Infection Control and Management of COVID-19: Challenges for Paediatric Tertiary Care Hospitals

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Abstract

PURPOSE: To describe infection control measures and patient management at a tertiary children's hospital in southern Germany during the COVID-19 pandemic.

METHODS: Prospective, observational study of infection control measures, patient management, clinical and virologic data of paediatric patients treated at our hospital during the COVID-19 pandemic from February to May 2020. Infection control measures were documented beginning with preparation for the pandemic. All paediatric patients with suspected SARS-CoV-2 infection were prospectively included in the study.

RESULTS: With local triage, restraint of patient admission and testing strategies implemented, healthcare capacity remained adequate and no healthcare-associated infections occurred. Workload in the paediatric emergency department significantly decreased following the lockdown of schools and kindergartens. 7 of 174 (4%) children with and 2 of 208 (1%) children without typical symptoms, respectively, were diagnosed with COVID-19 by PCR. Six out of nine inpatients treated for COVID-19 had underlying comorbidities, two were admitted to the intensive care unit. One patient died shortly after discharge.

CONCLUSIONS: While COVID-19 generally causes mild disease in children, severe illness and fatal cases may occur, particularly among children with underlying diseases. Tertiary children's hospitals may face challenges with treating potential high-risk patients during the pandemic. Thus, timely establishment of effective testing and triage strategies is crucial.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused the pandemic of coronavirus disease 2019 (COVID-19) with more than 14 million cases and close to 600.000 deaths globally until 20 July 2020. This outbreak challenges healthcare systems worldwide [1]. Children generally develop milder disease than adults; the majority of infections are asymptomatic or manifest as upper respiratory tract infection or mild pneumonia [2–4]. Nevertheless, severe and fatal cases have been reported in children [5]. In particular, infants and young children appear to have an increased risk for a critical course of disease [6, 7]. Several risk factors for severe illness and mortality due to COVID-19 have been identified among adult patients, such as hypertension, diabetes and coronary heart disease [8]. Elevated rates of arrhythmia, cardiac injury, myocarditis or coagulation abnormalities occur among patients with underlying cardiovascular disease [9]. Among patients with solid and haematological cancers, higher rates of severe disease and death have been reported [10–12]. However, at present, our knowledge about risk, prevention, course of disease and outcome of COVID-19 in children with different comorbidities is extremely limited. While most studies of COVID-19 in children have found an increased rate of hospitalisation and intensive care unit (ICU) admission in children with comorbidities [5, 13, 14], some studies did not find a difference in admission rates in children with underlying chronic health conditions [15]. It has been hypothesised that children with chronic kidney disease have an elevated risk for the acquisition of COVID-19 due to their immunocompromised state and frequent exposure to the hospital setting [16]. While an increased rate of Kawasaki-like multi-system inflammatory disease has been reported among children with COVID-19 [17], it is still unclear if patients with immunodeficiency or immunomodulatory treatment are at higher risk. First reports on COVID-19 in patients with cystic fibrosis did not show an apparent effect of the cystic fibrosis on COVID-19 severity [18].

Taking these potential risks into account, tertiary care children's hospitals with a high proportion of children with comorbidities face challenges with organisational and clinical management during the pandemic. A particular challenge is the maintenance of medical care for children with suspected COVID-19 combined with provision of specialised care for risk groups [19]. Although the usual turnaround time for SARS-CoV-2 testing was less than 24 hours at our hospital, fast and effective triage procedures are hampered while waiting for the test result. This is aggravated by limited testing capacities e.g. due to lacking testing reagents, forcing healthcare professionals to define decision criteria whom to test with priority. An additional burden for the health care system can be presumed by coincidence of the COVID-19 pandemic with the peak of the influenza and respiratory syncytial virus (RSV) season [20].

The aim of this study was to describe particular challenges in the management during the first wave of the COVID-19 pandemic for a tertiary children's hospital in southern Germany and to report risks and outcomes in children treated for COVID-19 in the hospital.

Methods

The University Children's Hospital Tuebingen is a large tertiary care facility in southern Germany with a total of 170 beds, comprising departments for paediatric oncology and haematology, cardiology and pulmonology, surgery, neuropaediatrics, and neonatology. Each year, 40–50 patients undergo haematopoietic stem cell transplantation (HSCT), 15–20 receive solid organ transplant; 140 patients undergo thoracic, cardiac or vascular surgery. Treatment is also provided for children with rheumatologic diseases, cystic fibrosis and those requiring home ventilatory support. The hospital has a paediatric intensive care unit (PICU) with a capacity of 14 beds and a neonatal intensive care unit (ICU) with a capacity of 17 beds. It also has an emergency department (ED) as well as several outpatient clinics for high-risk patients and serves as regional primary and secondary care referral centre.

