Title: A prospective cohort of SARS-COV2 infected health care workers: Clinical characteristics, outcomes and follow up strategy.

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ABSTRACT

Background: During the COVID-19 outbreak health care workers (HCWs) were at a high risk of infection. Strategies to reduce in-hospital transmission between HCWs and to safely manage infected HCWs are lacking. Our aim was to describe an active strategy for the management of COVID-19 in SARS-CoV-2 infected HCWs and investigate its outcomes.

Methods: A prospective cohort study of SARS-CoV-2 infected health care workers in a tertiary teaching hospital in Barcelona, Spain, was performed. An active strategy of weekly PCR screening for SARS-CoV-2 on HCWs was established by the Occupational Health department. Every positive HCW was admitted to the Hospital at Home Unit with daily assessment online and in-person discretionary visits. Clinical and epidemiological data were recorded.

Results: Of the 590 HCWs included in the cohort, 134 (22%) were asymptomatic at diagnosis, and 15% (89 patients) remained asymptomatic during follow up. A third of positive cases were detected during routine screening. The most frequent symptoms were cough (68%), hyposmia/anosmia (49%) and fever (41%). 10% of the patients required specific treatment at home, while only 4% of the patients developed pneumonia. Seventeen patients required a visit to the Outpatient clinic for further evaluation, and six of these (1%) required hospital admission. None of the HCWs included in this cohort required ICU admission or died.

Conclusions: Active screening for SARS-CoV-2 among HCWs for early diagnosis and stopping in-hospital transmission chains proved efficacious in our institution, particularly due to the

high percentage of asymptomatic HCWs. Follow up of HCWs in Hospital at Home units is safe and effective, with low rates of severe infection and readmission.

INTRODUCTION

Since its outbreak in Wuhan, China, in December 2019, the novel coronavirus disease (COVID-19) pandemic has reached more than 47 million infected individuals and 1.2 million deaths worldwide [1]. The rapid spread of the virus and the severity of the disease has been a real challenge to health systems globally. Alternatives to conventional hospitalization, such as home care in Hospital at Home units (HaH) or other outpatient resources have previously been proposed to manage the risk of health system collapse in other high demanding situations[2,3].

HCWs, defined as any paid professional involved in the care of patients, are at high health risk during pandemics [4]. Risks observed by the Prevention Service, and also acknowledged by the WHO, include pathogen exposure, long working hours, psychological distress, fatigue, occupational burnout, stigma, and physical and psychological violence[5]. HCW nosocomial infection by COVID-19 has been widely reported to be highly prevalent in countries such as the USA, China or Italy[6–9]. In Spain nearly 41,000 HCWs were infected during the first wave, with 53 fatalities[10]. In many cases, personal protection equipment shortage was an issue, greatly endangering professionals on the front line of care provision. Different strategies for control and surveillance of health workers at risk have been proposed by international organisations, however, no global strategy has been defined for caring for infected health care workers.

Our aim in this study is to describe the characteristics and outcomes of an active strategy of COVID-19 management of infected HCWs in a HaH Unit in coordination with the Human Resources and Occupational Health departments in the Hospital Clinic Barcelona, Spain.

METHODS

Design: Prospective cohort study including HCW with a confirmed SARS-CoV-2 infection by real-time polymerase chain reaction (rt-PCR) on nasopharyngeal swabs between March 9th and May 4th 2020.

Setting: Hospital Clinic is a public, tertiary teaching hospital with 6,403 health care workers, serving 560,000 people in the metropolitan area of Barcelona, Spain. The Hospital Clinic's Hospital at Home Unit (HaH) started providing hospital-level, specialized, health care to patients at home in 1996 [11]. Care of infected HCW during HaH admission included daily virtual medical and nurse visits (phone and video calls), a round the clock call centre, medical and nurse visits at home on demand, blood tests, and transfer to an adapted Outpatient Hospital facility for either further tests (eg. chest X-ray) or planned conventional hospitalisation if required. Patients were discharged from HaH a week after symptom remission, with guidelines for re-consulting in case of clinical deterioration. Working reinstatement was decided by the Human Resources and Work Health department according to government protocols.

