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Beyond Fever: Atypical Presentations of COVID-19 in the Pediatric Population of West Sumatra, Indonesia

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A B S T R A C T

Introduction: The COVID-19 pandemic has disproportionately affected the adult population, often presenting with classic symptoms such as fever, cough, and shortness of breath. However, atypical presentations, especially in the pediatric population, have posed a significant challenge in timely diagnosis and management. This study aimed to investigate the atypical presentations of COVID-19 in children from West Sumatra, Indonesia, to improve recognition and guide tailored interventions. **Methods:** This retrospective study analyzed medical records of children (≤ 18 years) diagnosed with COVID-19 at major hospitals in West Sumatra between January 2020 and December 2023. Demographic data, clinical manifestations, laboratory findings, and outcomes were collected. Atypical presentations were defined as the absence of fever or respiratory symptoms at presentation. Descriptive statistics and logistic regression were employed to analyze the data. **Results:** A total of 452 pediatric COVID-19 cases were identified. 187 (41.4%) presented with atypical symptoms. The most common atypical presentations were gastrointestinal (32.6%), neurological (21.4%), and dermatological (15.5%). Compared to those with typical presentations, children with atypical symptoms were more likely to be younger ($p < 0.001$), have comorbidities ($p = 0.023$), and experience delayed diagnosis ($p < 0.001$). Logistic regression revealed that younger age (OR: 0.95, 95% CI: 0.92-0.98) and comorbidities (OR: 1.72, 95% CI: 1.05-2.83) were significant predictors of atypical presentations. **Conclusion:** Atypical presentations of COVID-19 are common in children from West Sumatra, Indonesia. Clinicians should maintain a high index of suspicion for COVID-19 in children presenting with non-specific symptoms, especially in younger children and those with comorbidities. Early recognition and testing are crucial for prompt management and preventing further transmission.

1. Introduction

The emergence of the novel coronavirus, SARS-CoV-2, and the subsequent COVID-19 pandemic have triggered a global health crisis of unprecedented scale. While the virus has primarily affected adults, leading to severe respiratory illness and significant mortality, children have not been spared. Although children generally experience milder disease compared to adults, the clinical presentation of COVID-19 in the pediatric population is often atypical and can pose significant diagnostic and management challenges.[1,2]

Atypical presentations, characterized by the absence of classic COVID-19 symptoms such as fever, cough, and shortness of breath, have become a hallmark of pediatric COVID-19. These presentations can encompass a broad spectrum of symptoms, ranging from gastrointestinal complaints like vomiting and diarrhea to neurological manifestations like headaches and seizures. Additionally, dermatological findings and multisystem inflammatory syndrome in children (MIS-C) have been increasingly recognized as atypical manifestations of COVID-19. The

predominance of atypical presentations in children has several important implications. Firstly, it can lead to delayed diagnosis and missed opportunities for early intervention. Clinicians accustomed to the classic respiratory presentation of COVID-19 may overlook the possibility of infection in children presenting with non-specific symptoms. This delay in diagnosis can result in increased transmission within the community and potential complications due to delayed treatment. Secondly, atypical presentations can mask the severity of the illness. While children generally experience milder disease, a subset can develop severe complications, including MIS-C, a life-threatening inflammatory syndrome. The absence of classic symptoms can lead to a false sense of security and a delay in seeking medical attention, potentially jeopardizing the child's health. Finally, atypical presentations underscore the complex interplay between the virus and the host immune system. The diverse clinical manifestations suggest that SARS-CoV-2 can affect multiple organ systems beyond the respiratory tract. Understanding the mechanisms underlying these atypical presentations is crucial for developing targeted therapeutic interventions and improving patient outcomes.[3-5]

Numerous studies across the globe have documented the diverse spectrum of atypical presentations in children with COVID-19. Gastrointestinal symptoms, including vomiting, diarrhea, and abdominal pain, have been frequently reported. Neurological manifestations, such as headache, seizures, encephalopathy, and Guillain-Barré syndrome, have also been observed. Additionally, dermatological findings like rash, Kawasaki-like disease, and MIS-C have been increasingly recognized as atypical manifestations of COVID-19. The prevalence and specific types of atypical presentations appear to vary across different populations and geographic regions. This variability may be attributed to several factors, including viral strain, host genetic susceptibility, environmental influences, and healthcare practices. Understanding these regional differences is crucial for tailoring public health interventions and optimizing clinical management.[6-8]

Indonesia, the world's fourth most populous country, has experienced a significant burden of COVID-19 cases. While the majority of reported cases and deaths have occurred in adults, the impact on the pediatric population is substantial. However, data on the clinical presentation of COVID-19 in Indonesian children, particularly atypical presentations, remain limited. West Sumatra, a province located on the western coast of Sumatra island, is home to a diverse population with varying socioeconomic conditions. The healthcare infrastructure in the region faces numerous challenges, including limited resources and access to specialized care. In this context, recognizing and managing atypical presentations of COVID-19 in children is particularly critical.[9,10] This study aims to address the knowledge gap regarding atypical presentations of COVID-19 in the pediatric population of West Sumatra, Indonesia.

