Clinical Manifestation of digestive problems among children with COVID-19: A Literature Review

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Abstract. This review explores digestive problems in children with COVID-19. Researchers examined studies (2019-2021) focusing on "children," "Covid 19," and "digestive issues." They prioritized original English-language research on hospitalized children (0-16) with digestive problems, MIS-C, or other health conditions. The review highlights a concerning trend: digestive issues like nausea, vomiting, abdominal pain, and diarrhea are common in children with COVID-19, especially those with MIS-C or other conditions. Viral proteins found in intestinal cells suggest the virus directly attacks the digestive tract, potentially explaining the prevalence of diarrhea. This points to diarrhea as a key digestive symptom and raises the possibility of fecal-oral transmission, a potentially overlooked route. Given these findings, the review proposes rectal swabs with fecal RT-PCR testing alongside nasopharyngeal swabs for diagnosing COVID-19 in children. This approach could improve detection and lead to better control measures. Recognizing diarrhea and the possibility of fecal-oral transmission can help healthcare professionals refine diagnosis and implement appropriate infection control to protect children.

Keywords: Children; Covid 19; Clinical Manifestations; Digestive Problems; Diarrhea.

1 Introduction

Currently, the situation of COVID-19 cases in the world is increasing, including Indonesia in a state of emergency. Data from the World Health Organization (WHO) in July 2021 showed that Indonesia was ranked second after India in the number of confirmed cases of COVID-19 and deaths, which amounted to 2,313,829[1]. At the beginning of the COVID-19 pandemic, the disease caused by the corona virus was rarely experienced by children. However, in June 2021, in Indonesia, a fairly high number of COVID-19 cases occurred in children, which was around 11-12%. The number of under-five deaths due to COVID-19 has also increased, by 50%, where there are 1,000 child deaths every week. This case is included in the highest cases of covid 19 in children in Asia[1]. The clinical conditions experienced by children with COVID-19 have milder symptoms than adults. However, due to the high population of children, it is the main cause of community spread of SARS-CoV-2 in children[2]. For this reason, it is important to know what clinical signs may occur in children with COVID-19.

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The most common symptoms that occur in children are respiratory problems, such as pneumonia, bronchiolitis, tachypnea. Other symptoms include gastrointestinal problems, fever, and neurological disorders. In children who are confirmed to have COVID-19 and are hospitalized, the majority have Multisystem Inflammatory Syndrome in Children (MIS-C), or multisystem inflammation. In COVID-19 children with MIS-C, symptoms that are more common, apart from respiratory problems, are gastrointestinal disturbances. It was reported that 90% of gastrointestinal symptoms were experienced by children with covid 19 [3][4][5].

Children are more susceptible to digestive problems because the immune system in children is immature, which may weaken the immune system in the digestive tract [7]. In COVID-19 patients, the presence of viral nucleocapsid proteins has been verified in almost the entire gastrointestinal lumen, such as the stomach, duodenum and anus. The process of entry of corona virus cells into the digestive tract begins with the entry of 2 proteins, namely the enzyme receptor that converts angiotensin 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) [19]. The digestive problems that appear in children with COVID-19 are diarrhea, nausea, vomiting and abdominal pain. Children with COVID-19, whether they have mild, moderate or severe symptoms, all have diarrhea. The average duration of diarrhea in children is 3.7 days, with varying severity of diarrhea. Most children with diarrhea can recover on their own, but there is a group of children who experience a higher severity of diarrhea during the course of their illness. Children who have diarrhea are also very at risk of dehydration, which will aggravate the disease [4] [6]. In addition, it was seen that between PCR tests of faecal and respiratory specimens showed that virus particles persisted longer in the digestive tract than in the respiratory tract. It is very possible that the virus can spread easily through faces [7]. Previous studies have described the respiratory characteristics of COVID-19 children, but have not described their gastrointestinal conditions. This study aims to to describe the clinical manifestations of digestive problems in children infected with SARS-Cov-2, so that the public can know and prevent the risk of severity and spread of COVID-19 disease.

2 Method

The literature search uses two databases, namely PubMed and ScienceDirect. Key words included were pediatric, covid 19 and gastrointestinal characteristic. The selected articles focus on original research, in English, and published from 2019 to 2021, with inclusion criteria: the subject is a child, Multisystem Inflammatory Syndrome Children (MIS-C), has comorbidities and has clinical signs of digestive problems.

The results of the literature search found 19 articles from PubMed and 6 articles from ScienceDirect. Of the 25 articles that were screened, 10 articles were excluded due to duplication. A further 5 articles were excluded because the title, aim and content did not match. Furthermore, from 10 articles were screened again and 4 articles were excluded because they did not meet the inclusion criteria, so there were 6 articles that were eligible.

Data extraction was carried out on all articles found, with the selection of: first author, year, place of study, purpose, population, comorbid and gastrointestinal characteristics. The purpose of this literature analysis is to to describe the clinical manifestations of digestive problems in children infected with SARS-Cov-2.

