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Clinical Characteristics and Mortality Risk Factors of Hospitalized COVID-19 in Children: An Experience of Two Years Pandemic in Regional Referral Hospital

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Abstract

Coronavirus disease 2019 (COVID-19) has spread worldwide rapidly. COVID-19 in children is relatively mild compared to adults. However, several studies showed high mortality rates in children with underlying diseases. This study aimed to describe the clinical characteristics and outcomes of pediatric COVID-19 cases in regional referral hospital. This study was retrospective observational study using data from Medical Record Dr. Moewardi General Hospital between October 1st, 2020 and October 30th, 2022. The epidemiological and clinical data were extracted from the database and were compared with outcomes of patients. All statistical analyses were performed by SPSS software version 27. This study enrolled 371 (19,9%) children with confirmed RT-PCR SARS CoV-2 from 1856 hospitalized suspected children whereas 55% were males, and 63% aged under 5 years old. Moderate-severe patients accounted for 18% of the cases. Cough (74,4%), fever (66,6%) and shortness of breath (22,6) are the most common symptoms while 99 (26,7%) patients who had chronic diseases with the most common diseases being congenital heart disease, hematological malignancy and neurological disorders. Patient outcomes were significantly related to age, degree of severity and

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chronic disease with p=0.004, p< 0.001, and p< 0.001 respectively. After performing multivariate regression analysis, degree of severity [*p<0.001;* adjusted OR = 28.03, 95% CI (10.73–73.21)] was found to be significant predictors for mortality. The clinical and epidemiological data revealed that the majority symptom were cough, fever and shortness of breath. Mortality rate during hospitalization was higher in children with moderate-to-severe COVID-19.

Keywords: Clinical characteristic, COVID-19, Children, Pandemic

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, has had a profound impact on global health, affecting populations across various age groups with differing levels of severity. Since its emergence, the virus has led to widespread illness and fatalities worldwide, challenging healthcare systems, economies, and societies. According to data reported to the World Health Organization (WHO) as of June 2024, there have been approximately 775,364,261 confirmed cases of COVID-19 globally, with 7,046,320 deaths. These numbers illustrate the extensive reach and deadly potential of the virus, despite ongoing public health interventions, vaccination efforts, and treatments. In Indonesia, COVID-19 has also taken a significant toll. As of June 2024, the country has reported 6,417,490 confirmed cases and 157,966 deaths, placing it eleventh globally in terms of COVID-19 fatalities. However, Indonesia's case fatality rate (CFR) is lower than the global average, which stands at 0.9%. This suggests that, although the country has experienced a high number of deaths, the rate of death per confirmed case is comparatively lower, possibly reflecting improvements in treatment, healthcare infrastructure, and access to COVID-19 vaccines (Mnyambwa et al., 2022).

The variation in COVID-19 impact across different regions, including Indonesia, underscores the virus's complex nature. The difference in outcomes may be attributed to factors such as healthcare accessibility, population density, prevalence of comorbid conditions, and the speed and effectiveness of public health responses. In Indonesia's case, large-scale efforts to control COVID-19 spread, including lockdowns, social distancing measures, and mass vaccination campaigns, may have contributed to a relatively lower case fatality rate despite a high infection rate. Globally, these statistics emphasize the need for sustained vigilance, particularly as variants continue to emerge. Lessons from countries like

Indonesia highlight the critical role of adaptable healthcare policies and targeted interventions in managing the pandemic's toll on both lives and healthcare systems. Continuing to analyze data from diverse regions helps provide a more comprehensive understanding of COVID-19's ongoing challenges and can guide global efforts to prevent further loss of life and control future outbreaks effectively (Poignon et al., 2020).

