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COVID-19: Hotspot hospital? - seroprevalence of SARS-CoV-2 antibodies in hospital employees in a secondary care hospital network in Germany: Intermediate results of a prospective surveillance study

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ARTICLE INFO

Keywords:
SARS-CoV-2
Coronavirus
COVID-19
Antibodies
Healthcare workers

ABSTRACT

Purpose: The objective of the ongoing study was to investigate how SARS-CoV-2 infection spread within two hospitals in North Rhine-Westphalia, Germany by testing the employees working in high-risk, intermediate-risk and low-risk-areas for the presence of SARS-CoV-2 IgG antibodies. Presented intermediate results evaluate the first infection period until the end of September 2020.

Methods: The study “COVID-19: Hotspot hospital? - Seroprevalence of SARS-CoV-2 antibodies in hospital employees in a secondary care hospital network in Germany” is a prospective, single centre observational cohort study conducted at the St. Vincenz Hospital Datteln with 316 beds. The presented data include one other hospital: St. Laurentius Stift Waltrop, Germany with 172 beds.

Results: Between June 2020 and September 2020 we analyzed serum samples of 907 employees which represents 62.1% of all employees. Thirteen employees (1.4%), respectively 13/696 healthcare workers (HCWs) (1.9%) had detectable SARS-CoV-2 IgG antibodies. Among them, 4 (30.8%) were aware of COVID-19 exposure, and 5 (38.5%) reported clinical symptoms. HCWs working in high-risk areas had a seroprevalence rate of 1.6% (1/64), HCWs working in intermediate-risk area 1.7% (11/632) and 0.5% employees (1/211) in low-risk areas with no contact to patients were seropositive.

Conclusion: Even if we treated COVID-19 positive patients, we found no clear evidence that infection was transmitted to HCWs in contact to these patients. As knowledge about SARS-CoV-2 transmission evolves, the concept of infection prevention must be continuously reviewed and adapted as needed to keep hospitals a safe place.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel beta coronavirus that was first identified in December 2019 in Wuhan, China (Huang et al., 2020; Ralph et al., 2020). At the beginning of 2020 the virus spread and became pandemic (Abebe et al., 2020; Whitworth, 2020). The WHO declared a global health emergency on January 31, 2020; subsequently, on March 11, 2020, they declared it a pandemic situation (Dhama et al., 2020). SARS-CoV-2 infection is presented clinically as corona virus disease 2019 (COVID-19) with a broad range of symptoms from asymptomatic and mild to critical courses (Guan et al., 2020; Pergolizzi et al., 2020). There are no specific symptoms that can suggest COVID-19 compared to symptoms of respiratory illnesses caused by other viruses, such as influenza and common cold (Abebe et al., 2020). The gold standard for diagnosing COVID-19 is the detection of SARS-CoV-2 viral nucleic acid using a quantitative real time-PCR (qRT-PCR) from respiratory tract samples (e.g. throat swabs) (Abebe et al., 2020). Rapid antigen tests provide a promising scheme for timely monitoring and eventual control of the global pandemic (Li et al., 2020). Antibody testing surveys can aid the investigation of an ongoing outbreak and retrospective assessment of the attack rate or extent of an outbreak. However, serological tests cannot be applied to early infection (Li et al., 2020).

The primary means of transmission is person to person through...
droplets that occurred during coughing or sneezing, through personal contact (shaking hands), or by touching contaminated objects (Abebe et al., 2020). Additionally, aerosols from infected persons may pose an inhalation threat even at considerable distances and in enclosed spaces, particularly if there is poor ventilation (Meselson, 2020).

As a consequence nosocomial transmission of inadequately protected healthcare workers (HCWs) can occur during aerosol generating procedures (Patel et al., 2020), but also in the regular contact to patients with delayed diagnosis of COVID-19 and in close contact to asymptomatic or presymptomatic virus carriers (patients or colleagues) which can also spread the virus (Chou et al., 2020a, b; Khonyongwa et al., 2020; Zhao et al., 2020).

In summer 2020, more than 1.3 Mio HCWs have been tested positive for SARS-CoV-2 worldwide (Fischer-Fels, 2020). Hence it is of great importance to implement infection prevention strategies in the health care sector and provide sufficient personal protection equipment (Chou et al., 2020a).