Participants: As hospital policy, weekly control rt-PCR was performed by the Prevention Service on every HCW working in COVID-19 areas in our hospital. Additional rt-PCRs were performed on all HCW self-reporting symptoms compatible with COVID-19. All HCW from the Hospital Clinic Barcelona with a positive rt-PCR were admitted to the HaH Unit. Only those HCW with baseline comorbidities or showing moderate symptoms underwent chest X-ray and blood tests at the time of admission. Active protocols at the time were followed to provide specific COVID-19 treatment. All patients initiating treatment underwent an ECG to

rule out QT segment abnormalities to prevent potential pro-arrhythmic effects associated with antiviral treatment.

Patients were followed up in HaH until symptom remission. Those who remained asymptomatic had a minimum follow-up of one week.

Patient consent statement: The study protocol was evaluated and approved by the Ethical Board of the Hospital Clínic (HCB/2020/0444). A waiver for informed consent was provided due to the state of infectious disease emergency. Admission to the Hospital at Home programme was voluntary, as was every medical procedure performed.

Statistical analysis: Categorical variables collected included sex, type of HCW occupation (administration, maintenance, nurses, physicians, other) active smoking habit, comorbidities (dyslipidaemia, hypertension, chronic lung disease, ischaemic heart disease, chronic kidney disease, neoplasm), reason for performing nasopharyngeal swab for SARS-CoV-2 diagnosis through rt-PCR (routine, high-risk contact, symptoms, unknown), presence of symptoms at diagnosis, presence of symptoms during follow-up, type of symptoms (cough, fever, dyspnoea, hyposmia/anosmia, dysgeusia, gastrointestinal symptoms including diarrhoea and abdominal pain), performance of blood analysis, performance of chest X-ray, radiological findings (normal, unilateral interstitial infiltrates, bilateral infiltrates), administration of antiviral treatment (lopinavir/ritonavir, hydroxychloroquine, azithromycin, remdesivir, tocilizumab), treatment received at home, treatment withdrawal, oxygen requirements at home, outpatient clinic visit, readmission to hospital, admission to intermediate care-ICU, mechanical ventilation (invasive or non-invasive), and death. Continuous variables included number of HCW admissions per day in the HaH, age, time from symptom initiation to diagnosis, time from diagnosis to symptom initiation in

asymptomatic patients at diagnosis, serum C reactive protein concentration, procalcitonin, lymphocyte count, lactate dehydrogenase, d-dimer, ferritin, aspartate aminotransferase, alanine aminotransferase, gammaglutamyl transferase, alkaline phosphatase, bilirubin, and length of stay at HaH. Categorical variables are reported as percentages and continuous variables as medians and interquartile ranges (IQR). Data was analysed with SPSS v21.0.

RESULTS

A total of 590 HCW (9.21% of the institution's total staff) tested positive for COVID-19 during the study period and were therefore admitted to the HaH (Figure 1). Main patient characteristics are summarised in Table 1. They were predominantly female (76%) with a median age of 40 years. A small proportion of patients in our cohort presented comorbidities, including hypertension (4.6%) and dyslipidaemia in 3.7%. Notably 6% had a history of chronic lung disease (mainly asthma). The largest professional group was composed by nursing staff who accounted for 34% of HCW, followed by nurse aide assistants (25%), and physicians (18%). Almost a third (32%) of the positive cases were detected by routine screening, while nearly half of the positive tests (49%) were performed in HCWs actively seeking attention due to self-reported symptoms.

Clinical features

Globally, 77% COVID-19 positive patients reported some symptom when specifically asked in the first assessment. Mean time from showing symptoms to diagnosis was 4.16 days. The most frequent symptom reported in this group of patients was cough (222 patients, 48.8%), followed by fever (156 patients, 34%), hyposmia/anosmia in 10.5%, dyspnoea in 4% (17 patients), gastrointestinal symptoms (diarrhoea) in 13 patients (3%), and 5 (1.1%) patients

reported dysgeusia. The most frequent combination of symptoms was fever and cough, present in 16.5% of the patients at the time of diagnosis (table 2).

