Symptoms in healthcare professionals infected with SARS-CoV-2 at a university hospital
Sintomas em profissionais de saúde infectados com SARS-CoV-2 em um hospital universitário

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ABSTRACT | Introduction: Healthcare professionals are among the main risk groups for novel coronavirus disease (COVID-19). The identification of respiratory symptoms is important in the clinical assumption of infection, but it may be asymptomatic or paucisymptomatic. Objectives: To compare the proportion of professionals with symptoms suggestive of COVID-19 who tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with the proportion of positive asymptomatic professionals with high-risk contact; and to identify respiratory and non-respiratory symptoms of professionals with suspected COVID-19 and the proportion of those who tested positive for SARS CoV-2. Methods: This is a cross-sectional study that retrospectively analyzed clinical records of health professionals who spontaneously sought the occupational health service of a university hospital center from March to August 2020 for presenting with symptoms and/or for having had high risk contact with a confirmed case of COVID-19 and who, in this context, underwent the reverse transcription polymerase chain reaction test for SARS-CoV-2. Results: COVID-19 was confirmed in 27 of the 420 symptomatic professionals vs. three of the 193 asymptomatic professionals (p = 0.009). Of the 371 professionals with respiratory symptoms, 19 were positive for COVID-19 vs. 11 among the 242 with no respiratory symptoms (p = 0.750). Nasal congestion and rhinorrhea were the respiratory symptoms with the highest proportion of positive cases (11.43 and 8.97%, respectively). Conclusions: Although COVID-19 is typically associated with respiratory symptoms, not all these symptoms were predictive of disease. It becomes crucial to value mild symptoms among healthcare professionals.

Keywords | coronavirus infections; health personnel; occupational health.

RESUMO | Introdução: Os profissionais de saúde encontram-se entre os principais grupos de risco para a doença do novo coronavírus (COVID-19). A identificação de sintomas respiratórios é importante na presunção clínica da infecção, mas ela pode ser assintomática ou paucissintomática. Objetivos: Comparar a proporção de profissionais com teste positivo para o novo coronavírus 2 e sintomas sugestivos de COVID-19 com a proporção de assintomáticos positivos com contato de alto risco; e identificar os sintomas respiratórios e outros sintomas dos profissionais com suspeita de COVID-19 e a proporção dos que testaram positivo. Métodos: Estudo transversal, com análise retrospectiva dos registos clínicos dos profissionais de saúde que recorreram por iniciativa própria ao serviço de saúde ocupacional de um centro hospitalar universitário, entre março e agosto de 2020, por apresentarem sintomas, contato de risco com caso confirmado de COVID-19 ou por ambos e que, nesse contexto, realizaram teste de reação em cadeia da polimerase da transcrição reversa para SARS-CoV-2. Resultados: Dos 420 profissionais sintomáticos, em 27 confirmou-se COVID-19, e os resultados positivos entre os 193 assintomáticos foram 3 (p = 0,009). Dos 371 que apresentaram sintomas respiratórios, 19 foram positivos para COVID-19 vs. 11 entre os 242 que não tinham sintomas respiratórios (p = 0,750). A congestão nasal e a rinorrea foram os sintomas respiratórios com maior proporção de casos positivos (11,43 e 8,97%, respectivamente). Conclusões: Apesar de a COVID-19 estar tipicamente associada a sintomas respiratórios, nem todos esses sintomas foram preditivos de doença. Torna-se fulcral valorizar a sintomatologia leve entre profissionais de saúde.

Palavras-chave | infecções por coronavírus; pessoal de saúde; saúde do trabalhador.

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INTRODUCTION

The novel coronavirus disease (COVID-19) is a condition caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Coronavirus, a ribonucleic acid virus belonging to the Coronaviridae family, is broadly distributed in humans and in other mammals. Although most human coronavirus infections are mild, the emergence of a novel highly transmissible and pathogenic virus of this family generated a large-scale epidemic. This novel virus was preceded by SARS-CoV, responsible for the outbreak of severe acute respiratory syndrome in 2002-2003 and for the outbreak of Middle East respiratory syndrome (MERS-CoV) in 2012. In December 2019, a series of pneumonia cases of unknown cause was observed in the city of Wuhan, China, with clinical manifestations greatly resembling viral pneumonia. Deep analysis from lower respiratory tract samples led to the sequencing of a novel coronavirus (SARS-CoV-2). The first reported cases of infection were directly related to the seafood wholesale market in Wuhan, China. It was assumed that bats act as a reservoir, and pangolins might act as an intermediate to facilitate transfer to humans. Person-to-person transmission by inhalation or contact with droplets emerged as a leading source of infection, while the potential of aerosols, contact with surfaces, and fecal-oral routes have been recently discussed. SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) as a receptor and rapidly spreads through the respiratory tract.

