Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Letter in response to article in journal of infection: "High SARS-CoV-2 antibody prevalence among healthcare workers exposed to COVID-19 patients"

To the editor

We have read with interest the recent paper of Chen Y et al., about antibody prevalence among healthcare workers (HCWs) exposed to COVID-19[1]. They found a significant incidence of asymptomatic HCWs previously exposed to COVID-19 patients. We have performed a cross-sectional descriptive study to assess the clinical and epidemiological characteristics of mildly symptomatic COVID-19 in a series of Spanish HCWs outpatients with reverse transcription polymerase chain reaction (RT-PCR)-confirmed disease. Nowadays, Spain has the highest number of confirmed cases of COVID-19 among its HCWs around the world. The study protocol was approved by the clinical research ethics committee of the Hospital Clinico San Carlos de Madrid and complied with the clinical research guidelines of the Declaration of Helsinki. Criteria for inclusion in our study were: age over 18 years, laboratory (RT-PCR)-confirmed COVID-19; clinical cure (lack of symptoms except olfactory and gustatory symptoms), healthcare worker (both hospital and community care staff) and reading comprehension of Spanish. Exclusion criteria were hospitalization, symptom persistence at the study outset or no laboratory confirmation of COVID-19 infection. Clinical and epidemiological data was collected though a voluntary, anonymous, self-administered online questionnaire, accessible from Google Docs. The questionnaire consisted of three general questions (about age, sex and occupation), two about general clinical issues (comorbidities and systemic treatments), and two about COVID-19 symptoms. Questionnaire data were transferred to an Excel database. Statistical analysis was performed using the Statistical Package for the Social Sciences for Windows (SPSS version 22,0; IBM Corp, Armonk, NY, USA). Categorical variables are provided as counts and percentages and continuous measurements as the mean, standard deviation (SD) and range. We compared means for continuous variables through independent group t tests. Proportions of categorical variables were compared using the $\chi 2$ test. Significance was set at $P < 0.05$.

The final study population comprised 1177 patients fulfilling the inclusion and exclusion criteria. Mean patient age was 41.7 (11.6) years (range 19–68). There were 866 women (73.6%). There were no differences in age according to gender ($p = 0.09$). Most patients were physicians (62.2%) or nurses (29%). 405 patients (34.4%) had allergies (to pollens, dust mites, epithelia of animals, etc.). Most frequent concomitant diseases were arterial hypertension (6.9%), asthma (6.6%) and high blood cholesterol (5.7%).

Fever at some time during the disease course was reported by 842 patients (71.5%) (Table 1). Each patient described a mean of 7.88 (3.26) symptoms.

Significant differences emerged between both sexes in the frequencies of most of the symptoms listed (15 of 21).

In Table 2 we provide symptom frequencies by age group.

So, while the symptoms most frequently reported were similar to those described in hospitalized patients (fatigue, fever and cough)[2,3], other symptoms appeared with greater frequency (myalgia, headache, nasal congestion, sore throat, diarrhea or chills). In fact, in several studies regarding hospitalized patients, several symptoms that are common in outpatients with mild infection have been reported as infrequent[4]: myalgia (21.2–36.2%), headache (9.9–18.6%), nasal congestion (0.4–3.9%) or diarrhea (4.8–12.6%). Similarly, other common symptoms in mildly symptomatic patients seen here and in other studies were not mentioned in hospitalized patients, even in the larger series[2,3], like anosmia and ageusia, which have been reported with similar incidence to the present study (71.6%) in a study among 202 mildly symptomatic outpatients from Italy (64.4%).[5] Besides, in another recent study, anosmia was strongly and independently associated with outpatient care in a trial designed to identify risk factors for hospital admission, suggesting that this factor could be a marker of milder manifestations of COVID-19.[6] The results of our study indicate that loss of smell is even more frequent in mildly symptomatic patients under 40 years of age. Rates of asymptomatic patients from 1.4% to 11.6% of patients have been provided.[4] In our study, this rate was 1.9%, thus, within the lower range of reported prevalence. However, the purpose of our study was not to detect asymptomatic patients. Besides, diagnostic tests for healthcare staff in the initial stages of the epidemic in our country were practically restricted to symptomatic cases, so these asymptomatic patients were HCWs in contact with confirmed COVID-19 cases who were tested because of epidemiological or occupational health risks (and have positive RT-PCR, unlike the HCWs in Chen Y at alś study). Finally, differences emerged between men and women in the presentation of most symptoms [just like Chen Y et al. study,[1] the proportion of females in our study was high (73.6%) and may be attributed to the inclusion criteria (HCWs, 70% of which in Spain are women)]. Some symptoms were also more frequent depending on patient age.