One hundred and thirty four patients (22%) in the cohort were asymptomatic at the time of diagnosis. Of these, 89 (66.4%, 15% of the total cohort) did not develop symptoms at any time during follow up. The remaining 45 patients (33.6%, and 7.6% overall) had at least one symptom during follow up. Median time from positive PCR to having symptoms was 2.6 days (IQR 1.25-3 days) in these patients. Median time to each of the symptoms is represented in Figure 2. When comparing baseline characteristics (age, comorbidities, occupation) between symptomatic and asymptomatic patients we did not find any differences (data not showed).

Outcomes

Median length of stay in HaH was 15 days (IQR 12-15). Only 47 (8%) patients underwent blood analysis (CRP, basic metabolic panel, complete blood count, ferritin, D-dimer, procalcitonin). Main blood analysis findings are depicted in Table 3. Regarding blood analysis, patients had low median levels of C reactive protein (3.07 mg/dL), ferritin (330 (ng/mL), D-dimer level (550 ng/mL) and procalcitonin (0.14 ng/mL). Notably, no concomitant bacterial infections or superinfections were detected. Nine percent (n= 55) of the patients required a chest X-ray, which showed abnormalities in 63% of these, with bilateral infiltrates in 20 patients (36% of the X-Ray performed). Ten percent of the HCW started treatment at home. All of them received a combination of hydroxychloroquine and azithromycin, whereas just a third (31%) of the patients started lopinavir/ritonavir treatment. Seven patients (1.2%) required oxygen treatment at home.

Seventeen patients (2.9%) required hospital assessment during HaH stay, and only 6 patients (1%) required hospital admission. Of these 6 patients, 4 received anti-IL6 treatment with tocilizumab, and 3 (4.9%) received antiviral treatment with remdesivir. None of the patients required ICU admission or mechanical ventilation. None of the patients died.

DISCUSSION

During the first wave of COVID-19 in Spain, 590 HCWs were infected by SARS-CoV-2 in our institution, representing 9.21% of the overall Hospital Clinic Barcelona staff and 6,7% of the total of COVID-19 patients diagnosed in the hospital in the same period (n=8,768). In Italy 26,675 HCW were reported positive, accounting for 11.7% of the total confirmed cases in Italy[6]. In the US, among 315,531 COVID-19 cases reported to CDC from February 12 to April 9, 9,282 (19%) were identified as HCW[8]. In Spain 41,000 HCW were reported to be infected on April 16, namely 24% of the total cases [10]. However, variations in population-testing strategies within health systems and pandemic timings must be considered when interpreting this data. In Spain this percentage is probably overestimated, as testing strategy was prioritised in HCW. It was carried out irregularly in the general population, depending on setting and test availability. It is interesting to point out that 76% of the infected HCWs were female workers, reflecting the higher proportion of women in our centre (72% of the workers).

In our institution both technical actions (assessment of protection equipment, training in occupational risk prevention, action protocols) and health actions (active and passive surveillance of the population) were carried out in order to guarantee the safety and health of HCW. Weekly screening of SARS-CoV-2 in every HCW was established in order to

minimise transmission between HCWs or from HCW to patients. Also, screening PCR was performed in those HCW self reporting symptoms. This strategy has been perceived as positive amongst HCWs, as it brings confidence and ease regarding reduction in the risk of transmission to relatives outside the hospital. From the public health point of view, this strategy allowed our centre to detect and separate 590 HCWs from the system onto sick leave, preventing potential horizontal transmission. It is interesting to note that 32% of these PCRs were performed as screening on asymptomatic workers who had symptoms only 2.59 days after a positive PCR. Moreover, 22% never had any symptoms, suggesting that active screening for SARS-CoV-2 between HCWs may be fundamental in the early detection of asymptomatic but potentially contagious HCWs and therefore stopping in-hospital transmission chains. When analysing the temporal trends in the number of infected HCWs, it is noticeable that the peak of incidence occurs within the first 14 days of confinement (figure 1), suggesting that a great burden of infection has an extra-hospital origin, mitigated afterwards by mobility and social restrictions, as well as in-hospital preventive measures.

