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Characteristics of children with confirmed SARS-CoV-2 infection in Indonesia

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ABSTRACT

Objective: COVID-19 in children poses a significant challenge due to the atypical/asymptomatic presentations. The study is aimed to help understand clinical characteristics in Indonesian children for better management and control of transmission.

Methods: clinical characteristics of children with confirmed COVID-19 were retrospectively analysed from the database dating from March to November 2020.

Results: the study revealed a high prevalence (67.3%) of asymptomatic cases from contact tracing population. The most common symptoms in children with confirmed COVID-19 were cough and fatigue. Among symptomatic patients, 14/21 (66.7%) had either radiological and/or clinical evidence of pneumonia.

Conclusion: children with respiratory symptoms especially those with contact history should be screened for possible COVID-19 infection regardless of disease severity.

1. Introduction

As of 31 October 2020, Indonesia has the unenviable highest number of coronavirus disease 2019 (COVID-19) cases in Southeast Asia with more than 400,000 confirmed cases and 13,000 deaths [1]. Although children were initially thought to be less affected with milder symptoms [2], it is now known that children can be severely affected and that the infection is more common in children than previously thought [3,4]. However, there is limited data on paediatric COVID-19 especially in the region. Our aim was to investigate the characteristics of Indonesian children with confirmed COVID-19 based on their demographic, clinical, laboratory data, and chest X-ray (CXR) findings available at the Eijkman Institute for Molecular Biology (EIMB).

2. Methods

Our study retrospectively analysed the data of laboratory confirmed COVID-19 children from 0 to <18 years of age [15] including those from contact-tracing available at EIMB from March to November 2020. The laboratory diagnosis was performed in accordance with WHO recommended real-time RT-PCR assays developed by Charité Institute of Virology - Universitätsmedizin Berlin (modified), US-Centers for Disease Control (modified), and Hong Kong University, all with similar analytical sensitivities for SARS-CoV-2 [5] detection, as well as the Cobas® 6800, a reliable commercially available SARS-CoV-2 assay [6]. To compare the clinical characteristics according to age, the patients were divided into groups of <1, 1–5, 6–10, and 11-<18. Clinical characteristics between asymptomatic and symptomatic subjects were compared using either the Wilcoxon–Mann Whitney U test for continuous variables or Fisher's exact test for categorical variables. Symptom clusters were summarised and visualised in an upset plot to present the co-occurring symptoms. All statistical analyses were carried out in R version 4.0.2 with R Studio version 1.3.1073.

3. Results

Out of a total of 46,452 patients in which specimens were submitted to EIMB between March and November 2020, 1973 were children <18 years old. Two hundred and eight (10.5%) were positive for COVID-19 comprising 140 asymptomatic (67.3%) and 68 symptomatic cases (32.7%) (Fig. 1), the age group and gender proportion were not significantly different between these two categories. The paediatric specimens were from 190 private hospitals and public health facilities in Banten,

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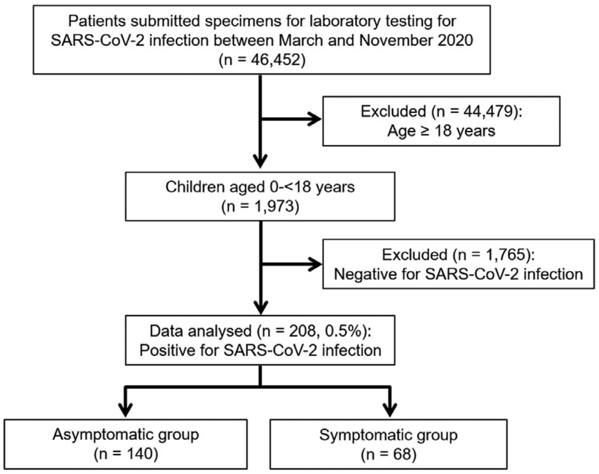

Fig. 1. Patient selection flow chart. Nasopharyngeal and/or oropharyngeal swab specimens, including those from contact-tracing, submitted to the Eijkman Institute for Molecular Biology from March to November 2020 were tested for SARS-CoV-2 using real-time RT-PCR assays developed by Charité Institute of Virology - Universitätsmedizin Berlin (modified), US-Centers for Disease Control (modified), and Hong Kong University, [5], as well as the Cobas® 6800 assay [6]. Specimens from patients aged ≥18 years old [15] and those who tested negative for SARS-CoV-2 were excluded from the analysis.

