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Research Article

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Convalescence and Post-covid-19 Conditions Comparison between Long Covid and Post Acute Covid

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Abstract

***Objective:** To compare clinical-epidemiological characteristics of patients with Long covid-19 (prolonged symptoms beyond 12 weeks) with post-acute covid-19 syndrome (persistent symptoms beyond 4 weeks) in the same population in general medicine.*

***Methodology:** Comparison of secondary data among tow previous observational, longitudinal and prospective studies: 1) patients with post-acute COVID-19 syndrome from March 15, 2020 to March 31, 2021; and 2) patients with Long covid-19 from March 15, 2020 to October 31, 2022, in the same population in general medicine.*

***Results:** 27 cases of Long covid-19 and 33 of Post-acute covid-19 syndrome were included. Long covid-19 vs. Post-acute covid-19 syndrome had fewer people with some type of labor specialization (15% vs. 51%; p= .003026), fewer cases of Moderate-severe severity of primary infection (30% vs. 51%; p= . 044129), and fewer General symptoms (14% [asthenia, arthralgia, malaise] vs. 36% [discomfort, asthenia, myalgia, fever, arthralgia]; p= .001337). In Long covid-19, Respiratory (27%) and ENT (20%) symptoms predominated, while in Post-acute covid-19 syndrome they were General (36%) and Respiratory (32%). In Long covid-19 there were more symptoms ENT (29% vs. 14%), Neurological (18% vs. 7%), Psychiatric (9% vs. 5%), Circulatory (4% vs. 0%), Genitourinary (4% vs. 0%). In post-acute covid-19, General (36% vs. 14%), Respiratory (32% vs. 27%), Digestive (5% vs. 4%), and Skin (1% vs. 9%) symptoms predominated.*

***Conclusion:** Convalescence from covid-19 beyond 4 but less than 12 weeks, probably caused by variants of the original Wuhan virus and alpha variant, appears to be more acute, severe, general, and debilitating, and may require specialized convalescent care, while beyond 12 weeks appears to be more multi-organ and chronic, requiring long-term outpatient care.*

Keywords: Covid-19, Sars-Cov-2, Post-Covid-19 Condition, Convalescence, Rehabilitation, General Practice, Epidemiology

Introduction

Despite many efforts to learn from the coronavirus disease 2019 (covid-19) pandemic over the last 3 years, our knowledge remains fragmentary and incomplete about the causative agent, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and on its acute and post-acute clinical manifestations. In addition, it is now recognized that a dangerous new phase of the pandemic is opening that requires urgent attention [1].

Some people who have been infected with SARS-CoV-2 may have long-term effects from the infection, known as post-COVID-19 illnesses or persistent COVID-19 illnesses. These post-covid-19 conditions have taken various names, such as persistent covid-19, prolonged covid-19, long-lasting covid-19, post-acute covid-19, post-covid-19 syndrome, long covid-19, long-term effects of covid-19 or chronic covid-19. There is no consensus on the name or duration or symptoms of this Post-covid-19 condition [2,3].

It is recognized that Post-covid-19 condition represents many potentially overlapping entities, likely with different biological causes and different sets of risk factors and outcomes. The terms and definitions for these conditions have evolved since the start of the pandemic and will continue to evolve as more is learned about the symptoms and conditions associated with covid-19 [4].

Although it is accepted that Post-covid condition can represent a global health crisis, its clinical and epidemiological characterization is difficult [5]. Persistent Covid-19 is a complex and multifaceted condition that involves a variety of physical, cognitive, psychological, and social implications, and the evidence base is limited and fragmented [6].

One of the problems is that Post-covid-19 condition is the difficulty of measuring other indicators of covid-19 different from the usual of hospitalizations or deaths, and there is an absence of biomarkers, no imaging tests, and the pathophysiology of many Post-covid-19 symptoms remains unresolved [7-12]. Thus, the diagnostic criteria for Post-covid condition is controversial, although regarding Long covid-19 there are definitions from both the WHO and the National Institute for Health and Care Excellence, which provided a useful outline [13,14].