By the end of February 2020, the local virology department implemented testing for SARS-CoV-2 ribonucleic acid (RNA). During the study period, assessment for SARS-CoV-2 RNA was performed by real-time reverse transcription polymerase chain reaction (RT-PCR), either with the RT-PCR Assay RealStar SARS-CoV-2 (Altona Diagnostics, Hamburg, Germany) or using RT-PCR with primers and probes of TIB MolBiol (Berlin, Germany). From 8 May, SARS-CoV-2 PCR tests were additionally performed using an Xpert cartridge system (Cepheid, Sunnyvale, California, USA). SARS-CoV-2 serology tests were locally available in May, but not used for routine patient care during the study period.

The ED workload was assessed by counting all paediatric emergency visits of patients aged under 18 years from 1 January to 17 May 2020. Visits in the paediatric surgery department and scheduled outpatient visits were not included. These data were compared to the arithmetic mean of the number of patient-visits during the corresponding weeks in the 5-year period 2015–2019 using a paired t-test. A two-sided p-value < 0.05 was considered statistically significant.

In addition, local guidelines that were developed during the course of the pandemic were systematically documented and analysed. Patient data were collected prospectively and retrieved from hospital records. We used the standardised International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) questionnaire as part of the ISARIC study [21, 22]. Data on demography, clinical presentation and course, treatment and outcome as well as virology results were collected in a standardised and pseudonymised manner.

We used REDCap 10.0.3 (Vanderbilt University, Nashville, Tennessee, USA), Microsoft Excel (Microsoft Excel 2010 v14.0, Microsoft Corporation, Redmond, Washington, USA) and SPSS (IBM SPSS Statistics 26, IBM, Armonk, New York, USA) for data collection and analysis. Figures were created using Microsoft Excel and Microsoft Powerpoint (Microsoft Powerpoint 2010 v14.0, Microsoft Corporation, Redmond, Washington, USA).

Results

Management of patients with suspicion of COVID-19

Due to the reports about COVID-19 spreading in Wuhan, China, a local task force was founded at the University Hospital Tuebingen, including specialists for infectious diseases, hospital hygiene and intensive care as well as virologists. This task force created the first local guidelines by the end of January 2020. In mid-February, guidelines for testing and triage of patients with suspected COVID-19 were released by the World Health Organization (WHO) and the German Public Health Institute Robert Koch Institute (RKI) [23]. Local procedures mainly followed the recommendations of the RKI, additionally guidelines were more and more adapted to local conditions during the course of the pandemic.

Initial triage measures in the children's hospital comprised the installation of separate waiting and examination areas for suspected COVID-19 patients in the ED, including separation of patient flow. Later, a fever clinic for examination and testing of children with suspected COVID-19 was established in another part of the town. As only 18 children made use of this facility during the 2 weeks that it was operational, it was discontinued. While initially single patient rooms with airlock chambers were kept ready for paediatric COVID-19 inpatients, a separate COVID-19/respiratory infections ward with a capacity of ten beds was established by the end of May. As the ward accommodated both suspected and confirmed COVID-19 cases, it was physically separated into two areas, using a folding screen for division of the corridor. Furthermore, patients in the two areas received care provided by separate teams of nurses. Non-urgent, scheduled outpatient visits and admissions were postponed or cancelled by mid-May.

For hospital staff with direct contact to patients, a general obligation to wear surgical masks covering mouth and nose was set up by mid-March. Full personal protective equipment, including filtering facepiece (FFP) 2 masks, gowns, gloves, operation caps and goggles was provided to hospital staff involved in direct handling of patients with confirmed or suspected COVID-19. By the end of March, all patients had to wear surgical masks while being outside their rooms. By mid-May, voluntary SARS-CoV-2-RNA testing of asymptomatic hospital staff working with COVID-19 patients or in defined risk areas (haematology, PICU, ED) was established. Staff screening comprised a throat swab tested for SARS-CoV-2 RNA which was performed in the hospital and, from mid-June, also serological testing. No healthcare-associated infections with COVID-19 occurred at the children's hospital among patients and health care staff.

