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IN THE HOSPITAL

COVID-19 Pandemic Experience in a Tertiary Care Center in Turkey: What have We Learned?

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ABSTRACT

Coronavirus disease 2019 (COVID-19) has become a public health threat to people all over the world and it has stretched hospital resources since the beginning of the pandemic. Available reports to date showed that COVID-19 seems to be less common in children. However, the number of pediatric patients is increasing and a lower number of pediatric patients does not necessarily mean that children are less susceptible to the infection. On the other hand, it is shown that preparedness and response to the COVID-19 disease pandemic in the hospital caring for children are extremely variable. The main target during a pandemic is to maintain high quality and high-efficiency care, with emphasis on patient and provider safety. A documented pandemic plan, simulation training, appropriate use of personal protective equipment (PPE), and appropriate isolation areas in the hospital and also in the emergency department are essential components of pandemic response. Therefore, respiratory hygiene, proper patient placement/ isolation, handling and cleaning of patient care equipment, devices, and environment and procedure safety are all important for effective working flow and reliable working environment in the hospital.

Early recognition and isolation of a patient with COVID-19 may help decrease exposure to the other patients and healthcare personnel. The use of a strict surveillance and management protocol during outbreaks of highly virulent viruses such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), through dedicated patient pathways, adoption of personal protective equipment for health care personnel, and use of nasopharyngeal screening of all admitted children and possibly all healthcare personnel should be recommended. Therefore, we developed a protocol addressing reception, risk management, and hospitalization of suspected SARS-CoV-2 cases at the pediatric emergency department, pediatric wards, and outpatient clinics aimed at containing intrahospital transmission of the infection. Our pandemic response planning was characterized by close collaboration among the head of our hospital, department of pediatrics, pediatric emergency department, pediatric infection control committee, and front-line staff as well as optimization of communication channels. In this article, we aimed to share our experiences of how to handle pediatric patients with COVID-19 in our university hospital from all aspects including prevention of possible transmissions during the first few months of the COVID-19 pandemic.

Key words: COVID-19, severe acute respiratory syndrome coronavirus 2, children, management in hospital, pandemic

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INTRODUCTION

An outbreak of novel coronavirus-2019 (COVID-19) infection is a public health emergency of international concern and was first discovered in Wuhan, China [1,2]. The number of cases rapidly increased, particularly in North and South America in addition to Europe which was the most affected region outside of China. At the beginning of the COVID-19 pandemic, pediatric patients were extremely rare [3], whereas, in the later stages of the pandemic, patients with COVID-19 from the whole age spectrum from all over the world [4,5] and in Turkey were reported. In Turkey, the first case of infection with SARS-CoV2 was announced on March 11, 2020. Currently, the documented cases increased up to 8,178,901 on November 20, 2021[6]. Available data regarding SARS CoV2 infections in children on children are limited worldwide as well and confirmed pediatric cases with COVID-19 who had commonly milder disease course compared with adults consisting of 1-5% of all cases with the lack of universal diagnostic and treatment modalities [7,8]. There are still concerns about the transmission route of the SARS-CoV-2. However, respiratory secretions in droplets produced by an infected person during coughing or sneezing seem the predominant way. Additionally, the possibility of airborne spread of COVID-19 and the existence of viable viruses on environmental surfaces and in feces should be taken into consideration [3,9-12].

Hacettepe University Ihsan Dogramaci Children's Hospital is a 272-bed tertiary care pediatric hospital in Ankara, Turkey. It is a pediatric hospital with 16-bed pediatric intensive care unit, 22-bed neonatal intensive care unit, and 4-bed hematopoietic bone marrow unit in addition to general pediatric wards. A total of 273 physicians and/or researchers, 224 nurses, and 429 administrative staff work in the hospital. As of July 14, 2020, 117 confirmed and 235 suspected COVID-19 pediatric cases were admitted to the hospital. Up to July 14, 2020, 6 HCWs were diagnosed with COVID-19, which was attributable to out-of-hospital exposure (the sources were mainly their spouses).

Few data are available regarding management strategies and infection control practices in children with COVID-19 [13,15]. In the period 16 March-14 July 2020, 6 (0.6%) of health care workers (HCWs) were found positive in Hacettepe University Ihsan Dogramaci Children's Hospital and the percentage of positive test results was really low when compared with some hospitals located in Europe [16,17]. We aimed to share our experiences regarding how to handle pediatric patients with COVID-19 in a pediatric referral and tertiary care university hospital from all aspects including prevention of possible transmissions during the first few weeks of the COVID-19 pandemic.

The Algorithm of Pandemic in a Tertiary Care Pediatric University Hospital

Preparation of Hospital and Pediatric Emergency Department (PED)

1. General applications in Hospital

After the declaration of the COVID-19 pandemic worldwide and in Turkey, Hacettepe University Ihsan Dogramaci Children's Hospital implemented a "Pandemic Action Plan" on March 16, 2020 (Table 1) as well as additional measures according to Covid 19 Guidelines created by The Turkish Ministry of Health. Interns (6th-grade medical students) and grade 4 and 5 medical students who have been a part of the trainee program in the hospital withdrew from the hospital environment. All meetings, conferences, and lectures of medical students were cancelled and later completed online. New elective admissions were cancelled and only emergency cases and chronic patients were served. Pediatric residents started to work in shifts to prevent them from contacting high viral load as well as suffering from burnout syndrome.