Yet another problem resides in the variety and heterogeneity of the methods used in clinical-epidemiological studies, including differences in the selection of patient populations and response rates, different follow-up periods, and inconsistent terms used to describe symptoms and conditions of adverse health. In addition, any symptom has often been included in interviews and questionnaires, regardless of whether it existed before covid-19 [7].

On the other hand, covid-19 is an opportunity to re-examine the importance of convalescence after acute illness. Doctors used to bet on the slow recovery period known as convalescence. Some experts say that re-adopting it could be beneficial for a number of long-term illnesses and injuries. When there was no cure, patients were left to live the natural history of the disease. Now, in the case of diseases that can be cured, there is no room for maneuver, it is presumed that if the patient is microbiologically cured, he does not deserve more rest, and it is accepted that perhaps the symptoms are imaginary or psychological [15].

In short, the chronology of convalescence from covid-19 is confusing. Consequently, there is a need to determine the long-term effects of covid-19, and especially in adult covid-19 survivors living in the community. In this context, we present a study to try to clarify the differences between Post-covid-19 conditions. Thus, clinical-epidemiological characteristics of patients with Long covid-19 (presence of prolonged symptoms for at least 12 weeks) are compared with Post-acute covid-19 syndrome (persistent symptoms beyond 4 weeks from the onset of symptoms), in the same population in general medicine.

Material and Methods

Design and emplacement

Comparison of secondary data among two previous studies:

1. An observational, longitudinal and prospective case series study of patients with Long covid-19 from March 15, 2020 to October 31, 2022 [16].

2. An observational, longitudinal and prospective study of patients with Post-acute covid-19 syndrome from March 15, 2020 to March 31, 2021 [17].

Both studies were carried out in the same population of patients treated in a general medicine office in the Health Center Santa Maria de Benquerencia, Toledo (Spain), which has a list of 2,000 patients> 14 years of age (in Spain, the general practitioners [GPs] care for people > 14 years of age, except for exceptions requested by the child's family and accepted by the GP).

Objective

1.To compare clinical-epidemiological characteristics of patients with Long covid-19 (presence of prolonged symptoms for at least 12 weeks, lasting at least 2 months, after acute covid-19 infection, and that are not explained by an alternative diagnosis) with post-acute covid-19 syndrome (persistent symptoms and / or delayed or long-term complications beyond 4 weeks from the onset of symptoms) in the same population in general medicine.

Criteria of Long-covid-19

The diagnostic criteria for Long covid-19 have already been published [16]. Basically Long-covid-19 was diagnosed by the presence of prolonged symptoms for at least 12 weeks, lasting at least 2 months, after acute covid-19 infection that are not explained by an alternative diagnosis [5, 13, 18, 19].

Criteria of Post-acute covid-19

The diagnostic criteria for Long covid-19 have already been published [17]. It was defined as a syndrome characterized by persistent symptoms and / or late or long-term complications beyond 4 weeks from the onset of symptoms [20].

Statistic analysis

The bivariate comparisons were performed using the Chi Square test (X2) with Yates correction or Fisher Exact Test when necessary, (according to the number the expected cell totals) for percentages.

