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EFFECTS OF LONG COVID IN DIFFERENT COUNTRIES DURING THE PANDEMIC: A NARRATIVE REVIEW

EFEITOS DA COVID LONGA EM DIFERENTES PAÍSES DURANTE A PANDEMIA: UMA REVISÃO NARRATIVA

EFECTOS DEL COVID PROLONGADO EN DIFERENTES PAÍSES DURANTE LA PANDEMIA: UNA REVISIÓN NARRATIVA

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ABSTRACT

Objective: To evaluate the effects of long COVID in different countries, during the pandemic.

Methods: This is a narrative review conducted through an advanced search in the MEDLINE database, using descriptors identified in Medical Subject Headings (MeSH).
The search was carried out on September 26, 2023.

Results: The study found 88 studies, of these 62.02% were conducted in Europe, 22.98% in America, 10.34% in Asia, and 4.59% in Africa. Fatigue, shortness of breath, headaches, muscle pain, loss of taste, sore throat, and memory loss were the symptoms most prevalent among the patients. Additionally, the onset of the symptoms varied from four weeks to six months after the infection.

Conclusion: The evidence suggests that long COVID symptoms are heterogeneous, with a higher prevalence of physical symptoms, occurring between 4 weeks to 6 months after infection. Thus, new studies are needed to better understand this condition, which will be critical to developing effective prevention, diagnosis, and treatment strategies.

Keywords: COVID-19. Long COVID. Clinical Characteristics. Symptons. Studies Prevalence. Countries. Onset Symptoms.

RESUMO

Objetivo: Avaliar os efeitos da COVID longa em diferentes países durante a pandemia.

Métodos: Trata-se de uma revisão narrativa realizada por meio de uma busca avançada na base de dados MEDLINE, utilizando descritores identificados nos Medical Subject Headings (MeSH). A busca foi realizada em 26 de setembro de 2023.

Resultados: O estudo encontrou 88 estudos, dos quais 62,02% foram realizados na Europa, 22,98% na América, 10,34% na Ásia e 4,59% na África. Fadiga, falta de ar, dores de cabeça, dor muscular, perda de paladar, dor de garganta e perda de memória foram os sintomas mais

prevalentes entre os pacientes. Além disso, o início dos sintomas variou de quatro semanas a seis meses após a infecção.

Conclusão: As evidências sugerem que os sintomas da COVID longa são heterogêneos, com maior prevalência de sintomas físicos, ocorrendo entre 4 semanas e 6 meses após a infecção. Assim, novos estudos são necessários para melhor compreender essa condição, o que será fundamental para o desenvolvimento de estratégias eficazes de prevenção, diagnóstico e tratamento.

Palavras-chave: COVID-19. COVID Longa. Características Clínicas. Sintomas. Prevalência de Estudos. Países. Início dos Sintomas.

RESUMEN

Objetivo: Evaluar los efectos del COVID prolongado en diferentes países durante la pandemia.

Métodos: Se trata de una revisión narrativa realizada mediante una búsqueda avanzada en la base de datos MEDLINE, utilizando descriptores identificados en los Medical Subject Headings (MeSH). La búsqueda se llevó a cabo el 26 de septiembre de 2023.

Resultados: El estudio encontró 88 estudios, de los cuales el 62,02% se realizaron en Europa, el 22,98% en América, el 10,34% en Asia y el 4,59% en África. La fatiga, la falta de aire, los dolores de cabeza, el dolor muscular, la pérdida del gusto, el dolor de garganta y la pérdida de memoria fueron los síntomas más prevalentes entre los pacientes. Además, el inicio de los síntomas varió de cuatro semanas a seis meses después de la infección.

Conclusión: La evidencia sugiere que los síntomas del COVID prolongado son heterogéneos, con mayor prevalencia de síntomas físicos, presentándose entre 4 semanas y 6 meses después de la infección. Por lo tanto, se necesitan nuevos estudios para comprender mejor esta condición, lo cual será fundamental para desarrollar estrategias eficaces de prevención, diagnóstico y tratamiento.

Palabras clave: COVID-19. COVID Prolongado. Características Clínicas. Síntomas. Prevalencia de Estudios. Países. Inicio de los Síntomas.

1 INTRODUCTION

More three years after the onset of the COVID-19 pandemic, it is estimated that 65 million or more people are still living with a variety of mid and long-term effects from COVID-19 [1], named post-COVID-19 conditions or long COVID. Although still disputed, the World Health Organization (WHO) describes it as symptoms arising within three months of infection with SARS-CoV-2 and lasting at least two months without an alternative diagnosis [2]. Its causes are also elusive, with a recent meta-analysis suggesting a series of risk factors associated with the development of this condition, such as female sex, older age, having a high body mass index, smoking, and especially underlying comorbidities [3].