Data from German HCWs are scarce so far and mainly focussed on university hospitals (Bahrs et al., 2020; Brehm et al., 2021; Korth et al., 2020). The primary objective of this study was to investigate the SARS-CoV-2 infection spread within two hospitals of a secondary care hospital network in North Rhine-Westphalia, Germany by testing employees for the presence of SARS-CoV-2 IgG antibodies. Secondary objectives were to identify potential risk factors for infection and clinical symptoms of seropositive employees. Furthermore, we wanted to evaluate the results with regard to the number of treated COVID-19 positive patients and employees that were tested with PCR within the scope of contact tracking during the first period of SARS-CoV-2 infection.

2. Methods

2.1. Study design

The study “COVID-19: Hotspot hospital?- Seroprevalence of SARS-CoV-2 antibodies in hospital employees in a secondary care hospital network in Germany” is a prospective, single centre observational cohort study conducted at the St. Vincenz Hospital Datteln with 316 beds. The hospital belongs to the group Vestische Caritas Kliniken GmbH. Until end of September 2020 one other hospital of this group also took part in our study so far: St. Laurentius Stift Waltrop with 172 beds. The study is designed from June 2020 to June 2021. We want to publish intermediate results for the period June 2020 to September 2020 in order to look at the first surge of the new pandemic virus.

Research was conducted in accordance with the declaration of Helsinki and national standards. The study protocol was approved by the local ethics committee: Ärztekammer Westfalen-Lippe and Westfälische Wilhelms Universität Münster (approval no.2020-478-F-S). The study was registered at the German Clinical Trials Register (DRKS00022941).

2.2. Enrolment and data management

Participants were recruited since June 1, 2020. All employees of the St. Vincenz Hospital Datteln and St. Laurentius Stift Waltrop working with (HCWs) and without patient contact were addressed to take part. They received information about the study via intranet platform. Participation was voluntary and free of charge.

Employees were included if they put their laboratory number on a 3 paged document so that we could assign the sample to the person. This written informed consent included a questionnaire and agreement on providing a blood sample (not exceeding 9 ml of venous blood). Pseudonymized blood samples were sent to our central laboratory for testing of antibodies against SARS-CoV-2. Data from pseudonymized questionnaires were collected and processed with MS Excel 2010.

2.3. Questionnaire

The questionnaire included information on personnel data like name, address, telephone number and working area for future contacting. Individual medical history contained clinical symptoms within the last two months such as fever, taste disturbances and smell disorders, dry cough, headache, growing pains, cold-like symptoms, exposure to confirmed COVID-19 cases, results of previous polymerase chain reaction (PCR) or previous serology.

2.4. SARS-CoV-2 antibody testing

Presence of SARS-CoV-2 antibodies were investigated with a chemiluminescence-based immunoassay Elecsys, Anti-SARS-CoV-2 (Roche, Basel, Switzerland). The immunoassay targets recombinant nucleocapsid protein and was carried out according to manufacturers’ instructions. Sensitivity and specificity as provided by the manufacturer was high (>99%). Volunteers with positive test results were regarded as SARS-CoV-2 seropositive. Re-testing was offered to all participants during the test period June 2020 to June 2021. We now only present results of the first point of testing.

2.5. Outcomes

The primary outcome of the study was to assess the seroprevalence of SARS-CoV-2 antibodies in hospital employees using an IgG detecting immunoassay. The study is still running. As we could see a clearly marked first pandemic infection period until end of September 2020, we decided to evaluate these data and publish intermediate results.

Secondary outcomes were: (i) differentiation between HCWs working in high-risk areas with contact to COVID-19 positive patients, HCWs working in intermediate-risk areas with contact to non-COVID-19 positive patients and employees working in low-risk areas with no contact to patients at all (personnel working in administration, kitchen, cleaning service, and others), (ii) potential risk factors and clinical symptoms for seropositive employees and (iii) evaluating the results with regard to infection risk of HCW according to the number of treated COVID-19 positive patients and employees that were tested with PCR within the scope of contact tracking.