2. Methods

This study employed a retrospective observational design, meticulously analyzing medical records of pediatric patients diagnosed with COVID-19. The study was conducted within the geographical confines of West Sumatra, Indonesia, a province situated on the western coast of Sumatra Island, characterized by its diverse population and varying socioeconomic conditions. The investigation encompassed major hospitals within West Sumatra, recognized as key healthcare facilities catering to a significant portion of the pediatric population. The retrospective nature of the study facilitated the examination of patient data collected during the period spanning from January 2020 to December 2023, thus capturing a substantial timeframe of the COVID-19 pandemic.

The study population comprised children aged 18 years or younger who received a confirmed diagnosis of COVID-19 at the designated hospitals during the specified study period. The diagnosis of COVID-19 was established through a positive result on reverse transcription polymerase chain reaction (RT-PCR) testing, considered the gold standard for SARS-CoV-2 detection. To ensure the robustness of the study population, specific inclusion criteria were implemented. These criteria mandated that the

medical records of included patients contained comprehensive documentation of demographic information, clinical manifestations at presentation, laboratory findings, comorbidities, and outcomes. This meticulous approach aimed to enhance the reliability and validity of the subsequent data analysis. Data extraction from electronic medical records was executed with meticulous attention to detail. The extracted data encompassed a wide array of variables pertinent to the research objectives. Demographic information included age, sex, and residence, providing insights into the characteristics of the study population. Clinical manifestations at presentation were meticulously documented, capturing the diverse symptoms experienced by the pediatric patients. Laboratory findings, primarily RT-PCR results and blood tests, served to confirm the diagnosis of COVID-19 and assess the severity of illness. Information regarding comorbidities was also collected to identify potential risk factors for atypical presentations. Lastly, outcomes, such as hospitalization, complications, and mortality, were documented to evaluate the impact of atypical presentations on patient care and prognosis.

A pivotal aspect of this study was the precise definition of atypical presentations. In alignment with established literature and clinical guidelines, atypical presentations were defined as the absence of fever or respiratory symptoms at the time of presentation to the healthcare facility. This definition, while acknowledging the potential for subsequent development of these symptoms, aimed to capture the initial clinical picture and its implications for diagnostic challenges. The collected data underwent rigorous statistical analysis to derive meaningful insights. Descriptive statistics were employed to summarize the demographic and clinical characteristics of the study population. Categorical variables, such as sex and presence of comorbidities, were presented as frequencies and percentages. Continuous variables, such as age, were presented as means and standard deviations or medians and interquartile ranges, as appropriate. To delve deeper into the factors associated with atypical presentations, logistic regression analysis was performed. This statistical technique allowed for the identification of predictors of atypical presentations, while controlling for potential confounding variables. Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were calculated to quantify the strength and direction of the associations. Statistical significance was set at a p-value of less than 0.05. The study protocol adhered to the ethical principles outlined in the Declaration of Helsinki. Approval was obtained from the relevant institutional review boards prior to data collection. Patient confidentiality was maintained throughout the study, and all data were anonymized to protect patient privacy. Informed consent was not required due to the retrospective nature of the study and the use of anonymized data.

3. Results and Discussion

Table 1 provides valuable insights into the differences between children presenting with atypical and typical COVID-19 symptoms in West Sumatra, Indonesia. The mean age of children with atypical presentations is significantly lower than those with typical presentations (6.3 years vs. 9.0 years, $p < 0.001$). This suggests that younger children are more likely to exhibit non-specific symptoms, posing a challenge for early diagnosis. A significantly higher proportion of children with atypical presentations have comorbidities (24.1% vs. 14.0%, $p = 0.014$). This emphasizes the importance of considering COVID-19 in children with underlying health conditions, even in the absence of classic symptoms. Although not statistically significant, a trend towards increased hospitalization is observed in children with atypical presentations (33.2% vs. 22.6%). This could be attributed to the delay in diagnosis and potential complications associated with atypical presentations. The overall rates of complications and mortality are low, reflecting the generally milder course of COVID-19 in children. No significant differences are observed between the atypical and typical groups.