2. Applications in the Pediatric Emergency Department

Our Pediatric Emergency Department (PED) is the frontline of our children's hospital, serving as the main point for triaging patients as non-infected versus infected (suspected/confirmed patients) with COVID-19 as in many hospital emergency departments.

At the beginning of the pandemic, our major aim was to protect the HCWs from SARS-CoV-2 infections and to prevent the spread of this infection from patient to patient. Therefore, respiratory hygiene, proper patient placement/ isolation, handling and cleaning of patient care equipment, devices, and environment and procedure safety

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Table 1. Timeline of key pediatric infectious disease team interventions.

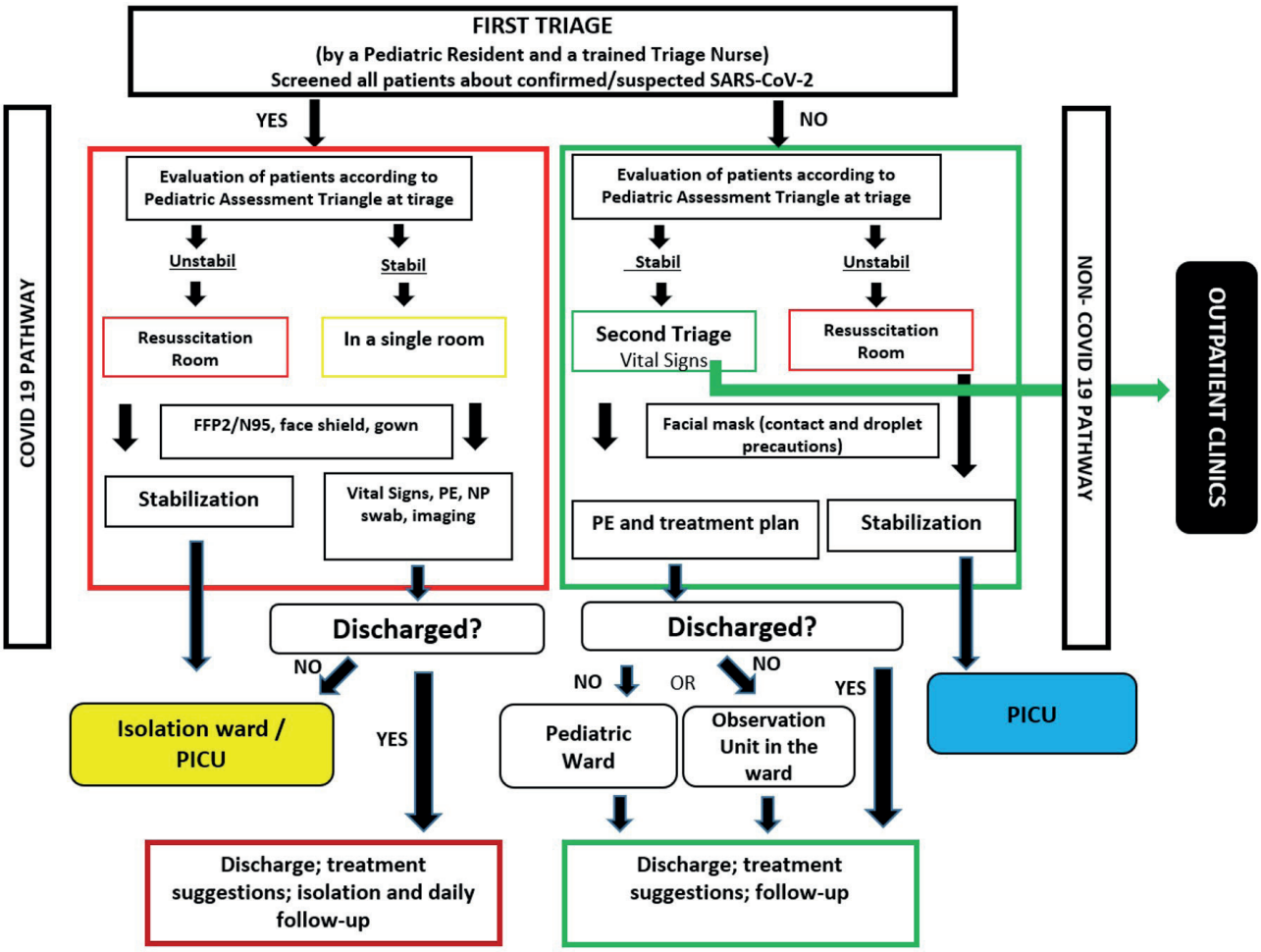
Date	Intervention	Rationale
15-31 Jan 2020	Small groups in hospital, particularly including HCWs of pediatric emergency department, pediatric intensive care unit department, department of infectious diseases etc. started to be notified about disease as well as precautions of hospital infection control committee HCWs were continued to be informed about the last situation of COVID-19 worldwide and updated the infection control practices.	Increasing number of imported cases worldwide
4 Feb 2020	Stock levels of PPEs were strictly started to be monitored via a software program day by day and the certain levels were determined for each PPE in each area of hospital to manage the decline of equipment under the critical threshold.	Possible PPE requirement due to the number of patients likely to increase
10 Feb 2020-11 March 2020	The last meeting in face to face about the last position of COVID-19 pandemic in a big conference hall was organized and HCWs in small groups were continued to be informed about the last situation of COVID-19 worldwide.	Increasing local transmission in several countries.
16 March 2020	Hospital "Pandemic Action Plan" was put into practice	Containment and isolation purposes since the first case in our country were diagnosed on March 11, 2020
18 March 2020	A specific ward consisting of 12-rooms beds with negative airway pressure was arranged and the pressure of rooms were continuously controlled by technical team of the hospital.	Local transmission was reported in Turkey. Reported asymptomatic pediatric cases who had a possibility of high viral load.
19 March 2020	"Diagnosis and Treatment Algorithm for Children" was prepared for our hospital in the light of the accumulated literature and then, was revised two times according to the dynamic nature of pandemic.	Limited data on management procedures of children worldwide.
20 March 2020	Video-assisted training was programmed by Children's Hospital Infection Control committee and shared with target groups on WhatsApp. • Small videos (approximately 5 minutes) about putting on PPE and removing PPE were prepared and shared with all HCWs, including doctors, nurses, and administrative staff who contact with patients and required appropriate use of PPE during pandemic. • Accumulated literature knowledge about COVID-19 from many different aspects was prepared using Zoom: video conferencing and shared via WhatsApp.	Need of continuous education
22 March 2020	"Risk Assessment Score for HCWs" was prepared for the early management of risky behavior of HCWs.	Evidence of infected HCWs with COVID-19 in Turkey
23-26 March 2020	The brochures about "putting on and removing PPE", "management algorithms of pediatric cases", and "warning about confirmed case with COVID-19" were prepared. The rules and brochures about "prolonged or extended use of N95" were prepared.	Increasing local transmission in Turkey. The first pediatric case with COVID-19 was confirmed in our hospital.
1-7 April 2020	Video-assisted education was continued to be programmed by Children's Hospital Infection Control committee • Short new videos (approximately 2 minutes) about putting on PPE and removing PPE were prepared one more time and shared with all HCWs. • Short videos (13 pieces about 2-3 minutes) about cleaning and disinfection procedures were prepared and shared via organized WhatsApp group with the target team. • A literature review on the experiences of different countries about COVID-19 was prepared using Zoom: video conferencing and shared via WhatsApp with the target groups.	Growing number of cases in Turkey
1 June 2020	Beginning of the normalization in the hospital as well as in the country	Decreasing number of cases with COVID-19, although cases increased again.