From a clinical stand our data is comparable to previous studies describing the clinical features of COVID-19[9]. The most frequent clinical presentation of COVID-19 in those symptomatic at diagnosis was cough (49%) followed by fever (34%) and hyposmia (10.5%). Other symptoms were less frequently reported, such as dyspnoea in less than 4%, gastrointestinal symptoms (mainly diarrhoea) in 3% and dysgeusia in only 1%. It is interesting to point out that a vast majority (84.9%) of the HCWs in our cohort developed symptoms at some point of the follow up, with cough the most frequent (68%), followed by fever (41%). Symptoms less frequently reported at diagnosis appeared later in the course of

the disease, such as hypo/anosmia in half of the patients, dysgeusia in 44% or gastrointestinal symptoms in 30%.

It is of great interest to point out that 15% of our cohort never developed symptoms of COVID-19. To date, only small studies had reported data regarding the frequency of asymptomatic COVID-19 infection, with different results ranging between 18 and 88%[12,13]

Overall, the clinical course was benign in our cohort. Only 10% of our patients required antiviral treatment following local protocol. Less than 3% of the patients required in-hospital admission and a marginal 1% required readmission to hospital. None of the patients required ICU admission or died, in contrast to other cohorts of HCW such as reported by the CDC in the USA, where 2% of them required ICU admission and 0,3% died[8]. This can be explained by an evident selection bias, but also can be attributed to a relatively healthy and young cohort, and to the active surveillance provided by close monitorisation in Hospital at Home Unit.

Our study has two main limitations. Firstly, data regarding the origin of infection was scarce and in most cases, it was impossible to determine. Secondly, our cohort included only patients with a mild-moderate clinical course who may have not provided epidemiological data in a different setting, but cannot be extrapolated to severe COVID-19 patients. This data could serve to better depict the epidemiology and clinical evolution in non-severe patients and give a further understanding of the disease.

In conclusion, during global challenges to health systems such as the actual COVID-19 pandemic, HCWs are at great risk of biohazard exposure due to increased demand for

health assistance, compounded by the difficulties in guaranteeing adequate provision of protective equipment. According to our data, asymptomatic infection is as frequent as 15%, therefore an active strategy of SARS-CoV-2 screening is critical in stopping in-hospital transmission. Close monitoring of clinical status and early complication detection is critical in the follow up of HCW with COVID-19. In the context of the current COVID-19 pandemic, an active strategy of monitoring and treatment at home by Hospital at Home Units seems to be a safe and efficacious alternative to self-monitoring or conventional hospital admission.

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Conflicts of interest

The authors declare that they have no relevant or material financial interests that relate to the research described in this paper.

Authorship contributions

DN and JMP designed the study; FS, AA, AC, EB, GA and PM systematically collected the data; JMP and DN obtained permissions; JMP and DC performed the statistical analyses and drafted the tables; DNO and OT-M wrote the first draft of the manuscript; all other authors contributed by gathering data, critically revising the manuscript and providing final approval.

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Table 1. Baseline characteristics of 590 health care workers with COVID-19 admitted to the Hospital at Home during the study period.

