scans, heart function via cardiac ultrasound, and neurologic and cognitive issues using brain magnetic resonance imaging, among others. It is essential to note that various diagnostic instruments may be employed to assess characteristics of LC, including the validated "symptom burden questionnaire for LC" (SBQ-LC), tests for orthostatic intolerance related to postural orthostatic tachycardia syndrome (POTS), cardiac magnetic resonance imaging for cardiovascular anomalies and residual pathology, electrocardiograms revealing novel QRS fragmentation due to cardiac injury, and pulmonary function tests, among others. Most diagnostic tools for LC remain in development, including hyperpolarized magnetic resonance for identifying pulmonary gas exchange abnormalities, imaging for detecting microclots or small fiber neuropathy. Additionally, various tests have been employed in patients with ME/CFS and dysautonomia, such as serum or salivary cortisol measurement, detection of antibodies against herpesviruses, total immunoglobulin concentration assessments (IgG, IgA, IgM, IgG3), natural killer cell function tests, and evaluations for orthostatic intolerance.

4. Biomarkers of Systemic Inflammation

In reaction to a viral infection during the acute phase, the immune system mobilizes various cells (such as T cells and macrophages) and secretes a range of inflammatory mediators, including cytokines and chemokines. SARS-CoV-2 infection may induce a "cytokine storm," marked by a moderate surge of proinflammatory cytokines linked to significant monocyte dysregulation [66]. Acute respiratory distress

syndrome (ARDS), a primary cause of mortality in COVID-19 patients, is mostly induced by the cytokine storm [67]. The diverse and recurrent symptoms of LC may be attributed to elevated cytokines resulting from an aberrant immunological response [68].

Over the last two years, many case-control, prospective, and retrospective studies have examined inflammatory biomarkers in lung cancer, with inconsistent results. A preliminary meta-analysis of 15 studies regarding the incidence of long-term effects in LC, including laboratory abnormalities, indicated little evidence of systemic inflammation roughly 4 months post-infection [20]. Specifically, 8% of patients had raised CRP and ferritin levels, whilst 3% and 4% demonstrated increased concentrations of IL-6 and procalcitonin, respectively [20]. This was an early meta-analysis that included a limited number of studies investigating laboratory abnormalities with a modest participant count. A recent meta-analysis of 23 studies (14 prospective and 9 retrospective case-control) encompassing 18 meta-analyzed biomarkers revealed that survivors of LC exhibited elevated levels of CRP, D-dimer, lactate dehydrogenase (LDH), and leukocytes compared to controls without LC; however, the effect sizes were minimal [65]. Following sensitivity analysis, lymphocytes and IL-6 were substantially higher in patients with LC. Notably, variations in D-dimer, LDH, and lymphocyte levels were significant in patients exhibiting organ abnormalities identified by imaging and functional assessments, while discrepancies in IL-6 levels were noted in patients with persistent symptoms [65]. Moreover, variations in the levels of LDH, leukocytes, and N-terminal pro b-type natriuretic peptide (NT-Pro-BNP) were seen in patients exhibiting symptoms for less than 6 months, while changes in D-dimer levels were noted in patients with symptoms persisting for more than 6 months. IL-8, a chemokine that activates neutrophils at the site of inflammation, was seen to be higher in liver cirrhosis patients compared to healthy controls, according to just two investigations [64]. A recent meta-analysis of 22 case-control observational studies revealed that IL-6 levels were elevated in patients with LC relative to healthy persons and those without post-acute sequelae of COVID-19, however lower than in patients during the acute phase of COVID-19 [65]. IL-6, a significant indicator of systemic inflammation and negative outcomes in acute COVID-19, may work as a valuable predictor of long-term COVID (LC) after four weeks post-infection, indicating the "early stage" of LC [65]. Numerous investigations indicated that elevated IL-6 levels persisted for as long as 7 months in individuals with LC [69,70]. Similarly, several studies indicate that CRP, an acute-phase protein originating from the liver and enhanced after IL-6 production by macrophages and T cells, remains consistently high in liver cirrhosis patients from the early phase and persists for up to 7 months thereafter.