HCWs: Health care workers, PPE: Personel protective equipment

were all important for effective workflow and a reliable working environment in our PED. Thus, PED in our hospital had five different roles during the outbreak and these roles will continue even though the pandemic is over. These roles can be listed as follow: First, identifying patients with suspected COVID-19 in the pre-triage area (triage 1) by screening and later administering the test for suspected COVID-19 patients. Second, admitting suspected/confirmed patients with COVID-19 to the isolation ward and starting their initial treatment. Third, collaborating and communicating with the head of our hospital, the pediatric infection control team, and the department of pediatrics to initiate the pandemic plan. Fourth, reporting suspected/confirmed cases to the National Health Center/Public Health Department of Ankara. Lastly, to continue to the standard pediatric emergency care like trauma, suicidal attempt, home accidents, surgical emergencies, poisoning, and more.

2a. Triage, Screening, and Initial Approach to Patients at risk for COVID-19

In the PED, our team focused on identifying and isolating patients at risk for COVID-19 infection. Triage was the first step of early recognition and rapid initiation of infection control precautions. Therefore, a clinical pathway amongst pediatric emergency physicians, infectious disease specialists, and Hospital Administrators was created and regularly updated to safely evaluate COVID-19 patients according to our National Ministry of Health COVID-19 guideline during the pandemic (Figure 1). Two triage areas were created in front of the PED: Pre-triage (triage 1), located at the entrance of the hospital, and the non-COVID-19 area called Triage 2, located inside of the hospital. Triage in both areas was applied not only for the PED but for every patient admitted to our hospital. However, almost all admissions were accepted to the PED at the beginning of the pandemic.



PE: Physical examination, NP: Nasopharyngeal swab, PICU: Pediatric intensive care unit

Figure 1. Clinical pathway at the pediatric emergency department from the triage to the disposition for all patients.

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During pre-triage, the screening chart included questions about The presence of fever, cough, dyspnea, or signs of a respiratory illness, nausea, vomiting, diarrhea, and contact history with a confirmed/suspected case according to the Turkish Ministry of Health COVID-19 Guideline was asked to all patients and their caregivers/parents. All changes were closely followed and our PEDs and hospitals' working plan were updated according to the principles and criterias defined by the revised guideline of the Scientific Board of the Turkish Ministry of Health. During the screening for COVID-19, the initial triage and assessment were done at least 6 ft or 2 meters away from the patient and started only after the patient and the parents/caregivers (only one) don facemasks. After screening, all of the patients were evaluated according to the pediatric assessment triangle to determine the stable and unstable patients. Unstable and critically ill patients with or without suspected COVID-19 infections were directly taken to the resuscitation room. There was only one resuscitation room in our PED. Therefore, all HCWs in this area wore full personal protective equipment (PPE) including N95/FFP2 or N99/FFP3 with a surgical mask.

