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Clinical Profile of Children Hospitalized with COVID-19 in One of Indonesia's District Hospitals: A First-Year Pandemic Wave Single Center Study

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ABSTRACT

Introduction: Children are known to be less infected by Coronavirus disease 2019 (COVID-19) rather than adults. However, they are still a vulnerable group and the incidence of patients' admission to the hospital continues to increase. As Indonesia's district hospitals have limited resources during the pandemic wave, the data on occurring cases were still underreported specifically those involving children. Therefore, this study aimed to describe the clinical characteristics of children with COVID-19 who were treated at the main referral district hospital in Jember Regency.
Methods: This retrospective observational study collected data on pediatric cases aged 0 – 18 years, who were hospitalized at Dr. Soebandi Hospital, Jember, and confirmed to have COVID-19, from March 2020 to the end of March 2021.
Results: A total of 40 children were hospitalized and confirmed COVID-19 positive during the study period, the majority were 15 – 18 years old (40%), male (65%), and had a history of contact (67.5%). The commonest symptoms were cough (85%), fever (67.5%), and shortness of breath (40%). The laboratory results showed that the majority had decreased neutrophils, increased lymphocytes, and normal chest X-rays (52.5%). Four died out of the five pediatric patients who experienced multimorbidity, and the recorded mortality rate reached 10%. All these four had common underweight clinical morbidity, while acute respiratory distress syndrome dominated the cause of their death.
Conclusion: The majority of pediatric patients were found to have mild to moderate symptoms with good outcomes. The case mortality rate in this study was lower than the national data. Meanwhile, the underweight comorbidity in children with COVID-19 worsened the outcomes.

Keywords: clinical profile; children; COVID-19; district

INTRODUCTION

The World Health Organization (WHO) has determined COVID-19 as a respiratory infectious disease caused by the Novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The first case was reported in December 2019 in the city of Wuhan, Hubei, China but at that time it was believed to be pneumonia of unknown etiology. Shortly, the disease spread to all parts of the world and was declared a pandemic in March 2020[1].

In the first-year situation of the pandemic, WHO confirmed 110,749,023 cases with more than 170 countries involved[2]. It was reported that cases of children were much lower than in adults in some countries with higher rates of asymptomatic infection[3,4,5]. Indonesia is a developing country and is included country with a high population density. Indonesia is on the list of five

countries with the highest number of new cases in Southeast Asia[6]. Indonesia reported 1,278,653 active cases spread across 34 provinces. Meanwhile, infected children of 0 – 18 years age range amounted to 11.9% of the total confirmed cases in February 2021[7], indicating that they were much higher.

Most coronavirus infections in children emerged to be asymptomatic or with mild symptoms. However, recent studies showed some children require hospitalization and intensive care[4,8]. Risk factors for severe disease in pediatric populations have not been clearly identified and the high prevalence of SARS-CoV-2 in Indonesia offers an opportunity to describe severe pediatric disease in more detail. The district shown has limited resources compared to other big cities, and particularly limited data on clinical profile, manifestation, and mortality of children with COVID-19. Therefore, this study aimed to describe reliable data on children with COVID-19 admitted to one of the district hospitals located in Jember, Indonesia. Hence, a better understanding will be provided of situations requiring further pediatrician intervention and government strategies implemented in this region.

METHODS

This observational descriptive study collected data retrospectively and was performed at Dr. Soebandi Jember Hospital located in the East Java region, Indonesia. Data were obtained from the medical records of pediatric patients, aged 0-18 years, who were hospitalized due to COVID-19 infection from March 2020 to the end of March 2021. Only laboratory-confirmed patients according to the gold standard, reverse transcriptase-polymerase chain reaction (RT-PCR) were used as participants. This study also included those hospitalized with other initial diagnoses and later confirmed positive for COVID-19 while being inpatients.

Data were collected in the form of demographic and clinical characteristics of patients consisting of age, gender, nutritional status, clinical symptoms during admission, history of close contact with COVID-19 infected individuals, laboratory examinations, imaging, comorbidities, and outcomes. All the symptoms observed during the admission were reported and classified according to the Indonesian Pediatric Society's Guidelines[9]. Further results of mortality cases were presented in more detail including clinical onset, length of stay, and cause of death. The data were processed using Microsoft Excel and IBM SPSS 22.0. The results were presented as the frequency and percentage of each variable. Additionally, the data were presented as median and range for particular results. The Ethical Committee of the Faculty of Medicine Universitas Jember approved this study with reference code 1497/H25.1.11/KE/2021.

