First reported nosocomial outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a pediatric dialysis unit

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Summary: Forty-eight cases were involved in a nosocomial outbreak of SARS-CoV-2 infections in a pediatric dialysis unit due to person-to-person transmission. Our results outline strategies to trace and monitor SARS-CoV-2 infected health care workers including virology testing and infection control measures.

Abstract

Background: Coronavirus disease 2019 (COVID-19) is a life-threatening respiratory condition caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was initially detected in China in December 2019. Currently, in Germany over 140,000 cases of COVID-19 are confirmed. Here we report a nosocomial outbreak of SARS-CoV-2 infections in the pediatric dialysis unit of the University Hospital of Münster (UHM).

Methods: Single-step real-time RT-PCR from nasopharyngeal swaps was used to diagnose the index patient and identify infected contacts. Epidemiological links were analyzed by patient interviews and chart reviews. In addition, each contact was assessed for exposure to the index case and monitored for clinical symptoms. Threshold cycle (C_t) values of all positive test results were compared between symptomatic and asymptomatic cases.

Results: Forty-eight cases were involved in this nosocomial outbreak. Nine contact cases developed laboratory confirmed COVID-19 infections. Two SARS-CoV-2 positive cases remained clinically asymptomatic. Eleven cases reported flu-like symptoms without positive results. C_t values were significantly lower in cases presenting typical COVID-19 symptoms, suggesting high viral shedding ($p = 0.007$).

Conclusion: Person-to-person transmission was at the heart of a hospital outbreak of SARS-CoV-2 between healthcare workers (HCWs) and patients in the pediatric dialysis unit at the UHM. Semi quantitative real-time RT-PCR results suggest that individuals with high viral load pose a risk to spread SARS-CoV-2 in the hospital setting. Our epidemiological observation highlights the need to develop strategies to trace and monitor SARS-CoV-2 infected HCWs in order to prevent COVID-19 outbreaks in the hospital setting.

Keywords: nosocomial SARS-CoV-2 outbreak, COVID-19, super-spreader, exposure-based risk classification, infection control measures

Introduction

In December 2019, SARS-CoV-2, a novel B lineage betacoronavirus was discovered in Wuhan City, Hubei province, China [1,2]. SARS-CoV-2 causes COVID-19, a severe respiratory syndrome that is associated with fever, cough, dyspnoea, myalgia and fatigue [3]. On March 11th, 2020 the WHO declared COVID-19 a pandemic and currently SARS-CoV-2 infections pose a serious threat to health care systems worldwide [4]. SARS-CoV-2 is the third member of the *coronaviridae* family, with the Severe Acute Respiratory Syndrome-Coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Virus (MERS-CoV), to cause major epidemic outbreaks in the last twenty years [2,5,6]. Recent studies demonstrate that SARS-CoV-2 is more contagious than SARS-CoV and MERS-CoV [7]. While persistence of SARS-CoV-2 has been described on inert surfaces, person-to-person transmission via droplets is believed to be the main mode of transmission followed by an incubation period of five days on average before onset of illness [2,7,8].

Several publications have described nosocomial transmission for the current COVID-19 pandemic [9,10]. It has been estimated that more than 3,300 health care workers (HCWs) in China have been infected with SARS-CoV-2 during the outbreak and in Italy, an estimated 20% of those infected were HCWs [11]. However, detailed epidemiological characterization of transmission chains in the hospital setting remains scarce. Consequently, there is concern that infection control measures are not adequate to prevent SARS-CoV2 transmissions between individuals in healthcare settings.

The first COVID-19 case in Germany was diagnosed on January 27th, 2020 and the first case of SARS-CoV-2 infection at the UHM was detected on February 29th, 2020 [12]. The UHM is a 1,500-bed university hospital in the federal state of North-Rhine-Westphalia (NRW), Germany with a catchment area of 310,000 inhabitants. By the beginning of April over 140,000 cases of COVID-19 have been detected in Germany and over 29,000 cases of COVID-19 in the region of NRW [13].