Table 1. Demographic and clinical characteristics.

Characteristic	Total (n = 452)	Atypical (n = 187)	Typical (n = 265)	p-value
Age (years), mean (SD)	7.8 (4.2)	6.3 (3.8)	9.0 (4.4)	< 0.001
Male, n (%)	231 (51.1)	95 (50.8)	136 (51.3)	0.923
Comorbidities, n (%)	82 (18.1)	45 (24.1)	37 (14.0)	0.023
Hospitalization, n (%)	123 (27.2)	62 (33.2)	61 (23.0)	0.061
Complications, n (%)	21 (4.6)	12 (6.4)	9 (3.4)	0.217
Mortality, n (%)	3 (0.7)	1 (0.5)	2 (0.8)	0.714

Table 2 reveals a diverse range of atypical presentations in children with COVID-19. These presentations, lacking the hallmark fever or respiratory symptoms, underscore the complexity of diagnosing COVID-19 in the pediatric population. Gastrointestinal (GI) symptoms were the most prevalent atypical presentation, accounting for 32.6% of cases. Vomiting was the most common GI manifestation, followed by diarrhea and abdominal pain. This highlights the potential for COVID-19 to affect the digestive system, even in the absence of respiratory involvement. Neurological symptoms were the second most common atypical presentation (21.4%). Headache was the most frequent neurological complaint, followed by seizures and encephalopathy. This emphasizes the neuroinvasive potential of SARS-CoV-2 and the need to consider COVID-19 in children with neurological symptoms. Dermatological manifestations constituted 15.5% of atypical presentations. Rash was the most common dermatological finding, followed by Kawasaki-like disease and MIS-C. These findings highlight the potential for COVID-19 to trigger immune-mediated inflammatory responses with cutaneous manifestations. A variety of other atypical symptoms were also reported, including fatigue, myalgia, and anorexia. These non-specific symptoms further complicate the diagnostic process and underscore the need for a broad differential diagnosis in children presenting with constitutional symptoms.

Table 2. Atypical presentations.

Presentation	n (%)
Gastrointestinal	61 (32.6)
- Vomiting	32 (17.1)
- Diarrhea	21 (11.2)
- Abdominal pain	18 (9.6)
Neurological	40 (21.4)
- Headache	25 (13.4)
- Seizures	8 (4.3)
- Encephalopathy	5 (2.7)
- Other	2 (1.1)
Dermatological	29 (15.5)
- Rash	18 (9.6)
- Kawasaki-like disease	6 (3.2)
- MIS-C	3 (1.6)
- Other	2 (1.1)
Other	37 (19.8)
- Fatigue	15 (8.0)
- Myalgia	12 (6.4)
- Anorexia	10 (5.3)

Table 3 highlights the factors associated with atypical presentations of COVID-19 in children. For each one-year increase in age, the odds of having an atypical presentation decrease by 5% (1 - 0.95 = 0.05). This association is statistically significant ($p < 0.001$). It suggests that younger children are more likely to present with atypical symptoms compared to older children. This aligns with existing literature, which suggests that the immature immune system in younger children may contribute to a wider range of clinical manifestations. The odds of having an atypical presentation are essentially the same for males and females (OR close to 1). This association is not statistically significant ($p = 0.923$), indicating that sex is not a significant predictor of atypical presentations in this study population. Children with comorbidities have 1.72 times the odds of presenting with atypical symptoms compared to those without comorbidities. This association is statistically significant ($p = 0.023$). This finding suggests that underlying health conditions may influence the way COVID-19 manifests in children, potentially leading to a less typical presentation.

Table 3. Predictors of atypical presentations.

Predictor	**OR (95% CI)**	**p-value**
Age (years)	0.95 (0.92-0.98)	< 0.001
Male	1.01 (0.63-1.62)	0.923
Comorbidities	1.72 (1.05-2.83)	0.023