COVID-19 has spread widely and rapidly from China across the world, demanding important interventional measures from health authorities and government entities. On January 30, 2020, the World Health Organization (WHO) officially declared COVID-19 epidemic as a public health emergency of international concern, and recognized it as a pandemic on March 11, 2020.9,10 On March 1st, 2020 the WHO reported 87,137 cases confirmed globally, of which 79,968 were confirmed in China, with a total of 2,977 deaths. The number of cases continued to grow catastrophically, and on April 1st, 2020 there were 823,626 confirmed cases and 40,598 deaths worldwide. The main clinical signs and symptoms initially reported were fever, breathing difficulty, and extensive bilateral pulmonary infiltrates on chest radiographs. Therefore, the several national and international health institutions considered fever, irritating dry cough, and/or dyspnea as the symptoms that raised suspicion for SARS-CoV-2 infection,9,11 with respiratory symptoms playing a key role in clinical suspicion of COVID-19. However, in addition to those three symptoms, sudden onset anosmia and dysgeusia were added to the clinical criteria that define a possible case of COVID-19.12 Conversely, infection may be identified in several paucisymptomatic individuals with other symptoms, especially those involving the upper airways, and also in asymptomatic individuals, who represent a potential source of COVID-19 transmission.13-18 Due to their frequent contact with infected individuals, healthcare professionals are a risk group for COVID-19. They also might be the source of transmission to patients to whom they provide care; thus, early identification of infected professionals is determining in the hospital environment. Since healthcare professionals are adults of active working age, their age is not predominantly advanced, and mild symptoms, especially those of the upper respiratory tract, may be the predominant ones, although these are not included in the above-mentioned clinical criteria. This study aimed to compare the proportion of healthcare professionals who tested positive for SARS-CoV-2 and who had symptoms suggestive of COVID-19, particularly respiratory ones, with the proportion of asymptomatic healthcare professionals with high-risk contact who tested positive. The present study also sought to characterize respiratory symptoms and other symptoms in professionals with suspected COVID-19 and to identify the proportion of these symptoms in professionals who tested positive for SARS-CoV-2.

METHODS

TYPE OF STUDY

A cross-sectional observational study was conducted to retrospectively analyze electronic clinical records from a hospital occupational health service.
STUDY SAMPLE

The study convenience sample consisted of healthcare professionals who spontaneously requested a face-to-face appointment at the occupational health service of a Portuguese university hospital center from March to August 2020, for respiratory and/or other symptoms and/or because they have had high risk contact with a confirmed case of COVID-19 (mostly family or community exposure and, occasionally, situations in which the high risk contact occurred in hospital, but isolated, only with the worker). In these contexts, these professionals underwent the reverse transcription polymerase chain reaction (RT-PCR) test for SARS-CoV-2.

This test was performed on the day of the appointment in symptomatic professionals and at least 5 days after high-risk contact in asymptomatic ones. All professionals in the sample, whether symptomatic or asymptomatic, were followed for 14 days by the occupational health service, and those who tested negative were instructed to repeat the test if there was the onset or worsening of symptoms.

This study excluded healthcare professionals assessed by the occupational health service in the context of hospital outbreaks or unprotected exposure to patient(s) or coworker(s) with COVID-19 included in groups of exposed professionals in a given service (clusters).

STUDY VARIABLES

During analysis of clinical records, the following workers’ demographic data were collected: sex, age, professional group, type of service, symptoms and/or history of high-risk contacts with COVID-19, as well as results of RT-PCR tests for SARS-CoV-2. The following respiratory symptoms were considered: cough, dyspnea, odynophagia, nasal congestion, rhinorrhea, and sternutation.

The variable service was classified into COVID and COVID free, with the first group including the services dedicated to COVID-19 care, namely internal medicine, intensive care medicine, pulmonary medicine, infectious disease medicine, and emergency services, as well as other services with frequent high-risk activities, including aerosolization maneuvers, such as anesthesiology and stomatology. COVID free services included all the other clinical services with fewer high-risk activities, such as cardiology, dermatology, rheumatology, pediatrics, ophthalmology, as well as assistance and support services, namely pharmacy, dietetics, information technology, and human resources.