Here we describe an outbreak of SARS-CoV-2 among 28 HCWs, 13 patients and seven accompanying persons (ACP) at the pediatric dialysis unit of the UHM. Recently the European Dialysis (EUDIAL) working group of the European Renal Association-European Dialysis Transplant Association (ERA-EDTA) has classified uremic patients on hemodialysis as a risk group for COVID-19 infection due to an impaired immune system, high burden of comorbidities and frequent hospitalization [7].

As the pandemic continues to spread, it will be important to establish effective infection control strategies to protect frontline HCWs and patients from nosocomial SARS-CoV-2 infections. Here we provide a detailed contact investigation including clinical and laboratory findings of all individuals associated with the outbreak. Our observation emphasizes that nosocomial SARS-CoV-2 outbreaks require effective infection control strategies to prevent transmission within the hospital setting.

Methods

Epidemiological data collection

Individuals with laboratory-confirmed SARS-CoV-2 infection were recorded as COVID-19 cases. Contacts were identified based on potential exposure to the index case on the day of the index case's symptom onset. For the purposes of this outbreak investigation, day 0 was considered as two days prior to the day of first symptoms for the index case. Cases were classified as hospital-acquired, if SARS-CoV-2 real time reverse transcriptase polymerase chain reaction (RT-PCR) was positive after contact to the index case without any alternative source of transmission (e.g. SARS-CoV-2 positive household contacts).

Patients, ACP and HCW were interviewed to identify COVID-19-typical symptoms (n=11) each day, for ten days, and trace additional individuals that had contact with the index case while symptomatic.

Exposure risk classification, monitoring of contacts and hygienic measures

Persons with contact to SARS-CoV-2 infected individuals were assessed for their type of exposure with the help of a risk-based questionnaire, adopted from the guidelines issued by the Robert-Koch Institute (RKI), Germany's national Public Health Institute. The criteria considered for the different types of exposure were duration of exposure, personal protective equipment (PPE) used during exposure, distance to the infective source and potential infectivity of body fluids (table 1). In case of suspected or confirmed SARS-CoV-2 infections personnel was instructed to wear filtering face peace (FFP)-2 masks, unsterile gloves and gowns for PPE. For aerosol-generating procedures goggles were additionally recommended.

The outbreak was defined as two or more COVID-19 infections resulting from a common exposure, that was either suspected or laboratory-confirmed as SARS-CoV-2. After identification, the outbreak was reported to the local public health department. In addition,

following the recommendations of the RKI for hygienic measures (table 1), patients were pre-emptively isolated. Alternatively, if an outpatient treatment was necessary due to their underlying diseases, *i.e.* hemodialysis, patients were cohorted together with their ACP.

Swab sampling and laboratory testing

Following internal standard operating procedures for specimen collection, nasopharyngeal swabs of all persons with contact to the index case were collected from day 5 onwards ((after the index case was confirmed on day 4). If first test showed a negative result but contact cases presented new or worsened symptoms, testing was repeated.SARS-CoV-2 was detected by specific assays targeting two separate genes via real-time RT-PCR as described previously [14]. Detection of envelope (E) gene was used as a screening test and detection of RNA-dependent RNA polymerase (RdRp) gene was used for confirmation. The threshold cycle value (C_t value), which is inversely proportional to the viral load, was documented for every SARS-CoV-2 positive sample.

Statistical analysis

Statistical analysis was performed using the Student's t-test. Statistical significance was declared at $p < 0{\cdot}05$.

Results

Involved outbreak cases and outbreak dynamics

48 cases (28 HCWs, 13 patients, and seven ACP) were involved in the outbreak, including index case and contact cases. The average age of HCWs was 46 years, of patients was 10 years and of ACP was 32 years. In total 15 cases were of male, 33 of female sex. All patients suffer from chronic kidney disease with the majority being on regular hemodialysis.

