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COVID-19

Prevalence, characteristics and risk factors in a Moroccan cohort of Long-Covid-19

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Abstract

Introduction Covid-19 can involve persistence of nonspecific symptoms and sequelae that last weeks to months after initial recovery, but the definition of this situation is lacking. Thus, the aim of our study is to estimate the prevalence, symptoms, and signs extending beyond the acute phase of Covid-19 compared to the general population not infected with the virus and to assess the factors influencing the occurrence of these symptoms in developing countries like Morocco.

Patients and methods This study recruited 118 healthcare workers who endured the Covid-19 infection and 118 matched controls that had never experienced it. We have defined Long-Covid-19 according to guidance for NICE, and we used a survey made of direct questions and short answers sent to the recruiters via mail to evaluate the demographic parameters, severity and duration of the Covid-19 symptoms, vaccination against SARS CoV-2, and pulmonary involvement, and a series of general symptoms were looked for.

Findings Our study found that the prevalence of Long-Covid-19 was 47.4%. Compared to the general population, the symptoms with statistical significative results were predominated by asthenia, myalgia, and brain fog. The severity of the pulmonary involvement on chest CT scan was the only risk factor to their occurrence, whereas no effect of the vaccination anti-SARS-CoV-2 was found.

Conclusion Comparing to the literature, this study showed that nearly half of the patients who have been infected with SARS-CoV-2 will experience a variety of symptoms after the acute phase of this infection, and that it would be a real burden even in the youngest. We also found that vaccination against SARS-Cov-2 has no impact on this prevalence, which is to the best of our knowledge has never been previously studied.

Keywords Long terms · Covid-19 · Vaccination · Comparative study

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was detected in China in December 2019. To date, more than 328 million people worldwide have been infected, and over 5.54 million people have died from the coronavirus disease 2019 [1]. Covid-19 can involve persistence symptoms and sequelae that last weeks to months after initial recovery, but the definition of this situation has been confusing and not standardized. Since first reported, there has been a vast amount of social media patient groups, polls, comments, and scientific articles aiming to describe the chronicity of Covid-19 [2]. The pathophysiology is poorly understood, and some hypotheses are suggested to explain the persistence of these manifestations (e.g., long-term tissue damage and pathological inflammation related to viral

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persistence and immune dysregulation) [3]. Guidance for NICE (National Institute for Health and Care Excellence) describes "Long-Covid-19" as symptoms that continue or develop after acute Covid-19 including both "ongoing symptomatic Covid-19" that arises from 4 to 12 weeks and "post-Covid-19 syndrome" continuing for more than 12 weeks after an infection and cannot be explained by another cause [4]. The prevalence of infected patients with SARS-CoV-2 that developed one or more long-term symptoms was estimated at 80%, but this prevalence is very variable in the studies mainly for lack of precise definition [5]. Moreover, the reported manifestations of "Long-Covid-19" remain mostly nonspecific and can be found in the general population not infected with SARS-CoV-2.

Here, we perform a comparative study to estimate the prevalence, symptoms, and signs extending beyond the acute phase of Covid-19 compared to the general population not infected with the virus and to assess the factors influencing the occurrence of these symptoms. Such data from developing countries like Morocco are scarce.

Methods

The following transversal case–control study recruited 236 healthcare staff working in Ibn Rochd University Hospital (Casablanca, Morocco) during the period from February 2021 to April 2021. Our population included doctors and other healthcare workers (nurses, medical assistants, technicians, physiotherapists, and psychologists), of which 118 endured the Covid-19 infection confirmed by a positive nasopharyngeal PCR test (group A) and 118 manually matched controls that had never experienced symptoms of Covid-19 (group B). We have defined "Long-Covid-19" as symptoms that continue or develop after acute Covid-19, including both "ongoing symptomatic Covid-19" that arises from 4 to 12 weeks and "post-Covid-19 syndrome" continuing for more than 12 weeks. We have excluded patients who were hospitalized in the intensive care units to avoid including patients who have severe Covid-19 complications. We used a survey made of direct questions and short answers sent to the recruiters via e-mail. The different sections of the survey were the following: demography, comorbidities, severity and duration of the Covid-19 symptoms, and vaccination against SARS CoV-2. At the time of study, 53.4% had received the vaccine in group A (all of them after contracting the Covid-19 infection), and 49.2% was vaccinated in group B. The pulmonary involvement was studied in 30 patients who had realized a chest CT scan mainly for a reason of dyspnea and was stratified in 3 groups according to the percentage of lung damage in CT scan (< 5%, 5–20%, > 20%). In both groups, all of the following symptoms were looked for: fatigue, anorexia, hypo/anosmia, dysgeusia, tinnitus, dyspnea, cough, chest pain, palpitations, fever, chills, myalgia, arthralgia, abdominal pain, nausea, diarrhea, itching, headache, dizziness, sensitive disorders, sleep disorders, anxiety, and "brain fog," characterized by forgetfulness and the lack of focus and mental clarity. For the statistical analysis, we used SPSS (20.1), and the statistical threshold was fixed at $p < 0.05$. Informed consent was obtained from all the population study to complete the questionnaire and use the data for this study.