Results

27 cases of Long covid-19 and 33 of Post-acute covid-19 syndrome were included. In Long covid-19 (from March 15, 2020 to October 31, 2022) vs. Post-acute covid-19 syndrome (from March 15, 2020 to March 31, 2021) there were fewer people with some type of labor specialization (15% vs. 51%; X2= 8.7919. p= .003026), fewer cases of Moderate-severe severity in primary infection (30% vs. 51% ; X2= 4.0516. p= .044129) and fewer General symptoms (14% [asthenia, arthralgia, malaise] vs. 36% [discomfort, asthenia, myalgia, fever, arthralgia]; X2= 10.2908. p= .001337). In Long covid-19, Respiratory (27%) and ENT (20%) symptoms predominated, while in Post-acute covid-19 syndrome they were General (36%) and Respiratory (32%). In Long covid-19 there were more symptoms ENT (29% vs. 14%), Neurological (18% vs. 7%), Psychiatric (9% vs. 5%), Circulatory (4% vs. 0%), Genitourinary (4% vs. 0%). In post-acute covid-19, General (36% vs. 14%), Respiratory (32% vs. 27%), Digestive (5% vs. 4%), and Skin (1% vs. 9%) symptoms predominated. There were no statistically significant differences by age, sex, or affectation in health workers, Ethnic minority, Complex family, or Chronic diseases (TABLE 1, TABLE 2, TABLE 3). Based on the dates of the included cases of Post-acute covid-19 syndrome, these were probably caused by variants of the original Wuhan virus and alpha variant.

Table 1: Comparison of Variables in Long and Post-Acute Covid-19

VARIABLES	LONG COVID-19 N=27	POST-ACUTE COVID-19 SYNDROME N=33	STATISTICAL SIGNIFICANCE
> = 65 years	7 (26)	7 (21)	X2= 0.1845. p= .667574. NS
< 45 years	11 (41)	8 (24)	X2= 1.868. p= .171707. NS
< 18 years	1 (4)	0	Fisher exact test= 0.45. NS
Women	13 (48)	19 (58)	X2= 0.5303. p= .466479. NS
Social-occupancy class of patients (people with some type of labor specialization)	4 (15)	17 (51)	X2= 8.7919. p= .003026. Significant at p < .05.
Health Care Workers	1 (4)	0	Fisher exact test= 0.45. NS
Ethnic minority	3 (11)	9 (27)	X2= 2.4242. p= .119471. NS
Complex family	1 (4)	0	Fisher exact test= 0.45. NS
Moderate-severe severity of primary infection	7 (30) [pneumonias]	17 (51)	X2= 4.0516. p= .044129. Significant at p < .05.
Hospitalization in acute phase	7 (30)	14 (42)	X2= 1.7767. p= .18255. NS
Readmission after hospital discharge	3 (11)	2 (6)	Fisher exact test = 0.6494. NS
Presence of Chronic diseases	15 (56)	18 (54)	X2= 0.0061. p= .937635. NS
( ): Denotes percentages; NS: Not significant			

Table 2: Ccomparison Of Chronic Diseases in Long and Post-Acute Covid-19

CRHONIC DISEASES ACCORDING TO WHO, ICD-10 GROUPS *	LONG COVID-19 N=27	POST-ACUTE COVID-19 SYNDROME N=33	STATISTICAL SIGNIFICANCE
-I Infectious	0	Fisher exact test= 1. NS	RR= NaN
-II Neoplasms	0	3 (4)	Fisher exact test = 0.2451. NS
-III Diseases of the blood	2 (3)	0	Fisher exact test = 0.2337. NS
-IV Endocrine	11 (17)	15 (21)	X2= 0.4982. p= .480306. NS
-V Mental	8 (12)	7 (10)	X2= 0.1558. p= .693085. NS
-VI-VIII Nervous and Senses	13 (20)	7 (10)	X2= 2.5466. p= .11053. NS
-IX Circulatory system	6 (9)	13 (19)	X2= 2.5404. p= .110965. NS
-X Respiratory system	2 (3)	3 (4)	Fisher exact test = 1. NS
-XI Digestive system	9 (13)	5 (7)	X2= 1.5511. p= .212967. NS
-XII Diseases of the skin	2 (3)	2 (3)	Fisher exact test = 1. NS
-XIII Musculo-skeletal	7 (11)	9 (13)	X2= 0.1658. p= .683845. NS
-XIV Genitourinary	6 (9)	6 (9)	X2= 0.0114. p= .914989. NS
TOTAL chronic diseases*	66 (100)	70 (100)	---
( ): Denotes percentages; NS: Not significant; NaN: Not a Number (result impossible to calculate); *Patients could have more than one chronic disease; the percentages are over the total of chronic disease			