After contact to the index case, nine contact cases (seven HCWs, one patient and one ACP) developed laboratory confirmed COVID-19 infections. All of these were categorized as type I or Ib-exposure, according to mentioned criteria (table 1). No contact was categorized as Ia. In total, four of eight type I and seven of seven type Ib contacts became infected. No type II contact was tested SARS-CoV-2 positive. Additionally, two patients were tested positively for SARS-CoV-2 but did not present apparent COVID-19 symptoms. Another 11 HCWs affirmed common cold symptoms without being tested positively. No case reported dyspnea (figure 1, table 2).

In total, during the outbreak 12 cases were confirmed SARS-CoV-2 positive by real-time RT-PCR. Of these, six individuals presented with symptoms at the time they were tested. C_t values of symptomatic cases were significantly lower compared to asymptomatic cases (22.55, range 16.03-23.50 vs. 29.94, range 21.89-37.49; $p = 0.007$), indicating an approximately 200-fold higher viral load (table 2).

After establishing adequate hygienic measures (table 1) for all HCWs, patients and ACP from day 4 on, no further laboratory confirmed COVID-19 infection was uncovered.

Discussion

Covid-19 is currently a public health relevant pandemic that will increase hospital admissions for severe acute respiratory disorders. In addition, hospital acquired COVID-19 infections are a potential route of transmission and pose a threat to vulnerable inpatients and HCWs.

We characterized a nosocomial outbreak of SARS-CoV-2 on a pediatric dialysis unit that involved 48 cases including patients, ACP and HCWs. Detailed contact investigation and initial laboratory testing identified an index case and infected contact cases confirming previous findings that person-to-person transmission is also the most likely mode of transmission in the hospital setting [15].

Part of our outbreak investigation was a detailed assessment of clinical symptoms associated with COVID-19 infection. Interestingly, two infected children with chronic kidney disease either presented a very mild phenotype or even remained asymptomatic, despite considered to be at particular risk for respiratory infections because of hemodialysis [16,17]. This might confirm reports that children suffering from COVID-19 often present with relatively mild symptoms [18]. However, the majority of confirmed cases became symptomatic with body aches accompanied with flank and loin pain, fatigue and headache. Similar to influenza, infected individuals described loss of taste and smell several days after onset of illness. This is consistent with statements of the British Association of Otorhinolaryngology and the American Academy of Otolaryngology-Head and Neck Surgery reporting dysgeusia and anosmia in COVID-19 patients [19,20]. This particular symptoms should be investigated in larger epidemiological cohorts [21].

Previous studies suggest better positive predictive values if tests are performed in symptomatic individuals [22]. Our findings in HCW25 seem to corroborate these findings: whereas the initial test was negative after contact to the index case without any symptoms, the HCW was positively tested three days later after development of clinical signs of a SARS-CoV-2 infection. Since lower C_t values and therefore higher viral load were detected

in symptomatic patients and HCWs, our observations give a first hint to support this testing strategy for the hospital setting. For example HCW1 (index case) experienced fever on day 2 resulting in a low C_t value when she was tested two days later. As many healthcare systems are facing the problem of reduced laboratory testing capacity, based on our results we are cautious to recommend testing asymptomatic contacts but would preferably monitor clinical key symptoms. On the other hand, individuals with high viral load could potentially serve as a source of transmissions, supporting the theory of so-called super-spreaders [23].

During the outbreak management, we classified contacts according to duration and severity of exposure (see table1). While only cases with type I/Ib exposure became symptomatic, several other cases with type I/Ib exposure did not develop symptoms. This result suggests that an exposure-based classification is not specific enough to discriminate high risk from no risk contacts. However, this recommendation in combination with infection control measures allows key personnel to continue work while self-monitoring symptoms. This strategy can be used to maintain an adequate healthcare service while facing staff shortages during the current SARS-CoV-2 pandemic.

Summarizing, our investigation suggests that application of appropriate infection control measures including contact tracing, assessment of exposure and optimal symptom-based testing strategies are essential to prevent outbreaks of SARS-CoV-2 within hospital settings.