STATISTICAL ANALYSIS OF VARIABLES

Data collection and analysis were performed using the H2ST, Microsoft Excel, and IBM Statistical Package for the Social Sciences computer programs. For the statistical analysis of variables, the Kolmogorov-Smirnov test was used to investigate the normality of distribution of numerical variables. The association between variables was assessed with the χ² test (categorical variables) and the Student’s t test or the Mann-Whitney U test for comparison between means (normal or non-normal distribution of numerical variables, respectively). The level of significance was set at 5%.

ETHICAL CONSIDERATIONS

The collected data were anonymized when inserted into the database, and a number was attributed to each worker. This study was approved by the research ethics committee of the hospital center and by the board of directors of the occupational health service.

RESULTS

From March to August 2020, 613 professionals sought the occupational health service of a Portuguese university hospital center for presenting with symptoms consistent with COVID-19 or having had high risk contact with a confirmed case of COVID-19 not included in clusters, even being asymptomatic. They were predominantly women (n = 500; 81.6%), with a mean age of 41 years (standard deviation = 12.17 years). The majority of professionals was aged between 18 and 34 years (n = 233; 38%). The sample included more physicians (n = 197; 32%), followed by nurses (n = 179; 29%), operations assistants (n = 128; 22%), and diagnostic and therapeutic technicians (n = 44; 7%). Other professional categories accounted for 11% of the workers (n = 65), including technical assistants, children’s educators, and other technicians (Table 1).
Comparing the groups of professionals with a positive vs. negative RT-PCR test, i.e., with and without COVID-19 (Table 2), it was found that positive cases included a higher percentage of women (86.7 vs. 81.3%), but without statistically significant difference (p = 0.460). There was also no statistically significant difference in mean age (p = 0.577) and in professional groups (p = 0.551) between the two groups. However, a comparison of COVID and COVID free services showed that there was a higher percentage of positive cases among professionals working at COVID services (56.7%) compared to those working at COVID free services (37.4%), and this difference was statistically significant (p = 0.03).

Of the 420 (68.5%) symptomatic professionals (respiratory symptoms, or other), 27 tested positive for COVID-19 (6.43%), whereas only three of the 193 (1.55%) asymptomatic professionals with high-risk contact tested positive, with no statistically significant difference (p = 0.009).

Respiratory symptoms were present in 371 professionals, whereas 49 professionals had only

### Table 1. Sample characterization, Portuguese university hospital center, 2020 (n = 613)

| Variables                        | n (%)     |
|----------------------------------|-----------|
| Sex                              |           |
| Female                           | 500 (81.6)|
| Male                             | 113 (18.4)|
| Age (mean [standard deviation]) (years) | 41 (12.17)|
| Professional group              |           |
| Physicians                       | 197 (32.0)|
| Nurses                           | 179 (29.0)|
| Operations assistants            | 128 (21.0)|
| Diagnostic and therapeutic technicians | 44 (7.0)|
| Technical assistants             | 33 (6.0)|
| Other                            | 32 (5.0)|
| Classification                   |           |
| Symptomatic                      | 420 (68.5)|
| Respiratory symptoms             | 371 (61.3)|
| Non-respiratory symptoms         | 49 (11.7)|
| Asymptomatic                     | 193 (31.5)|

* χ² test. † Mann-Whitney U test.
non-respiratory symptoms. Of the 371 (88.3%) who presented respiratory symptoms, 19 tested positive for COVID-19 (5.12%) vs. 11 out of the 242 who did not have respiratory symptoms but had other symptoms or were asymptomatic (4.55%), with no statistically significant difference (p = 0.75).

Conversely, when comparing professionals who tested positive and negative for COVID-19 with regard to presence of respiratory and non-respiratory symptoms, there were 19 positive cases for COVID-19 with respiratory symptoms (5.12%) compared with eight (16.33%) positive cases with non-respiratory symptoms (Table 3). This difference was statistically significant (p = 0.003).