The number of ED visits were significantly higher from calendar weeks 2 to 12 with a mean difference of 31.5 (95% confidence interval [CI]: 15.1–47.8, $P = 0.002$) visits per week in 2020 compared to the mean number of visits during the corresponding period in 2015–2019. This completely changed from calendar weeks 13 to 19, where the number of visits to the ED was significantly lower than in the previous years with a mean difference of − 72.3 (96% CI: −86.5 to −58.1, $P < 0.001$) weekly visits. Figure 1 shows the ED workload, testing, triage and infection control measures during the study period.

Testing strategy and capacity

Patients were tested for SARS-CoV-2 RNA in Tuebingen starting in mid-February. While first samples were sent to the national reference centre and consultant laboratory for coronaviruses of the RKI in Berlin, testing was available locally by the end of February. Local testing capacity was rapidly increased. While initial test runs were performed once daily, capacity was soon expanded to three PCR runs per day, reducing the sample-to-result time to about half a day. With availability of cartridge based tests from May, the delay could be further reduced to two to three hours for a limited number of samples; thus some patients could be kept in the ED or in designated holding areas until test results were obtained. This saved the capacities of the respiratory infections ward.

Between 29 February and 17 May 2020, a total of 450 respiratory specimens were collected from patients aged under 18 years for SARS-CoV-2 RNA RT-PCR testing. These correspond to 392 different cases defined as outpatient visits and hospital admissions of a total of 346 patients. The median age of the 346 children tested was 3.5 years (IQR: 1–11 years) years, of whom 10 (3%) were aged < 1 month, 67 (19%) were aged 1–12 months, 138 (40%) were aged 1–6 years, 60 (17%) were aged 7–12 years and 71 (21%) were aged 13–18 years; and 165 (48%) were female.

In 175 (45%) out of 392 cases, symptoms suspicious of COVID-19 (any of: fever, respiratory symptoms other than rhinitis, diarrhoea, loss of smell or taste) were present. 207 (53%) cases presented without any of these typical symptoms, and in 10 (3%) cases the symptoms were unknown. Among the 175 suspected cases, SARS-CoV-2 infection was present in 7 (4%), while among the 207 cases without typical symptoms, SARS-CoV-2 was detected in 2 (1%). These latter two patients presented with orbital swelling and livid discoloration of the legs, respectively (Table 1). There were no asymptomatic cases of COVID-19 diagnosed.

For 220 (56%) of the 392 cases, SARS-CoV-2 tests were performed on or shortly before hospital admission, 94 (24%) tests were done for inpatients and 75 (19%) for outpatients; 201 (51%) tests were done in children admitted to a general paediatric department (ED or general ward including patients from neurology, gastroenterology, rheumatology and nephrology), 79 (20%) to haemato-oncology (outpatient clinic or ward), 44 (11%) to cardiology, 31 (8%) to surgery, 25 (6%) to the PICU, 5 (1%) to neonatology and 7 (2%) to other departments.

The COVID-19 epidemic in Tuebingen coincided with the end of the acute respiratory infection season. The last cases of RSV and influenza were recorded on 28 March. Until then, during the first 3 months of 2020, 82 (67%) out of 108 tested cases had symptoms of COVID-19. Among these, 12 (15%) were diagnosed with RSV, 5 (6%) with influenza, and 2 (2%) with SARS-CoV-2.

Characteristics of patients admitted with COVID-19

Between 26 March and 20 July 2020, nine patients with COVID-19 were admitted to our children's hospital. All were admitted to the paediatric COVID 19/respiratory infections ward. Eight were diagnosed on admission and one was diagnosed prior to admission. Data on the clinical course, treatment and outcome are presented in Table 1

The presenting symptoms included fever in six patients (one developed fever later), respiratory symptoms in five patients, and gastrointestinal symptoms in two patients. One patient presented with orbital swelling and another one with livid discoloration of the legs as the initial symptom. Six patients had underlying comorbidities, of whom three had an impaired immune system due to immunosuppressive treatment (two cases) or after haematopoietic stem cell transplantation (HSCT).

Four patients required oxygen therapy. Two patients required admission to the PICU: an 18-year-old boy with hypoplastic left heart syndrome and a 16-year-old girl who had received kidney transplantation 12 years previously. The girl required invasive ventilation. Experimental treatments were used in two out of nine patients: one patient with distinct thrombocyte activation received treatment with defibrotide to prevent blood clotting. Another patient who had undergone HSCT a year before received ribavirin treatment.

