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POST COVID-19 CONDITION: NEEN FOR CONSENSUS DEFINITION

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პოსტ-COVID-19 მდგომარეობა: აუცილებელია შეთანხმებული განსაზღვრება

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რეზიუმე

ლიტერატურის მიმოხილვისას ხშირად ვხვდებით SARS-CoV2 ინფექციასთან დაკავშირებული გახანგრძლივებული დაავადების განსხვავებულ განმარტებებს და ინტერპრეტაციას, რაც სერიოზულ პრობლემას ქმნის შემთხვევების სისტემატურ დახასიათებაში ეპიდემიოლოგიური და კლინიკური მონაცემების მიხედვით. ჩვენი კვლევა ეხება პოსტ-COVID-19-ის სიხშირის შეფასებას შემთხვევის განსაზღვრების კონტექსტში, რასაც მნიშვნელოვანი გავლენა აქვს მონაცემების ანალიზისათვის. განხილულ კვლევებზე დაყრდნობით, პოსტ-COVID-19 მდგომარეობის პრევალენტობა 10%-დან 77.8%-მდე მერყეობს და ის დროთა განმავლობაში გაიზრდება SARS-CoV2 ვირუსის მუტაციის პარალელურად. პოსტ-COVID-19 მდგომარეობის განსაზღვრებაში კონსენსუსის მიღწევა აუცილებელია COVID-19-ის გამოვლინების ყველა ფორმის კლინიკური, პათოფიზიოლოგიური, ლაბორატორიული, რადიოლოგიური და ეპიდემიოლოგიური მახასიათებლების იდენტიფიცირებისა და დახასიათებისთვის. ეს დაგვეხმარება უკეთ გავიგოთ შესასწავლი დაავადება, განვსაზღვროთ მისი სიხშირე, ეპიდემიოლოგიური და კლინიკური მახასიათებლები, ჩამოვყალიბოთ მოვლის საუკეთესო პრაქტიკის სტანდარტები და შევიშუშაოთ ეფექტური კონტროლისა და პრევენციის ღონისძიებები.

Introduction: The worldwide scientific community is forging ahead to characterize a wide range of outcomes associated with SARS-CoV-2 infection; however, the underlying assumptions in these studies have varied so widely that the resulting data are difficult to compare (Rando). Relatively little is known about the clinical course of COVID-19 and return to baseline health for persons with milder, outpatient illness (Mark W. Tenforde). Less is known about the clinical evolution of COVID-19 patients after hospital discharge (Lledó). During literature review we come across to different definitions of prolonged illness associated with SARS-CoV2 infection, which made it difficult to characterize and compare COVID-19 cases by epidemiological and clinical patterns. Our study is an attempt to assess post-COVID-19 frequency in the context of the case definitions.

Methods: Literature review was performed in PubMed Central, ScienceDirect and Willey Online Library. Search key words included: post-Covid-19 and Long Covid-19, Acute and chronic post-COVID-19. As for the study design we considered for inclusion clinical trials, observational longitudinal comparative and non-comparative studies, cross-sectional and case series.

Results: The frequency of long COVID-19 widely varied by countries, patients' population and medical institutions even within the same countries due to differences in the case definitions. Post COVID-19 condition occurs in many different sets of patients, such as those hospitalized with COVID-19 illness of varying severity, those who have not been hospitalized or those having recovered from a pauci- or asymptomatic acute illness (WHO, Post COVID-19 condition: A webinar to expand our understanding of this condition). The syndrome can take many forms, from post-intensive care unit syndrome¹ to pulmonary fibrosis secondary to aggressive COVID-19 pneumonia. (McGroder CF). Substantial subset patients continue to complain of persistent symptoms after several months. (Garrigues E), (Huang C), (Fortini A), (Chopra V), (ONS), (S. K. Nalbandian A).