Notes

Authors' contributions

VS, JCK, AM, CC, HO, MK, TK and SK provided contact investigation and collected epidemiological data. JCK, TK, HO, MK provided clinical care to the patients and provided clinical case histories. JK evaluated and provided laboratory test results. VS and SK performed data analysis, interpretation, drafted and revised the manuscript. All authors reviewed, revised and approved the final manuscript.

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Potential conflicts of interest

The authors declare that they have no potential conflicts of interest.

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Table1: Risk classification and infection control measures of HCWs and patients after contact to COVID-19 confirmed cases*

Risk	Type of exposure	Measures		
		HCWs		Patients
		Shortage of personnel	No shortage of personnel	
I	Cumulative 15-minutes face-to-face contact, without usage of PPE			Home quarantine (14 days[#]) Symptom monitoring (14 days[#]) In case of typical COVID-19-symptoms: further diagnostics after contact to local health authorities
Ia	HCWs with direct exposure to respiratory secretions, body fluids or aerosols of confirmed COVID-19 cases, without usage of PPE	Home quarantine for 7 days; if no symptoms, continue work while wearing a surgical face mask	Home quarantine (14 days[#]) Symptom monitoring (14 days[#]) In case of typical COVID-19-symptoms: further diagnostics after contact to local health authorities	

Ib	HCWs exposed during treatment or nursing in a distance of ≤ 2 meters, without PPE	Continue work while wearing a surgical face masks In case of of typical symptoms, SARS-CoV-2 test when possible and home quarantine until infection excluded/confirmed Excluded infection: continue work Confirmed infection: home quarantine 14 days	Home quarantine (14 days[#]) Symptom monitoring (14 days[#]) In case of typical COVID-19-symptoms: further diagnostics after contact to local health authorities	
II	Shared indoor environment without cumulative 15-minutes face-to-face contact HCWs exposed during treatment or nursing in a distance of > 2 meters, without PPE	Symptom monitoring (14 days[#]) If contact to respiratory secretions, body fluids or aerosols of confirmed COVID-19 cases, -> see Ib If no contact to respiratory secretions, body fluids or aerosols of confirmed COVID-19 cases, -> see III		Symptom monitoring (14 days[#])

III	HCWs exposed during treatment or nursing in a distance of > 2 meters HCWs exposed during treatment or nursing using in a distance ≤ 2 meters, using PPE	Symptom monitoring for 14 days Continue work, if possible while wearing surgical face mask	

COVID19 =coronavirus disease 2019; SARS-CoV-2–=severe acute respiratory syndrome coronavirus 2; PPE=appropriate personal protective equipment (surgical masks, unsterile gloves and gowns, and for aerosol-generating procedures filtering face peace (FFP-)2 masks and additional goggles); HCWs=health care workers

[#]after last exposure

*adopted according to the Robert Koch Institute, Germany; 21/04/2020; https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/HCW.html

Table 2: Type of exposure and symptoms at time of testing

Person	Type of exposure	SARS-CoV-2 rtPCR test result	New symptoms at time of testing	C_t value
HCW1	Index person	+	yes	17.96
P1	I	+	yes	20.62
HCW2	Ib	+	no	21.89
HCW3	Ib	+	no	25.25
HCW4	Ib	+	yes	23.85
HCW5	Ib	+	no	32.98
HCW6	Ib	+	no	31.50
HCW7	II	-	no	----
HCW8	II	-	no	----
HCW9	II	-	no	----
HCW10	II	-	no	----
HCW11	II	-	no	----
HCW12	II	-	yes	----
HCW13	II	-	no	----
HCW14	II	-	no	----
HCW15	II	-	yes	----
HCW16	II	-	no	----
HCW17	II	-	no	----
HCW18	II	-	yes	----
HCW19	II	-	no	----
HCW20	II	-	no	----
HCW21	II	-	no	----
HCW22	II	-	no	----
HCW23	II	-	no	----