In the early stages of the COVID-19 pandemic, infections were predominantly detected among middle-aged and elderly individuals, reflecting a demographic trend where older populations faced a higher risk of severe symptoms and complications. However, as the pandemic persisted globally, a significant shift occurred with a marked increase in the number of reported cases among children in various countries. Particularly, children aged 5 to 14 have shown a higher proportion of cases than those under the age of 5, with statistics indicating that they accounted for approximately 6.3% (6,020,084 cases) of the total global infections reported between 2019 and 2021. In contrast, children under 5 years made up about 1.8% (1,695,265 cases) of these infections (Poignon et al., 2020).It's important to note that these figures might not fully capture the extent of COVID-19 cases among children, as many young individuals infected with the virus tend to exhibit few or no symptoms, leading to lower detection rates. Consequently, the actual incidence among children could be higher than the reported data suggests. This asymptomatic nature of COVID-19 in children poses challenges in identifying and tracking infections in this age group, potentially impacting public health responses and strategies tailored for younger populations (Irfan et al., 2021).

In children, COVID-19 often appear to have a mild clinical course compared adult with an array of symptoms such as fever, cough, diarrhea, vomiting, headache, and appetite loss.[3] However, a number of variables, including the characteristics of the virus, co-infections, and the underlying medical conditions, affect a child's vulnerability to severe clinical consequences such as hospitalization, need of intensive care and mortality.[4,5] Understanding the mortality rates and risk factors associated with COVID-19 in children is crucial for developing effective public health strategies and clinical practices (Allotey et al., 2020).

METHODS

Dr. Moewardi General Hospital, a regional referral facility in Solo, Central Java, Indonesia, served as the study site. Every pediatric patient whose had SARS-CoV-2 detected in nasopharyngeal swab between October 1st, 2020 and October 30th, 2022, had their electronic medical data examined. The following three factors were required for inclusion in this cross-sectional research: (1) inpatient hospitalization; (2) symptoms that aligned with COVID-19 as reported in the literature; and (3) age under eighteen years old. Asymptomatic patients who received positive test result during screening for hospital admission or prior to surgical procedure were excluded from further analysis (Sugiyono, 2018).

Data collection and Study definition

For patients who met eligibility criteria, the following groups of variables were collected from the electronic medical record: sex, age, presenting symptoms, comorbid conditions, disease severity, and clinical outcome. Age group was categorized as follow: ≤ 5 years old and 6-18 years old. All symptoms reported at time of presentation were documented included: fever (temperature ≥37.5°C), cough, shortness of breath, sore throat, congestion or runny nose, vomiting, diarrhea, abdominal pain, gastrointestinal bleeding, and/or constipation. Moderate-severe disease was defined as requirement for the use of noninvasive positive pressure ventilation (NIPPV) or mechanical ventilation during hospitalization. Comorbid conditions as documented in the electronic medical record include congenital heart disease, hematologic malignancy, neurologic disorder, other malignancy, renal disease, gastrointestinal disorder, hematologic disorder, prior lung disease including asthma or tuberculosis, SLE, HIV, or DM type 1.

Statistical Analysis

Data cleaning was performed by removing duplicates. Data analysis was conducted using SPSS version 27. A descriptive analysis in the form of frequencies and percentages was conducted. Bivariate analysis was conducted using the Chi-squared test to study factors that associated with mortality risk in COVID-19 hospitalized children, and multivariable logistic regression analysis was conducted at 95% confidence level and $p < 0.05$.

RESULTS

Group of pediatric patients included in a study on COVID-19. In this study, researchers examined children who were suspected of having SARS-CoV-2, the virus responsible for COVID-19. Over the span of two years, from October 1, 2020, to October 30, 2022, a total of 1,856 children underwent testing to determine if they were infected with the virus. Out of these, 371 children were confirmed to have tested positive for SARS-CoV-2, representing 19.9% of the total tested population. These 371 cases were specifically chosen because they met certain inclusion criteria established by the researchers, which might have been based on factors such as age, confirmed positive diagnosis, and perhaps other health characteristics necessary for the study's goals (Almalki et al., 2020). This selection process is essential for ensuring that the study population reflects the characteristics needed to answer the research questions effectively. By narrowing the focus to these confirmed positive cases, the study can provide insights into how COVID-19 affects children, examine patterns in symptoms, or identify risk factors that are particularly relevant to pediatric patients. In summary, this paragraph explains the scope and selection of the study's participants, emphasizing that out of all tested children, those with confirmed positive cases who met specific criteria were included in the research analysis (Lazzerini et al., 2021).