If the patient had complaints other than COVID-19 infection or any other diseases and these patients were stable, s/he were directed to Triage area 2. They were screened again by a pediatric resident and/or triage nurse in this triage area.

During the pandemic, not only suspected or confirmed COVID-19 cases but also patients with other complaints including patients which require life-saving interventions, traumatic injuries, poisoning and metabolic problems such as diabetic ketoacidosis continued to be admitted to our PED. In addition, the triage acuity level of presenting patients was higher and the number of less urgent patients admitted to PED decreased markedly.

2b. Pediatric Emergency Department Setting

Pediatric emergency care was given in two different areas for the isolation of the infected and non-infected patients. These two areas are the suspected COVID-19 area and the non-COVID area. The entrance to both of these areas was also separated. When all patients and caregivers/parents entered these areas of the hospital, all patients and their caregivers/parents were asked to wear a facemask to reduce the risk of transmission to others in the immediate vicinity.

Our main emergency area was used as a suspected COVID-19 assessment area. Thus, children presenting with symptoms related to COVID-19 to the PED were separated from other patients. There were no negative pressure rooms in this area, instead, there were single isolated rooms without washrooms for the suspected COVID-19 patients. A radiology imaging room in this area was used for obtaining chest x-rays for the suspected COVID-19 patients. Clinically stable suspected COVID-19 patients identified at the pre-triage were placed in a single room with the door closed. However, critically ill patients and patients contacted with persons contaminated with COVID-19 have been placed in the resuscitation room. After stabilization of the critically ill patients, they have been placed in a negative pressure isolation room with high-efficiency particulate air (HEPA) filtration of the recirculated air in our COVID- 19 isolation service. This COVID- 19 isolation service was located outside of the PED and in a different place from the pediatric ward. After March 27, 2020, a container was placed outside in front of the PED. After this date especially high-risk patients with suspected COVID-19 who had close contact with confirmed COVID-19 cases were evaluated in this container. Portable plain radiography was placed within the container and chest x-ray of the high-risk patients were obtained in it. Alternatively, the radiology imaging room in the main emergency area continued to be used for suspected COVID-19 patients.

Once a possible COVID-19 patient was identified, the appropriate pediatric resident /pediatric emergency fellow and a nurse have been notified in an expeditious manner. The physician took the patient's medical history and performed physical examination. The pediatric emergency nurse obtained the required laboratory investigations of the patients. The most crucial point was to wear a face mask during his/her interactions with health care providers (e.g., performing a physical examination, blood drawn) in the room.

Our pediatric emergency workers used alcohol-based hand sanitizers or washed their hands with soap and water before and after contact with a suspected COVID-19 patient according to the recommendation of the Pediatric Infectious Disease Control Committee. They have been trained for the

appropriate use of PPE according to our hospital guidelines, including techniques to safely doff equipment protecting mucous membranes.

Staff cleaned each room after possible COVID-19 patients left the room according to the recommendations of the Pediatric Infectious Disease Control Committee. This staff followed the droplet, contact, and standard precautions with eye protection. Pediatric Infection Disease Control Committee nurses visited the PED frequently and controlled the compliance of the emergency team to the precautions. Patients leaving their treatment room wore face masks, performed hand hygiene, and were educated in proper respiratory hygiene.

2c. Personal Protective Equipment of Pediatric Emergency Department Health Care Workers

Pediatric emergency care for suspected COVID-19 cases or anyone in the same room or area with such patients was given with standard, contact, and airborne precautions, including the use of eye protection (face shield and/or goggles). If patients were critically ill or if an aerosol-generating procedure (e.g., endotracheal intubation, suctioning of the airway, sputum induction) was needed in other areas, HCWs escalated to airborne precautions with the use of a fitted N95/FFP2 or N99/FFP3 respirator instead of a surgical mask.

All our pediatric residents, pediatric emergency fellows, nurses, and other health care providers practiced wearing and doffing PPE regularly. Doffing of PPE was the procedure with the highest risk of infection during the patient-physician interaction, in terms of the spread of SARS-CoV-2. Therefore, posters adopted by the CDC (Centers for Disease Control) showing a simple step-by-step approach to proper doffing of PPE after evaluation of a suspected or confirmed COVID-19 patient were placed inside the rooms.

2d. Training of Pediatric Emergency Workers and Airway Management

All HCWs exercised caution if aerosol-generating procedures, such as bag valve mask (BVM) ventilation, oropharyngeal suctioning, endotracheal intubation, intubation with video laryngoscopy, nebulizer treatment, continuous positive airway pressure (CPAP), biphasic positive airway pressure (BİPAP), or resuscitation involving emergency intubation or cardiopulmonary resuscitation (CPR) were necessary [18,19]. During this training and in real patients, we used an "aerosol box" which consisted of a transparent plastic cube and two circular ports to perform the airway procedure [20]. However, this box extremely restricted the hand movement of the clinicians, especially during the evaluation of smaller children. Therefore, it was not used frequently.