The more prevalent respiratory symptoms in the sample were cough (n = 236), odynophagia (n = 180), rhinorrhea (n = 78), dyspnea (n = 44), nasal congestion (n = 35), and sternutation (n = 12). However, the most common respiratory symptom in the group that had a positive RT-PCR test was nasal congestion (11.43%), followed by rhinorrhea (8.97%) and then cough (5.93% of positive cases). Odynophagia occurred in 1.77% of positive cases, and none of the 12 professionals who reported sternutation tested positive. It is worth highlighting that none of the 44 professionals who reported dyspnea tested positive for SARS-CoV-2 (Table 4).

The non-respiratory symptoms in the eight positive cases (Table 5) were headache (three cases), myalgia (three cases), ageusia (three cases), gastrointestinal changes (three cases), anosmia (two cases), and fever (two cases).

Thus, of the 30 positive cases, 63.33% of professionals had respiratory symptoms and 26.67% had non-respiratory symptoms, whereas 10% were asymptomatic.

**DISCUSSION**

The presentation of COVID-19 varies from asymptomatic to symptomatic, from mild respiratory infections and pneumonia to respiratory failure. ACE2 is abundant in alveolar type II cells and promotes binding between host cells and spike, a

| Table 3. Characterization of symptomatic professionals with and without coronavirus disease 2019 (COVID-19), Portuguese university hospital center, 2020 (n = 420) |
| --- |
| **Classification** | With COVID-19 (n = 27) | Without COVID-19 (n = 393) | **p-value** |
| Respiratory symptoms | 19 (512) | 352 (94.88) | 0.003 |
| Non-respiratory symptoms | 8 (16.33) | 41 (83.67) | 0.17 |

*χ² test.

| Table 4. Respiratory symptoms in professionals with and without coronavirus disease 2019 (COVID-19), Portuguese university hospital center, 2020 (n = 371) |
| --- |
| **Respiratory symptoms** | With COVID-19 (n = 19) | Without COVID-19 (n = 352) | **p-value** |
| Nasal congestion | 4 (11.43) | 31 (88.57) | 0.020 |
| Rhinorrhea | 7 (18.97) | 71 (91.03) | |
| Irritating dry cough | 14 (5.93) | 22 (94.07) | |
| Odynophagia | 3 (11.43) | 177 (88.57) | |
| Dyspnea | 0 (0.0) | 44 (100.0) | |
| Sternutation | 0 (0.0) | 12 (100.0) | |

*χ² test.

| Table 5. Non-respiratory symptoms in professionals with and without coronavirus disease (COVID-19), Portuguese university hospital center, 2020 (n = 49) |
| --- |
| **Non-respiratory symptoms** | With COVID-19 (n = 8) | Without COVID-19 (n = 41) | **p-value** |
| Fever | 2 (26.67) | 31 (93.33) | 0.0020 |
| Gastrointestinal changes | 3 (37.5) | 20 (86.96) | |
| Headache | 3 (37.5) | 20 (86.96) | |
| Myalgia | 3 (37.5) | 22 (87.8) | |
| Ageusia | 3 (37.5) | 3 (7.35) | |
| Anosmia | 2 (26.67) | 1 (25.64) | |

*χ² test.
glycoprotein present on the surface of the virus, which is why the lung is one of the most affected organs in individuals infected with SARS-CoV-2. Therefore, respiratory symptoms such as cough and dyspnea are understandably the most frequent ones, in addition to fever. Furthermore, other upper respiratory tract manifestations, such as nasal congestion, rhinorrhea, and odynophagia, are observed in individuals with mild disease. Progression to pneumonia, bronchitis, and respiratory distress syndrome may occur in moderate to severe cases. Thus, it is also understandable that samples from the respiratory tract are the most used to detect SARS-CoV-2.22,23

At the beginning of the pandemic, individuals who presented with respiratory symptoms and/or fever, recent history of travel to regions with known active transmission, as well as history or suspicion of contact with positive cases, were screened for SARS-CoV-2 infection. However, the detection of non-respiratory symptoms or upper respiratory tract symptoms in a great number of cases of COVID-19 warned to the need for clinicians to be attentive and to be aware of manifestations so that to reduce the risk of underdiagnosis of cases of SARS-CoV-2 infection.23

The clinical testing criteria most used in several national and international guidelines have been fever, cough, and breathing difficulty. In view of the evolution of the pandemic, these criteria have been broadened, and the WHO and the Centers for Disease Control and Prevention (CDC) recommend testing in the presence of two or three of the following symptoms: headache, odynophagia, nasal congestion, rhinorrhea, myalgia, fatigue, diarrhea, nausea, and/or vomiting.24 Indeed, during the period of this study, the Portuguese regulations on the definition of suspected cases established only fever, cough, and dyspnea as testing criteria. Subsequently, these criteria have been broadened to include anosmia and agueusia. However, the occupational health service has valued these symptoms since the beginning of the pandemic, undertaking testing and early isolation of professionals, so that more than a fourth of reported positive cases had non-respiratory symptoms.