All of our nine patients were discharged alive, two with mild residual symptoms. However, the 18-year-old boy died at home, 11 days after discharge. Autopsy of the brain showed cerebral vasculitis probably associated with COVID-19 [24, 25].

Discussion

Management of patients with suspicion of COVID-19

Outbreaks of respiratory pathogens in paediatric healthcare settings are well described in the literature [26, 20]. During the COVID-19 pandemic children's hospitals have faced particular challenges because of the novelty of this virus. Effective infection prevention strategies needed implementation in very little time and with an obvious lack of experience and data regarding spread and clinical course of infection.

Triage and infection control strategies:

Overall, local infection control measures have proven effective, since no overload of local capacities was noted. All cases of confirmed paediatric COVID-19 were treated on-site and no cases of healthcare-associated infection occurred in the children's hospital. A reason might be the early planning of local infection control strategies, almost two months before admission of the first paediatric COVID-19 case. This allowed quick implementation of infection control measures with local spread of the pandemic. Scheduled outpatient visits were cancelled early not only for infection prevention but also to conserve resources for adult patients. Whether the cancellation of scheduled visits and admissions has led to increased morbidity or mortality in children remains unclear and needs to be closely monitored on a local and national level.

Implementation of a separate ward for COVID-19 and respiratory infections was just in time, as the first paediatric COVID-19 patients were admitted only a few days later. Since many patients required admission to the infection ward while waiting for their SARS-CoV-2 RT-PCR results (which depending on sample collection had a turnaround time of up to 24 hours in the beginning), temporarily up to eight out of ten beds in the ward were occupied. This underscores the necessity of a separate inpatient area of sufficient capacity, as long as SARS-CoV-2 rapid tests are unavailable or highly limited.

While outpatient fever clinics outside the hospital have been reported to be an effective triage measure in prevention of healthcare-associated infections [27], the fever clinic in our setting was hardly used by children and was therefore discontinued after 2 weeks. We suspect that the low utilisation had several causes: First, the paediatric fever clinic opened shortly after the end of the respiratory infection season. Second, around this time, children were no longer going to school because of the full lockdown, so it is likely that spread of respiratory viruses decreased in general. Third, it is assumed that there was a low incidence of SARS-CoV-2 infection in children in our region of only about 2% [28]. Hence, we believe that these clinics might become an essential feature for infection control if local COVID-19 incidence increases. As the infrastructure has now been developed, this service can be rapidly reopened if required.

The paediatric ED workload was significantly higher than in previous years until mid-March and then rapidly decreased –to become 57% lower than in previous years, in parallel to the increase of COVID-19 cases in Germany. This is in line with reports from Italy [29]. The natural decrease of acute respiratory infection incidence in the beginning of spring does not explain these differences; neither does the implementation of a fever clinic outside the hospital, as only few patients attended the fever clinic. The most likely cause is reduced transmission of respiratory infections due to the school and kindergarten lockdown and the implementation of hygiene measures in the population [20]. The delay of about a week between these control measures and the decrease in emergency visits corresponds to the incubation time of respiratory infections. Another reason might be a restraint of parents and children in seeking medical care due to anxiety of being infected with COVID-19 in the hospital [30]. As this behaviour poses a risk especially for children with chronic diseases [29], paediatricians should make special efforts to follow up these cases proactively. Moreover, health education on COVID-19 needs to consider this aspect.

The so far low rate of children seeking emergency care at our and other hospitals during the pandemic [29] should only be regarded with caution for future projections. With re-opening of schools and kindergartens, coincidence of SARS-CoV-2 with other respiratory infections and habituation of the population to the COVID-19 threat, ED workload might increase considerably during the next autumn and winter. Children's hospitals should keep strategies ready for rapid increase in ED capacities, including redundancy in healthcare personnel and the implementation of isolation areas flexible in size.

Testing procedures

With local spread of COVID-19 and increasing test capacities, test criteria shifted from travellers and contact persons to all patients with suspicious symptoms and were complemented by standardised screening procedures for asymptomatic patients. This shift of test criteria was likewise reported from other children's hospitals in Europe (unpublished data). The total number of tests performed in children doubled from end of April to mid-May, probably due to broadening of the test criteria and implementation of screening procedures.