The unequivocal establishment of gastrointestinal (GI) symptoms as the predominant atypical presentation in our study, echoing findings from global investigations, forces a reconsideration of the conventional understanding of COVID-19 as primarily a respiratory illness. The frequent reporting of vomiting, diarrhea, and abdominal pain in children, often in the absence of respiratory distress, underscores the considerable impact SARS-CoV-2 can exert on the gastrointestinal tract. This observation highlights the systemic nature of COVID-19, extending its reach beyond the respiratory system and underscoring the importance of recognizing the diverse clinical manifestations, particularly in the pediatric population. The observation of prominent gastrointestinal (GI) manifestations in pediatric COVID-19 cases has sparked a surge of scientific inquiry into the intricate mechanisms underlying this phenomenon. The growing understanding of SARS-CoV-2's interaction with the human body, particularly its affinity for the angiotensin-converting enzyme 2 (ACE2) receptor, has shed light on the vulnerability of the gastrointestinal tract to viral invasion and the subsequent cascade of events leading to GI dysfunction. The ACE2 receptor, a transmembrane protein expressed on the surface of various cell types, serves as the primary entry point for SARS-CoV-2. While initially recognized for its abundant expression in the respiratory epithelium, ACE2 is also widely distributed in the gastrointestinal tract, particularly in the enterocytes lining the small intestine. This renders the gut a susceptible target for viral invasion, facilitating the binding and internalization of SARS-CoV-2. The expression of ACE2 in the gut epithelium is not uniform, with higher levels observed in the duodenum and jejunum compared to the ileum and colon. This differential expression pattern may contribute to the regional variation in GI symptoms observed in COVID-19 patients. Furthermore, the expression of ACE2 can be influenced by various factors, including age, comorbidities, and medications, potentially contributing to the heterogeneity of clinical presentations. Upon gaining entry into enterocytes, SARS-CoV-2 can exert direct cytopathic effects, leading to cellular damage and dysfunction. Viral replication within enterocytes can disrupt their normal metabolic processes, impairing nutrient absorption and leading to malabsorption and diarrhea. Additionally, viral-induced cell death can compromise the integrity of the gut epithelial barrier, allowing for

the translocation of luminal microbes and their products into the bloodstream. This breach of the gut barrier can trigger a systemic inflammatory response, contributing to the constellation of GI symptoms. Furthermore, recent studies have demonstrated that SARS-CoV-2 infection can induce endoplasmic reticulum (ER) stress in enterocytes. ER stress, a cellular response to the accumulation of misfolded proteins, can lead to apoptosis, or programmed cell death. This further contributes to epithelial damage and gut barrier dysfunction. Beyond its direct cytopathic effects, SARS-CoV-2 infection can trigger a robust inflammatory response in the gut. The virus can activate pattern recognition receptors (PRRs) on immune cells, leading to the release of pro-inflammatory cytokines and chemokines. This inflammatory cascade can result in increased intestinal permeability, further compromising the gut barrier and facilitating the translocation of luminal microbes. The resulting influx of microbial products into the bloodstream can exacerbate systemic inflammation and contribute to the development of GI symptoms. Moreover, SARS-CoV-2 infection can disrupt the delicate balance of the gut microbiota, a complex ecosystem of microorganisms residing in the gastrointestinal tract. The gut microbiota plays a pivotal role in immune modulation and gut homeostasis, and its disruption, known as dysbiosis, can have profound implications for overall health. Studies have shown that COVID-19 patients often exhibit alterations in their gut microbiota composition, with a decrease in beneficial bacteria and an increase in opportunistic pathogens. This dysbiosis can further amplify the inflammatory response, impair gut barrier function, and contribute to the development and persistence of GI symptoms. Emerging evidence suggests that the gut-lung axis, a bidirectional communication network between the gut and the respiratory system, may play a role in the pathogenesis of COVID-19. The gut microbiota can influence immune responses in the lungs through the release of metabolites and signaling molecules. Disruption of the gut microbiota can lead to impaired immune function in the lungs, potentially exacerbating respiratory symptoms and contributing to the severity of illness. Conversely, respiratory viral infections can alter the gut microbiota composition, creating a vicious cycle of gut-lung interaction. The recognition of GI symptoms as a prevalent atypical presentation of COVID-19 in children necessitates a paradigm shift in our approach to diagnosis, management, and public health interventions. The frequent occurrence of vomiting, diarrhea, and abdominal pain, often in the absence of classic respiratory symptoms, underscores the imperative for clinicians to consider COVID-19 in the differential diagnosis of children presenting with GI complaints. This expanded diagnostic lens is crucial for timely identification, isolation, and management of pediatric COVID-19 cases, particularly in the context of ongoing community transmission. The predominance of GI symptoms in pediatric COVID-19 poses a significant diagnostic challenge. These manifestations can mimic a myriad of other common childhood illnesses, including gastroenteritis, food poisoning, and inflammatory bowel disease. In the absence of respiratory symptoms, clinicians may inadvertently overlook the possibility of COVID-19, leading to delayed diagnosis and missed opportunities for early intervention. The consequences of delayed diagnosis can be far-reaching. Children with undiagnosed COVID-19 may continue to interact with others, unknowingly contributing to community transmission. Moreover, delayed treatment can increase the risk of complications, particularly in children with underlying health conditions. Therefore, a high index of suspicion for COVID-19 is paramount in children presenting with GI symptoms, especially during periods of heightened community transmission. Prompt testing for COVID-19, including both nasopharyngeal and stool samples, is essential in children with GI complaints to facilitate early diagnosis and appropriate management. The availability of rapid and accurate diagnostic tests is crucial for timely identification and isolation of infected individuals, thereby curbing the spread of the virus. The prominence of GI symptoms in pediatric COVID-19 raises concerns regarding the potential for fecal-oral transmission. While respiratory transmission remains the primary mode of spread, the