Our study has several obvious limitations. First, data were self-reported, so recall biases are likely. However, our study was conducted mid-pandemic and participants had just recovered. In addition, it was based on a cross-sectional survey, although only recovered patients with no active symptoms were included to obtain data for the whole disease course. The only exception was that we accepted patients with persisting olfactory and gustatory alterations, because has been reported that 56% of patients show persistent olfactory dysfunction over the days following resolution of the general clinical manifestations of COVID-19[7]. Finally, to avoid possible infections, this was an online-based voluntary study, so the possibility of selection bias exists.

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Table 1
Symptom frequencies: overall and by sex.

SIGNS AND SYMPTOMS	TOTAL ($n=1177$) (%)	MEN ($n=310$) (%)	WOMEN ($n=866$) (%)	p
Fever	842 (71.5)	241 (78.5)	600 (71.5)	0.018
< 37.5 °C	192 (22.8)*	34 (14.1)*	158 (26.3)*	
37.6–38 °C	393 (46.7)*	105 (43.6)*	287 (47.8)*	<0.001
38.1–39 °C	232 (27.6)*	91 (37.8)*	141 (23.5)*	
> 39 °C	25 (3)*	11 (4.6)*	14 (2.3)*	
Fatigue	878 (74.6)	216 (69.7)	662 (76.4)	0.02
Cough	827 (70.3)	216 (69.7)	610 (70.4)	0.8
Myalgia	822 (69.8)	223 (71.9)	599 (69.2)	0.36
Headache	814 (69.2)	186 (60.0)	628 (72.5)	<0.001
Anosmia	625 (53.1)	130 (41.9)	495 (57.2)	<0.001
Nasal congestion	570 (48.4)	117 (37.7)	453 (52.3)	<0.001
Sore throat	552 (46.9)	115 (37.1)	436 (50.3)	<0.001
Diarrhea	511 (43.4)	111 (35.8)	399 (46.1)	0.002
Chills	509 (43.2)	129 (41.6)	380 (43.9)	0.49
Ageusia	405 (34.4)	78 (25.2)	327 (37.8)	<0.001
Dysgeusia	380 (32.3)	106 (34.2)	274 (31.6)	0.41
Nausea	243 (20.6)	29 (9.4)	214 (24.7)	<0.001
Stabbing chest pain	240 (20.4)	44 (14.2)	196 (22.6)	0.002
Shortness of breath	218 (18.5)	38 (12.3)	180 (20.8)	0.001
Hyposmia	200 (17)	59 (19)	141 (16.3)	0.27
Abdominal pain	167 (14.2)	25 (8.1)	142 (16.4)	<0.001
Conjunctivitis	104 (8.8)	21 (6.8)	82 (9.5)	0.15
Dizziness	86 (7.3)	9 (2.9)	77 (8.9)	0.001
Mouth and tongue sores	79 (6.7)	12 (3.9)	67 (7.7)	0.02
Vomiting	55 (4.7)	5 (1.6)	50 (5.8)	0.003
Skin rash	15 (1.3)	2 (0.6)	13 (1.5)	0.25
Asymptomatic	23 (1.9)	10 (3.2)	13 (1.5)	0.06

(* among patients with fever).

Table 2
Symptom frequencies: overall and by age group.