As presentation with atypical symptoms has frequently occurred in our cohort as well as other cohorts of paediatric COVID-19 patients [2, 3, 5], broadening of test criteria is justified. Although we did not observe asymptomatic SARS-CoV-2 infection in our cohort, routine testing of asymptomatic children at risk is essential, since transmission of COVID-19 can occur prior to symptom onset or patients may show very little or atypical symptoms [31]. This is the reason why clear test criteria for asymptomatic patients at risk (e.g. solid-organ transplant, dialysis, haemato-oncology, immunosuppressed) were defined later in the course (Fig. 1D, calendar week 19).

Among five neonates tested in our neonatology department, two were the children of women with SARS-CoV-2 infection. In both cases, infection was not transmitted from mother to child, which is in line with literature describing neonatal transmission as rare [3].
Characteristics of patients admitted with COVID-19
Given the reported complications of COVID-19 (such as acute respiratory distress syndrome, cardiac involvement, thromboembolic complications, exuberant inflammatory response, renal failure, secondary infections) [8], some of the patient groups seeking specialised care at our hospital might be at increased risk of severe disease or death due to COVID-19. Among the nine patients admitted to our hospital with COVID-19, five had serious underlying health conditions, among them two patients in need of PICU admission. This is a high rate compared to literature reporting of only a fourth of the children admitted for COVID-19 having underlying health conditions [2], which might point at an increased risk in our patient population.

In the two cases with atypical clinical presentation it remains unclear, whether infection with SARS-CoV-2 has been causative or an incidental finding, as asymptomatic infection with respiratory viruses is a common finding among young children [32]. Circulatory disorders due to increased blood clotting have been described in the literature [9] but orbital swelling related to COVID-19 has not been reported to date.

While fever as the most common symptom among adults [21] was present in seven patients in our cohort, the second most frequent symptoms dyspnoea and cough were only present in four patients. This is in line with other reports that found respiratory symptoms less frequently in paediatric patients [2, 3, 5],

Four patients required respiratory support, which is lower than around 65% in need of oxygen treatment reported among adults [21], but higher compared to other reports on paediatric COVID cases [2, 3]. This might point at an elevated risk of severe disease among our patient population although these findings are inconclusive due to the small number of patients.

Limitations

Despite a relatively high number of patients tested (n = 346), the small number of children admitted with COVID-19 at our hospital limits strong conclusions on risk factors, clinical course and outcome. Due to shifts in the testing strategy during the local course of the pandemic, the characteristics of the observed cohort changed and thus conclusions have to be drawn with caution. Although triage, testing and hygiene precautions reported from our hospital were highly effective, they were adapted to local conditions and might need modification in other situations and settings.

Conclusions

Although COVID-19 generally causes mild disease in children, severe illness and fatal outcomes occur. These cases of severe disease might be more frequent among children with underlying health conditions. Clinical presentation might differ between these patients and healthy children or adults.

Therefore, it is crucial for children's hospitals that treat children with high-risk conditions to be especially proactive in the timely establishment of sufficient testing and triage strategies.

Declarations

Ethics approval and consent to participate: The study protocol was approved by the local ethical review board at the University Hospital Tuebingen (project No. 164/2020BO1).

Consent to publish: During the first three months of the pandemic a waiver of informed consent was obtained from the local ethics committee due to the urgency of acquisition of clinical data. Afterwards, written informed consent was obtained from all parents/guardians, with assent from children when appropriate for their age.

Availability of data and materials: No reprints are available. Data assessed from children admitted with COVID-19 (Table 1) was shared with the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC). We confirm that the patients mentioned in this manuscript have not been reported in any other submission. However, there is a case report about patient N°5 in Table 1 under consideration for publication in the Journal of the Pediatric Infectious Diseases Society (22/08/2020).

Competing interests: none

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Authors' contributions: JR and HR conceived the study and designed the study protocol; OH and HR conceived and implemented local infection control measures. TG managed virologic test procedures. JR, TG, MKV and HR performed the data analysis. JR drafted and TG, MKV, HR and RH critically revised the manuscript. All authors contributed and approved of the final manuscript.