Table 1. Demographic, Clinical Presentation and Comorbidities in Hospitalized Covid-19 Children

Characteristic	N (%)
Male sex	204 (54.98)
Age under 5 y.o	235 (63.34)
Moderate-severe case	65 (17.52)
Mortality	38 (10.24)
Sign or symptoms at time of admission	
Cough	276 (74.39)
Fever	247 (66.58)
Congestion/runny nose	102 (27.49)
Shortness of breath	84 (22.64)
Sore throat	58 (15.63)
Vomitting	37 (9.97)
Diarrhea	35 (9.43)

Abdominal pain	14 (3.77)
Gastrointestinal bleeding	6 (1.62)
Constipation	1 (0.27)
Comorbidities	
Congenital heart disease	21 (5.66)
Hematologic malignancy	18 (4.85)
Neurologic disorder	14 (3.77)
Other malignancy	12 (3.23)
Renal disease,	10 (2.69)
Gastrointestinal disorder	6 (1.61)
Hematologic disorder	5 (1.34)
Lung disease	5 (1.34)
HIV	3 (0.81)
SLE	2 (0.54)
Liver disease	2 (0.54)
DM type-1	1 (0.27)

Source: Author's Analysis

Table 1 provides an overview of the demographic characteristics, clinical presentation, and comorbidities observed in pediatric patients hospitalized with COVID-19. This data gives insight into the common traits, symptoms, and underlying health conditions of children affected by the virus. Among the hospitalized children, 54.98% (204) were male, showing a slight predominance of male patients. A significant portion, 63.34% (235), were under five years old, indicating that younger children represented the majority of the cases. The severity of cases varied, with 17.52% (65) classified as moderate to severe. Mortality among the hospitalized children was recorded at 10.24% (38), reflecting the impact of severe COVID-19 in some pediatric patients (Jamalidoust et al., 2023). The table also details the clinical symptoms observed at the time of hospital admission. The most common symptom was cough, present in 74.39% (276) of the patients, followed closely by fever at 66.58% (247). Other symptoms included congestion or a runny nose in 27.49% (102), shortness of breath in 22.64% (84), and sore throat in 15.63% (58). Less common symptoms such as vomiting (9.97%), diarrhea (9.43%), abdominal pain (3.77%), gastrointestinal bleeding (1.62%), and constipation (0.27%) were also noted (Shahbaznejad et al., 2021).

Additionally, several children had comorbid conditions, which could impact the severity and outcomes of their COVID-19 infections. Congenital heart disease was the most prevalent comorbidity, present in 5.66% (21) of cases. Hematologic malignancies were seen in 4.85% (18) of the patients, and neurologic disorders in 3.77% (14). Other comorbidities included various types of cancer (3.23%), renal disease (2.69%), gastrointestinal disorders (1.61%), hematologic disorders (1.34%), lung disease (1.34%), and HIV (0.81%). Some rare conditions included systemic lupus erythematosus (SLE) and liver disease (each affecting 0.54%), and type 1 diabetes mellitus (DM type-1) in 0.27% (1) of the patients. This table highlights the demographic spread, symptomatology, and presence of underlying conditions among COVID-19 pediatric inpatients, providing a snapshot of the population most affected by severe COVID-19 within the study group. This information is crucial for identifying vulnerable groups and understanding how the virus presents in hospitalized children (Nowak et al., 2020).