Further investigations into cytokines and chemokines have demonstrated an increase in IL-2 (which promotes the proliferation of helper, cytotoxic, and regulatory T cells), IL-17 (linked to inflammation and autoimmunity), interferon (IFN)-γ (essential for both innate and adaptive immunity against viral infections), CCL3, and CCL5 during the initial phase of LC [25,71,72]. Patients with LC exhibiting cognitive symptoms have shown increased levels of CCL11, which correlates with the suppression of neurogenesis, aging, and cognitive function, in contrast to those with LC without cognitive symptoms [73,74]. Conflicting findings were seen regarding the anti-inflammatory cytokines IL-4 and IL-10, which were described as either diminished or increased in individuals with LC [75]. In comparison to recovered patients, IFN-γ was raised at 2 months, tumor necrosis factor-α (TNF-α) at 4 months, and IFN-β and IFN-λ1 at 11 months in lung cancer patients [73]. The AA genotype of the IFNG gene was more prevalent among LC patients [76]. Additional acute phase proteins that react to proinflammatory cytokines and elevate in response to inflammation and tissue damage, including serum amyloid 1 (SAA1) and SAA4, were shown to be elevated in the microclots of patients with LC at three months [69].

Certain phenotypes of LC correlate with elevated biomarkers of systemic inflammation; nevertheless, the data are restricted. These biomarkers may possess predictive potential for identifying people at risk of liver cancer, as well as diagnostic relevance for certain liver cancer morphologies. Additional long-term studies are necessary to determine if the elevation trend of certain cytokines mirrors that seen in ME/CSF, where some cytokines decline after an initial increase in the early years of the illness, despite ongoing symptoms [78].

5. Immunological Profiling in Long COVID

Research examining immunological dysregulation in individuals with LC has shown several changes in immune cells. Elevated inflammatory monocytes (CD14+, CD16+, CCR5+) were seen before the onset of LC and throughout the convalescent chronic phase [78], with increased non-classical monocytes, which are linked to several chronic inflammatory and autoimmune disorders [74]. Research has recorded an elevation in natural killer (NK) cells displaying memory and activation markers, and an increase in plasmacytoid dendritic cells expressing CD86 and CD38 markers, which are crucial for antiviral immunity and are associated with the onset and progression of various autoimmune and inflammatory diseases, alongside a reduction in conventional dendritic cell numbers [74,76].

Individuals with LC exhibit persistent B and T cell abnormalities for a minimum of one year, characterized by a reduction in naive B and T cells; an increase in B cells and double negative B cells, which proliferate in older adults and accumulate prematurely in autoimmune and infectious diseases; a decrease in CD4+ and CD8+ effector memory cells; variable levels of SARS-CoV-2 CD8+ T cells expressing cytotoxic markers in patients with respiratory or gastrointestinal symptoms, respectively; a reduction in exhausted lymphocytes (CD4+/CD8+ expressing PD1) before clinical manifestations of LC; and an increase in exhausted lymphocytes during the convalescent phase of LC [25,74,76,79].

No definitive conclusions can be made on the changes of T regulatory (Treg) cells in LC owing to ambiguous findings [75]. Following their first SARS-CoV-2 infection, individuals with long COVID have a dysregulation of Treg cell functionality. These cells are essential for self-tolerance by suppressing T cell growth and cytokine production, hence averting autoimmunity. Contradictory evidence exists on the frequency of Treg among CD4+ cells in individuals with LC compared to those who have recovered, with a decreased percentage of Treg seen in 121 patients with LC relative to controls [76-78].

Despite the absence of a distinct immunological signature attributable to the variability of LC, the immunophenotypic abnormalities seen in LC patients highlight a sustained antiviral immune response, prevalent after chronic exposure to viral antigens and viral persistence. Numerous studies involving a limited participant pool, alongside case series and reports, have identified elements of viral persistence that may elicit symptoms of long COVID, particularly gastrointestinal manifestations, including the presence of viral proteins (spike and nucleocapsid) and/or SARS-CoV-2 RNA in feces, plasma, urine, the brain, muscles, eyes, lymph nodes, cardiovascular organs, liver, and lung tissue [80]. A histological examination of infected tissues via autopsy on 44 COVID-19 patients revealed the widespread presence of SARS-CoV-2 RNA in 84 different anatomical locations up to 230 days post-infection. Notably, although viral RNA was undetectable in plasma among all deceased cases, viral persistence was observed in various tissues through high-sensitivity droplet digital PCR, indicating the continued presence of a low viral load in biospecimens of COVID-19 patients [8].