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Tables

	Mo of admission	Age-range	Past medical history	Clinical presentation	Radiologic findings	Hospital LOS (days)	PICU LOS (days)	Respiratory support	Pharmacological treatment	Co-Infections
1	March	Neonate	Healthy	Fever, diarrhoea, vomiting	—	4	—	—	—	None
2	March	≥ 16 y	Kidney transplantation 2008, immunosuppressive treatment	Fever, productive cough, dyspnoea, rhinorrhoea, sore throat, chest pain, myalgia, headache, abdominal pain	chest X-ray: bilateral infiltrates, unilateral pleural effusion	15	9	Oxygen therapy, invasive ventilation	Antibiotic, antifungal agents, heparin	None
3	March	≥ 16 y	Hypoplastic left heart syndrome	Cough, hypoxaemia	Normal chest X-ray	13	11	Oxygen therapy	—	None
4	April	6 - 12y	Rhabdomyosarcoma	Sore throat	—	11	—	—	Antibiotic	None
5*	April	6 - 12y	Healthy	Fever, headache, abdominal pain, anorexia	Chest X-ray: bilateral infiltrates and pleural effusions	18	—	Oxygen therapy	Antibiotic, heparin, defibrotide	None
6	April	≥ 16 y	Severe immunodeficiency syndrome with T-cell-disorder, HSCT 2019	Fever, cough, rhinorrhoea, vomiting	CT: bilateral infiltrates, pericardial effusion	16	—	Oxygen therapy	Antibiotic , antifungal agents, ribavirin, valganciclovir	Throat swab: HSV-1, CMV, EBV, HHV-6, *Enterobacter cloacae*
7	May	6 - 12y	Oesophageal atresia, multiple interventions	Fever, vomiting, orbital swelling	—	8	—	—	Antibiotic	—
8	May	Infant	Healthy	Circulatory disorder in lower extremities	—	6	—	—	—	—
9	May	6 - 12y	Asthma, obesity	Fever, cough, sore throat, wheezing, rhinorrhoea, dyspnoea, chest pain, headache, anosmia	—	2	—	—	Inhaled beta-2-mimetics	—

**A case report about this patient is currently under consideration for publication in "The Journal of Pediatric Infectious Diseases". We will cite the reference as soon as a decision is made.*

Figures

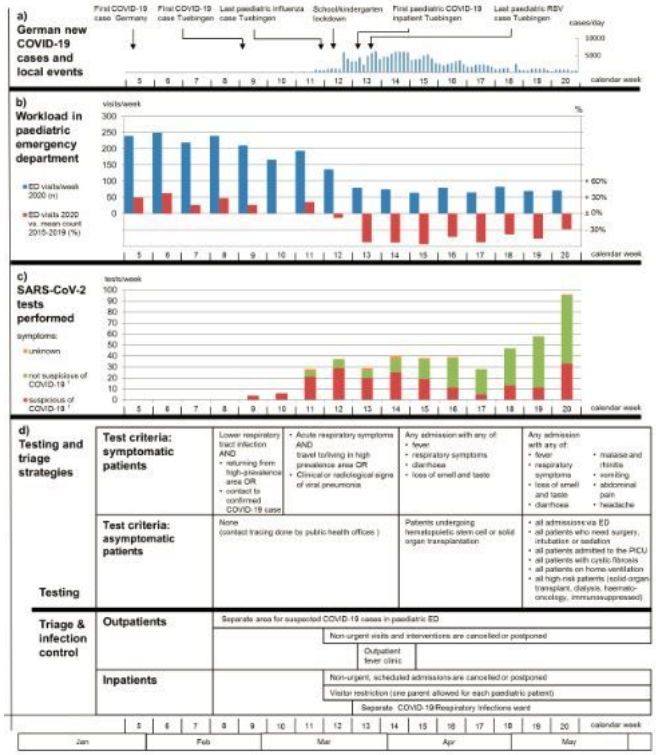

Figure 1

Local infection control measures a) chronology of COVID-19 cases in Germany and local events in relation to the pandemic [33]. b) workload in paediatric emergency department; blue bars: emergency visits/week; red bars: emergency visits/week in 2020 compared to mean visits/week 2015-2019 during the same time of the year. c) number of SARS-CoV-2-RNA tests performed on children <19 years in local virology lab. 1) COVID-19 suspicion defined as presence of any of the following symptoms: fever >38.0 °C, respiratory symptoms other than rhinitis, diarrhoea, loss of smell or taste. d) chronology of local testing, triage and infection control measures. Abbreviations: ED, emergency department; PICU, paediatric intensive care unit.