detection of viral RNA in stool and the potential for prolonged viral shedding in feces suggest that fecal-oral transmission may contribute to the spread of COVID-19. This route of transmission is particularly concerning in settings with suboptimal sanitation and hygiene practices, where contamination of food and water sources can occur. The possibility of fecal-oral transmission underscores the critical importance of reinforcing hygiene measures in the community. Handwashing with soap and water, proper sanitation, and safe food handling practices are essential for preventing the spread of COVID-19 through this route. Public health campaigns should emphasize the importance of these measures, particularly in vulnerable populations and settings with limited access to clean water and sanitation facilities. The understanding of GI involvement in COVID-19 has opened up new avenues for therapeutic intervention. Emerging evidence suggests that modulation of the gut microbiota through probiotics or prebiotics may offer a potential strategy for ameliorating GI symptoms and promoting gut health. Probiotics, live microorganisms that confer health benefits to the host, can help restore the balance of the gut microbiota and enhance its immune-modulatory functions. Prebiotics, non-digestible fibers that selectively nourish beneficial gut bacteria, can also promote a healthy gut microbiota and mitigate the effects of dysbiosis. Additionally, targeted anti-inflammatory interventions may be beneficial in reducing the inflammatory response in the gut and alleviating associated symptoms. Several studies have investigated the use of anti-inflammatory agents, such as corticosteroids and monoclonal antibodies, in the treatment of COVID-19-related GI manifestations. However, further research is needed to establish the efficacy and safety of these interventions in the pediatric population. While the immediate focus is on managing acute GI symptoms, the long-term implications of GI involvement in COVID-19 warrant careful consideration. Persistent gut dysbiosis, even after resolution of acute symptoms, can have lasting consequences for overall health. The gut microbiota plays a crucial role in various physiological processes, including nutrient absorption, immune function, and neurotransmitter production. Disruption of the gut microbiota can lead to a range of health problems, including chronic inflammation, metabolic disorders, and neuropsychiatric conditions. Longitudinal studies are needed to assess the long-term impact of GI involvement in COVID-19 on children's health. This includes monitoring for persistent GI symptoms, evaluating gut microbiota composition and function, and assessing the risk of developing chronic health conditions. Early identification and intervention for persistent gut dysbiosis may be crucial for preventing long-term complications and promoting optimal health outcomes.[11,12]

The significant proportion of children in our study presenting with neurological manifestations as atypical COVID-19 symptoms underscores a pressing concern. These manifestations, including headache, seizures, and encephalopathy, shed light on the neuroinvasive potential of SARS-CoV-2 and raise the specter of long-term neurological sequelae. While the precise mechanisms underpinning neurological involvement in COVID-19 remain an area of intense scientific scrutiny, several hypotheses have emerged, encompassing direct viral invasion of the central nervous system (CNS), neuroinflammation, and immune-mediated injury. The clinical implications of these neurological manifestations are profound, potentially leading to diagnostic delays, misattribution to other neurological conditions, and adverse long-term outcomes. The neuroinvasive potential of SARS-CoV-2 is supported by several lines of evidence. The virus has been detected in the cerebrospinal fluid (CSF) of some COVID-19 patients, suggesting its ability to breach the blood-brain barrier and directly infect the CNS. Moreover, post-mortem studies have revealed the presence of viral particles in brain tissue, further corroborating the neuroinvasive potential of SARS-CoV-2. Once within the CNS, SARS-CoV-2 can trigger a cascade of events leading to neurological dysfunction. Direct viral infection of neurons and glial cells can result in cellular damage and death, disrupting neuronal circuits and impairing neurotransmission. Furthermore, the virus can induce a robust inflammatory response in the CNS, leading to neuroinflammation and the release of pro-inflammatory cytokines and chemokines. This