Table 2. Cross-tabulation and Pearson Chi-square Test for Factors Associated with Mortality in Hospitalized Covid-19 Children

Factors Associated with Mortality	No (%)		*P* value
	Survivor	Deaths	
Male sex	184	20	0.78
Age under 5 y.o	219	16	0.004
Moderate-severe case	35	30	< 0.001
With Comorbidities	76	22	< 0.001

Source: Author's Analysis

Table 2 presents a cross-tabulation and Pearson Chi-square test results to analyze factors associated with mortality in children hospitalized with COVID-19. This statistical analysis helps to identify which demographic and clinical factors are linked to a higher risk of death in the pediatric COVID-19 population. The table compares survivors and deaths across several categories, providing insight into potential risk factors. For instance, 184 of the survivors were male, while 20 of the deceased were also male, resulting in a p-value of 0.78. This suggests that male sex is not significantly associated with mortality in this group, as the p-value is above the typical threshold for significance (0.05). However, age appears to play a significant role in mortality outcomes. Among children under the age of 5, 219 were survivors, whereas 16 did not survive, yielding a p-value of 0.004. This result indicates a statistically significant association between younger age (under five years old) and

mortality, suggesting that younger children may have a higher risk of fatal outcomes when hospitalized with COVID-19 (Sedighi et al., 2022).

The severity of the COVID-19 case was another crucial factor. Of the moderate to severe cases, 35 were survivors, while a notably higher proportion, 30, were among the deaths. This difference is statistically significant, with a p-value of less than 0.001, underscoring that moderate to severe cases are strongly associated with increased mortality in this pediatric population. Lastly, the presence of comorbidities also showed a strong association with mortality. Among those with underlying health conditions, 76 were survivors, and 22 were among those who passed away, resulting in a p-value of less than 0.001. This finding suggests that comorbidities significantly elevate the risk of death in children hospitalized with COVID-19, highlighting the vulnerability of children with pre-existing health issues. Overall, this analysis indicates that age under 5, moderate to severe COVID-19 cases, and the presence of comorbidities are statistically significant factors associated with mortality in pediatric COVID-19 patients. Understanding these risk factors is essential for clinicians to identify high-risk patients early, manage their care more effectively, and potentially improve outcomes in this vulnerable population (Thevarajan & Buising, Kirsty Cowie, 2020).

Table 3. Adjusted OR, 95% CI for Factors Associated with Mortality in Hospitalized Covid-19 Children

Factors Associated with Mortality	**OR**	**95% C.I**	***P* value**
Age under 5 y.o	1.4	(0.6-3.4)	0.004
Moderate-severe case	28.0	(10.7-73.2)	< 0.001
With Comorbidities	1.1	(0.4-2.7)	< 0.001

Source: Author's Analysis

Table 3 provides the adjusted odds ratios (OR) with 95% confidence intervals (CI) for factors linked to mortality among children hospitalized with COVID-19. This table offers insights into the likelihood of mortality in relation to specific patient characteristics while adjusting for other variables, allowing a more precise understanding of each factor's independent impact on mortality risk. The first factor analyzed is age under five years old, which shows an adjusted OR of 1.4 with a 95% CI ranging from 0.6 to 3.4. The p-value of 0.004 indicates a statistically significant association, suggesting that children under five may have an increased likelihood of mortality when hospitalized with COVID-19 compared to

older children, though the wide confidence interval implies some variability in this estimate. The severity of the case, classified as moderate to severe, exhibits a substantial effect on mortality risk, with an adjusted OR of 28.0 and a 95% CI of 10.7 to 73.2. This highly significant p-value (<0.001) and the large odds ratio highlight that children with moderate to severe COVID-19 cases are much more likely to experience fatal outcomes compared to those with milder cases. This strong association underlines the impact of disease severity on survival and suggests that more intensive monitoring and treatment may be critical for children presenting with more severe symptoms.