Baseline characteristics	
Age, years (median, IQR)	40 (30-50)
Male sex, n (%)	141 (24)
Occupation, n (%)	
- Administration	34(5.8)
- Maintenance	13 (2.2)
- Certified Nurse Assistants	150 (25.4)
- Nurses	199 (33.7)
- Physicians	107 (18.1)
- Other	33 (5.6)
Current smoking habit, n (%)	26 (4.4)
Dyslipidaemia, n (%)	22 (3.7)
Hypertension, n (%)	27 (4.6)
Chronic lung disease, n (%)	34 (5.8)
Ischaemic heart disease, n (%)	4 (0.7)
Chronic Kidney disease, n (%)	3 (0.5)
Neoplasm, n (%)	16 (2.7)
Characteristics of the infection	
Reason for performing nasopharyngeal swab, n (%)	
- Routine	189 (32)
- High-risk contact	10 (1.7)
- Symptoms	293 (49.5)

- Unknown	98 (16.6)

Table 2. Clinical features of 590 health care workers with COVID-19 admitted to the Hospital at Home during the study period

Clinical features	
Symptomatic at diagnosis, n (%)	455 (77.1)
Time from symptom initiation to diagnosis (days, mean IQR)	4.16 (1-5)
- Cough	222 (48.8)
- Fever	156 (34.3)
- Dyspnoea	17 (3.7)
- Hyposmia/anosmia	48 (10.5)
- Dysgeusia	5 (1.1)
- Gastrointestinal symptoms	13 (2.9)
- Fever + cough	75 (16.5)
- Fever + dyspnea	7 (1.5)
- Fever + hyposmia	6 (1.3)
- Fever + gastrointestinal symptoms	4 (0.9)
Asymptomatic at diagnosis, n (%)	**135 (22.9)**
Never developing symptoms during follow up	89 (15.1)
Time from diagnosis to symptom initiation (days, mean (IQR)	2.59 (1.25-3)
Symptoms at any point of follow up, n (%)	**501 (84.9)**

- Cough	342 (68.3)
- Fever	207 (41.3)
- Dyspnoea	108 (21.6)
- Hyposmia/anosmia	246 (49.1)
- Dysgeusia	222 (44.3)
- Gastrointestinal symptoms	155 (30.9)

Table 3. Clinical assessment and outcomes of 590 health care workers with COVID-19 admitted to the Hospital at Home during the study period

Blood analysis results	
Blood analysis performed, n (%)	47 (8)
C Reactive Protein, mg/dL, median mg/dL (IQR)	3.07 (0.4-4.82)
Procalcitonin, median ng/mL (IQR)	0.14 (0.03-.0.78)
Lymphocytes per 10^6/L, median (IQR)	810 (220-1325)
Lactate dehydrogenase, median U/L (IQR)	218 (168-262)
D-dimer, median ng/mL (IQR)	550 (200-550)
Ferritin, median ng/mL (IQR)	330 (132-405)
Aspartate aminotransferase, median U/L (IQR)	29 (20-37)
Alanine aminotransferase, median U/L (IQR)	27 (16-34)
Gammaglutamyl transferase, median U/L (IQR)	32 (15-41)
Alkaline fosfatase, median U/L (IQR)	63 (49-72)
Total bilirubin, median mg/dl (IQR)	0.49 (0.4-0.6)
Radiological findings, n (%)	
Chest X-ray performed	55 (9.3)
Normal chest X-ray	26 (47.3)
Unilateral interstitial infiltrates	4 (7.3)
Bilateral infiltrates	20 (36.4)

Treatment characteristics, n (%)	
Received treatment at home	61 (10.3)
Lopinavir/ritonavir	19 (31.1)
Hydroxicloroquine	59 (96.7)
Azithromycin	60 (98.4)
Remdesivir	3 (4.9)
Tocilizumab	4 (6.5)
Treatment withdrawal	4 (6.5)
Oxygen requirements at home	7 (1.2)
Outcomes	
Total HaH length of stay, days (median, IQR)	15 (12-19)
Outpatient clinic visit	17 (2.9)
Readmission to hospital	6 (1)
Admission to intermediate care-ICU	0
Invasive or non-invasive mechanical ventilation	0
Death	0

Figure legends

Figure 1. Timeline of admissions and prevalence (total number of admissions per day) of positive HCW in the Hospital at Home Unit.

Figure 2. Symptom onset diagram in patients asymptomatic at diagnosis who presented symptoms during follow-up (days from positive PCR to symptom manifestation) (n=46)

Figure 1.