2.6. Statistical analysis

In descriptive analysis participants demographics, professions, symptoms, and other attributes of COVID-19 exposure were determined and compared for the whole cohort and stratified by antibody test result using absolute and relative frequencies. Associations of characteristics with test results was statistically tested by Fisher exact test. Alterations of risks for a positive antibodies test result was estimated by univariable logistic regression, giving odds ratios and 95% confidence intervals versus the reference level for each main category of the characteristics or change per unit (for number of symptoms). We applied a significance level of 0.05. Analyses were done using the statistical programming software R (R Core Team (2020). R: A language and environment for statistical computing. R foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Characteristics of the study participants

From June 2020 to the end of September 2020 nine hundred seven of 1460 (62.1%) employees of two hospitals (St. Vincenz Hospital Datteln, St. Laurentius Stift Waltrop) with together 488 beds took part in our study (Table 1).

Among the 907 participants 136 (15.0%) were males and 771 (85.0%) were females. We categorized three age groups: 16–25 years (n
A cluster of 7 seropositive HCWs (58.3%) worked on one psychiatric ward. One of these employees reported an exposure to a COVID-19 positive family member, but received an initially negative PCR result. Therefore this employee kept working with a surgical face mask until the second PCR test turned out to be positive. This happened at the beginning of April 2020, when we did not have established universal masking in the hospital, yet. Furthermore, we were not working generally with FFP-2 masks at that time. As the St. Laurentius Stift in Waltrop had no COVID-19 positive patient in the first infection period (Table 1), sero-positive HCWs in this hospital presumably acquired their infection not in contact with patients, but more likely during break times or private contact.

Among the altogether 13 employees with detectable SARS-CoV-2 IgG antibodies we found the following characteristics: Twelve (92.3%) were HCWs, 1 (7.7%) was working with no direct contact to patients in the laboratory. The profession and risk group at work had no statistic significant influence on the risk of positive SARS-CoV-2 IgG antibody detection (Table 2).

Only 1 employee (7.7%) was working in contact with COVID-19 positive patients. Four (30.8%) reported known exposure to COVID-19 positive persons (at work or at home) and 10 (76.9%) had previously known positive PCR results. Statistical analysis revealed significance for the risk of SARS-CoV-2 positive antibody test in case of known contact to a COVID-19 positive person (p = 0.005) and previously performed PCR test (p < 0.001) (Table 2).

Three employees (23.1%) got to know about their previous infection only through the result of the SARS-CoV-2 antibody test. Only 5 employees (38.5%) reported clinical symptoms within the last two months: cold-like symptoms (2), fever (3), headache (3), cough (1) and taste or smell disorders (2). The number of clinical symptoms was not statistical significant. However, we found statistical significance for fever (p = 0.036) and taste or smell disorders (p = 0.047) as expected (Table 2).

### 3.4. Context to PCR positive patients and staff

From March 2020 to September 2020, we treated 53 SARS-CoV-2 positive patients in the St. Vincent Hospital Datteln: 29 patients were hospitalized in our COVID-19 ward, 2 of them were treated on the ICU, 4 patients died and 24 outpatients were seen at the emergency department. Surprisingly no COVID-19 positive patients were treated in the St. Laurentius Hospital Waltrop during the first period of infection (Table 1). Although we established general testing of patients on admission not until August 2020, all patients who were admitted from other hospitals to the hospital in Waltrop were tested for SARS-CoV-2 since April 2020 (Table 3).

On 27-Apr-2020 mandatory masking for all employees at the hospitals was implemented. Therewith we were nearly four weeks later than other regions in Germany, e.g. the University Hospital in Jena which implemented mandatory masking on 20-Mar-2020 (Bahrs et al., 2020).

We did not test employees routinely for SARS-CoV-2, but according to the recommendations of the Robert Koch Institute (RKI) at that time, employees were tested with PCR in case of cold-like symptoms of any severity, exposure to COVID-19 positive persons and returning from a region at risk (Robert Koch Institute, 2020). According to the RKI definitions we initiated 812 SARS-CoV-2 PCR tests in employees until the end of September 2020. Four employees working at the St. Vincenz Hospital Datteln were tested SARS-CoV-2 PCR positive, in 2 of them we found SARS-CoV-2 IgG antibodies in our study (Table 1).