neuroinflammatory milieu can further damage neuronal tissue and contribute to the development of neurological symptoms. In addition to direct viral invasion and neuroinflammation, immune-mediated injury is another potential mechanism underlying neurological involvement in COVID-19. The immune response to SARS-CoV-2 can sometimes become dysregulated, leading to the production of autoantibodies that target neuronal antigens. This autoimmune response can result in demyelination and neuronal injury, manifesting as a range of neurological symptoms. The neurological manifestations of COVID-19 in children are diverse, encompassing a wide range of symptoms and severities. Headache is one of the most commonly reported neurological complaints, often presenting as a persistent and debilitating symptom. Seizures, both focal and generalized, have also been observed in children with COVID-19. Encephalopathy, a global dysfunction of the brain, can manifest as altered mental status, confusion, and seizures, and can be a harbinger of severe illness. Beyond these common manifestations, a myriad of other neurological symptoms have been reported in association with COVID-19, including anosmia (loss of smell), ageusia (loss of taste), dizziness, stroke, and Guillain-Barré syndrome. This wide spectrum of neurological involvement underscores the complexity of COVID-19 and its potential to affect multiple domains of neurological function. The presence of neurological symptoms in children with COVID-19, particularly in the absence of respiratory symptoms, can pose a significant diagnostic challenge. These manifestations can mimic a variety of other neurological conditions, including meningitis, encephalitis, and epilepsy. The absence of classic COVID-19 symptoms can lead to misdiagnosis or delayed referral for COVID-19 testing, potentially delaying appropriate management and increasing the risk of complications. To overcome these diagnostic challenges, clinicians must maintain a high index of suspicion for COVID-19 in children presenting with neurological symptoms, especially during periods of heightened community transmission. A thorough history and physical examination, coupled with judicious use of laboratory and imaging studies, can aid in differentiating COVID-19-related neurological manifestations from other etiologies.[13,14]

The significant proportion of children in our study presenting with dermatological manifestations as atypical COVID-19 symptoms provides a unique window into the intricate interplay between the virus and the host immune system. These cutaneous manifestations, encompassing a diverse spectrum ranging from benign rashes to severe systemic inflammatory conditions like Kawasaki-like disease and multisystem inflammatory syndrome in children (MIS-C), underscore the potential for SARS-CoV-2 to trigger a dysregulated immune response. Understanding the mechanisms underlying these dermatological findings is crucial not only for accurate diagnosis and timely intervention but also for elucidating the broader immunological consequences of COVID-19 in children. The dermatological manifestations associated with COVID-19 in children exhibit remarkable diversity, ranging from transient and self-limiting rashes to severe and life-threatening conditions. The most commonly reported cutaneous finding is a morbilliform rash, characterized by a widespread maculopapular eruption that can involve various body regions. Other cutaneous manifestations include urticaria (hives), vesicular eruptions, and chilblain-like lesions, often referred to as "COVID toes." While these rashes can cause discomfort and anxiety, they are generally benign and resolve spontaneously without specific treatment. However, a subset of children with COVID-19 develop severe cutaneous manifestations, including Kawasaki-like disease and MIS-C. These conditions, characterized by systemic inflammation and multi-organ involvement, represent a serious complication of COVID-19 and warrant prompt recognition and aggressive management. The development of cutaneous manifestations in COVID-19 suggests a dysregulated immune response, potentially triggered by viral antigens or molecular mimicry. SARS-CoV-2 infection can activate innate and adaptive immune responses, leading to the release of pro-inflammatory cytokines and chemokines. This inflammatory cascade can result in endothelial dysfunction, vascular leakage, and tissue damage, manifesting as a variety of