A national cohort study performed in Israel verified the long-term clinical outcomes in over 1.9 million people with mild COVID-19. Anosmia and dysgeusia, concentration and memory impairment, dyspnoea, weakness, streptococcal tonsillitis, and dizziness had significant hazard ratios throughout the year after diagnosis, peaking at four months, and slowly declining [4]. Another recently published study examined data from 9,764 adults, including 8,646 who had COVID-19 and 1,118 controls. The authors identified the 12 most common symptoms, among them post-exertional malaise, fatigue, brain fog, dizziness, gastrointestinal symptoms, heart palpitations, and loss of smell or taste. This study also provided an initial symptom-based scoring system to classify their as a condition specific to SARS-CoV-2 infection [5]. Although the general understanding of the clinical features of long COVID is progressively increasing, there are still many gaps, particularly in developing countries.

Thus, given the heterogeneity of symptoms, it is of significant public health and scientific importance to better research the principal manifestations of long COVID throughout the pandemic in order to provide insights into prevention and treatment strategies for a condition, that affects the health and well-being of millions of people. In this context, this study aimed to evaluate the effects of long COVID in different countries, during the pandemic.

2 METHODS

This work is a narrative literature review that aims to describe the main clinical characteristics of long COVID (such as symptoms and its onset), as well as the prevalence of studies in various countries, during the pandemic. Therefore, through an advanced search carried out on September 26, 2023, with the use of descriptors identified in Medical Subject Headings (MeSH): (((Post-Acute COVID-19 Syndrome) AND

(Prevalence)) AND (symptoms)), we select the files for composing the synthesis.

The literature search was realized in one independent database, MEDLINE, which contains more than 30 million references in the medical area. With the aforementioned descriptor terms, 782 related articles were delimited. After the selection of research that followed the following parameters: (i) full and free texts, (ii) case reports, (iii) clinical study, (iv) clinical trial, (v) comparative study, (vi) study multicenter, (vii) observational study and controlled, and (viii) randomized test, the final number was of 88 articles, which were effectively used in the development of this work. The process subsequently, involved study selection and data extraction performed independently by one of the investigators.

We extracted data on study, objective, study design, patient time span, country, sample size (n), groups, criterion to define Long COVID, outcomes, statistical analysis, results, limitation, conclusion, and observations. All data extracted were added in Supplementary Table 1.

Abstract texts, associated data, books and documents, meta-analyses, and systematic reviews were excluded, as well as publications that were more than five years old.

3 RESULTS

After screening 782 articles, a total of 88 studies were included in this analysis (complete data in Supplementary Table 1). Of these, 62.02% of studies were carried out in Europe, 22.98% in America, 10.34% in Asia, and 4.59% in Africa. The three countries with the most studies were the United States (N= 12), Spain (N= 8), and United Kingdom (N= 6).

Among the analyzed studies, 18 were performed with a modest sample of 501– 2,000 patients, and 34 used even a smaller sample, with less than 500 patients. Only nine studies used a sample with more than 10,000 patients (Table 1).

Table 1

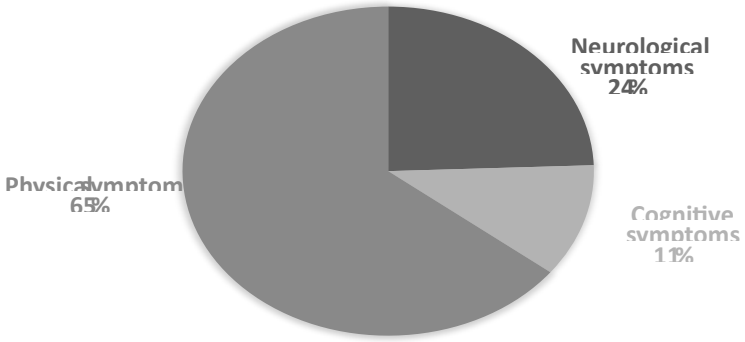
Sample ranges used in each study

Sample ranges	Number of studies (N)
1 - 50	9
51 - 100	7
101 - 500	18
501 – 2,000	25
2,001 – 10,000	9
>10,000	9
Information not available	11

Forty-five symptoms were identified in the different studies and subsequently categorized into physical, mental, and cognitive impairments, represented in Figure 1. Of these, the most common symptoms were fatigue (N= 15), lack of shortness of breath (N= 16), headaches (N= 10), muscle pain (N= 8), loss of taste (N= 3), pain in throat (N= 3) and memory loss (N= 2). In most studies, the time of onset of long COVID ranged from 4 weeks to 6 months.

Figure 1

Proportion of symptoms reported in different studies.