Prolonged illness is well described in adults with severe COVID-19, especially among older adults (Fortini A), (Grasselli G); (Guan WJ). COVID-19 can result in prolonged illness, even among young adults without underlying chronic medical condition. Among persons aged 18-34 years one in five had not returned to their usual state of health (Mark W. Tenforde). According to WHO, around 10%–15% of patients may present persistent symptoms after acute infection (WHO). (GCMSC) (Trisha Greenhalgh). The Office of National Statistics (ONS) estimating the prevalence of long COVID symptoms in the national Coronavirus (COVID-19) Infection Survey (CIS), concluded that: Around 1 in 5 respondents testing positive for COVID-19 exhibited symptoms for a period of 5 weeks or longer. Around 1 in 10 respondents testing positive for COVID-19 exhibited symptoms for a period of 12 weeks or longer. A substantial percentage of COVID-19 patients (77.8%) continue to complain of symptoms 3–6 months after hospital discharge (Lledó) and even longer (A. R. Sebastian Havervall, Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers.), (Tenforde). Evidence of persisting COVID-19 symptoms is accumulated; however, no consensus has yet been reached on the definition and chronology associated with persistent illness. The terms “prolonged COVID-19”, “prolonged sequelae”, “post-acute COVID-19”, “post-acute COVID-19 Syndrome (PACS)”, “persistent COVID-19 symptoms”, “post-COVID-19 manifestations”, “long-term COVID-19 effects”, “post-COVID-19 syndrome”, “post-acute COVID-19 sequelae”, “chronic COVID syndrome”, among others, have been used by different authors (Rando), sometimes – interchangeably (S. K. Nalbandian A) . There is currently no agreement on which outcomes should be measured and how they should be measured. (Munblit). The Multidisciplinary Collaborative Group for the Scientific Monitoring of COVID-19 in its third report (June 2021), which was focused on persistent symptoms among convalescent patients, highlighted the need to establish a clear and common definition for Post-Acute COVID-19 syndrome (GCMSC). From all the existing definitions of Post COVID-19, the authors of the report support the use of the term **Post-Acute COVID Syndrome**, englobing two non-mutually exclusive sub-entities or scenarios: i) **Long-COVID** refers to symptoms that persist or appear beyond 4 weeks after infection, and which may be permanent, recurrent or progressively improve, ii) **Sequelae** refers to irreversible damage to organs 12 weeks after the infection, leading to different grades of permanent dysfunction and symptoms. In the absence of agreed definitions, some authors define post-acute covid-19 as extending beyond three weeks from the onset of first symptoms and chronic covid-19 as extending beyond 12 weeks (Trisha Greenhalgh) , (Shah). WHO had established the ICD-10 code for the Post COVID-19 condition and by January 2021, had published its initial guidance on clinical management of patients after acute illness. WHO’s clinical case definition of post COVID-19 condition by Delphi methodology that includes 12 domains, available for use in all settings (6 October 2021). (WHO, A clinical case definition of post COVID-19 condition by a Delphi consensus). The U.S. Centers for Disease Control and Prevention (CDC) issued the following definition and offered detailed interim guidance for healthcare providers. The term “Post-COVID Conditions” is an umbrella term for the wide range of physical and mental health consequences experienced by some patients that are present four or more weeks after SARS-CoV-2 infection, including by patients who had initial mild or asymptomatic acute infection (CDC) . The time frame of four or more weeks provides a rough approximation of effects that occur beyond the acute period, but the timeframe might change as we learn more. Both organizations readily acknowledge that their definitions are likely to change as understanding of post-COVID conditions increases ((APTA)). In this regard it noteworthy that NIH launched the RECOVER (Researching COVID to Enhance Recovery) Initiative in February 2021 to bring together researchers and scientists to identify the causes and the means to prevent and treat post-acute sequelae of SARS-CoV-2 infection PASC, including what is commonly called Long COVID or long-haul COVID (NIH). As yet it is unclear how long chronic post-COVID condition’s symptoms may persist. Although literature on this topic is scarce, in one of the cohort studies Bosscolo-Rizzo et al. observed a variable range of COVID-19 symptoms beyond 12 months after the onset of the infection (P Bosscolo-Rizzo). A systematic review of 25 observational studies with moderate to high methodological quality, considering 5440 participants none of the studies assessed the duration of signs/symptoms (Ana Luiza Cabrera Martimbianco). Post-COVID-19 condition could become a significant global health burden

(Munblit D). We consider that along with consensus definitions on post-COVID-19 conditions, there is a need in standard approach to and understanding of:

- Natural history of COVID-19, in general, and the duration of the acute clinical phase of the disease, in particular;
- Diagnostic criteria for post COVID-19 conditions;
- Clinical and laboratory indicators of fully recovery from acute COVID-19.

Conclusion: Prevalence of post-COVID-19 condition ranges from 10% up to 77.8% over the reviewed studies and tends to increase over time along with mutation of the SARS-CoV-2 virus. Consensus definition of Post-COVID Conditions is essential for identification and characterization of clinical, pathophysiological, laboratory, imaging and epidemiologic features of all forms of COVID-19 manifestation. It will help us better understand the disease entity, set up best-practice standards of care and elaborate effective control and preventive measures.

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SUMMARY

During literature review we come across to different definitions of prolonged illness associated with SARS-CoV2 infection, which made it difficult to characterize and compare COVID-19 cases by epidemiological and clinical patterns. Our study is an attempt to assess post-COVID-19 frequency in the context of the case definitions. Prevalence of post-COVID-19 condition ranges from 10% up to 77.8% over the reviewed studies and tends to increase over time along with mutation of the SARS-CoV-2 virus. Consensus definition of Post-COVID Conditions is essential for identification and characterization of clinical, pathophysiological, laboratory, imaging and epidemiologic features of all forms of COVID-19 manifestation. It will help us better understand the disease entity, set up best-practice standards of care and elaborate effective control and preventive measures.

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СОСТОЯНИЕ ПОСЛЕ COVID-19: НЕОБХОДИМО ИМЕТЬ СОГЛАСОВАННОЕ ОПРЕДЕЛЕНИЕ

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РЕЗЮМЕ

При обзоре литературы мы сталкиваемся с различными определениями и интерпретациями продолжительного заболевания, связанного с инфекцией SARS-CoV2, что создает серьезную проблему для систематической характеристики случаев по эпидемиологическим закономерностям и клиническим проявлениям для их эффективного ведения и контроля. Наше исследование представляет собой попытку оценить частоту пост-COVID-19 в контексте определений случаев, поскольку это имеет важное значение для анализа. Распространенность пост-COVID-19 состояния, по рассмотренным исследованиям, колеблется от 10% до 77,8% и имеет тенденцию к увеличению по мере мутации вируса SARS-CoV-2. Согласованное определение пост-COVID-19 состояний необходимо для идентификации и характеристики клинических, патофизиологических, лабораторных, радиологических и эпидемиологических особенностей всех форм проявления пост-COVID-19. Это поможет нам лучше понять сущность заболевания, определить его частоту, эпидемиологические и клинические характеристики, установить стандарты лечения и разработать эффективные меры контроля и профилактики пост-COVID-19 состояний.