The presence of comorbidities, such as congenital heart disease, neurological disorders, or hematologic malignancies, also shows an adjusted OR of 1.1, with a 95% CI of 0.4 to 2.7. Although the p-value is less than 0.001, suggesting statistical significance, the odds ratio close to 1.0 and the wide confidence interval indicate that while there is an association, comorbidities alone may not drastically increase the odds of mortality compared to other factors like disease severity. However, it still points to a higher risk for children with underlying health conditions, emphasizing the need for special attention in managing these cases. In summary, this table suggests that moderate to severe COVID-19 cases have the strongest association with mortality in hospitalized pediatric patients, while younger age and the presence of comorbidities are also risk factors, albeit to a lesser extent. These findings are valuable for healthcare providers to assess risk and prioritize care for children most vulnerable to severe outcomes, aiding in targeted intervention strategies to improve survival rates among pediatric COVID-19 patients.

DISCUSSION

This study provides valuable insights into the clinical characteristics and mortality risk factors among children hospitalized with COVID-19 over a two-year period at a regional referral hospital. The data reflects patterns in demographic distribution, common symptoms, severity of disease, and the role of underlying health conditions. Understanding these factors is critical in informing healthcare practices, especially in pediatric populations that may differ significantly from adult patients in both clinical presentation and disease progression.

Clinical Characteristics of Hospitalized Children with COVID-19

The demographic analysis reveals that males made up a slight majority of the hospitalized children, though gender did not appear to be a significant predictor of mortality. The finding that younger children, particularly those under five years old, were more frequently hospitalized aligns with global observations that younger children are generally more susceptible to respiratory infections due to underdeveloped immune responses and smaller airways. This finding underscores the importance of closely monitoring young children with COVID-19, especially in hospital settings. The clinical symptoms at the time of hospital admission also provide a clear picture of how COVID-19 manifests in children. Cough, fever, and congestion were the most common symptoms, consistent with symptoms seen in adults, though gastrointestinal symptoms such as vomiting and diarrhea were present in a smaller percentage of pediatric patients. These variations emphasize the need for a tailored approach to diagnosing COVID-19 in children, as symptoms may not always align perfectly with those typically seen in adults (Alhumaid et al., 2021).

Mortality Risk Factors

One of the most notable findings is the strong association between the severity of COVID-19 cases and the risk of mortality. The adjusted odds ratio for moderate to severe cases was significantly high, suggesting that children presenting with more severe symptoms are at much higher risk of poor outcomes. This finding highlights the importance of early assessment and intervention for children who show signs of more severe disease. Such patients may benefit from immediate intensive care, oxygen support, and potentially antiviral or other supportive therapies to mitigate the risk of deterioration. Additionally, age under five years was associated with an increased risk of mortality, albeit to a lesser extent than disease severity. This outcome could reflect the increased vulnerability of younger children to severe infections, especially as their immune systems are still developing. The presence of comorbidities, though statistically significant, had a more modest impact on mortality risk compared to disease severity. Nevertheless, children with pre-existing health conditions, such as congenital heart disease or hematologic disorders, represent a vulnerable group that requires careful monitoring and possibly proactive measures to prevent severe outcomes (Salva et al., 2021).

Implications for Pediatric Care

These findings carry significant implications for pediatric care in hospital settings, especially when treating COVID-19 in young patients. The clear association between moderate to severe cases and an elevated risk of mortality highlights the necessity for early and accurate identification of symptoms that indicate a higher risk of deterioration. Key indicators such as respiratory distress, hypoxia, and rapid progression of symptoms are especially relevant in predicting poorer outcomes. By recognizing these severity markers early on, healthcare providers can prioritize high-risk patients and implement more intensive, targeted interventions from the outset, potentially improving survival rates. Implementing severity-based protocols specifically for pediatric COVID-19 patients would allow hospitals to stratify care based on each patient's risk profile. These protocols could include fast-tracking critical care for children presenting with severe respiratory symptoms, tailored oxygen therapy, or early initiation of antiviral and anti-inflammatory treatments. This approach could help ensure that children who are more likely to experience severe outcomes receive the prompt, specialized care they need, preventing complications and supporting recovery (Lota-Salvado et al., 2023).

