

Health Service Research

Infection with SARS-CoV-2 in primary care health care workers assessed by antibody testing

Korbinian Lackermair^a, Frederic William^b, Noelle Grzanna^b,
Elke Lehmann^b, Stephanie Fichtner^{a,e}, Hans Bernd Kucher^c, Karl Wilhelm^b
and Heidi Estner^{a,*}

^aDepartment of Medicine I, University Hospital Munich, Ludwig Maximilians University, Marchioninstr. 15, DE-81377 Munich, Germany, ^bMedizinisches Versorgungszentrum Dachau, Münchner Straße 64, 85221 Dachau, Germany and ^cLabor Augsburg MVZ GmbH, August-Wessels-Straße 5, 86154 Augsburg, Germany

*Correspondence to Heidi Estner, Department of Medicine I, University Hospital Munich, Ludwig Maximilians University, Marchioninstr. 15, DE-81377 Munich, Germany; E-Mail: Heidi.Estner@med.uni-muenchen.de

Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused a pandemic threat of public health during the last month causing more than 10 million infections and 500 000 deceased patients worldwide. Nevertheless, data about risk of infection for health care workers are sparse.

Methods: In a large primary care facility, 151 workers underwent SARS-CoV-2 immunoglobulin G (IgG) testing. In addition, participants had to complete a survey regarding symptoms and their individual risk of infection.

Results: Symptoms suspicious for COVID-19 occurred in 72%, fever in 25% of all subjects. Four workers (2.6%, 95% confidence interval 0.8–7.1%) had a positive SARS-CoV-2 antibody testing. None of these was free from COVID-19 suspicious symptoms. Source of infection was presumably professional in three of four individuals.

Conclusion: Our systematic analysis of SARS-CoV-2 infection in a cohort of health care workers in a large outpatient centre revealed an apparently low rate of 2.6% past SARS-CoV-2 infections. Relative risk for infection following health care profession cannot be derived as data about infection rates in the corresponding general population are lacking.

Keywords: Antibody testing, COVID-19, health care workers, infection rate, primary care, SARS-CoV-2.

Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) originating from Wuhan, China, emerged to a worldwide threat of public health with greater than 10 million infections and about 500 000 caused deaths so far. The infectious disease caused by SARS-CoV-2 was named COVID-19 by the World Health Organization at the beginning of the current year (1). COVID-19 presents with a large variety of severity ranging from acute respiratory distress syndrome with pronounced mortality to (nearly)

asymptomatic disease (2). SARS-CoV-2 testing is less frequent in patients with little or no symptoms, which might cause a high number of undiagnosed COVID-19 cases, as well as an underestimation of infection with SARS-CoV-2.

As SARS-CoV-2 is transmitted via airborne droplet infection and in direct contact to COVID-19 patients, all kinds of health care workers are at high risk of infection, in particular, if shortages of personal protection equipment exists (3,4). In Italy, infection rates of up to 25% of health care workers are reported (5).

Key messages

- The rate of infection with severe acute respiratory syndrome coronavirus 2 in a cohort of primary health care workers was 2.6%.
- No employee experienced asymptomatic COVID-19 infection.
- Estimation of professional relative infection risk is not possible.

Gold standard for the testing for SARS-CoV-2 infection is the proof of virus-specific nucleic acid using real-time polymerase chain reaction (RT-PCR) (6). Samples can be taken as a nasopharyngeal or oropharyngeal swab, from lower respiratory tract (e.g. sputum and bronchoalveolar lavage) or from specimens of blood or faeces (6). It has been shown that the traceability of SARS-CoV-2 within the described modalities of RT-PCR testing may change during the course of COVID-19 disease with pharyngeal tests converting to negative prior to COVID-19 recovery (7). Therefore, a random sample RT-PCR testing, especially from pharyngeal specimens, might be appropriate for the diagnosis of acute infections but not for the estimation of the total rate of overcome SARS-CoV-2 infections in a specific cohort.