RESULTS

A total of 40 children confirmed with COVID-19 cases were used as participants. Furthermore, the majority were in their adolescent age 15-18 years (40%), while the lowest population was under 1 year old (7.5%). Male (65%) was also the largest gender and most persons had a history of contact with COVID-19 patients (67.5%). Malnutrition is quite a concern in this study, where the underweight had the largest portion (52.5%) (table 1). Cough (85%), fever (67.5%), and shortness of breath (40%) were the most common symptoms detected. None of the patients recorded experienced Multisystem Inflammatory Syndrome in Children (MIS-C).

A blood routine examination was conducted for all the patients, where hemoglobin count (Hb), white blood cell count (WBC), and platelet count were found to be normal in most persons. Decreased neutrophil counts with a median value of 51.5% were diagnosed in the majority (range 22% - 87%).

In contrast, the lymphocyte count was elevated in most persons with a median value of 36% (8% - 64%) as presented in table 2. All the pediatric patients had chest X-ray imaging and most were found to be normal (52.5%), while the rest had pneumonia (42.5%). However, none had chest CT examinations either during initial admission or for evaluation purposes.

Among all patients who suffered comorbidity, five (12.5%) experienced more than one comorbidity. The comorbidity recorded varied, with the commonest results being underweight (52.5%) and overweight (10%), while tuberculosis, gastrointestinal bleeding, and an abscess had an equal portion in 5% of total cases. Notably, in multimorbidity patients, four died during admission, and calculation showed the mortality rate reached 10%.

DISCUSSION

Among the 40 inpatient children recorded, most were admitted with mild to moderate symptoms according to Indonesian guideline classification. The study in the United Kingdom reported that only 0.9% of pediatric patients infected with COVID-19 were hospitalized, while there were 2% in China and 1.7% in North America. The death cases in this current study reached 10%, which was lower compared to the national data, and two tertiary referral hospitals in Indonesia also reported 46% and 40% respectively[10,11].

Based on the results, the males accounted for a higher proportion of cases. Besides, a meta-analysis study of all ages concluded that there was no difference in the proportion of male and female COVID-19 patients. However, the males had three times the tendency to be admitted to the Intensive Care Unit (ICU) and a higher risk of experiencing severe symptoms and death[12]. This current study shows a similar situation where 3 out of the 4 dead patients were males.

The classic clinical COVID-19 symptoms of cough, fever, and shortness of breath were initially found in most patients during admission. While most had symptoms, three of those hospitalized were asymptomatic. One of the asymptomatic patients was born to a mother with COVID-19. The other two were admitted after the district implemented centralized isolation at a referral hospital during the earlier period of the pandemic. Horizontal transmission is believed to be the main source of newborns' infection, but a recent systematic review concluded there is strong evidence of vertical transmission when pregnant women are infected in the third trimester[13,14].

In this study, a blood laboratory examination was conducted for all pediatric patients diagnosed with COVID-19. The majority of hemoglobin, leukocyte, and platelet components were found to be normal. Meanwhile, the neutrophil count mostly decreased and the lymphocytes tended to increase. In contrast, the previous systematic review stated only 5.5% of children showed lymphopenia, while it was more common in adults infected with COVID-19[15]. Other studies reported significant differences between infected children and adults. In children, the leukocyte count tended to be normal, accompanied by a decrease in the neutrophil count and an increase in lymphocytes, which is inversely proportional to the results reported in adults who were predisposed to leukopenia[6,16] .

As presented in case 3, table 4, one patient who had a fatal outcome recorded elevations in d-dimer, ALT, and AST. Another study at a tertiary hospital in Jakarta, Indonesia also noted nine persons examined for d-dimer among 40 infected pediatric patients experienced an overall increase, of which 6 later died[11] .

Table 1. Clinical characteristics and symptoms presented in pediatric COVID-19 patients at Dr. Subandi Jember Hospital, Indonesia