Jakarta, West Java, Central Kalimantan, East Nusa Tenggara, South Sulawesi, and North Sulawesi provinces.

Demographic and clinical characteristics, as well as laboratory results of 208 SARS-CoV-2 confirmed cases are shown in Supplementary Tables S1 and S2. The median age of the patients was 9 years (interquartile range, IQR 4–14 years), and the proportion of age for <1, 1–5, 6–10 and 11-<18 years were 9.6%, 21.6%, 21.6%, and 47.1%, respectively. The ratio of female to male was 46.6% to 53.4%. One hundred and eighteen subjects (56.7%) reported close contact with either confirmed or suspected COVID-19 cases, majority with the family members (84/118, 71.2%). Underlying diseases were reported in 7 of 208 patients (3.4%), consisting of immunodeficiency (2/7, 28.6%), cancer (2/7, 28.6%), both immunodeficiency and cancer (1/7, 14.3%), cardiovascular disease/hypertension (1/7, 14.3%) and epilepsy (1/7, 14.3%). The underlying diseases were only reported in the symptomatic patients (7/65, 10.8%; $p < 0.001$). Sixteen of 36 patients (44.4%) had CXR results consistent with pneumonia, 2 had underlying disease.

The most frequently reported symptom was cough (57.4%), followed by fatigue (39.7%) and fever (36.8%) (Fig. 2A). Shortness of breath, the common manifestation of COVID-19 in adults, was observed in 15/68 (22.1%) mostly in infants. Characterisation of symptom clusters using an upset plot showed that the most common symptom cluster was cough only (8/68, 11.8%), followed by runny nose only (6/68, 8.8%) (Fig. 2B).