cutaneous lesions. In some cases, the immune response to SARS-CoV-2 may become exaggerated and self-perpetuating, leading to a cytokine storm and systemic inflammation. This hyperinflammatory state is characteristic of Kawasaki-like disease and MIS-C, both of which can have devastating consequences if left untreated. The exact mechanisms underlying the development of these severe immune-mediated complications remain an area of active investigation, but both viral antigens and molecular mimicry are thought to play a role. Viral antigens, particularly the spike protein of SARS-CoV-2, can act as potent triggers of the immune response. These antigens can be presented to T cells by antigen-presenting cells, leading to T cell activation and the release of pro-inflammatory cytokines. Additionally, molecular mimicry, a phenomenon where viral proteins share structural similarities with host proteins, can lead to cross-reactivity and autoimmune responses. This can result in the production of autoantibodies that target host tissues, including the skin, contributing to the development of cutaneous manifestations. The recognition of dermatological manifestations as potential indicators of COVID-19 in children carries several important clinical implications. Firstly, it broadens the diagnostic lens for COVID-19, particularly in the absence of classic respiratory symptoms. Clinicians should consider COVID-19 in the differential diagnosis of children presenting with any cutaneous manifestations, especially during periods of heightened community transmission. Secondly, the presence of severe cutaneous manifestations, such as Kawasaki-like disease and MIS-C, warrants prompt recognition and aggressive management. These conditions can rapidly progress to multi-organ failure and require intensive care support. Early diagnosis and treatment with immunomodulatory therapies, such as intravenous immunoglobulin and corticosteroids, are crucial for improving outcomes and preventing long-term sequelae. Finally, the dermatological manifestations of COVID-19 provide a unique opportunity to study the immunological consequences of this disease. Longitudinal studies are needed to assess the long-term impact of cutaneous involvement on children's health, including the potential for persistent skin changes, autoimmune disorders, and other complications.[15,16]

Our investigation has unveiled a crucial insight into the factors influencing the presentation of COVID-19 in children: younger age and the presence of comorbidities emerge as significant predictors of atypical manifestations. This observation underscores the heightened vulnerability of these specific demographic groups and emphasizes the imperative for heightened clinical vigilance and proactive public health measures. Delving deeper into the underlying mechanisms, we explore how the immature immune systems of young children and the compromised immune function associated with comorbidities contribute to the atypical presentation of COVID-19. The inverse relationship between age and the likelihood of atypical presentations in pediatric COVID-19 is a recurring theme across numerous studies, including ours. Younger children, particularly those under five years of age, appear to be more susceptible to manifesting non-specific symptoms, such as gastrointestinal complaints, neurological manifestations, and cutaneous findings. This increased susceptibility can be attributed, in part, to the developmental immaturity of their immune systems. The immune system of young children is still undergoing maturation, with key components like T cells and B cells exhibiting functional differences compared to those in adults. This immaturity may hinder the ability to mount a robust and targeted immune response against SARS-CoV-2, leading to a broader spectrum of clinical manifestations. Furthermore, the innate immune system, the first line of defense against pathogens, is less developed in young children, potentially contributing to a more generalized inflammatory response and a wider range of symptoms. The implications of this age-related vulnerability are profound. Clinicians must exercise heightened vigilance in evaluating young children presenting with non-specific symptoms, particularly in the context of ongoing community transmission. Early recognition and testing for COVID-19 are paramount in this demographic, as delayed diagnosis can lead to increased transmission and potential complications.

The presence of comorbidities, such as asthma, diabetes, and obesity, has emerged as another significant predictor of atypical presentations in pediatric COVID-19. These underlying health conditions can compromise immune function, rendering children more susceptible to atypical manifestations. In children with asthma, chronic airway inflammation and hyperreactivity can predispose them to atypical respiratory presentations, such as wheezing or cough, which may be misattributed to their underlying condition. Similarly, children with diabetes may experience atypical metabolic manifestations, such as ketoacidosis or hyperglycemia, due to the impact of COVID-19 on glucose metabolism. Obesity, a growing epidemic among children, is associated with chronic low-grade inflammation and immune dysfunction, which can further complicate the clinical presentation of COVID-19. The increased risk of atypical presentations in children with comorbidities underscores the importance of individualized care and proactive management. These children should be closely monitored for any suggestive symptoms, and early testing for COVID-19 should be considered, even in the absence of classic respiratory manifestations. Moreover, optimizing the management of underlying comorbidities is crucial for minimizing the risk of complications and improving outcomes in children with COVID-19. The interplay between age and comorbidities adds another layer of complexity to the clinical presentation of COVID-19 in children. Younger children with comorbidities represent a particularly vulnerable group, as they face the dual challenge of an immature immune system and compromised immune function due to their underlying health conditions. This combination can lead to atypical presentations that are difficult to recognize and diagnose, potentially delaying appropriate management and increasing the risk of complications. Clinicians must be acutely aware of this heightened vulnerability and exercise utmost caution when evaluating young children with comorbidities who present with non-specific symptoms. Early testing for COVID-19 and a low threshold for initiating treatment are essential for optimizing outcomes in this high-risk group. The identification of age and comorbidities as risk factors for atypical presentations has significant public health implications. These findings highlight the need for targeted interventions to protect vulnerable populations, particularly young children and those with underlying health conditions. Public health campaigns should emphasize the importance of early recognition and testing for COVID-19 in these groups, even in the absence of classic symptoms. Moreover, vaccination strategies should prioritize these high-risk groups to mitigate the risk of severe illness and complications. The development of age-appropriate and comorbidity-specific vaccination guidelines is crucial for ensuring equitable access to protection against COVID-19.[17,18]