Results

One-hundred and eighteen cases (group A) and 118 manually matched controls (group B) were included in this study. Clinical symptoms of the acute phase of Covid-19 infection in the group A were dominated by myalgia (73%), anosmia/hyposmia (69.4%), and headache (56.8%). One patient was asymptomatic and had a positive PCR Covid-19 test as part of the screening of contact cases (Table 1).

In this study, the prevalence of Long-Covid-19 was 47.4% because at least one symptom was observed in 56 of the 118 patients after the acute phase of the Covid-19 infection. Compared to the controls (group B), population previously infected with SARS-CoV-2 (group A) had a statistically significant higher prevalence of asthenia (25.3%), "brain fog" (14.4%), myalgia (13.3%), headache (12%), sleep disorders (12%), and anosmia/hyposmia (9.6%) (Table 2). The asymptomatic case had developed

Table 1 Demographic and clinical characteristics of the 118 cases infected with SARS-CoV-2

	Group A ($n = 118$) Effective (percentage)
Gender	
Male	34 (29%)
Female	84 (71%)
Average age-median (years)	29 (21–54)
Profession	
Doctors	92 (78%)
Other health workers	26 (22%)
Clinical symptoms in the acute phase	
Anosmia/hyposmia	81 (69.4%)
Dysgueusia	60 (51.4%)
Arthralgia	47 (40.5%)
Myalgia	85 (73%)
Digestive signs	43 (36.9%)
Dyspnea	26 (22.5%)
Cough	46 (39.6%)
Dizziness	24 (20.7%)
Headache	66 (56.8%)

Table 2 Long-term effects in group A (Covid-19 +) compared to group B (Covid-19 −)

	Group A (Covid-19 +) ($n = 118$) (percentage%)	Group B (Covid-19 −) ($n = 118$) (percentage%)	p-value
Gender			
Male	34 (29%)	34 (29%)	
Female	84 (71%)	84 (71%)	
Average age-median (years)	29 (21–54	29 (21–54)	
Vaccination status			
Not vaccinated	55 (46.6%)	60 (50.8%)	
Vaccinated	63 (53.4%)	58 (49.2%)	0.93
Sinopharm	44 (37.8%)	35 (29.76%)	
Astrazeneca	19 (16.2%)	23 (19.84%)	
At least one symptom	**56 (47.4%)**	**14 (11.8%)**	**0.0001**
Asthenia	25.3%	11.8%	**0.0001**
Anorexia	0	2.9%	0.31
Anosmia/hyposmia	9.6%	0	**0.0001**
Dysgeusia	6%	0.85%	**0.003**
Tinnitus	7.2%	0.85%	**0.005**
Dyspnea	3.6%	1%	0.19
Cough	4.8%	2%	0.08
Chest pain	8.4%	1%	**0.0001**
Palpitations	10.8%	2.9%	**0.008**
Fever	0	1%	0.45
Chills	0	0	
Myalgia	13.3%	3.4%	**0.014**
Arthralgia	9.6%	2.5%	0.3
Abdominal pain	4.8%	0.85%	**0.0001**
Nausea	0	0.85%	0.02
Diarrhea	6%	1%	0.085
Itching	1.2%	0.85%	0.3
Headache	12%	4.4%	**0.014**
Dizziness	8.4%	2%	0.3
Sensitive disorders	1.2%	0	**0.0001**
Sleep disorders	12%	9.3%	**0.022**
Anxiety	21.7%	9.3%	0.3
Attention disorders, memory impairment "brain fog"	14.4%	4.9%	**0.001**

symptoms of Long-Covid-19 (asthenia, myalgia, and anorexia) 4 weeks after the positivity of the PCR Covid-19 test with a negative nasopharyngeal PCR test at the time of these symptoms.

Among the population of "Long-Covid-19" ($n = 56$), 71.5% were women, and the average age was 29 years. At the time of this study, the sample population with an ongoing Covid-19 and post-Covid-19 was respectively 16 (28%) and 40 patients (72%). Among the four factors studied (age, gender, anti-Covid-19 vaccination, and the severity of the pulmonary involvement in chest CT scan), only this latter was statistically associated with the occurrence of "Long-Covid-19" symptoms (Table 3).

Discussion

At the beginning of the Covid-19 pandemic in December 2019, hardly anyone would have thought that the disease might be chronic. However, that soon changed, and the term "Long-Covid-19" started gaining traction among social media patient groups, comments, and started gaining recognition in the scientific and medical communities [2]. While the actual definition is lacking, a review identified that the most frequent symptoms of "Long-Covid-19" are fatigue and dyspnea [6, 7]. Other less typical symptoms include cognitive and mental disorders, headache,

Table 3 Factors influencing "Long-term-Covid-19" symptoms in group A ($n=118$)