During COVID-19, virus-specific antibodies against SARS-CoV-2 become detectable throughout the clinical course (8–13). Cross-reaction to harmless coronavirus subtypes challenges the development of COVID-19 antibody tests (14). Nevertheless, assays with a strong performance with respect to sensitivity and specificity as early as the fourth day after symptom onset have become available (8). This makes antibody tests an important complementary approach in testing, especially to overcome SARS-CoV-2 infection (15). Therefore, we sought to investigate SARS-CoV-2 infection by the measurement of SARS-CoV-2-specific immunoglobulin G (IgG) antibodies in a cohort of health care workers of a ‘high-volume COVID-19’ outpatient centre in Bavaria, Germany.

Methods

The ‘Medizinisches Versorgungszentrum Dachau’ (MVZ Dachau) is a medical supply centre in Bavaria, Germany, that covers a total of eight locations with 46 family doctors and 38 medical specialists. A total of 84 physicians and a total of 153 of receptionists and doctors’ assistants are working in this network. In normal times, 124 000 patients per year have been treated in the different locations.

About 150 000 people inhabit the district of Dachau. The first COVID-19 was diagnosed in the beginning of March. The Government of Bavaria imposed a generalized lockdown on 21 March. At the time of our study, 422 people were diagnosed with COVID-19 by PCR testing in the district of Dachau.

During the epidemic outbreak of SARS-CoV-2, the institution changed the way of supply and admission to the practices: before entering the institution, every patient was investigated for possible symptoms of COVID-19, known contact to COVID-19 patients or temporary residence in high-risk COVID-19 regions. In addition, body temperature was taken.

If one question was answered positive or the patient had elevated body temperature, they were not admitted to the practice and were being cared for in a separate treatment area where the staff was dressed in complete protective clothing, aiming to prevent any contact with healthy persons (medical staff and patients). Otherwise, the treatment was undertaken without specific personal protection equipment neither for the physician nor the patients. In cases where the patients felt healthy but a PCR test was indicated due to other

reasons (e.g. contact to COVID-19 patients), the patients were advised to take the diagnostic dipstick test by themselves. The test kit was deposited in a safe place together with a written instruction to enable the patients to take the test in the correct way by themselves. If a patient was not able to take the test by himself, the sample was taken by the medical staff in the separate COVID-19 treatment area.

The physicians and doctors’ assistants did not wear protective dresses in their regular consultation hours. During their rest or lunch hours, no particular protection arrangements have been established until the beginning of April. In the time from the outbreak until 3 April, a total of 2326 PCR tests have been undertaken, 236 of which were tested positive (56% of all 422 diagnosed patients in the district of Dachau).

Blood samples of every health care professional were taken from 2 to 6 April. Measurement of SARS-CoV-2 was performed using commercially available IgG Immunoassay (ELISA) Kits according to the manufacturer’s instruction (EUROIMMUN, Lübeck, Germany). During the clinical course of COVID-19 disease, IgG responses after 1 week and maintains at high levels for at least 6 weeks, most likely longer (16). The S1 protein, important for viral host cell entry, serves as target antigen. S1 protein shows very little homology with other human pathogen coronaviruses, except for SARS-CoV-1 and MERS-CoV. Thus, the applied assay ensures discrimination from other coronaviruses often causing trivial common cold. In addition, participants were asked to complete a standardized survey. Items were: contact with COVID-19 patients (private or professional); temporary residence in high-risk SARS-CoV-2 regions [i.e. Egypt, Italy, Austria, France, Iran, Switzerland (Canton Tessin, Waadt and Genf), Spain, South Korea (Daegu and Gyeongsangbuk-do) and USA (California, New York, New Jersey and Washington)], if yes: when; and symptoms suspicious for COVID-19 (dry cough, shortness of breath, sniff, fever, chills, fatigue, sore throat, headache, limb pain, impaired sense of taste and diarrhoea), if yes: time course. The questionnaire about COVID-19 suspicious symptoms referred to the whole period since SARS-CoV2 became present in Germany in the beginning of March.