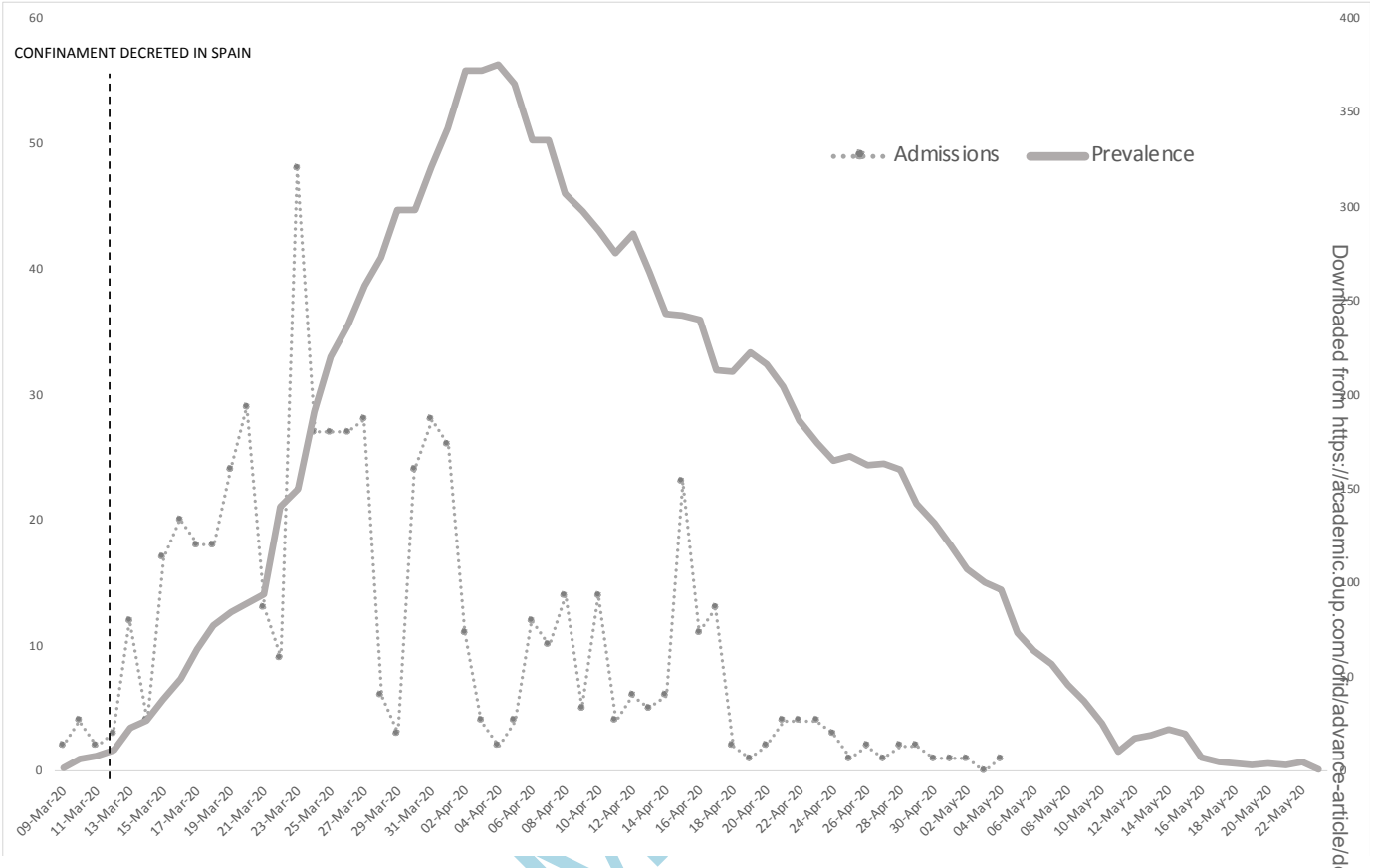

Figure 2.