Variable	Results (%)
Sex (n = 40)	
Male	26 (65)
Female	14 (35)
Age, median (range) (n = 40)	13.0 (0 – 18.0)
< 1	3 (7.5)
1 – 4	6 (15)
5 – 9	7 (17.5)
10 – 14	8 (20)
15 – 18	16 (40)
BMI (n = 40)	
Normal	15 (37.5)
Underweight	21 (52.5)
Overweight	4 (10)
History of contact (n=40)	
Yes	27 (67.5)
No	13 (32.5)
Clinical symptoms (n = 40)	
Fever	27 (67.5)
Cough	34 (85.0)
Shortness of breath	16 (40.0)
Sore throat	9 (22.5)
Rhinorrhoea	12 (30.0)
Nausea	6 (15.0)
Vomiting	3 (7.5)
Diarrhea	5 (12.5)
Abdominal pain	4 (10)
Malaise	4 (10)
Anosmia	7 (17.5)
Chest X-ray	
Pneumonia	18 (45)
Normal	21 (52.5)
Comorbid history	
Yes	8 (20)
No	32 (80)
Comorbidities	
Tuberculosis	2 (5)
Gastrointestinal bleeding	2 (5)
Abscess	2 (5)
Underweight	21 (52.5)
Overweight	4 (10)
Cardiovascular disease	1 (2.5)
Cerebral palsy	1 (2.5)
Malignancy	1 (2.5)
Hirschsprung's disease	1 (2.5)
Open fracture	1 (2.5)
Hepatitis B	1 (2.5)
Number of comorbidities	
Single	3 (7.5)
Multiple	5 (12.5)
Outcome	
Discharged alive	22 (55)
Ongoing care	14 (35)
Died	4 (10)

Tabel 2. Laboratory interpretation (n = 40)

Parameter	Normal Value	Median (*range*)	Increased	Normal	Decreased
Haemoglobin (g/dL)	12.0 – 16.0	13.0 (4.3 – 16.7)	2	28	10
White blood cells (109/L)	4.5 – 11.0	7.3 (2.0 – 36.9)	7	32	1
Platelets (109/L)	150 – 450	316.5 (6 – 881)	8	26	6
Neutrophils (%)	54 – 62	51.5 (22.0 – 87.0)	10	14	16
Lymphocytes (%)	25 – 33	36.0 (8.0 – 64.0)	19	18	3

On the first day of admission, all patients had a chest x-ray which indicated 45% had pneumonia. This contradicts a study in the UK, where 90% of pediatric patients with COVID-19 had abnormal chest X-rays. Additionally, it was found that the imaging was nonspecific while most results showed peribronchial thickening and Ground Glass Opacity (GGO), both unilateral and bilateral[17]. Similar results to this current study were reported in Turkey, where most of the chest X-rays were normal and pneumonia was detected in 46% of the samples used. Furthermore, Chest CT analysis was conducted continually and 86% of the recorded cases were found to have an abnormality with GGO in most imaging[18]. In this current study, there was no Chest CT imaging either during initial admission or followed-up evaluation from chest X-ray abnormality. This is probably because the clinical guidelines at the beginning of the pandemic in Indonesia did not include a chest CT as a supporting examination for the insured. Hence, the hospital costs will be a burden due to insurance limitations and low socioeconomic status.

Four pediatric patients died during the treatment performed, two of which were below a year old, while the other two were eight and 17 years old, respectively. Meanwhile, previous national study data recorded that most cases of child mortality were at the age of 10-18 years, i.e. 42 out of 159 cases (26%), followed by the age of 29 days to 1 year reaching 23%[10]. One hypothesis explains that infants have a higher risk because their immune systems are still underdeveloped and will fully mature in the first 7-8 years of life. Moreover, the association between angiotensin-converting enzyme 2 (ACE-2) receptors is high in the lungs despite low levels of the nasal epithelium in children and there is the inadequate use of PPE. The four mortality cases shown from the results were similar to experiencing more than one comorbidity. The highest comorbidities reported in the previous national study data were malignancy and malnutrition. Meanwhile, the most common cause of death was respiratory failure[10,19]. Similarly, the four mortality cases discovered in this current study had underweight nutritional status, one experienced malignancy comorbidity, and three deaths were recorded due to respiratory failure.

Underweight nutritional status was one of the comorbidities that worsened the prognosis. The three mortality cases (1-3) presented in Table 4 were noted to experience hypoalbuminemia. Although the pathogenesis continues to be debated that malnutrition causes a decrease in the supply of amino acids to the liver, leading to a reduced albumin production. However, the low serum albumin is believed to be closely related to the inflammatory process, and common in patients with critical conditions or malnutrition[20,21]. Hypoalbuminemia will decrease oncotic pressure and increase the shifting extravasation of fluid from the intravascular space to the interstitial space.