The role of comorbidities in increasing mortality risk further indicates that children with chronic health conditions, such as congenital heart disease, neurologic disorders, or immunocompromised states, require tailored management plans that address both COVID-19 and their underlying health issues. For these patients, standard treatment may be insufficient; instead, healthcare providers should consider specialized protocols that might include higher levels of monitoring, proactive management of their chronic conditions, and multidisciplinary care involving pediatric specialists. Regular follow-up and close monitoring for any signs of deterioration are crucial in this group, as prompt action could prevent the escalation of symptoms, leading to improved outcomes. Additionally, younger children, particularly those under the age of five, have been shown to be more vulnerable to severe disease. This finding suggests a need for policies that prioritize preventive measures and early intervention in this age group. Early testing, even at the onset of mild symptoms, can aid in quick diagnosis and prompt management before the disease progresses. Emphasis on preventive care, such as the reinforcement of hygiene practices, physical distancing where possible, and reducing exposure to known cases, could minimize the chances of infection among younger children. Furthermore, vaccination, if eligible and available for the age group, remains a vital tool for reducing the risk of severe

illness and mortality. Immunization policies should aim to protect the youngest and most vulnerable children, ultimately reducing hospital admissions and fatalities in this demographic (Letelay et al., 2023).

In summary, these findings underline the need for a multifaceted approach in pediatric COVID-19 care within hospitals. By focusing on early detection of severity markers, establishing risk-based treatment protocols, offering specialized management for children with comorbidities, and emphasizing preventive care and vaccination for young children, healthcare systems can improve outcomes for hospitalized pediatric patients. This approach will also support a more effective, resource-efficient response to COVID-19 in children, ultimately enhancing the quality of care and reducing mortality rates in this vulnerable population.

Limitations and Future Research

While this study offers meaningful insights, it also has limitations. First, the study is based on data from a single regional hospital, which may limit the generalizability of the findings. Differences in healthcare infrastructure, patient demographics, and COVID-19 variants across regions may affect outcomes, suggesting a need for further multicenter studies to validate these results. Moreover, this study did not include long-term outcomes post-hospitalization, which could provide a fuller picture of COVID-19's impact on pediatric patients, particularly those with pre-existing conditions. Future research should focus on examining the effects of emerging COVID-19 variants on pediatric populations, as well as the role of interventions such as vaccination in preventing severe cases and reducing mortality. Additionally, exploring long-term follow-up studies could shed light on post-acute sequelae of COVID-19 in children, contributing to a better understanding of potential lasting impacts on pediatric health. This study highlights critical factors influencing mortality in children hospitalized with COVID-19, with disease severity, younger age, and comorbidities emerging as significant predictors of poor outcomes. These insights underscore the importance of early assessment, severity-based treatment protocols, and special considerations for younger children and those with pre-existing health conditions. These findings can guide healthcare professionals and policymakers in optimizing pediatric care protocols during ongoing and future COVID-19 waves, ultimately aiming to reduce mortality and improve health outcomes for hospitalized pediatric patients (Flores-Alanis et al., 2022).

CONCLUSION

This research on the clinical characteristics and mortality risk factors among children hospitalized with COVID-19 over two years at a regional referral hospital provides key insights into the pediatric population's vulnerability to the virus. The study concludes that younger children, particularly those under five, and those with moderate to severe COVID-19 cases are at a significantly higher risk of mortality. Disease severity emerged as the most critical predictor of poor outcomes, highlighting the importance of prompt identification and intensive care interventions for children presenting with severe symptoms. While comorbidities also contributed to an elevated risk, their impact was less pronounced than disease severity, although children with underlying health conditions still represent a group requiring careful monitoring and specialized management. These findings emphasize the need for hospitals to establish severity-based treatment protocols for pediatric COVID-19 cases and advocate for preventive measures, including vaccination where possible, to protect younger children and those with pre-existing conditions. This study underscores the importance of early recognition of severe disease indicators and targeted care strategies to improve survival outcomes among hospitalized pediatric patients with COVID-19. Further multicenter studies and long-term follow-up research could broaden these insights, helping refine pediatric COVID-19 care and informing future pandemic responses to reduce child mortality rates.

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