Eight patients on regular wards turned out to be SARS-CoV-2 positive so that we did contact tracing and testing of contact patients and employees. At the time we did not have universal masking, one positive patient resulted in up to 54 contact persons that were not protected properly. Fortunately, none of the contact persons of these 8 patients was infected through the exposure.

We reduced the number of exposed persons in COVID-19 positive patients by implementation of universal masking of employees and patients in situation of close contact and training of the awareness of adequate protection.

### Table 1
Basic information on the conditions in both hospitals in general and with regard to SARS-CoV-2 infections during the first infection period (until the end of September 2020).  

| Basic information | St. Vincenz Hospital Datteln | St. Laurentius Stift Waltrop | Total number |
|-------------------|-------------------------------|-------------------------------|--------------|
| Beds              | 316                           | 172                           | 488          |
| Employees         | 1085                          | 375                           | 1460         |
| SARS-CoV-2 IgG antibodies tested employees | 671 (61.8%) | 236 (62.9%) | 907 (62.1%)^a |
| **COVID-19 patients** |                               |                               |              |
| Hospitalized patients | 29                          | 0                             | 29           |
| Patients on intensive care unit | 2                          | 0                             | 2            |
| Patients died | 4                             | 0                             | 4            |
| Outpatients       | 24                            | 0                             | 24           |
| **SARS-CoV-2 infection in employees**^b |                        |                               |              |
| IgG antibodies positive | 5                           | 8                             | 13           |
| PCR positive      | 4                             | 0                             | 4            |
| PCR positive, IgG antibodies negative | 2                           | 0                             | 2            |

^a Total number of all tested employees is 907.

^b Multiple answers possible.

= 124), 26–40 years (n = 254) and >40 years (n = 515). The background for this was the assumption that participants in these 3 categories might have different composition of their households (e.g. <25 years: less children, 26–40 years: young children, >40 years: older children) and consequently different risks for acquiring SARS-CoV-2 infection outside the hospital. However, we unfortunately did not collect these data (Table 2). The most common professions were nurses (n = 488; 53.8%), followed by medical doctors (n = 98; 10.8%), care workers (n = 78; 8.6%) administration staff (n = 81; 8.9%), therapists (n = 37; 4.1%), cleaning personnel (n = 31; 3.4%) and employees working in the kitchen service (n = 20; 2.2%). Six hundred ninety-six employees (76.7%) were HCWs with close contact to patients. Sixty-four HCWs (7.1%) were working in high-risk areas with regular contact to COVID-19 positive patients in the emergency department, COVID-19 ward or intensive care unit (ICU). Six hundred thirty-two employees (67.8%) were SARS-CoV-2 IgG antibodies positive, 205 (41.7%) worked in contact with COVID-19 positive patients. Four (30.8%) reported known exposure to COVID-19 positive persons (at work or at home) and 10 (76.9%) had previously known positive PCR results. Statistical analysis revealed significance for the risk of SARS-CoV-2 positive antibody test in case of known contact to a COVID-19 positive person (p = 0.005) and previously performed PCR test (p < 0.001) (Table 2).

Three employees (23.1%) got to know about their previous infection only through the result of the SARS-CoV-2 antibody test. Only 5 employees (38.5%) reported clinical symptoms within the last two months: cold-like symptoms (2), fever (3), headache (3), cough (1) and taste or smell disorders (2). The number of clinical symptoms was not statistical significant. However, we found statistical significance for fever (p = 0.036) and taste or smell disorders (p = 0.047) as expected (Table 2).
As RKI recommendations were adapted continuously according to the knowledge of science we implemented infection control measures in both hospitals (Table 3).

### 4. Discussion

We found a low seroprevalence (1.4%) of SARS-CoV-2 IgG antibodies in the investigated employees of two hospitals belonging to a secondary care hospital network in North Rhine-Westphalia, Germany. Even if we also consider previously reported positive PCR results of seronegative employees we just reached an infection rate of 1.7%. Two other studies in Germany reported seroprevalence rates of hospital workers: 2.7% at the University hospital in Jena (Bahrs et al., 2020) and 1.8% at the University Medical Center Hamburg-Eppendorf (Brehm et al., 2021).