4 DISCUSSION

The present study conducted a comprehensive search on the clinical characteristics of long COVID in different countries, since the beginning of the pandemic. The study found that the majority of the studies (62.02%) were conducted in Europe, followed by America (22.98%), Asia (10.34%), and Africa (4.59%). Although there were only a few studies conducted in low-income and middle-income countries, the physical symptoms of COVID-19 were quite prominent. Fatigue, shortness of breath, headaches, muscle pain, loss of taste, sore throat, and memory loss were most prevalent among the patients. Additionally, the onset of the symptoms varied from four weeks to six months after the infection.

To date, more than 700 million people worldwide have been infected with SARSCoV-2 [6]. As of April, the estimate was that about 10% of adults infected with the virus continue to experience and suffer from the many symptoms termed together as long COVID [7]. Researchers and patients identified approximately 200 symptoms associated with long COVID, affects nearly every tissue and organ in the body, considerably impacting the quality of life and health of infected individuals. Thus, this study provides important updates on the clinical characteristics of long COVID, through a comprehensive narrative review with approximately 90 articles published in indexed journals.

The impact of long COVID is not clear yet, with disparate publications on the condition in different countries. Our results showed that countries such as the United States, Spain, and the United Kingdom were the most productive, leading positions scientific in this area. However, various countries that were epicenters of the pandemic have limited data, such as Brazil, with only three of the 88 studies analyzed [8-10]. In this context, O'Mahoney et al. (2023) identified regional discrepancies in the prevalence of long COVID, with significantly higher rates in Europe when compared to North

America and Asia, while earlier reviews have shown the highest prevalence in Asia [11]. Therefore, it is necessary to obtain more comprehensive data, especially from low- and middle-income countries.

Among 88 studies included in this analysis, we observed more than 40 symptoms in wide varied areas and organs of the body. After the categorization of these symptoms, we observed a higher prevalence of physical symptoms (64.4%), such as fatigue, dyspnea, and headache. These findings are in agreement with Kelly et al., (2023), that cite fatigue (29.3% [IC 95% 20.1-40.6%]) and dyspnea (19.6% [IC 95% 12.8-28.7%]), as the most frequent individual symptoms [12]. Additionally, O'Mahoney et al., (2023) showed that fatigue, disturbed sleep, and breathlessness were the most common symptoms among 735,006 participants of 194 studies included in the systematic review [11]. In this line, as mentioned Thaweethai et al., (2023) developed an initial symptom-based scoring system to improve future diagnosis and treatment, additionally, the researchers observed that individuals who were unvaccinated or who had COVID-19 before the Omicron strain emerged in 2021 were more likely to have long COVID and severe cases of the condition, in addition to, reinfections also linked to higher rates of long COVID frequency and severity, compared to those who had only contracted the virus once [5].

Another attention point is the onset of the symptoms. The WHO defines long COVID as symptoms that start (usually) within three months of COVID, last for at least two months, and can't be explained by another disease. However, in the present study, the onset of the symptoms varied from four weeks to six months after COVID-19. Similar to our findings described by O'Mahoney et al., (2023), Mizrahi et al., (2023), and Centers for Disease Control and Prevention (CDC [13]).

Long COVID is a condition that is not yet well understood, in this context, this narrative review contributes to better identification and management of this illness, particularly by the large amount of extracted data, avaliable in Supplementary Table 1. Despite this, there are limitations such as heterogeneous symptoms have generated widely divergent estimates of prevalence, lack of an uninfected comparison group, limited follow-up durations, as well as

measurement methods. Associated with the few studies realized in low-income and middle-income countries, some of them widely reached by pandemic, such as Brazil.

5 CONCLUSION

The evidence suggests that long COVID symptoms are heterogeneous, with a higher prevalence of physical symptoms, including fatigue, shortness of breath, headaches, muscle pain, and loss of taste. These symptoms usually occur between 4 weeks and 6 months after COVID-19 infection. Given the high prevalence, still limited knowledge, particularlly in low-income and middle-income countries, as well as the possible impact on the quality of life, more studies are needed, in order to better understand the underlying mechanisms and management of the disease, which will be critical to developing effective prevention, diagnosis, and treatment of the long COVID.

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LIST OF ABBREVIATIONS

CDC: Centers for Disease Control and Prevention WHO: World Health Organization

DECLARATIONS

Ethics Approval statement Not applicable.

Consent for publication

All authors give consent for publication of the work.

Availability of data and materials

Not applicable.

Conflict of Interest

The authors declare no conflict of interest.

Authors' contribution

Substantial contributions to the conception or design of the work: all authors.

Substantial contributions to the acquisition, analysis, or interpretation of data for the work: all authors.

Drafted the work: all authors.

Revised the manuscript critically for important intellectual content: all authors.

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