Furthermore, intestinal endoscopic investigations, especially in individuals with inflammatory bowel disease (IBD), have detected the presence of SARS-CoV-2 in the gut epithelium or feces up to six months following infection, indicating a possible viral reservoir that may provoke prolonged inflammatory responses in certain instances of LC [81]. Notably, detectable SARS-CoV-2 RNA in stool samples and elevated levels of circulating spike, S1, and nucleocapsid (N) antigens were observed in children with MIS-C compared to those with acute COVID-19 or controls, indicating that viral persistence may initiate the hyperinflammatory responses characteristic of MIS-C [3]. However, Sigal et al. could not demonstrate any persistence of the plasma spike antigen in a multicentric cohort investigation of children with MIS-C using an ultra-sensitive electro-chemiluminescent immunoassay [82].

Current research indicates that the persistence of SARS-CoV-2 infection may exceed the timeframe suggested by PCR-negative results from nasopharyngeal swabs or bronchoalveolar lavage fluids. Persistent low-grade multisystem inflammation in adults and children may be linked to a prolonged SARS-CoV-2 infection or reinfection [83]. The use of antiviral medicines against SARS-CoV-2, such nirmatrelvir combined with ritonavir, may eliminate viral reservoirs and alleviate symptoms of long COVID.

6. Constraints of Research and Obstacles

This paper evaluates and summarizes biomarkers associated with LC. Nonetheless, no distinct biomarker or laboratory test, nor a panel of biomarkers, can reliably distinguish LC from other disease types. Prior results indicate that several symptoms and various subdiagnoses may occur within the framework of LC; hence, the sequelae of COVID-19 are unlikely to stem from a singular pathogenetic mechanism. Furthermore, owing to the varied and complicated etiology of LC, the diagnostic and prognostic efficacy of most biomarkers is limited. Moreover, given that individuals meeting the criteria for LC may or may not have actual organ damage [67], potential biomarkers might effectively identify the subgroup of patients with target organ involvement. To present, data in this area remains unclear, as no biomarker demonstrates enough precision to differentiate particular patient categories with target organ damage, despite its high frequency among individuals with LC [67].

The studies assessing laboratory data and biomarkers for the prediction, diagnosis, and prognosis of LC exhibit several methodological shortcomings. Initially, there was a lack of a common definition for LC, resulting in the misclassification of individuals. Misclassification may occur when distinguishing long-term symptoms possibly linked to LC from symptoms arising from other illnesses, whether related or unrelated to LC, becomes challenging. A notable limitation was the dependence on self-reported data about LC status, potentially resulting in selection bias. The time of symptom onset is susceptible to recollection bias, especially when data is gathered several months post-acute COVID. Significantly, several research concentrated on hospitalized cohorts, which may not accurately reflect the general population. Additional concerns include the false negative rate of PCR testing, potentially misclassifying individuals as controls, alongside the restricted efficacy of antibody titers in assessing prior SARS-CoV-2 infection [11]. Conversely, several investigations did not establish a laboratory-confirmed diagnosis of COVID-19 and concentrated on prevalent symptoms and varying timeframes with significant variability [84].

Many studies were inadequately powered owing to limited sample numbers, especially among control groups, and included convenient cohorts with individuals who were retained during follow-up. Numerous studies used a retrospective approach, whereby the majority of biomarkers were assessed post-onset of LC symptoms; hence, the changed biomarkers may represent an epiphenomenon of LC. Ultimately, most research was performed during the first period of the pandemic, focusing on a restricted array of biomarkers; hence, the use of these biomarkers for LC in relation to Omicron subvariants remains ambiguous.

7. Therapeutic Viewpoints and Obstacles

While the majority of therapeutic strategies evaluated for LC have focused on symptom relief [85], a thorough assessment of symptoms and clinical signs in affected patients is essential to promptly identify "red flag" indicators that suggest underlying objective systemic disorders, which may significantly influence patient prognosis. Similarly, thorough laboratory, radiographic, and other functional assessments should be limited to patients displaying specific characteristics and not universally administered as a screening procedure for all instances of persistent symptoms after acute infection. To enhance patient access to appropriate treatment and alleviate the strain on secondary and tertiary hospitals, the assessment and initial management should be delegated to primary care units, after sufficient information dissemination and education of primary care doctors. Optimal primary patient care should rely on consistent assessment methods and established protocols. For patients displaying "red flag" symptoms or severe manifestations, a referral to specialist care should be made through interdisciplinary ambulatory COVID clinics, which provide streamlined access to specialized personnel and investigations, serving as a conduit between primary and hospital care [86].