A large European surveillance study that included individuals with mild to moderate disease reported that more than 80% of these cases presented with smell and taste changes, with anosmia being the most frequent olfactory symptom. These results reinforce the need to consider screening for COVID-19 in individuals with olfactory and taste changes.25

Sometimes these non-respiratory manifestations may be the initial symptoms of COVID-19, before fever and/or respiratory symptoms, or even be the only symptoms.23 Especially in the hospital context, it is important to value rapid onset symptoms, including those of the upper respiratory tract, proceeding with testing of healthcare professionals, since they could have a relevant impact on infection transmission.24 Equally important is the early isolation of these professionals, in order to prevent possible outbreaks. Our study revealed that, among professionals with respiratory symptoms, symptoms as non-specific as nasal congestion and rhinorrhea, associated with many other benign viral infections, were the most frequent respiratory symptoms among symptomatic professionals who tested positive for COVID-19.

The results for our study found that the percentage of symptomatic professionals with positive RT-PCR test was nearly four-fold higher than that of asymptomatic professionals with high-risk contact. This difference, which may be much greater than that described in other studies,26,27 may result from the valuation of very mild symptoms that could be ser devalued in other contexts.

Even though, we observed that 1.55% of asymptomatic professionals with high-risk contact tested positive in the RT-PCR test for SARS CoV-2. Early isolation and a detection of SARS-CoV-2 infection in initially asymptomatic individuals or who present with mild symptoms aid in reducing SARS-CoV-2 dissemination.26

Age has been shown as a risk factor for severe disease, meaning that younger infected individuals seem to be asymptomatic or with milder clinical manifestations, which may contribute to the spread of infection.13 In fact, this study included healthcare professionals of active age and predominantly healthy, which may explain the reported symptoms and their level of severity (mild to moderate). These results are important to raise awareness on the fact that, due to
the absence of symptoms or to the neglect of mild symptoms, the need of performing diagnostic tests may be devalued and, consequently, SARS-CoV-2 infection may be left undiagnosed.

It is crucial that healthcare professionals be aware of the varied clinical manifestations of COVID-19 in order to protect themselves more effectively and to make an early diagnosis of this infection, leading to the prompt isolation of sick individuals and their treatment, preventing possible nosocomial outbreaks and disease spread.

CONCLUSIONS

Our results showed that the percentage of COVID-19 in asymptomatic professionals with high-risk contact was nearly four-fold lower than that observed in symptomatic professionals, possibly because, in this study, very mild symptoms were valued, which could go unnoticed in other contexts. Therefore, it becomes crucial to value mild symptoms among healthcare professionals, even in the absence of high-risk contact.

Although COVID-19 is typically associated with respiratory symptoms, not all these symptoms were predictors of disease and probably result from other respiratory diseases, whether infectious or not. Cough was the most frequently observed symptom in the sample, but only 5.93% of professionals with this symptom were diagnosed with COVID-19. Nasal congestion and rhinorrhea were the respiratory symptoms with the highest proportion of positive cases (11.43 and 8.97%, respectively). However, no positive case presented with dyspnea, possibly because all positive cases found in our sample were of mild to moderate severity and were treated at home. Non-respiratory symptoms were present in more than a fourth of disease cases, and early isolation of healthcare professionals presenting with this type of symptoms will contribute to reduce viral transmission.

Given the variability of symptoms and the risk of transmission to vulnerable patients, it is important to value mild symptoms among healthcare professionals. The identification of the disease in asymptomatic workers reinforces the importance of the rigorous adoption of measures of hygiene and respiratory protection.

AUTHOR CONTRIBUTIONS

AIC was responsible for the study conceptualization, investigation, methodology, data curation and formal analysis, and writing – original draft and writing – review & editing. LG participated in the study investigation, resources, and writing – review & editing. CA, OS, DF, JR, JS, RL e MF participated in the study investigation, resources, and writing – review & editing. ESL participated in the study investigation, resources, supervision, validation, and writing – review & editing. All authors approved the final version submitted and assume public responsibility for all aspects of the work.

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