Table 3: Comparison of Symptoms in Long and Post-Acute Covid-19

SYMPTOMS*	LONG COVID-19 N=27	SYMPTOMS IN POST-ACUTE COVID-19 N=33	STATISTICAL SIGNIFICANCE
General	6 (14) [asthenia, arthralgia, malaise]	21 (36) [malaise, asthenia, myalgia, fever, artralgias]	X2= 10.2908. p= .001337. Significant at p < .05.
Respiratory	12 (27) [cough, dyspnea, chest pain]	18 (32) [cough, dyspnea, chest pain]	X2= 0.6061. p= .436275. NS
ENT	9 (20) [rhinitis, chronic odynophagia, epistaxis, anosmia/ageusia]	8 (14) [anosmia / ageusia, odynophagia, rhinorrhea, pharyngeal dryness-mucus, epixtasis]	X2= 0.6044. p= .436903. NS
Digestive	2 (4) [fecal incontinence, anorexia]	3 (5) [anorexia, nausea / vomiting, diarrhea, abdominal pain]	Fisher exact test = 1. NS
Neurological	8 (18) [headache, dizziness, paresthesias in lower limbs]	4 (7) [headache, dizziness]	X2= 2.8451. p= .091652. NS
Psychiatric	4 (9) [anxiety/depression, insomnia]	3 (5) [anxiety, insomnia]	X2 with Yates correction = 0.1443. p= .704035. NS
Circulatory system	2 (4) [peripheral venous insufficiency, tachycardia on exertion]	0	Fisher exact test= 0.1837. NS
Genitourinary	2 (4) [dysuria]	0	Fisher exact test= 0.1837. NS
Skin	0	1 (1) [chilblains]	Fisher exact test = 1. NS
Total symptoms*	44 (100)	58 (100)	
( ): Denotes percentages; * Patients could have more than one symptom; the percentages are over the total of symptoms			

Discussion

Main findings

The main finding of our study is that the clinical-epidemiological characteristics of the convalescence of acute covid-19, in relation to the time elapsed since infection (Post-acute covid-19 or Long covid-19) are different. In Post-acute covid-19 (beyond 4 weeks), probably caused by variants of the original Wuhan virus and alpha variant, it occurred in patients with more severe acute covid-19, with more general symptoms (followed by Respiratory, Digestive, and Skin) and in people of higher socioeconomic status. In Long covid-19 (beyond 12 weeks) respiratory symptoms predominated (followed by ENT, Neurological, Psychiatric, Circulatory, and Genitourinary), acute infection was less severe, and the patients had a lower socioeconomic level.

Comparison with other studies

Classic ideas about recovery and convalescence could offer an important perspective for the covid-19 pandemic. All kinds of illnesses have lingering effects. Convalescence is an opportunity to advance in the understanding of long-term mechanisms in viral diseases. Postviral symptoms have been documented in diseases ranging from SARS to dengue, but remain understudied. Dengue patients are fatigued for several weeks after infection, and chikungunya patients may be in pain for months [15]. The chronology of convalescence from covid-19 is confusing. Acute Covid-19 is refers to symptoms that last up to 4 weeks after contracting the infection. Recovery from covid-19 can take 10-14 days or longer depending on your symptoms; but, most people's symptoms improve after two weeks [21].

Since the beginning of the pandemic, several variants of the virus have been identified: alpha, beta, gamma, delta, and omicron. These variants differ in transmissibility, disease course, and disease severity. In addition, they can affect to disease, susceptibility to treatments, and vaccine-mediated protection, and potentially affect long-term health outcomes after SARS-CoV-2 infection. The pattern that has emerged during the pandemic has been of spikes in covid-19 cases followed by declines, known as covid-19 waves. Different viral variants became dominant in each wave of covid-19. Although the first symptoms of covid-19 remain quite similar in the different variants, what has changed is the course of the disease. People infected with the omicron variant are less likely to require hospitalization than in previous waves of coronavirus [22].

