

RESIDUAL SYMPTOMS AFTER SARS-COV2 INFECTION AMONG HEALTHCARE WORKERS: PREVALENCE AND ASSOCIATED FACTORS

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ABSTRACT

Health-care workers are on the front line of the COVID-19 pandemic. In this occupational group, infection is of great concern due to the risk of nosocomial spread of the disease and significant reduction in the number of employees, it also endangers patient safety and compromises the capacities of health care workers. This is a cross-sectional study conducted among healthcare workers of university hospital of Farhat Hached Sousse who were affected by COVID-19 during September 1, 2020 to February 28, 2021. Data collection was carried out using an anonymous questionnaire about socio-professional and medical characteristics. Severity level of the SARS-CoV-2 infection was assessed according to the criteria of the National Authority for Health Assessment and Accreditation guideline (INEAS). Of the 555 healthcare workers with COVID-19, 477 participated. The factors associated with residual symptoms of COVID-19 were: age ($p=0.002$), female gender ($p=0.001$), marital status ($p=0.015$), cardiovascular ($p=0.001$), endocrine ($p=0.002$) comorbidities, obesity ($p=0.004$), work position ($p=10^{-3}$), professional work seniority ($p=0.022$), duration of confinement ($p=10^{-3}$) and hospitalization ($p=0.037$). The use of antibiotics ($p=10^{-3}$), anticoagulants ($p=0.010$) and corticosteroids ($p=0.004$) were significantly associated with the persistence of symptoms. After binary logistic regression, the factors associated with persistent symptoms were female gender, para-medical category, antibiotic and corticosteroid use. Long-term follow-up of HCWs with COVID-19 is recommended to understand and treat persistent symptoms after recovery. Protective equipment should be provided as well as vaccination for prevention and management.

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1. Introduction

In December 2019, a series of pneumonia cases of unknown cause emerged in Wuhan, China, with clinical presentations resembling viral pneumonia [1]. Its clinical manifestations range from asymptomatic or mild symptomatic infections to severe respiratory symptoms and death [2, 3].

Since its identification, SARS-CoV-2 has spread rapidly around the world. As of June 22, 2020, 177 countries have reported cases of COVID-19, representing more than 8-9 million reported cases and 468,000 deaths worldwide [4].

Health-care workers are on the front line of the pandemic and are at increased risk of infection with SARS-CoV-2 and could potentially play a role in hospital transmission.

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As of March 8, 2021, more than 420,170 healthcare workers in the United States have been infected with SARS CoV-2 and 1,388 have died [5]. The National Health Commission of the People's Republic of China reported that as of February 24, 2020, a total of 3387 of 77 262 Covid-19 patients (4.4%) in China were healthcare workers or others working in medical facilities [6].

Communicable infectious diseases are not only occupational hazards for health care professionals, but also endanger patient safety and compromise the capabilities of health care workers. A WHO report published in 2020 highlighted the rights of healthcare professionals in addition to their roles and responsibilities [7]. Since the end of the first wave of COVID-19, many scientific works have reported that some continue to experience symptoms despite recovery [8,9]. Surveys of thousands of people have revealed more than 205 symptoms may persist such as fatigue, cough, shortness of breath, headache and muscle pain [10].

It is within this framework that we were interested in studying the particularities of this infection in the PS of the CHU Farhat Hached Sousse in order to:

- Describe the characteristics of the SARS-Cov 2 infection in the affected PS
- Identify the factors associated with residual symptoms

2. Material and methods

Study design and population

Our survey is a descriptive, cross-sectional and epidemiological study conducted among 555 HCWs affected by COVID-19 and who were followed up at the Occupational Medicine Department of the Farhat Hached University Hospital of Sousse during a 6-month period, between September 1, 2020 and February 28, 2021. Active health personnel including administrative agents, maintenance technicians, ambulance drivers, workers, medical and paramedical personnel were included in our study. Also the HCWs affected by COVID-19 during this period and confirmed by a biological test (RT-PCR or rapid antigenic test or COVID-19 serology) or imaging (thoracic scanner), the symptomatic personnel or during a contact tracing. HCWs who refused to participate, unavailable by phone and who did not answer the forms sent by Google Forms were not included in our study.