HCW24	II	-	no	----
HCW25	Ib	-; +	no; yes	21.35
P2	I	+	no	37.49
ACP1	I	+	yes	16.03
HCW26	Ib	+	yes	23.50
HCW27	II	-	no	----
HCW28	II	-	yes	----
P3	I	+	no	30.58
P4	I	-	no	----
P5	I	-	no	----
P6	I	-	no	----
P7	II	-	no	----
P8	II	-	no	----
P9	II	-	no	----
P10	I	-	no	----
ACP2	II	-	no	----
ACP3	II	-	no	----
ACP4	II	-	no	----
ACP5	II	-	no	----
P11	II	-	no	----
ACP6	II	-	no	----
ACP7	II	-	no	----
P12	II	-	no	----
P13	II	-	no	----

HCW=health care worker; ACP=accompanying person; P=patient;

SARS-CoV-2-rtPCR=severe acute respiratory syndrome corona virus 2 real time reverse transcriptase polymerase chain reaction; C_t=threshold cycle

Figure 1: Linelist of healthcare workers, patients and accompanying persons involved in the outbreak

Symptoms in healthcare workers (HCWs) (1A), patients (P) and accompanying persons (ACP) (1B) are marked in different colors. Onset and end of symptoms are represented in the timeline, whereby first day of investigation was two days prior to onset of index case's symptoms. Black (negative) and red (positive) lines indicate SARS-CoV-2 real-time RT-PCR test result.

Figure 1A

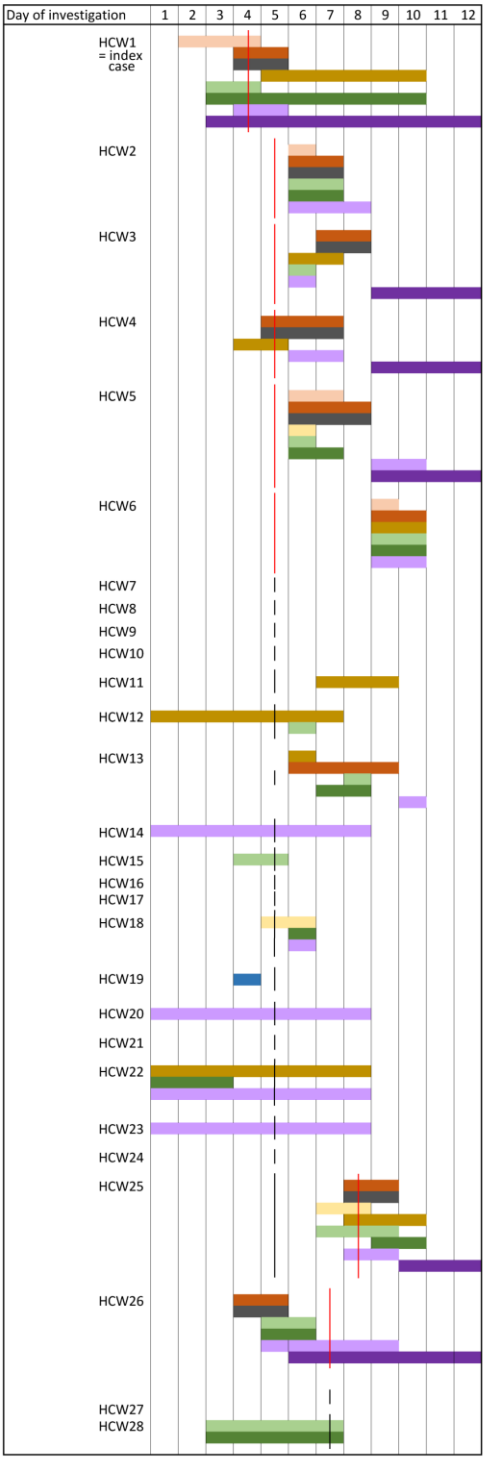

Figure 1B