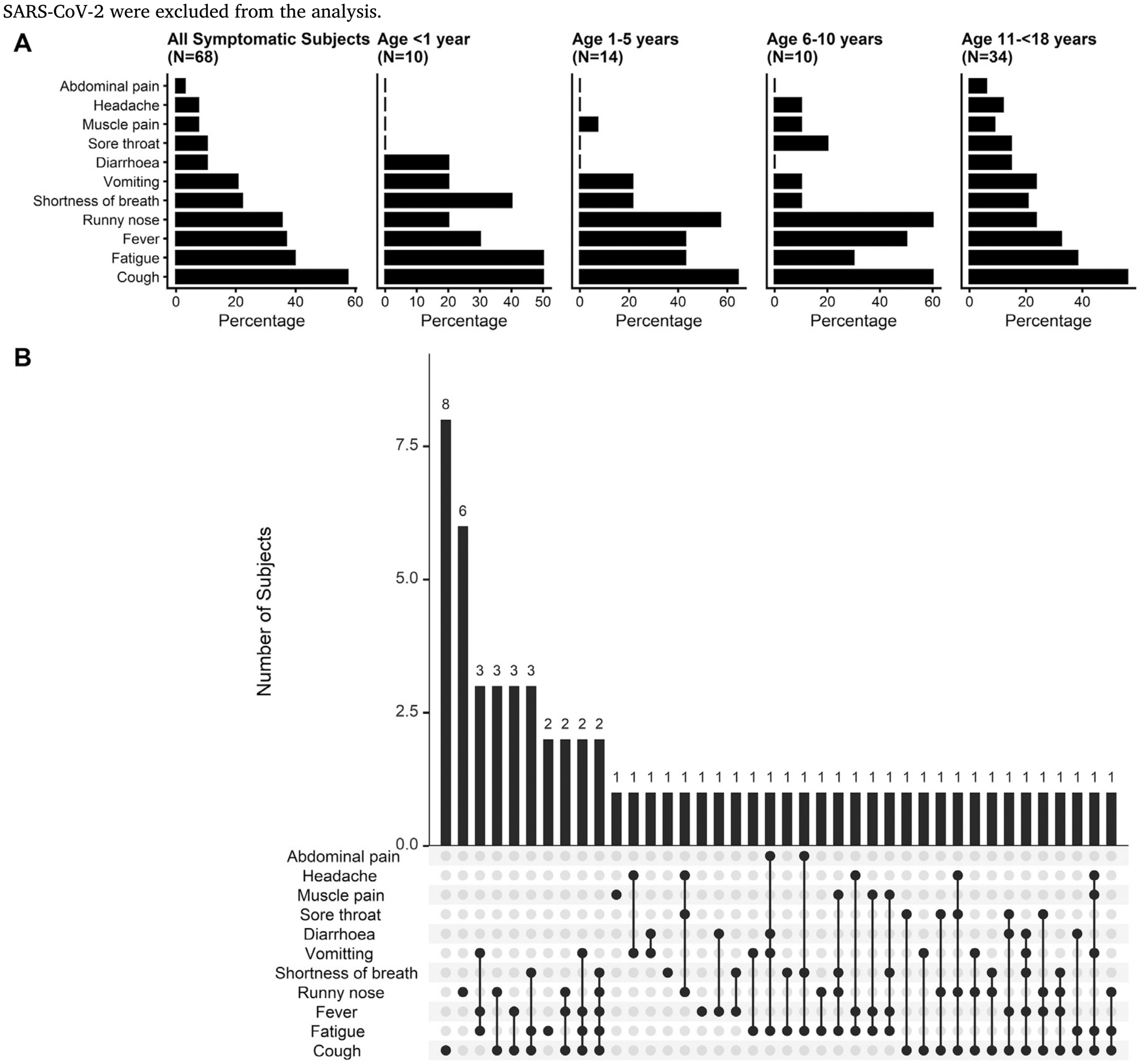

Fig. 2. Prevalence of symptoms among 68 symptomatic children from 0 to <18 years old with confirmed SARS-CoV-2 infection. (A) The prevalence of individual symptoms, in all symptomatic subjects and each age group (<1, 1–5, 6–10 and 11–<18 years), are shown as bar plots. (B) The symptom clusters are shown as an upset plot. The bar chart shows the number of subjects who reported symptom clusters. The black dots and connecting lines represent the combination of symptoms that make up each symptom cluster.

Table 1
Characteristics and laboratory results of asymptomatic and symptomatic children from 0 to <18 years old with confirmed SARS-CoV-2 infection.

Characteristic	Asymptomatic (N = 140)	Symptomatic (N = 68)	p
Gender [n/N (%)]			
Female	69/140 (49.3)	28/68 (41.2)	0.302
Male	71/140 (50.7)	40/68 (58.8)	
Age group [n/N (%)]			
>1 years	10/140 (7.1)	10/68 (14.7)	0.157
1–5 years	31/140 (22.1)	14/68 (20.6)	
6–10 years	35/140 (25.0)	10/68 (14.7)	
11-<18 years	64/140 (45.7)	34/68 (50.0)	
Hospitalised [n/N (%)][a]			
No	90/101 (89.1)	8/52 (15.4)	**<0.001**
Yes	11/101 (10.9)	44/52 (84.6)	
Underlying diseases [n/N (%)][b]			
No	135/135 (100.0)	58/65 (89.2)	**<0.001**
Yes	0/135 (0.0)	7/65 (10.8)	
Median leucocytes [x 10^9/L, IQR][c]	10.4 (9.3–20.6)	8.6 (3.1–24.1)	0.439
Leucopenia [n/N (%)] [c]			
No	7/8 (87.5)	12/20 (60.0)	0.214
Yes	1/8 (12.5)	8/20 (40.0)	
Median lymphocytes [x 10^9/L, IQR][d]	3.9 (0.4–382.7)	1.4 (0.5–3.9)	0.345
Lymphopenia [n/N (%)][d]			
No	5/8 (62.5)	8/18 (44.4)	0.673
Yes	3/8 (37.5)	10/18 (55.6)	
Median thrombocytes [x 10^9/L, IQR][c]	251.5 (159.8–458.0)	358.0 (155.5- 467.2)	0.666
Thrombocytopenia [n/N (%)][c]			
No	6/8 (75.0)	16/20 (80.0)	1.000
Yes	2/8 (25.0)	4/20 (20.0)	
Chest X-ray result [n/N (%)][e]			
No abnormality observed	3/7 (42.9)	5/21 (23.8)	0.133
Pneumonia	2/7 (28.6)	14/21 (66.7)	
Pneumonia not confirmed	2/7 (28.6)	1/21 (4.8)	
Bronchitis	0/7 (0.0)	1/21 (4.8)	
Radiological and/or clinical evidence of pneumonia [n/N (%)][f]			
No	11/13 (84.6)	8/25 (32.0)	**0.005**
Yes	2/13 (15.4)	17/25 (68.0)	