SIGNS AND SYMPTOMS	TOTAL ($n=1177$) (%)	< 30 years ($n=278$) (%)	31–40 years ($n=285$) (%)	41–50 years ($n=296$) (%)	51–60 years ($n=246$) (%)	> 60 years ($n=72$) (%)	p
Fever < 37.5 °C	842 (71.5) 192	168 (62.9) 35	212 (76.5) 50	228 (78.1) 59	176 (73) 33 (18.8)*	58 (82.9) 15	<0.001 0.86
37.6–38 °C 38.1–39 °C	(22.8)* 393 (46.7)*	(20.8)* 83 (49.4)*	(23.6)* 97 (45.8)*	(25.9)* 102 (44.7)*	85 (48.3)* 53	(25.9)* 26 (44.8)*	
> 39 °C	232 (27.6)* 25 (3)*	46 (27.4)* 4 (2.4)*	58 (27.4)* 7 (3.3)*	58 (25.4)* 9 (3.9)*	(30.1)* 5 (2.8)*	17 (29.3)* 0	
Fatigue	878 (74.6)	196 (70.5)	214 (75.1)	227 (76.7)	188 (76.4)	53 (73.6)	0.46
Cough	827 (70.3)	177 (63.7)	207 (72.6)	216 (73)	174 (70.7)	53 (73.6)	0.09
Myalgia	822 (69.8)	180 (64.7)	186 (65.3)	220 (74.3)	186 (75.6)	50 (69.4)	0.01
Headache	814 (69.2)	201 (72.3)	209 (73.3)	215 (72.6)	147 (59.8)	42 (58.3)	0.001
Anosmia	625 (53.1)	163 (58.6)	179 (62.8)	148 (50)	105 (42.7)	30 (41.7)	<0.001
Nasal congestion	570 (48.4)	158 (56.8)	160 (56.1)	130 (43.9)	96 (39)	26 (36.1)	<0.001
Sore throat	552 (46.9)	123 (44.2)	145 (50.9)	148 (50)	105 (42.7)	31 (43.1)	0.21
Diarrhea	511 (43.4)	107 (38.5)	126 (44.2)	131 (44.3)	115 (46.7)	32 (44.4)	0.4
Chills	509 (43.2)	93 (33.5)	117 (41.1)	154 (52)	111 (45.1)	34 (47.2)	<0.001
Ageusia	405 (34.4)	121 (43.5)	110 (38.6)	95 (32.1)	62 (25.2)	17 (23.6)	<0.001
Dysgeusia	380 (32.3)	76 (27.3)	94 (33)	98 (33.1)	89 (36.2)	23 (31.9)	0.29
Nausea	243 (20.6)	29 (9.4)	62 (21.8)	61 (20.6)	53 (21.5)	11 (15.3)	0.8
Stabbing chest pain	240 (20.4)	51 (18.3)	58 (20.4)	73 (24.7)	47 (19.1)	11 (15.3)	0.24
Shortness of breath	218 (18.5)	50 (18)	54 (18.9)	55 (18.6)	47 (19.1)	12 (16.7)	0.99
Hyposmia	200 (17)	45 (16.2)	41 (14.4)	45 (15.2)	54 (22)	15 (20.8)	0.13
Abdominal pain	167 (14.2)	32 (11.5)	39 (12.7)	45 (15.2)	41 (16.7)	10 (13.9)	0.53
Conjunctivitis	104 (8.8)	24 (8.6)	18 (6.3)	31 (10.5)	23 (9.3)	8 (11.1)	0.44
Dizziness	86 (7.3)	34 (12.2)	17 (6)	16 (5.4)	14 (5.7)	5 (6.9)	0.01
Mouth and tongue sores	79 (6.7)	24 (8.6)	28 (9.8)	15 (5.1)	6 (2.4)	6 (8.3)	0.005
Vomiting	55 (4.7)	11 (4)	12 (4.2)	15 (5.1)	17 (6.9)	0	0.14
Skin rash	15 (1.3)	4 (1.4)	4 (1.4)	4 (1.4)	1 (0.4)	2 (2.8)	0.58
Asymptomatic	23 (1.9)	8 (2.9)	3 (1.1)	4 (1.4)	5 (2)	3 (4.2)	0.3

(* among patients with fever).

To the best of our knowledge, this is the largest described clinical case series of mildly symptomatic HCWs COVID-19 disease outpatients. Their particular clinical spectrum could help physicians make a correct diagnosis and thus help avoid infection spread, as a health priority in most countries.

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