	Group A ($n=118$) (Covid-19+)		
	Long-term Covid-19 ($n=56$)	Acute Covid-19 ($n=62$)	p-value
Gender	Male 16 (28.5%) Female 40 (71.5%)	Male 18 (29%) Female 44 (71%)	0.85
Age (years)	< 35 47 (84%) > 35 9 (16%)	< 35 17 (27%) > 35 45 (73%)	0.07
Pulmonary involvement in chest CT scan	< 5% 11 (20%) > 5–20% 5 (9.1%) 20% 3 (5.4%)	< 5% 6 (9.6%) > 5–20% 4 (6.4%) 20% 1 (1.6%)	**0.001**
Vaccination status after the Covid-19 infection	• Not vaccinated 25 (44.6%) • Vaccinated 31 (55.4%) • Astrazeneca 7 (12.8%) • Sinopharm 24 (43.6%)	• Not vaccinated 30 (48.4%) • Vaccinated 32 (51.6%) • Astrazeneca 12 (19.3%) • Sinopharm 20 (32.3%)	0.93

myalgia, chest and joint pains, smell and taste dysfunctions, cough, hair loss, insomnia, wheezing, rhinorrhea, sputum, cardiac, and gastrointestinal issues [3]. It is important to point out that all these symptoms are nonspecific and frequently found in the general population, making crucial the need of comparative studies like ours, in order to correctly estimate their reality and the associated burden after the acute phase of the Covid-19 infection.

According to the literature, it seems illusive to define the p revalence of "Long-Covid-19" mainly for lack of precise definition [3, 8–10]. Also, most studies were performed in developed countries, but we did not find sufficient data from developing countries. Our study found that the prevalence of "Long-Covid-19" was 47.4%, and the symptoms with statistical significative results compared to the general population were asthenia, myalgia, "brain fog," headache, and sleep disorders. These findings are generally consistent with the literature (Table 4). An interesting fact has been reported that even initially asymptomatic patients may experience the "Long-Covid-19" symptoms, and our case illustrates such a situation. Indeed, this case tested positive for SARS-Cov-2 as part of the screening of contact cases, developed 4 weeks later a myriad of symptoms like myalgia, asthenia, and anorexia. In the study of Huang et al., 32% of the Long-Covid-19 patients were asymptomatic at the time of the PCR positivity of SARS-Cov-2 [21].

There are some risk factors influencing the occurrence of "Long-Covid-19" that were studied in the literature. Symptoms were reported to be more frequent in the elderly population [22, 23] which was not the case in our study,

Table 4 Symptoms prevalence of Long-Covid-19 population ($n=56$) in our study compared to the literature

Long-term-Covid-19 symptoms	Prevalence in our population (%)	Prevalence in the literature (%)
At least one symptom	47.4	74 [11]–87.4 [12] 38.7[13]–41 [14]
Myalgia	13.3	22 [11]–5.9 [15] 8.5 [13]–86.7 [16]
Asthenia	25.3	39 [11]–53.1 [12] 80 [17]
Sleep disorders	12	24 [11]–40 [17] 30.8 [18] 22 [14]
Headaches	12	< 5 [11]–53.6 [17] 6[13]
Anosmia/hyposmia	9.6	11 [11]–< 5 [15] 13.3 [18]
Dysgeusia	6	< 5 [11]–10.8 [18] 7 [19]
Chest pain	8.4	< 5 [15]–10.8 [18] 21.7 [12]
Palpitations	10.8	11 [19]–62 [20]
Attention disorders and memory impairments, brain fog	14.4	58.4 [17]–62 [20]

probably because of the inclusion of patients still in professional activity and, therefore, obviously younger. Also, we did not find that the gender would be associated with the occurrence of these symptoms [22, 23]. The severity of the pulmonary involvement in chest CT scan was a risk factor of developing "Long-Covid-19" symptoms in our population (p: 0.001), and the same findings were also reported [22–24]. To our knowledge, no study has ever discussed whether vaccination against SARS-CoV-2 plays a role in the occurrence of "Long-Covid-19." Since SARS-CoV-2 vaccination was associated with some side effects like myalgia, asthenia, headache, nausea, and fever[25], we tried to assess this link, and we found that it was not associated with this risk (p: 0.93), although more research is required to better assess this parameter.

While this study provides insights into the clinical presentation as well as the influencing risk factors of "Long-Covid-19" in a developing country like Morocco, it has some limits as the population studied was exclusively healthcare workers, and that the control group did not have a negative nasopharyngeal PCR Covid-19 test to eliminate asymptomatic cases, but we suppose that this would not have a major impact on the final results. More informations on prospective comparative studies are needed to better assess the natural course of the "post-acute phase" of the Covid-19 infection.

Conclusion

Our findings strengthen that nearly half of the patients who have been infected with SARS-CoV-2 will experience a variety of symptoms after the acute phase of this infection, and that it would be a real burden even in the youngest. We also highlight the fact that pulmonary involvement on chest CT scan is a risk factor to their occurrence, whereas no impact of the vaccination anti-SARS-CoV-2 was found.

Author contribution HEO researched literature and conceived the study. HEO, MB, and SN were involved in protocol development, patient recruitment, and data analysis. HEO and MB wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Declarations

Ethical approval All recorded data was confidential and was not used outside this study.

Consent to participate Informed consent was obtained from the population study to complete the questionnaire and use the data for this study.

Conflict of Interest The authors declare no competing interests.

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