[a] Available data: 101 asymptomatic subjects and 52 symptomatic subjects.
[b] Available data: 135 asymptomatic subjects and 65 symptomatic subjects.
[c] Available data: 8 asymptomatic subjects and 20 symptomatic subjects.
[d] Available data: 8 asymptomatic subjects and 18 symptomatic subjects.
[e] Available data: 7 asymptomatic subjects and 21 symptomatic subjects.
[f] Available data: 13 asymptomatic subjects and 25 symptomatic subjects.Classification: Leucopenia, leucocyte < 5 × 10^9/L; lymphopenia, lymphocytes < 1.55 × 10^9/L; thrombocytopenia, thrombocytes < 140 × 10^9/L. The p values were calculated with either Wilcoxon-Mann Whitney U test for continuous variables or Fisher's exact test for categorical variables. The significant p values are in bold ($p < 0.050$).

The majority of symptomatic patients (44/52, 84.6%) were hospitalised, 17/25 (68.0%) had either radiological and/or clinical evidence of pneumonia (Table 1). Radiologically confirmed pneumonia was found more in the 1–5 year age group (77%), followed by the 6–10 year age group (66.7%) (Fig. 3). Complete blood counts were only available for 28 subjects and showed no significant difference between these two groups (Table 1). Information was not available for poor oral intake, rash, and other reported manifestations of paediatric COVID-19 [7].

4. Discussion

Children make up almost one-third, about 83 million, of Indonesia's population of around 270 million [8]. More than 200 children under 18 in the country were reported to die from COVID-19 by mid-October [1], with >10% mortality in under-five children [9]. Many studies have reported that close contact within the family is the likely mode of SARS-CoV-2 infection in children [10], which is similar with the finding of this study (71.2%). The most effective prevention strategy to limit the spread of COVID-19 in children is through a family effort. Therefore, it is imperative for the whole family to apply simple and yet important preventive procedures such as hand hygiene, respiratory isolation, physical distancing, and surface disinfection. Study of paediatric COVID-19 is challenging, and the true situation could be distorted due to asymptomatic or atypical presentations. As with previous report [11], the paediatric patients with COVID-19 in our study were mostly asymptomatic and showed more upper respiratory symptoms. The most common symptoms in this study were cough followed by fatigue and fever, slightly different from most reports that showed fever followed by cough as major symptoms in children [12]. Although most of the SARS-CoV-2 infected children were reported as asymptomatic or with mild-moderate symptoms [12], children with underlying diseases are known to have an increased risk of developing a severe or critical illness [11]. The outcome of those with co-morbidities in our study was unknown, but 2 (40%) reported radiologically confirmed pneumonia. Asymptomatic children seen in the majority of cases as well as those with mild symptoms could be shedding high number of virus [13] and could play a significant role in community transmission. This study has limitations to be noted - First, the study population was small due to limited paediatric outbreak samples submitted to EIMB most likely due to the inapparent infection in this population. Second, detailed clinical information including multisystem inflammatory syndrome (MIS-C), recently reported to be associated with paediatric COVID-19 [14] as well as outcome data were not available due to the nature of this study. Third, there was no follow up