Data collection

Data were collected using a questionnaire at a distance from the infection and after returning to work. The questionnaire covered: socio-demographic and professional data, co-morbidities as well as lifestyle habits, personal pathological history, body mass index (BMI), lifestyle habits (smoking), clinical characteristics of the infection and therapy methods and the evolution. According to the National Institute for Health Assessment and Accreditation (INEAS), COVID-19 is an infectious disease that is limited in 7 to 14 days in most cases. However, in some patients, symptoms persists longer [11]. Figure n°1 shows the temporal distribution of the different types of residual symptoms of COVID-19 according to INEAS. In our study, symptoms that persisted for more than 14 days were considered residual symptoms.

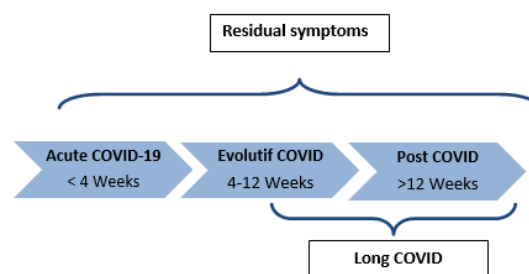


Figure 1. Temporal distribution of different types of residual symptoms of Long COVID

Statistical analysis

Data entry and analysis were performed by SPSS.22.0 software. Quantitative variables were expressed by their means and standard deviation and/or by the median. Qualitative variables were presented by the number and percentages. The analytical study was carried out by the chi-square test for qualitative variables; and by the Student's T test and/or Mann Whithney U test for quantitative variables. The significance level was set at 5%. Multivariate analysis was performed using binary logistic regressions.

Conflicts of interest

Our study was carried out with the informed consent of the participants and the respect of the anonymity and confidentiality. This survey was approved by the ethics committee of the Faculty of Medicine of Sousse (Tunisia) and there is no conflict of interest.

3. Results

Among the 555 HCWs with COVID-19 followed up at the Occupational Medicine Department between September 1, 2020 and February 28, 2021, 477 participated in the study, (85.9% response rate). The majority of confirmed COVID-19 cases in HCWs were observed during October 2020 and January 2021 with 126 cases (26.4%) and 150 cases (31.4%) respectively. Our study population was predominantly female (78.2%) with a sex ratio of 0.3. The median age was 38 years [24 to 61 years]. Nurses (32.1%) followed by physicians (28.1%) were the most affected by COVID-19 (Table 1).

Among the participants, 196 HCWs (41.1%) had at least one comorbidity. The most common medical history was hypertension (11.3%), allergic rhinitis (8.4%) and diabetes (6.9%). Obesity was found in 25.4% of respondents. The majority of HCWs were non-smokers (91.8%). Cigarette smoking was predominant (94.9%) with an average number of 14 pack-years. According to more than half of the HCWs, the most likely source of contamination was the work environment (54.9%) either through contact with a contaminated colleague (31.2%) or with a hospitalized patient (23.7%).

	Number	Percentage (%)
Job Position:		
Nurse	153	32.1
Physician	134	28.1
Technician	95	19.9
Laborer	34	7.1
Administration officer	28	5.9
Midwife	16	3.4
Maintenance	7	1.5
Ambulance men	4	0.8
Cook	3	0.6
Security	2	0.4
Pharmacist	1	0.2
Work schedule	255	53.4
Fixed day time Alternating	194	40.7
Fixed night shift	28	5.9
Hospital Department		
Medical department	129	27.04
Mother and child services	129	27.04
Emergency and resuscitation	49	10.27
Surgical department	44	9.22
Administration	24	5.03
Pharmacy	20	4.19
Others	82	17.19
Assignment to department managing COVID-19 patients		
No	245	51.4
Yes	232	48.6

Table 1. Occupational characteristics of health personnel in our study (n=477).

Contamination by the family environment was estimated at (15.3%). The source of contamination was not identified in 29.8% of cases. The delay between the onset of symptoms and the RT-PCR was 2.78 ± 2 days [1-19 days]. The HCWs were symptomatic in 96.6% of the cases while 3.4% were asymptomatic. The most frequent clinical signs were asthenia (88.7%), aches and pains (79.7%) and anosmia (62.7%). The different clinical signs are shown in Table 2.

	Number	Percentage (%)
Asthenia	423	88.7
Muscle soreness	380	79.7
Anosmia	299	62.7
Agueusia	278	58.3
Headache	278	58.3
Dry cough	233	48.8
Gastrointestinal disorders	202	42.3
Fever	128	26.8
Chills	121	25.4
Dyspnea	82	17.2
Odynophagia	59	12.4
Chest pain	51	10.7
Vertigo	16	3.4
Asymptomatic	16	3.4
Wet cough	13	2.7
Skin Rash	1	0.2

Table 2. Clinical signs of COVID-19 in healthcare workers in our study (n=477).