3 Result

The literature search results obtained 6 articles from pubmed and 19 articles from sciencedirect. Of the 25 relevant articles found, 6 articles were found that met the inclusion criteria, on Fig. 1 and design and characteristics of the studies on Table 1.

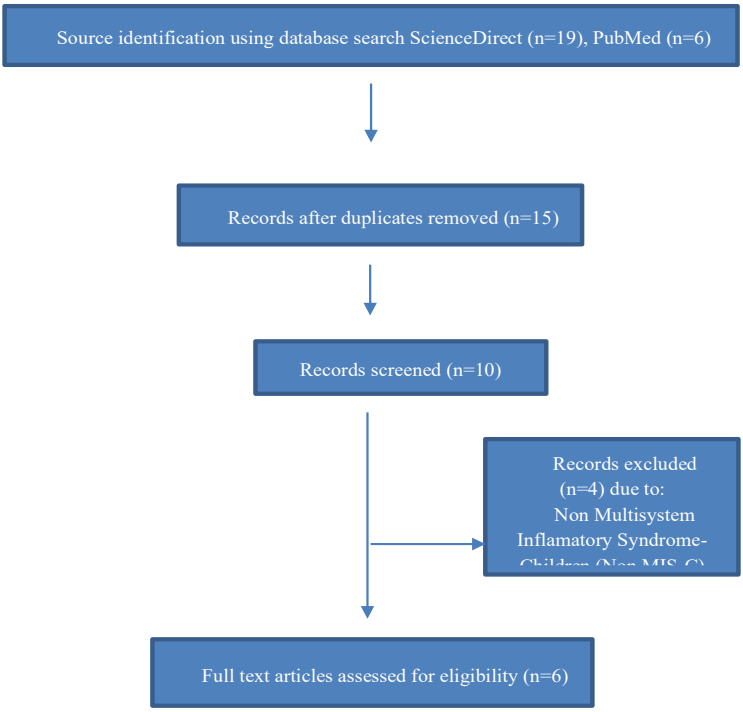

Fig. 1. PRISMA diagram of retrieved article

Table 1. Design and Characteristics of the Studies

Author and Location of studies	Barbosa – 2020 - Brazil	Setta, et. Al – 2020 - Brazil	Whittaker, et al – 2020 - England	Torres, et al - 2020 -Santiago, Chile	Al, et al (2021), Oman	Qiu, et al (2020), China
Aim	Describe the clinical characteristics of children and	Describe the clinical, laboratory and radiological	Describe the clinical and laboratory characteris-	Describe the clinical and epidemiological	Describe the epidemiology, clinical	Describe the Clinical and epidemiological

	adolescents admitted to intensive care with confirmed COVID-19	characteristics, as well as the outcomes of children with MIS-C	tics of hospitalized children	characteristics of hospitalized children with multisystem inflammatory syndrome in children (MIS-C) in Santiago, Chile	and laboratory features, and outcome of children hospitalized with coronavirus disease 2019 (COVID-19)	features of children with coronavirus disease (COVID-19)
Population	Patients aged 1 month to 19 years admitted consecutively (March May 2020) were included 79 children age average 4 years old, MIS-C	Conducted in 17 pediatric intensive care units in five states in Brazil, from March to July 2020 Patients from 1 month to 19 years who met the MIS-C diagnostic criteria	58 children from 8 hospitals in England admitted between March 23 and May 16, 2020, MIS-C	220 children, age 0-16 years old, who were admitted to the ICU with criteria MIS-C	56 children < 14 years old required hospitalization in 7 Omani centers over 5 month (February-July 2020), MIS-C	36 children (aged 0–16 years) with confirmed COVID-19 in three hospitals in Zhejiang, China, From Jan 17 to March 1, 2020, MIS-C
Comorbidities	Neuromuscular disease Chronic respiratory disease, Onomatological disease, Congenital heart defect, Undernutrition, Diabetes, Prematurity, Chronic liver disease, Obesity	Chronic neurological disease, Asthma, Congenital heart defect, Undernutrition, Obesity, Diabetes, Adrenoleukodystrophy (ADL)	Asthma, neutralizability, epilepsy, sickle cell trait, alopecia.	Overweight or obesity, asthma, primary immunodeficiency, GATA 3 deficiency, prematurity, and gestational age of 33 weeks	Sickle cell disease (SCD), chronic respiratory conditions, Asthma, cystic fibrosis) and severe neurological impairment	
Clinical Manifestation of digestive problems	On MIS-C Group: Diarrhea, feed refusal, vomiting, dehydration	Abdominal pain, diarrhea, vomiting, feed refusal, Dehydration, Lymphadenopathy, Enteritis	Abdominal pain, Diarrhea, vomiting	Abdominal pain, Diarrhea, vomiting	Vomiting, Diarrhea, Abdominal pain	Vomiting, Diarrhea

From the six literatures reviewed, it was found that the research subjects were children who were in the age range 0-16 years, were hospitalized and experienced MIS-C. Of the six journals there are five journals that show that children have comorbidities. The majority of comorbidities experienced are asthma, congenital heart disease, and neuromuscular disease. Judging from the research sites, they are spread all over the world, namely Brazil, England, Chile, Oman and China. All researchers conducted a study with the aim of describing the clinical characteristics of children with confirmed COVID-19, including gastrointestinal characteristics. From all the literature, it was found that the confirmed gastrointestinal symptoms experienced in children were diarrhea, nausea, vomiting, abdominal pain and dehydration.