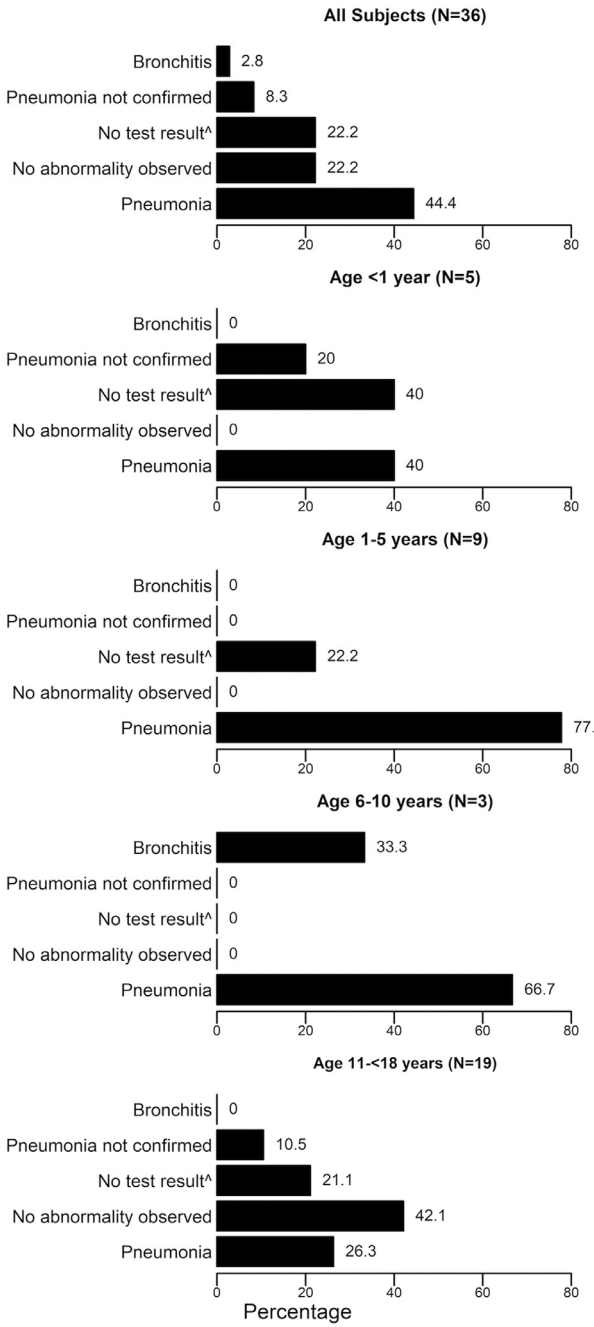

Fig. 3. Chest X-ray findings in 36 symptomatic children from 0 to <18 years old with confirmed SARS-CoV-2 infection. All symptomatic subjects and each age group (<1, 1–5, 6–10 and 11-<18 years) are shown as bar plots in percentage. ^No test result: Chest X-Ray examination was reported to be performed but no data available on the test result.

data and the asymptomatic population might be lower than stated as these children could later become symptomatic. Fourth, our study was based on data from only 4 provinces of Indonesia, and therefore, our findings could not be extrapolated to the entire country.

5. Conclusion

Our study provides insight into the clinical characteristics of COVID-19 in 208 Indonesian children, a population that might play a significant role in disease transmission. Although children have less frequent severe infection, emerging reports of Multisystem Inflammatory Syndrome in Children (MIS-C) necessitate continued surveillance in paediatric patients with respiratory symptoms. Children with contact history should be screened for possible COVID-19 infection regardless of disease severity. Further studies with large paediatric cohorts are needed for this vulnerable population to gain a better understanding of risk factors, outcomes, severity, role in community transmission, and appropriate management strategies.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethical approval

This study was performed in accordance with the human subject protection guidance provided by the Eijkman Institute Research Ethics Commission No. 127.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jcvp.2021.100027.

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