Regarding HCWs in our study, 1.7% of them (12/696) had detectable SARS-CoV-2 IgG antibodies. Similar results were published from Korth et al. with 1.6% seropositive HCWs (5/316) at the University Hospital Essen, which is a closely related region in North Rhine-Westphalia, Germany (Korth et al., 2020). We detected the highest seroprevalence in intermediate-risk HCWs (1.7%), followed by high-risk HCWs (1.6%)
and the lowest seroprevalence in low-risk employees (0.5%). Two other studies in Germany reported similar results: a higher seroprevalence rate in intermediate-risk HCWs (Essen: 5.4%; Jena: 2.9%) compared to high-risk HCWs (Essen:1.2%; Jena: 1.5%) (Bahrs et al., 2020; Korth et al., 2020). Bahrs et al. even found the highest seroprevalence rate in employees working in low-risk areas (3.3%) (Bahrs et al., 2020).

Another study at the University hospital in Münster, Germany investigated HCWs with PCR soon after reported exposure to COVID-19 positive persons. In this setting they found 5.4% of tested HCWs infected. As HCWs with no known exposure were not tested in this setting, infection rate in HCWs in total was probably lower (Schwierzeck et al., 2020). According to a recent analysis of SARS-CoV-2 infections reported to the RKI, in Germany 273 720 laboratory confirmed infections were recorded until the end of September 2020, 15 946 (5.8%) in employees in medical institutions (Kramer et al., 2020).

Seroprevalence rates among HCWs outside Germany range from 4.0% to 11.9% (Garcia-Basteiro et al., 2020; Goenka et al., 2020; Iversen et al., 2020; Self et al., 2020). A New York City (NYC) hospital even reported a SARS-CoV-2 antibodies seroprevalence rate of 27% in HCWs (Venugopal et al., 2020).

Personal protective equipment was available in our hospitals all the time. As the RKI recommendations to prevent infections in healthcare facilities were adapted continuously, we started to screen all visitors for symptoms of COVID-19 infection with a questionnaire and visitors used facemasks. Additionally we implemented universal masking of employees and patients in close contact at 27-Apr-2020. Later on we extended the use of facemasks to HCWs all the time and implemented a risk adapted screening of all patients resulting in a PCR test of high-risk patients. Since 10-Aug-2020 all patients in both hospitals were screened with PCR on admission. Even if we had no documented SARS-CoV-2 infection that clearly resulted from contact to a positive patient, we cannot rule out this scenario.

The strength of our study is the high percentage of employees that took part, representing 62.1% of all employees. Nevertheless, our study had limitations. As we did not test at defined points, we are not able to evaluate the effect of the described infection control interventions on prevention of nosocomial transmissions.

5. Conclusion

In our study we conclude that the two included hospitals were not hotspots for SARS-CoV-2 infection until the end of September 2020. The seroprevalence rate was low and we had no documented transmission of the infection that clearly resulted from contact to COVID-19 positive patients. Although we had numerically more HCWs with detectable SARS-CoV-2 IgG antibodies than employees with no contact to patients, community transmission might have played a larger role for COVID-19 infection than professional exposure during the first period of infection. However, this resulted from an overall low exposure of hospital employees to COVID-19 positive patients in the investigated hospitals at a time where the region was not a SARS-CoV-2 hotspot. As the knowledge about the way of transmission, symptoms and diagnosis of COVID-19 is increasing, it will be necessary to adapt the concept of infect prevention continuously to keep the hospital a safe place.

Funding

The study was financed by internal funding.

Availability of data and material

The datasets and materials used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Anke Hildebrandt and Oktay Hökelekli. Statistic analysis was performed by Henrik Rudolf. The first draft of the manuscript was written by Anke Hildebrandt and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval

Research was conducted in accordance with the declaration of Helsinki and national standards. The study protocol was approved by the local ethics committee: Arztekammer Westfalen-Lippe and Westfälische Wilhelms Universität Münster (approval no.2020-478-f-S). The study was registered at the German Clinical Trials Register (DRKS00022941).

Consent to participate

Informed consent was obtained from all included participants included in the study.

Consent for publication

Informed consent was obtained from all included participants that anonymized data will be published.

Declaration of competing interest

On behalf of all authors, the corresponding author states that there are no competing interests to declare.

Acknowledgements

We thank Wolfgang Mueller for the possibility of internal funding and Alide Vrielink for excellent technical support.
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