Due to limitations of nationwide test capacity for PCR testing, no systematic and repeated screening measurement of the staff took place in this early phase of the SARS-CoV2 pandemic in Germany. In addition, only subjects with a high pre-test probability plus suspicious symptoms underwent PCR testing in the beginning (i.e. fever plus known contact to COVID patients or residency in risk region). Nevertheless, during later study period as soon as the limitation of nationwide test capacity was overcome, every subject with suspicious symptoms underwent PCR testing. Ethical safety of our study was approved by the local ethics committee (accession number 20-311KB)

Results

Of 237 health care workers, 60 did not have direct contact with patients or other staff members (e.g. members of administration) or were off duty during the study period. One hundred seventy-seven workers underwent antibody testing. Twenty-six of these 177 did not complete

the above described survey and were, therefore, excluded from further analysis. The final cohort consisted of a total of 151 health care workers (54 physicians and 97 assisting health care workers).

In the survey, 108 (72%) probands reported symptoms suspicious for COVID-19 and 37 (25%) reported fever. Thirty-one subjects (21%) reported a temporary residence in a high-risk SARS-CoV-2 region. Forty-two health care workers (28%) reported a known, unprotected contact with a COVID-19 index patient. Characteristics are depicted in Table 1.

Positive SARS-CoV-2 IgG titre was found in four workers (2.6%, 95% confidence interval 0.8–7.1%). No significant differences between positive and negative IgG-tested workers were seen for sex, age, contact with index patients, temporary residence in a high-risk SARS-CoV-2 region, symptoms or occurrence of fever. In 48 workers (32% of the total cohort), a total of 87 prior RT-PCR tests from oropharyngeal swab were made. Two subjects of the SARS-CoV-2 IgG-positive group workers underwent prior RT-PCR testing, one with a positive result. RT-PCR from 46 workers with negative SARS-CoV-2 IgG titre were negative, except for one subject with acute COVID-19 infection and positive RT-PCR and IgG antibody testing 3 days after symptom onset, which was negative at that time.

The four health care workers (three physicians) with positive SARS-CoV-2 IgG titre had proven and direct contact with index patients in two cases (Table 2). None of the four subjects experienced infection without COVID-19 suspicious symptoms, one physician required in-hospital treatment, the duration of symptoms ranged from 2 days up to 3 weeks. The chain of infection was most likely starting in the family during the temporary residence in the high-risk region Tirol, Austria, in one worker. The three remaining cases were most likely derived from professional exposition.

Discussion

To the best of our knowledge, this is the first report studying infection with SARS-CoV-2 in a cohort of health care workers in a high-volume COVID-19 primary care centre.

Our major findings were:

- high proportion of subjects with COVID-19 suspicious symptoms (72%) and/or fever (25%)
- positive S1 protein binding IgG antibodies in 4 of 151 workers (2.6%)
- all had potential COVID-19 symptoms
- a most probable infection during professional practice in three of four subjects.

Data about SARS-CoV-2 infections of health care professionals are of poor scientific value and estimations of incidence are, in part, derived from preliminary scientific reports (that did not undergo peer review) or originate from local media. Especially, these reports describe horrifying infection rates in health care workers of up to 20% (17). The reports of these infection rates often fail to describe the way of identification of infected workers (clinical diagnosis, PCR testing and antibody testing) (3). This may lead to significant overestimation of infection rates when COVID-19 is diagnosed clinically, as 72% subjects of our cohort reported COVID-19 suspicious symptoms. The only certain knowledge is the number of deceased workers in some US federal states (18); still, the origin of disease, if private or professional, remains unclear even in that population.

Folgueira *et al.* described data from Madrid, Spain (19). Therein, a symptom or contact-driven PCR serial testing of 2085 hospital employees (30.6% of the total staff) retrieved positive results in 38% of all tested or 11.6% of all hospital employees.

Madsen *et al.* sought to investigate the infection of health care workers in a US emergency department systematically (20). A total of 279 employees underwent IgG antibody testing with the EUROIMMUN test assay. Employees participated voluntarily and were not selected for participation based on symptoms nor previous exposure to COVID-19. A proportion of about 82% was tested with a positive result in 5.9%.