In patients who had deterioration risk and required PICU (pediatric intensive care unit) care, our health care providers considered noninvasive ventilation (NIV), mechanical ventilation, or extracorporeal life support, if necessary. However, these advanced airway management techniques were performed in our isolation service for COVID-19, if enough time was present. During the preparation period, all of our hospital's storage of NIV devices, high-flow nasal cannula oxygen therapy (HFNC) devices, and ventilators were checked. In an effort to combat nosocomial spread and aerosolization of the SARS-CoV-2 virus, all filters were checked before using NIV and/or ventilator. The presence of a HEPA filter was verified in the expiratory limb of the mechanical ventilator prior to patient use at the beginning of the pandemic. Nebulization therapy for patients with acute bronchiolitis and asthma was not given because aerosol generating procedures increased the risk of infection. Instead of nebulized treatment with metered dose inhaler was given via a reusable holding chamber. In the event of a patient presenting with severe respiratory distress or failed prior use of NIV, intubation was performed by an experienced clinician who was previously trained for invasive ventilation and endotracheal tube intubation. Intubation is a high-risk procedure due to the aerosolization of respiratory droplets. Therefore, endotracheal intubation was performed under airborne precautions, including the use of a fitted N95 respirator and if possible, placement of the patient in an isolation room with negative pressure. The most experienced provider intubated with rapid sequence intubation (RSI). To reduce transmission risk, a surgical mask was placed on the patient over the device, especially a high flow nasal cannula (HFNC) or tracheostomy. Video laryngoscopy was preferred to direct laryngoscopy to increase the distance between the intubator and the patient. To reduce inadvertent contamination by touching one's face or hair, a full head cover including the neck was used. Wrist exposure was minimized with the use of long-sleeved gloves or

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vertically taping gloves to the gown. It was observed that circumferentially taping of the gloves made the doffing process of PPE more difficult.

During the pandemic, we had no inadequate access to personal protective equipment.

3. Infection Control Practices for Children with Suspected/Confirmed COVID-19, Organization of Healthcare Facility and Training of Health Care Workers

The main infection control measures taken during the COVID-19 pandemic and our standard practice are shown in Table 1, as well.

3a. General Measures in Pediatric Wards

- During the pandemic, visiting hours were cancelled and the change of parents/caregivers was strictly restricted.
- Mandatory standard precautions including hand-washing practices using water and soap and hand-rubbing via 70% alcohol-based solutions at least 20 seconds applied in all settings for all cases and were reminded repeatedly to HCWs in addition to parents/caregivers.

It was mandatory for HCWs to wear scrubs

- Surgical masks were provided to all HCWs, patients according to age, and parents/caregivers.
- N95/FFP2 or N99/FFP3 respirators were provided to HCWs performing aerosol generating procedures including the sampling of nasopharyngeal or oropharyngeal secretions, intubation, bronchoscopy, and tracheostomy [21].
- HCWs including physicians, nurses, and administrative staff not having contact with suspected/confirmed pediatric cases with COVID-19 were strictly separated from the areas where suspected/confirmed pediatric cases with COVID-19 were evaluated.

3b. Isolation of Suspected/Confirmed Pediatric Cases with COVID-19

A ward had been converted to an "isolation ward" and completely reserved for the monitoring of possible/definitive cases with COVID-19. Each room in this ward had a private toilet and bathroom. We aimed to avoid the contamination of other hospitalized cases. A total of 352 suspected cases were hospitalized in this ward. Patients who were confirmed negative PCR test results for SARS-CoV-2 by July 14, 2020, were transferred to other pediatric wards. When there was a suspicion about COVID-19 in terms of clinical and/or laboratory aspects, the patients were followed up in this ward until discharge. All confirmed cases with asymptomatic and mild disease course were discharged as soon as possible and instructed to quarantine at home for at least 14 days under the notification of The Public Health Department of Ankara to minimize the exposure of HCWs. However, the patients with moderate and critical disease courses were hospitalized in this ward until discharge or death. Moreover, extracorporeal membrane oxygenation (ECMO) and mechanical ventilation via tracheostomy were performed for both cases with critical disease courses in this ward, as well.

3c. Specific measures are taken in the rooms of the isolation ward for suspected/confirmed pediatric cases with COVID-19

Unlike adult hospitals, since the rooms of pediatric hospitals also include parents or caregivers, certain specific measures might be required, particularly when considered a high viral load in the air of the room is considered.

- HCWs wore scrubs that were washed in a cleaning room located in the same isolation ward after usage and they were not allowed to go out with scrubs.
- Disposable food boxes were delivered to the location of HCWs. At the entrance of the rooms, the brochures regarding "putting on and removing PPE" and "prolonged or extended use of N95" were hung on the wall to remind the appropriate use of PPE one more time. At the entrance of the rooms, small tables were placed which included gloves, gowns, masks (surgical and N95/FFP2 or N99/FFP3), bones, overalls, length overshoes, glasses, and face shields. Separate baskets were located outside the room for reusable glasses and face shields to sterilize them with the solution prepared with quarter ammonium after every single use.
- HCWs wore full PPE including N95/FFP2 or N99/FFP3 with surgical masks on before entering the rooms.