Paracetamol was the main treatment (67.7%) followed by antibiotics (12.6%) and vitamin therapy (8.1%). A combination of these three therapeutic was used in 11.1% of cases. Only 0.5% of the patients had recourse to oral corticosteroid therapy. In our study, 471 patients (98.7%) were initially managed at home and 6 (1.3%) were hospitalized in a medical ward. The treatment taken by the HCWs was dominated by paracetamol (91.7%), vitamin C (78.5%), azithromycin antibiotic (68.8%), zinc (65.8%) and vitamin D (63.9%). Only 6 participants required supplemental oxygen therapy. One antibiotic was used in 317 patients while dual therapy was used in 12 patients. During the period of home confinement, 73 HCWs (15.5%) required further care: 44 (60.3%) consulted the emergency room and 29 (39.7%) consulted a private physician. Dyspnea, chest pain and digestive disorders were the most frequent reasons for consultation. Ten HCWs required subsequent hospitalization, nine were managed in a medical ward and only one was hospitalized directly in an intensive care unit. The time from beginning of symptoms to hospitalization was 4.4 ± 3.8 days [1 and 15 days]. The duration of hospitalization ranged from 1 to 15 days, with an average of 6.3 ± 4.3 days. The clinical course was characterized by improvement in all patients. Only one patient was transferred to the intensive care unit with ($\text{SaO}_2=70\%$). The treatment of the two patients hospitalized in the intensive care unit was based on 3rd generation cephalosporins (C3G); anticoagulant with low molecular weight heparin (LMWH) and corticosteroid therapy. Both benefited from non-invasive ventilation (NIV). The average length of intensive care unit stay was 6.5 days. The clinical course was favorable in all our patients.

Residual symptoms in healthcare workers

During the return-to-work visit, 299 HCWs (62.7%) described persistent symptoms, predominated by fatigue (31.8%) and Dyspnea (29.4%) (Table 3). In this context, additional examinations were performed to eliminate complications of the acute phase or decompensation of underlying comorbidities (diabetes, hypertension, asthma, etc.) of COVID-19.

Two cases of pericarditis and one case of pulmonary embolism were diagnosed and referred to the emergency department. The majority of health workers (97.3%) had these symptoms for more than 4 weeks. (Figure 2)

	Number	Percentage (%)
Fatigue	95	31.8
Dyspnea	88	29.4
Memory impairment	29	9.7
Anosmia agueusia	26	8.7
Cough	26	8.7
Headache	24	8.1
Diarrhea	10	3.3
Earache	1	0.3

Table 3. Occupational characteristics of health personnel in our study (n=477).

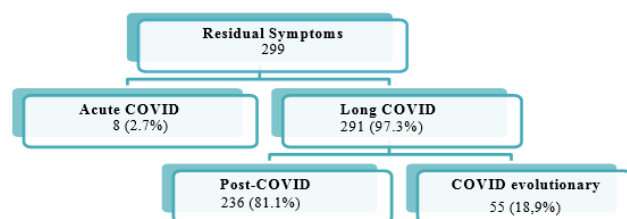


Figure 3. Residual symptoms in health workers in our study.

Factors associated with the development of residual symptoms

In our study, the factors associated with the presence of residual symptoms of COVID-19 were: age ($p=0.002$), female gender ($p=0.001$), marital status ($p=0.015$), cardiovascular ($p=0.001$) and endocrine ($p=0.002$) comorbidities, obesity ($p=0.004$), work position ($p=10^{-3}$), professional work seniority ($p=0.022$), duration of confinement ($p=10^{-3}$) and hospitalization ($p=0.037$). Regarding the effect of medication on these symptoms, the results showed that the use of antibiotics ($p=10^{-3}$), anticoagulants ($p=0.010$) and corticosteroids ($p=0.004$) were significantly associated with the persistence of these symptoms (Table 4).