It is unsurprising that, given the extensive range of symptoms and diseases included by the term "LC," no one treatment method has shown efficacies for all afflicted people. Nonetheless, some candidate medicines may be potentially beneficial for certain patient populations or symptom clusters. For individuals with chronic fatigue, strategies that have shown efficacy in ME/CFS may be beneficial, particularly lifestyle management (including pacing, energy optimization, and frequent rest) or pharmacological treatments

such as naltrexone [11,386]. In the setting of LC, therapy of dysautonomia with postural hypotension may be enhanced by a high intake of salt and fluids, beta-blockers, low-dose fludrocortisone, and desmopressin, among other treatments, contingent upon clinical presentation [87].

8. Conclusions

The constellation of symptoms and diseases associated with LC, although seldom life-threatening, significantly detracts from individual functional status and quality of life. Due to its significant frequency and prevalence after acute infection, LC is a disease that has major social and healthcare effects. As the rates of direct morbidity and death from acute infection decline owing to widespread vaccination and infection-induced immunity, together with the emergence of less virulent SARS-CoV-2 strains, the significance of long-term sequelae connected to SARS-CoV-2 infection is becoming more prominent.

It is essential to identify both the traits of individuals at high risk for LC and the particular qualities within patient populations that are most likely to gain from treatment interventions. Given that clinical risk factors alone are inadequate for this job, emphasis has shifted to identifying sensitive and accurate diagnostic biomarkers. Regrettably, this endeavor has produced few substantial outcomes so far, mostly hindered by methodological challenges associated with the predominantly retrospective epidemiological research available. Future endeavors should concentrate on assessing easily accessible serum, radiographic, or other biomarkers, which will further elucidate the underlying processes driving LC formation. Consequently, they should be evaluated within the context of randomized clinical trials of prospective therapeutic approaches to advance precision medicine in the treatment of afflicted patients.

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دور الفرق المخبرية والمؤشرات الحيوية في تشخيص وإدارة الاضطرابات النفسية المرتبطة بـ"كوفيد طويل الأمد": مراجعة شاملة

الملخص

الخلفية :أثرت جائحة كوفيد-19 بشكل كبير على الصحة العالمية، حيث يعاني عدد كبير من الناجين من أعراض مستمرة تُعرف باسم "كوفيد طويل الأمد .(LC) "يُعد فهم دور المؤشرات الحيوية والفرق المخبرية في تشخيص وإدارة الاضطرابات النفسية المرتبطة بـ LCأمرًا بالغ الأهمية لتحسين نتائج المرضى.

الطرق :تستعرض هذه المراجعة الأدبيات الحالية حول علم الأوبئة، النتائج المخبرية، والمؤشرات الحيوية المرتبطة بكوفيد طويل الأمد. تم تحليل بيانات من دراسات متعددة تركزت على انتشار الأعراض النفسية بين مرضىLC ، والعلامات المخبرية التي تشير إلى الالتهاب الجهازي، والملامح المناعية التي قد تكون وراء هذه الأعراض.

النتائج :يؤثر كوفيد طويل الأمد على حوالي 10% من الأفراد بعد الإصابة، مع ارتفاع معدلات الانتشار بين المرضى الذين تم إدخالهم المستشفى. وتشمل النتائج المخبرية الرئيسية مستويات مرتفعة من علامات الالتهاب مثل البروتين التفاعلي(CRP) C-، إنترلوكين-6(IL-6) ، والـD-dimer، والتي ترتبط بالأعراض الجسدية والنفسية على حد سواء. كما لوحظ خلل في التنظيم المناعي يتمثل في تغييرات في أعداد خلايا T و Bبين مرضى LC.تشير هذه النتائج إلى وجود مرض متعدد الجوانب قد يسهم في العبء النفسي الذي يعاني منه الناجون.

الخلاصة :يُبرز تقاطع المؤشرات الحيوية، الاضطرابات النفسية، وكوفيد طويل الأمد الحاجة إلى نهج متعدد التخصصات في رعاية المرضى. تلعب الفرق المخبرية دورًا حيويًا في تحديد المؤشرات الحيوية التي يمكن أن تُسهم في وضع استراتيجيات علاجية وتوجيه القرارات السريرية. ينبغي أن تركز الأبحاث المستقبلية على تطوير معايير تشخيصية موحدة وتدخلات علاجية فعالة للتعامل مع التأثيرات طويلة الأمد لكوفيد-19 على الصحة النفسية.

الكلمات المفتاحية :كوفيد طويل الأمد، المؤشرات الحيوية، الاضطرابات النفسية، الفرق المخبرية، خلل التنظيم المناعي.