- The patients, according to their ages and parents/caregivers were required to wear surgical masks in their rooms during all procedures performed by HCWs.
- In every patient room, patient-specific stethoscopes were placed. Monitors which show the vital signs of patients including blood pressure, oxygen saturation and heart rate were turned in the direction of the door for visibility. During clinical practice, glass doors of rooms were one of the most useful measures used during pandemics to evaluate the vital signs of patients as well as respiratory rate outside the room and to observe the clinical situation of the children, as well.
- Antimicrobial treatments with lower dose numbers or oral antimicrobials were preferred for patients requiring antibiotics to decrease the entrance of HCWs into the rooms.
- Salbutamol inhalation via nebulizer was discontinued and metered dose inhaler with a reusable holding chamber sterilized with the solution prepared with hydrogen peroxide was used instead even if the children were hospitalized in negative pressure isolation rooms.
- After the discharge of a pediatric patient with suspected/confirmed COVID-19, firstly all surfaces including the furniture and frequently touched surfaces in the room were physically cleaned and then disinfected using 1000 ppm bleach solution. The equipment with sensitive surfaces such as monitors, mechanic ventilators, etc. was disinfected using hydrogen peroxide-based solutions. Finally, a device (BioXeco 5) that rotates 360 degrees in the room and sprays 3% hydrogen peroxide was used in patient rooms (Figure 2).

3d. Extending the Use and/or Reusing Respirators

All HCWs who had contact with suspected/confirmed pediatric cases with COVID-19 were required to use appropriate PPE. One of the most important elements of PPE was N95/FFP2 or N99/FFP3 respirators and the appropriate regulation of the use of those respirators for the practice of infection control. Priority for the use of respirators was given to HCWs performing aerosol-generating procedures and working in the isolation ward where pediatric patients with suspected/confirmed COVID-19 were hospitalized [22]. As a result, we had to safely manage the extended use and/or reuse of respirators with proper hand hygiene because of the possibility of supply shortage. We prepared an extended reuse protocol and implemented it into our clinical practice. Therefore, we planned to keep adequate supplies during times of peak demands. Although the extended use and reuse of respirators were reported as 8 hours and 5 uses by CDC [23], respectively per device to ensure a safety margin, both the maximum length of continuous use and the possible number of safe reuses for a respirator were not determined in all settings for all cases. Thus, respirators were used by only a single wearer and commonly reused under the additional training and reminders (e.g., brochures) with the self-physical inspection in our hospital. Respirators were kept in a paper bag or on a paper labeled by the user in a room under UV light (Figure 3) between usages.

4. Clinical Aspects, Laboratory, and Radiologic Imaging

We diagnosed suspected cases, according to our national COVID-19 guidelines. Criteria was changed intermittently by the Coronavirus Scientific Advisory Board in Turkey in response to new data

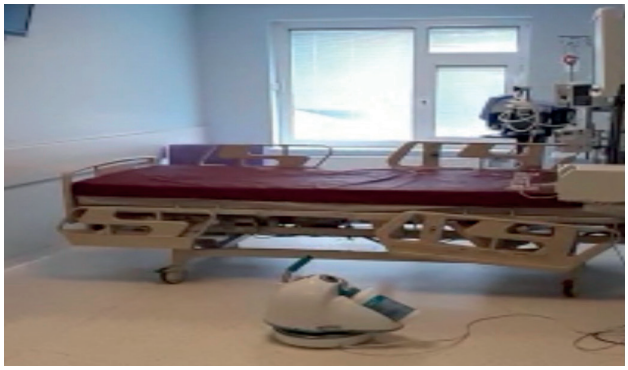

Figure 2. Hydrogen peroxide application in a patient room.

Figure 3. Respirators in a room under UV light between usages.

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regarding the disease [24]. Suspected cases with positive reverse transcriptase-polymerase chain reaction (RT-PCR) or serum-specific antibodies against 2019-nCoV were accepted as confirmed cases [13].

A nasopharyngeal swab and bronchoalveolar lavage fluid specimens were collected for RT-PCR testing according to the condition of the patients. However, at the triage, nasopharyngeal swabbing was the preferred sampling method as compared to feces, blood, urine, or others. Moreover, sputum sampling was actually difficult in our case series because of the nature of small children [25]. In dedicated intervals, a nasopharyngeal swab procedure video was shown to all providers [26]. Since the total positive rate of RT-PCR for nasopharyngeal swab samples was reported to be 30-60% at the initial presentation of COVID-19 [27], testing of a specimen of a suspected pediatric case via RT-PCR has been performed a maximum of five times, and positivity was revealed in maximum fourth sampling in our case series. Of all, (18/117) 15.4% of cases were confirmed by testing serum-specific antibodies despite two negative RT-PCR tests. When antibody testing was used after 14 days of the beginning of the symptoms, sensitivity was over 90% [28]. Therefore, RT-PCR from nasopharyngeal swab samples and/or antibody testing of blood samples were used to confirm the diagnosis of COVID-19 in our case series. Additionally, respiratory viral and/or bacterial panels for alternative diagnoses such as influenza or S. pneumonia have been considered for almost all patients under investigation. Complete blood count, CRP, procalcitonin, and chest x-ray were ordered for all patients. However, other investigations such as liver function tests, coagulation parameters, ferritin, and troponin were done according to the patient's clinical findings.