Variables	Residual symptoms		P
	Yes n (%)	No n (%)	
Socio-demographic Characteristics			
Age (Median \pm IQR)	38 years ; EIQ [34 , 50]	36 years ; EIQ [28 , 35]	0.002
Gender			
Female	248(66.5)	125(33.5)	0.001
Male	51(49.0)	53(51.0)	
Marital Status			
Married	223(66.2)	114(33.8)	0.015
Not married	76(54.3)	64(45.7)	
Professional Characteristics			
Position			
Medical	59(43.7)	76(56.3)	10 ⁻³
Paramedical	188(70.9)	77(29.1)	
Others	52(67.5)	25(32.5)	
Seniority (Median \pm IIQ)	9 years ; IIQ [4 , 15]	6 years ; IIQ [2 , 12, 2]	0.022
Work Covid			
Yes	141(60.8)	91(39.2)	0.402
No	158(64.5)	87(35.5)	
Medical and lifestyle Characteristics			
Cardio-vascular history			
Yes	47(82.5)	10(17.5)	0.001
No	252(60)	168(40)	
Respiratory History			
Yes	28(57.1)	21(42.9)	0.397
No	271(63.3)	157(36.7)	
Endocrine History			
Yes	52(80.0)	13(20.0)	0.002
No	247(60.0)	165(40)	
Obesity (BMI\geq30)			
Yes	89(73.6)	32(26.4)	0.004
No	210(59.0)	146(41.0)	
Smoking			
Smoker	12(48.0)	13(52.0)	0.119
Non-smoker	287(63.5)	165(36.5)	
Characteristics of the infectious episode			
Hospitalization			
Yes	14(87.5)	2(12.5)	0.037
No	285(61.8)	176(38.2)	
Length of hospitalization (Avg \pm SD)	6.6 \pm 4.4 days	4.5 \pm 4.9	0.550
Length of confinement (Avg \pm SD)	15.6 \pm 6.8 days	13.4 \pm 5 days	10 ⁻³
Medication			
Antibiotics			
Yes	245(73.1)	90(26.9)	10 ⁻³
No	54(38.0)	88(62.0)	
Corticosteroid therapy			
Yes	21(91.3)	2(8.7)	0.004
No	278(61.2)	176(38.8)	
Anticoagulation			
Yes	60(84.5)	11(15.5)	10 ⁻³
No	239(58.9)	167(41.1)	

Table 4. Results of univariate analysis of factors associated with the development of residual symptoms

The dose, the type and the duration of treatments varies according to the severity of the symptoms, comorbidity, age and drug allergy. The antibiotics used in our study were azithromycin 500mg/day during 3 to 5 days, amoxicillin or Amoxicillin and Clavulanic acid 1g, 3 per day, levofloxacin 500 to 1000 mg/day during one week.

Inhaled corticosteroid can be used (Pulmicort 0.25 to 4 mg per day or Cortis 250 μ g 3-4 times a day).

Systemic corticosteroids can be administered orally or intravenously (A daily dose of 6 mg of dexamethasone equivalent to 160 mg of hydrocortisone, 40 mg of prednisone or 32 mg of methylprednisolone were used in our patients during an average of 7 to 10 days).

After binary logistic regression, the factors associated with persistent symptoms were female gender and para-medical category, antibiotic and corticosteroid use (Table 5).

	OR	Confidence Interval 95%		p
		Lower	Upper	
Female Gender	2.08	1.27	3.40	0.003
Paramedical category	2.92	1.61	5.30	10 ⁻³
Corticosteroid	6.81	1.41	32.85	0.017
Antibiotic Therapy	3.65	2.34	5.68	10 ⁻³

Table 5. Results of multivariate analysis of factors associated with residual symptoms.