Tabel 4. Clinical characteristics of mortality cases

No	Age	Sex	History of contact	Symptoms related to COVID-19	Comorbidities	Laboratory results	Chest X-ray	Onset before admission (days)	Length of stay (days)	Cause of death
1 (MA)	3 Months	M	No	Shortness of breath, fever, cough, rhinorrhea	ARDS, cyanotic CHD (suspected TOF), abscess capitis, sepsis, gastrointestinal bleeding, anasarca, hypoalbuminemia, underweight	↓ Platelets, albumin, blood glucose level ↑ lymphocytes count, ALT	Right pneumonia	2	5	ARDS
2 (DO)	8 Years	F	No	Shortness of breath, sore throat, nausea, abdominal pain, diarrhea	Intra-abdominal tumors, hyponatremia, anemia, hypoalbuminemia, pulmonary edema, underweight	↓Hb, blood glucose level, albumin, sodium, lymphocytes count ↑Platelets, neutrophil count	Pulmonary alveolar edema	30	4	ARDS
3 (AP)	17 Years	M	Yes	Shortness of breath, cough, nausea, vomiting	Pulmonary tuberculosis, DIH, Hypoalbuminemia, thrombocytopenia, Hepatitis B, underweight	↓WBC, platelets, neutrophil count, blood glucose level, ↑ lymphocytes count, ALT, AST, bilirubin D-dimer, HBsAg +, Metabolic acidosis	Bilateral pneumonia	3	5	ARDS
4 (MK)	6 Months	M	No	Fever, convulsions	Hydrocephalus, subgaleal abscess due to an infected plate, sepsis, gastrointestinal bleeding, underweight	↓Hb, lymphocytes count, ↑WBC, platelets, neutrophil count, ALT, AST	Bilateral pneumonia	6	2	Syok sepsis

Abbreviations: ARDS, acute respiratory distress syndrome; CHD, congenital heart disease; TOF, tetralogy of Fallot; DIH, drug-induced hepatitis; ALT, alanine aminotransferase; Hb, hemoglobin; WBC, white blood cell; AST, aspartate aminotransferase; HbsAg, hepatitis B surface antigen

The described condition tends to cause pulmonary edema once extravascular fluid accumulates excessively in the lung parenchyma[22,23,24]. Once there is no compensation, this can progress to acute lung injury with severe hypoxemia and subsequent death[22].

One patient (4th case, MK) died from aggravated septic shock due to a subgaleal abscess, and the person also had underweight nutritional status. There is a close relationship between nutritional deficiencies that can slow wound healing and increase infection rate[25]. A study concluded that critically ill and underweight pediatric patients have a significant proportion of the tendency to stay longer in the Pediatric Intensive Care Unit (PICU) and experience an increased need for ventilators and a high frequency of fluid overload[26].

The analysis of its relation to COVID-19 shows that malnutrition is the main cause of immunodeficiency capable of affecting innate and adaptive immune responses, where body reserves and energy are needed in during viral proliferation inhibition[27]. Additionally, infection with the SARS-CoV-2 that enters the human body tends to cause an inflammatory response in the regulatory process of the immune system to eliminate the virus[28]. As previously mentioned, excessive inflammatory processes contribute to a decrease in serum albumin. Hence, in severe conditions, hypoalbuminemia pathways will increase the incidence of ARDS or multi-organ damage that can lead to death[24]. Strong interrelated associations were suspected between the morbidities that mortality patients had, including the incidence of exposure to COVID-19 and being underweight.

This study can not be separated from several limitations. First, patients with mild/no symptoms who were treated at home were not included as participants. Second, the association between variables as well as risk factors was not examined. Third, the laboratory tests including markers of infection were not performed in most patients but only in certain critically ill persons. Fourth, chest CT imaging was not conducted for the infected pediatric patients. Also, limitations and infrastructure in the district are a concern for pediatricians and policymakers. Still, this study was carried out in the first year of the COVID-19 pandemic while there were less centralized isolation places provided by the government. The selected hospital has been the main reference from the beginning of the pandemic. Therefore, this study can be a regional representation of the children's cases occurring at that time.

CONCLUSION

Cases of the children infected with COVID-19 were dominated by the age of 15-18 years, amounting to 16 of 40 cases (40%), with the majority being males. The commonest clinical symptoms were cough, fever, and shortness of breath with 90% of patients presenting a good outcome. The CFR in this study was 10% which is lower than the national data. Additionally, mortality cases had multimorbidity where all patients experienced underweight nutritional status. Further investigation is needed to understand the association of immunological pathways considering morbidity and mortality with the inflammatory process and nutritional status, thereby identifying the best therapy for COVID-19 patients.

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