Wild-type, alpha, and delta variants have been reported to result in similar long-term conditions [23]. However, the presence of 3 groups of symptoms according to variants have also been published; 1) a group of symptoms in the nervous system, such as fatigue, mental confusion and headaches, which was the most common subtype between the alpha variant, dominant in the winter of 2020-2021, and the delta variant, which was dominant in 2021; 2) a second group that had respiratory symptoms, such as chest pain and severe shortness of breath; It was the largest group of the original strain of coronavirus in the spring of 2020, when people were not vaccinated; 3) the third group included people who reported a wide range of physical symptoms, such as heart palpitations, muscle aches and pains, and skin and hair changes; this group had some of the most severe and debilitating multi-organ symptoms [24]. It has also been published that skin symptoms differ according to the covid-19 variant, being less frequent during the omicron wave than during the delta wave and ancestral strains [25]. In our study, the results can be considered along the same lines, but it must be taken into account that we are comparing cases of Post-acute covid-19 syndrome that occurred in 2020 [during 2020, variants of the original Wu-

han virus predominated in Spain], and the first three months of 2021 [in January 2021 alpha variant predominated] with cases of Long covid-19, which include the same period, but also last for the rest of the pandemic until October 31, 2022 [in Spain, from the summer-autumn of 2021 the delta variant was predominant, and from January 2022 to October 2022, the omicron variant predominated] [26-33].

Persistent symptoms during the convalescent period appear to be more likely after severe illness [3, 34-37]. Post-acute covid-19 syndrome has been published affects women more [37-39]. Other researchers have stated that sex had a lesser effect [23]. On the other hand, in a survey on Long covid-19, about a third of those surveyed were between 40 and 49 years old, and just over a quarter between 30 and 39 and between 50 and 59 years old [40]. Chinese researchers analyzed health data of more than 1,700 patients discharged from a hospital in Wuhan as cured between January 7 and May 29, 2020, found that they were 57 years old on average [41]. In another study patients with symptoms 60 days after the acute phase had a mean age of 56 years (range, 19-84 years) [42]. In our study, no statistically significant differences were found either by sex or by age.

Reports have shown that vaccination prior to SARS-CoV-2 infection partially reduced the risk of prolonged covid-19 [3, 23, 24]. In our study it is not possible to draw clear conclusions about the effects of vaccination, given the different time periods compared, and the fact that vaccination started from 2021.

Limitations and strengths of the study

1. The use of databases collected for specific purposes in the primary analysis, other than the secondary analysis, limits the analysis and interpretation of results.
2. The longitudinal studies that are compared have the strength of the continuous care of the GP. In addition, the population was the same in both studies, which minimizes demographic and socioeconomic biases. Furthermore, the investigator and GP were the same in both studies, which could allow the findings to be generalizable to similar populations.
3. The number of cases was small, which may hide differences between the groups.

Conclusions

Convalescence from covid-19 beyond 4 weeks, in relation to beyond 12 weeks, is more non-specific with respiratory symptoms, but general and debilitating symptoms predominate, in patients with more severe acute infection and higher educational level. In convalesce beyond 12 weeks, respiratory symptoms and symptoms of different organs and systems (ENT, Neurological, Psychiatric, Circulatory, and Genitourinary) were predominated. In summary, convalescence from covid-19 beyond 4 but less than 12 weeks, probably caused by variants of the original Wuhan virus and alpha variant, appears to be more acute, severe, and debilitating, while beyond 12 weeks, caused by variants of the original Wuhan virus, alpha, beta, gamma, delta, or omicron, appears to be more multi-organ and chronic. This may have implications for the GP, since convalescence care between 4-12 weeks may require medicalized rehabilitation, even hospitalization, or specialized convalescent care, while convalescence beyond 12 weeks may require chronic outpatient care where the patient is never given discharge, no matter how long is this period. But, a long recovery does not have to mean failure; It can be a slow process, but beneficial.

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