4. Discussion

The pandemic caused by COVID-19 has challenged health systems worldwide. Health workers have been particularly affected by this crisis. They have had to deal not only with a lack of personal protective equipment, but also with a shortage of personnel, which has had an impact on their well-being and on patient safety and satisfaction. Thus, special attention to their management is paramount to ensure an early return to work with the least number of complications [12]. In the present study, women were the most represented among the affected HCWs (78.2%). This was demonstrated by many scientific works [13,14]. These findings could be explained by the feminization of the health sector according to several studies [15,16]. However, the male gender is not spared in other studies in the literature [17,18]. It was also found that the median age of our population was 38 years with extremes from 24 to 61 years. These results were consistent with data from the national and international literature on HCWs with COVID-19 [19,20]. Clinically, the majority of the HCWs were symptomatic (96.6%), the most frequent clinical signs were of an influenza-like syndrome: asthenia (88.7%), aches and pains (79.7%), headache (58.3%), dry cough (48.8%), fever (26.8%). These results were in agreement with the meta-analysis of Do Nascimento et al [21] and the Tunisian study of Louhaichi S et al (70% of the HCWs were symptomatic) [22]. COVID-19 is causing several symptoms, the main ones dominated by fever (83-99%), cough (59-82%), fatigue (44- 70%). Non-specific symptoms (sore throat, nasal congestion, headache, diarrhea, nausea and vomiting) have also been reported. Anosmia or ageusia, preceding the respiratory symptoms, has also been described [23]. A total of 16 HCWs were hospitalized. All patients had a good outcome. According to a North American study, HCWs status was associated with a shorter duration of hospitalization and a lower probability of admission to intensive care unit compared to the general population [24], due to the young age of the population and low level of comorbidities. After the confinement, the HCWs had a medical visit to the occupational medicine department during which the occupational physician assessed the patient's ability to resume his professional activity or the need to prescribe explorations and to extend the rest period if necessary. The majority of the patients (62.7%) retained symptoms, which is in line with the data in the literature [25, 26]. General fatigue was the most frequent symptom in our study (31.8%) and in most studies [27, 28].

The authors believe that this could be due to neuroinflammation of the brain caused by the virus [29,30]. On the other hand, dyspnea (29.4%) was the most frequent residual symptoms, which is consistent with the literature [8, 31]. Studies have mentioned that some patients may have a restrictive defect and a minor respiratory disorder, which may persist [32]. Memory impairment was also mentioned by our HCWs (9.7%). The results of a large study including 84 285 participants cured of COVID-19, suggested a higher incidence of cognitive dysfunction compared to controls [33]. It has been suggested that the virus may enter the brain and cerebrospinal fluid [34]. However, data on the long-term effects and consequences on individuals' cognitive functions are still limited [33]. In addition, of the participants who kept residual symptoms, 97.3% retained these symptoms for more than 4 weeks (COVID-long), including 81.1% for more than 12 weeks (post-COVID) [11]. However, it has been reported in some studies that some patients retain symptoms for weeks or months after infection [35,36]. A systematic review including 25 observational studies reported a rate of long COVID of up to 80% [37]. There is no clear explanation for this phenomenon; some suggest that fragments of the virus may persist for months in the body [38]. In addition, chest pain, fatigue, shortness of breath and cough were the most frequently reported clinical manifestations attributed to the disease. Factors most frequently associated with persistent symptoms were age, female gender, comorbidities, hospitalization, and severe clinical status and acute oxygen use [37]. In the present study, the independent risk factors associated with persistence of symptoms were: female gender (OR=2.08; 95% CI [1.27; 3.40]), paramedical staff (OR=2.92; 95% CI [1.61 ;5.3]), antibiotic therapy (OR=6.81; 95% CI [1.41 ;32.85]), and corticosteroid therapy (OR=3.65; 95% CI [2.34 ;5.68]). Female gender was a major risk factor for the persistence of symptoms described in the literature [39]. Indeed, women are more likely to develop anxiety symptoms and emotional disturbance after being exposed to high stress. This psychological effect may be associated with physical symptoms, which is known as somatization [39]. Patients who received antibiotics and corticosteroids were three and six times more likely to have residual symptoms, respectively. This finding is in agreement with the Egyptian study by Abdel Hafiz et al [40]. It should be noted that in our population, overuse of antibiotics was observed even in the lack of indications. Several previous studies have reported side effects associated with the use of azithromycin, such as cardiotoxicity and vertigo [41]. The same is true for corticosteroids, which can cause cardiovascular, gastrointestinal, and neuropsychiatric impairment [42]. It is possible that the side effects of these drugs therefore contribute to the delayed recovery of these patients and the persistence of symptoms after recovery.

5. Conclusions

Based on the results of our study and the factors associated with residual symptoms, long-term follow-up of HCWs with COVID-19 is recommended to understand and treat persistent physical and psychological problems. Particular attention to female and paramedical HCWs is factors associated with persistence of symptoms after recovery. Self-medication with antibiotics and corticosteroids should also be limited, especially since in our study they were associated with residual symptoms.

The fight against the propagation of this virus continues with the respect of barrier actions, the training and information of the HCWs on the risk as well as the reinforcement of the preventive and the hospital hygiene measures.

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Conflicts of Interest: The authors declare that they have no conflicts of interest.

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