A clinical algorithm was created according to the severity of the pediatric cases; moreover, it was revised as our knowledge and experience accumulated. The severity of cases was categorized based on the clinical characteristics, laboratory results, and imaging findings as described [29]: a) asymptomatic infection; no clinical and/or radiological findings, b) mild disease; acute upper respiratory tract infection without clinical and radiological pneumonia, c) moderate disease; pneumonia with the symptoms of respiratory tract infection, d) severe disease; progressive respiratory disease with dyspnea and central cyanosis, e) critically ill cases; acute respiratory distress syndrome or respiratory failure, shock, organ dysfunction including encephalopathy, myocardial injury, coagulation abnormalities, and acute kidney injury.

Chest computed tomography (CT) seems to be a crucial radiological modality for the diagnosis of adult cases with COVID-19 showing typical imaging features like ground-glass opacities, multifocal patchy consolidation, and/or interstitial changes with a peripheral distribution [30]. However, a great majority of children had mild or moderate disease without severe pulmonary involvement, which was compatible with our results [7,13]. Therefore, radiological assessment of our pediatric cases with a suspicion of COVID-19 was coupled with clinical and laboratory examinations. As a result, CT was not used routinely for diagnosis because of its low diagnostic value and harmful effects on children and was performed only for patients with severe lower respiratory tract symptoms. When we decided whether to use CT, ultrasound (US) was often preferred as an alternative radiological modality. Ultrasound is repeatable and reliable, has no radiation, and is an inexpensive method. We used lung US as a way to screen patients with suspected COVID-19 pneumonia. Lung US is superior to standard chest radiography, with the additional advantage of the ease of use at the point of care, repeatability, absence of radiation exposure, and low cost [31].

Moreover, literature reports demonstrate that chest X-ray has a low sensitivity in the diagnosis of pulmonary involvement of COVID-19 [32]. Studies conducted in adults have shown that US results were correlated with chest CT, and US seemed as a reasonable diagnostic method in adult cases with COVID-19 pneumonia [33,34]. There is also an increasing number of studies about children which compared US and radiography features of pediatric cases with COVID-19 [35]. We preferred to use the US in addition to a chest x-ray as a diagnostic tool. The only problem with our US machine was it was not wireless. After use, it was cleaned with hydrogen peroxide.

Although data associated with the myocardial injury caused by COVID-19 is limited, particularly in the pediatric population, the cardiovascular system seems to be the second target of COVID-19.

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Patients with COVID-19 have presented with dysrhythmias, acute myocardial infarction, heart failure, myocardial injury, and even myocarditis from the start of the pandemic [36]. Contrary to popular belief, pediatric COVID-19 may be more serious than expected as in our cases, and serious conditions such as multisystem inflammatory syndrome in children (MIS-C) may arise which is related to the exposure to SARS-CoV-2 [37]. Moreover, myocarditis may have been underestimated because of its subtle symptoms in children and since fatality is commonly based on the lung involvement of the virus, clinicians can mainly focus on the respiratory tract symptoms of the patients [38]. Manifestations of myocardial involvement such as ejection fraction decline and myocardial enzyme elevation in addition to fulminant myocarditis have ranged between 10-20% of the patients with COVID-19. It should also be noted that cardiac involvement of COVID-19 may also occur without accompanying symptoms of respiratory tract infection [38,39]. Troponin elevations in patients with COVID-19 might have been directly associated with an increased risk of fatal outcomes [36]. However, as in our cases, the rapid resolution of systolic dysfunction together with mild troponin increase has suggested that the mechanism of systolic dysfunction is not only attributed to the myocardial damage [37]. Further data may have possibly shown us the actual mechanisms of cardiac involvement. We added a cardiac enzyme profile including troponin as well as electrocardiography routinely in the basic evaluation of pediatric cases in our hospital, particularly after we experienced pediatric cases consistent with the multisystem inflammatory syndrome in children (MIS-C).

5. Treatment procedures and follow-up of the confirmed pediatric patients

Currently, there is no specific treatment for patients with COVID-19. Supportive care is the mainstay of treatment, especially in children. Of approximately 1400 pediatric cases in a systematic review including one of the largest pediatric case numbers, 1.9% were admitted to PICU and required mechanical ventilation (MV). Nebulized interferon (IFN) was the most preferred agent for pediatric cases (51.5%), followed by other antivirals (38.4%) and antimicrobials (23.3%). The authors less frequently described the use of intravenous immunoglobulin (IVIG) and corticosteroids (5.2% and 5.8%, respectively) [8]. Of all patients, (1/117) 0.8% were required HFNC, (4/117) 3.4% MV and two of four cases needed ECMO in our case series. Additionally, corticosteroids were not used in any case and IVIG was used for the cases with severe/critical ill disease course (3/117, 2.5%), and anticoagulant therapy was used only for one case with critical disease course.