Our survey is comparable to Madsen's report (20) with respect to testing principle and selection of tested workers on a voluntary basis. The testing rate of our survey was almost the same (85 vs. 82%). Nevertheless, there was a distinct difference of SARS-CoV-2 IgG-positive workers (5.9 vs. 2.6%). Reported rates of COVID-19

Table 1. Clinical characteristics

	Total	SARS-CoV-2 IgG positive	SARS-CoV-2 IgG negative	P
<i>n</i>	151	4 [2.6]	147 [97.4]	–
Female sex, <i>n</i> [%]	126 [83]	2 [50]	124 [84]	0.13
Age	38 [26–47]	40 [24–45.5]	38 [26–48]	
Covid IgG titre	0.2 [0.1–0.3]	1.4 [1.2–4.7]	0.2 [0.1–0.3]	<0.01
Contact to index patient [%]	42 [28]	2 [50]	40 [27]	0.32
Temporary residence at high-risk SARS-CoV-2 region	31 [21]	1 [25]	30 [27]	0.8
Symptoms (i.e. cough or shortness of breath)	108 [72]	4 [100]	104 [71]	0.2
Fever	37 [25]	3 [75]	34 [23]	0.02
Pre-ceeding COVID-19 PCR, [%]	48 [32]	2 [50]	46 [31]	0.46
PCR positive, <i>n</i> [%]	2 [4]	1 [50]	1 [2]	0.18

Table 2. Characteristics of subjects with positive SARS-CoV-2 IgG titre

	Age	Sex	PCR	COVID-19 IgG titre	Symtoms (i.e. cough or shortness of breath)	Fever	Contact to index patient
Subject 1	19	Male	NA	1.4	Yes	No	No
Subject 2	41	Female	Positive	5.8	Yes	Yes	No
Subject 3	47	Female	Negative	1.1	Yes	Yes	Yes
Subject 4	39	Male	NA	1.4	Yes	Yes	Yes

infection in the district of Dachau were 334 cases/100 000 inhabitants and 103 cases/100 000 in Utah. However, these incidences are not comparable due to different modalities and indications for testing. As a consequence, an estimation of the relative risk for infection for health care workers in the current studies is not possible as real incidence of the referring population remains unclear.

Folgueira's study reported 38% positive SARS-CoV-2 PCR tests representing 11.6% of all hospital employees. Nevertheless, true incidence in this Spanish hospital was presumptively higher, as PCR testing is not suitable for the estimation of total rates of infection as described above and no asymptomatic employee was tested. Even so, no asymptomatic case of COVID-19 appeared in our current cohort.

In this context, our rate of 2.6% SARS-CoV-2 IgG-positive-tested health care workers appears to be rather low. One explanation could be that a high utilization of health care system with exhaustion and shortages of personal protection equipment increases infection rates in health care workers (17). The Reports by Madsen and Folgueira do not provide details about the utilization of hospital resources and availability of personal protection equipment. However, no shortage of the above described was present in our facilities within and prior to the study period.

Our study has several limitations: First, about 15% of the COVID-19-exposed cohort had to be excluded from analysis due to an incomplete survey. Second, as PCR testing was not done in each subject at the time of antibody testing, the used questionnaire was non-validated, and latency of antibody testing is up to 3 weeks an underestimation of infected workers is thinkable. Third, our results raise an urgent call for confirmation before generalization from our study results to other primary care facilities might become appropriate.

Conclusion

Our systematic analysis of SARS-CoV-2 infection in a cohort of health care workers in a large outpatient centre revealed an apparently low rate of 2.6% past SARS-CoV-2 infections. Relative risk for infection following health care profession cannot be derived as data about infection rates in the corresponding general population are lacking.

Declarations

Funding: none.

Ethical approval: ethical safety of our study was approved by the local ethics committee (accession number 20-311KB).

Conflict of interest: none.

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