4 Discussion

From the results of the literature review, it was found that the research subjects were children who were in the age range of 0-16 years. This shows that COVID-19 can be experienced by children of all age ranges, whether during infant, toddler, preschool, school or adolescent.

Symptoms of COVID-19 that occur in children are milder than adults, but multisystem inflammatory symptoms often appear which are very likely to aggravate the disease. Multisystem inflammation occurs due to the development of antibodies against the corona virus, especially IgG-mediated antibodies, which causes an increase in the severity of the disease. MIS-C in children can develop several weeks after COVID-19 infection [5]. The form of multisystem inflammation that occurs in children infected with corona virus is the occurrence of disorders in more than two organs, persistent fever, gastrointestinal symptoms and shock with cardiac dysfunction and Kawasaki disease, namely the occurrence of vascular vasculitis and cardiac ischemia [8]. Other specific symptoms of multiorgan inflammation are prolonged fever, usually more than five days, abdominal pain, diarrhea, vomiting, dyspnea or tachypnea, pallor or cyanosis of the extremities, decreased urine output, and conjunctivitis weakness, rash and neurological disturbances. Of these symptoms, the most prominent seen and felt by children are fever and digestive problems [8][9][10].

The results of a review of the journal showed that most of the children with confirmed COVID-19 experienced gastrointestinal symptoms. Digestive problems that appear in the form of diarrhea, nausea, vomiting and abdominal pain [5]. This is evidenced that 90% of children infected with the corona virus experience gastrointestinal symptoms. Children are more susceptible to digestive problems because the immune system in children is immature, which may weaken the immune system in the digestive tract [7]. In COVID-19 patients, the presence of viral nucleocapsid proteins has been verified in almost the entire gastrointestinal lumen, such as the stomach, duodenum and anus. The gastrointestinal epithelium also undergoes plasmacytic and lymphocytic infiltration, with manifestations of interstitial edema, especially in the esophagus, stomach, duodenum and rectum [11]. This problem can increase the possibility of transmission through feco-oral, as evidenced by the RT PCR test in the feces of children who are

positive for a long time. Although the results of the nasopharyngeal swab in children were negative, when a rectal swab was performed, the RT PCR results were still positive. It is very possible to transmit the infection via the fecal oral route [12]. In several pediatric studies, SARS-CoV-2 was present in the feces and was found to persist for several weeks. This is something that needs to be watched out for, that the possibility of fecal-oral transmission can still occur even though the child has finished the 14-day isolation period and the nasopharyngeal swab result is negative [13].

As long as a child is infected with the corona virus, the most felt gastrointestinal complaints are nausea, vomiting, diarrhea and abdominal pain. Of these symptoms, diarrhea is the most common and the main symptom. Diarrhea occurs one to 8 days after onset and the mean duration of diarrhea is 3 days. The process of entry of corona virus cells into the digestive tract begins with the entry of 2 proteins, namely the enzyme receptor that converts angiotensin 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) [14]. The presence of these two proteins is a very potential medium for entry and development of viruses. As type II alveolar cells enter the lungs and esophagus, enterocytes are also absorbed in the ileum and large intestine. After the virus enters, virus-specific RNA and proteins are synthesized in the cytoplasm of the cell, to assemble new virions, and are released into the digestive tract, where the virus is finally released into the feces. This proves that SARS-CoV-2 can be spread through feces [12].

Another possibility can also cause diarrhea in children with confirmed COVID-19. First, direct viral attack on the digestive tract can cause diarrhea, as evidenced by the detection of viral nucleocapsid proteins in epithelial cells. Second, children who are given antiviral drugs or traditional medicines can also cause nausea and diarrhea. Third, the consumption of antibiotics can also worsen digestive symptoms due to dysbiosis or an imbalance in the ratio of good and bad bacteria and microbes in the digestive tract, which is induced by antibiotics [7]. The occurrence of diarrhea can also be due to corona virus infection which changes intestinal permeability, with malabsorption by enterocytes. Corona viruses are also capable of altering the microbiome through regulation of the mucosal immune system [13].

5 Conclusion

This review of the literature demonstrates that diarrhea is the clinical sign of digestive issues in children infected with the corona virus. As shown by the identification of viral nucleocapsid protein in intestinal epithelial cells and the extended positive RT-PCR test of stool specimens, diarrhea is caused by a direct viral attack on the digestive system. This is the reason why feco-oral transmission of the virus is a potential. In addition to nasopharyngeal swab examination, rectal swab should be considered to determine RT PCR of stool specimens. From this literature review, it is hoped that the public can know and prevent the risk of the severity and spread of COVID-19 in children. For further research, an analysis of the characteristics of diarrhea in children with Covid-19 can be carried out.

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