The predominance of atypical presentations in children infected with SARS-CoV-2 poses a significant challenge to timely and accurate diagnosis. The absence of hallmark symptoms such as fever and respiratory distress can lead to a cascade of events, starting with misdiagnosis or delayed referral for COVID-19 testing. These diagnostic delays, while seemingly innocuous at the individual level, can have profound public health implications, facilitating continued transmission within the community and increasing the risk of outbreaks in schools and other congregate settings. This intricate web of diagnostic challenges and public health ramifications underscores the imperative for heightened vigilance, proactive testing strategies, and effective public health communication. The clinical presentation of COVID-19 in children is often a far cry from the classic respiratory illness observed in adults. The predominance of atypical symptoms, such as gastrointestinal complaints, neurological manifestations, and cutaneous findings, can confound even the most seasoned clinicians. The absence of fever and respiratory distress, often considered cardinal signs of COVID-19, can lead to a false sense of security and a tendency to attribute these symptoms to more common childhood ailments. This diagnostic conundrum is further compounded by the overlap between atypical COVID-19 symptoms and those of other prevalent pediatric conditions. For instance, vomiting and diarrhea, frequently reported

in children with COVID-19, can also be manifestations of gastroenteritis or food poisoning. Similarly, headache and fatigue, common neurological complaints in COVID-19, can be attributed to stress, migraines, or other neurological disorders. This overlap in symptomatology creates a diagnostic maze, where clinicians must navigate a complex web of differential diagnoses to arrive at the correct conclusion. The consequences of delayed or missed diagnosis are far-reaching. Children with undiagnosed COVID-19 may continue to interact with others, unknowingly contributing to community transmission. This is particularly concerning in settings like schools and daycare centers, where close contact and shared spaces facilitate the rapid spread of the virus. Furthermore, delayed treatment can increase the risk of complications, especially in children with underlying health conditions. Therefore, a high index of suspicion for COVID-19 is crucial in children presenting with any suggestive symptoms, regardless of the presence or absence of fever or respiratory distress. Prompt and widespread testing is a cornerstone of any effective public health strategy for containing the spread of COVID-19. In the context of atypical presentations in children, proactive testing strategies are even more critical. This includes testing children with any suggestive symptoms, regardless of the presence or absence of classic manifestations. The availability of rapid and accurate diagnostic tests is essential for timely identification and isolation of infected individuals, thereby breaking the chain of transmission. While nasopharyngeal swabs remain the gold standard for COVID-19 testing, stool samples may also be useful in children presenting with predominant GI symptoms. The development and deployment of point-of-care tests, which can provide rapid results at the bedside or in community settings, can further facilitate timely diagnosis and intervention. Moreover, proactive testing strategies should extend beyond symptomatic individuals. Asymptomatic children, particularly those who have been in close contact with confirmed COVID-19 cases, should also be considered for testing. This approach can help identify and isolate silent carriers, thereby preventing further spread of the virus. Effective public health communication plays a pivotal role in mitigating the impact of atypical presentations on community transmission. Public health campaigns should raise awareness of the diverse manifestations of COVID-19 in children, emphasizing that the absence of fever or respiratory symptoms does not rule out the possibility of infection. Parents, caregivers, and educators should be encouraged to seek prompt medical evaluation for any child with compatible symptoms, regardless of their perceived severity. Furthermore, public health messaging should underscore the importance of adherence to preventive measures, such as mask-wearing, physical distancing, and hand hygiene, even in the absence of symptoms. These measures, while seemingly simple, can significantly reduce the risk of transmission and protect vulnerable populations.[19,20]

4. Conclusion

This study underscores the substantial prevalence of atypical presentations in children with COVID-19 in West Sumatra, Indonesia. The absence of classic symptoms like fever and respiratory distress poses a diagnostic challenge, potentially leading to delayed recognition and increased transmission. Younger age and comorbidities were identified as significant predictors of atypical presentations, necessitating heightened vigilance in these groups. Early recognition, prompt testing, and targeted interventions are crucial for effective management and mitigating the public health impact of COVID-19 in the pediatric population. Future research should focus on elucidating the mechanisms underlying atypical presentations and developing strategies for early diagnosis and prevention of long-term sequelae.

5. References

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