There is no clear evidence associated with the safety and efficiency of antiviral treatment of children with COVID-19. The development of antiviral treatment was a dynamic process because of the changing and accumulating data in time. During the first days of the pandemic, we prepared a management algorithm that was mainly based on symptomatic and supportive care of pediatric cases without any antiviral targeted therapy. Because the published clinical treatment experiences mostly consisted of descriptive reports and case series from China and early affected countries from the pandemic. Additionally, CDC [40] and WHO [41] highlighted the absence of available specific treatment for patients with confirmed COVID-19 [42]. Although a number of clinical trials were performed to determine the effectiveness and safety of remdesivir, lopinavir/ritonavir, favipiravir, chloroquine/ hydroxychloroquine, and other drugs, few studies involved pediatric cases [43,44].

Many adult-based studies have postulated the mentioned drugs to be effective, whereas the ineffectiveness of some of them such as hydroxychloroquine was published recently despite some of these studies were retracted from the journals. These conflicting findings and suspicious data, as a result, lead us to evaluate the management procedures of cases with COVID-19, particularly in childhood where there is a huge knowledge gap. Lopinavir/ritonavir and arbidol were used in a couple of pediatric case series from China [45], whereas another expert team from the same country [13] did not recommend the use of lopinavir/ritonavir, ribavirin, or chloroquine phosphate in children in their second consensus statement. In a study from North America, remdesivir, hydroxychloroquine with/ without azithromycin, tocilizumab, and convalescent plasma were the therapeutic agents in children with a severe disease course [14]. Since it was reported in a current randomized, controlled trial

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that no beneficial effect of the use of lopinavir/ritonavir was present beyond the standard care in adult cases with COVID-19 [46], we did not prefer to use lopinavir/ritonavir from the beginning of the pandemic. A guideline prepared by The Science Board of Turkish Ministry of Health was published on April 12, 2020 including hydroxychloroquine with/ without azithromycin as a first choice and lopinavir/ritonavir in progressive disease. The revised guideline was published on June 3, 2020, included hydroxychloroquine as the first choice and lopinavir/ritonavir or favipiravir in progressive disease. However, none of the pediatric cases with asymptomatic or mild disease courses were treated with an antiviral agent. The Public Health Department was notified and patients with no significant comorbidities without concern for the deterioration of clinical condition were discharged as soon as possible and were instructed to quarantine at home for 14 days starting from the positive test date. During the first period of the pandemic, we planned to use hydroxychloroquine for the pediatric cases with a disease course that ranged between moderate and critical illness. Therefore, hydroxychloroquine was used in 4 children (4/117, 3.4 %) as a single agent in one pediatric case with a moderate disease course and in combination with favipiravir in the remaining 3 patients with a critical disease course. In the following days, increased radiological abnormalities in chest CT images despite antiviral therapy were detected in two of these patients while their clinical condition was improving. During the second period of the pandemic, none of the antiviral agents, except for one case with a critical disease course (favipiravir was used as a single agent), was used for the treatment of pediatric cases with COVID-19. Later, since it has been proven to be harmful, this recommendation was no longer used.

6. Conclusion and Future Direction

SARS-CoV-2 is a novel coronavirus that has affected an unprecedented number of people in the world. Patients typically presented with a combination of fever or cough and had a history of exposure to a person with COVID-19 or had traveled to an affected geographic area at the beginning of the pandemic. While most patients have mild disease, some may develop severe complications including ARDS and multi-organ failure. No curative treatment is currently approved. Early recognition and isolation of a patient with COVID-19 may help decrease exposure to other patients and healthcare personnel. During the pandemic, handling problems in unity, making clinical decisions together, and acting as a team including the head of our hospital, The Department of Pediatrics, the Pediatric Emergency Department, and the Pediatric Infectious Control Committee were important for success. Hopefully, this team will also stimulate further collaboration during the recovery period. From the beginning of the pandemic, the typical organization and structured workflow of our hospital were largely reorganized when anticipating how to limit the infectious spread and care for all patients. Our main target was to maintain high quality and high-efficiency care, with emphasis on patient and provider safety during the pandemic. We think that the key to success was to perform great teamwork during such kind of disaster. Otherwise, a single problem link in the chain could disrupt the whole process.

Lessons Learned:

1. Accurate and reasonable pre-triage is very important to screen for all patients who need care in PED or outpatient/inpatient clinics to keep the hospital "clean". Furthermore, accurate use of PPE in every setting of the hospital will be beneficial to maintaining "clean" areas.

2. Training of the HCWs again and again for personal protection and continued evaluation of compliance with the isolation rules are the crucial steps to maintain a healthy workplace. This may significantly reduce the contamination rates within HCWs.

3. Almost all our pediatric patients had close contact with confirmed/suspected SARS-CoV-2 cases who were commonly a family member at least within 14 days. Therefore, social isolation even within the family and among relatives is important.

4. SARS-CoV-2 infection seems to affect children less commonly and less severely than adults.

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Author contribution

Study conception and design and draft manuscript preparation: YÖ, ÖT, ÜMŞ, ENÖ, MC. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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