Journal of Multidisciplinary Healthcare

Dovepress
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ORIGINAL RESEARCH

Predictors of Mortality Among Children with Confirmed and Suspected Cases of COVID-19 in East Java, Indonesia

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Introduction: Coronavirus disease 2019 (COVID-19) increases rapidly and causes mortality in all groups, including children. However, the predictive risk factors of mortality among children remain inconclusive. This study aimed to analyse the predictors related to mortality among children with COVID-19.

Methods: Secondary data analysis was conducted using provincial COVID-19 data from April 2020 to May 2021. We selected 6441 children under age 18 to be included in this study. Chi-square and binary logistic regression were used to evaluate the predictors of mortality in children with COVID-19.

Results: This study showed that the prevalence of children who died COVID-19 was 2.7%. Age, case definition, treatment status, severity of illness, and travel history had a significant relationship with survival status in children with COVID-19. As the increasing age, the risk of death with COVID-19 will decrease [AOR=0.94; CI 95%=0.91–0.97]. Otherwise, suspected status [AOR=2.12; 95% CI=1.48–3.04], hospitalization with ventilators [AOR=22.25; 95% CI=5.73–86.42], severe illness [AOR=46.76; 95% CI=21.69–100.80], and travel history [AOR=1.78; 95% CI=1.22–2.60] were significantly related with an increased risk of death in children with COVID-19.

Discussion: Severe illness in children was the strongest predictor of mortality. Disease prevention and health promotion programs are the key to preventing hospitalizations in children and decreasing the mortality rate.

Keywords: child health, COVID-19, child mortality

Introduction

Coronavirus disease 2019 (COVID-19) poses a major risk of mortality worldwide.[1] Since COVID-19 was declared a worldwide pandemic by the World Health Organization in March 2020, the number of reported cases, deaths, and affected countries has continuously increased.[2] By June 2020, global reports of COVID-19 recorded 10 million cases and 503,862 deaths, with several countries categorized as having community transmission.[3] At the same time, Indonesia also reported a total of 55,092 confirmed cases, the third country in Southeast Asia with the highest number of confirmed cases.[3] Most provinces in the Java region reported an increase in cases and deaths.[4] The East Java Province became the first province in Indonesia, with the highest number of cases reaching 11,823 by June 2020.[5] The COVID-19-related fatality rate in East Java continues to increase, reaching 7.44%.[6,7] Moreover, based on data from online hospital applications, the East Java Provincial Health Office announced that the bed occupation rate (BOR) in East Java reached more than 80% and was categorized as a red zone area.[8] This fact requires special attention in overcoming the COVID-19 pandemic and reducing the number of confirmed cases and COVID-related deaths in East Java Province.[9]

Received: 6 October 2022
Accepted: 24 January 2023
Published: 7 February 2023

The COVID-19 data update in East Java was conducted by the COVID-19 task force and reported through online systems such as websites, mass media, and government accounts.[10,11] Although the trend of COVID-19 cases shows fluctuating data, the overall number cases in East Java have increased.[6] Each region implements strict health protocols to manage the outbreak of a small number of cases to reduce the likelihood of a larger number of cases. Public health protection is provided through several strategies: health promotion, early detection, physical and social restrictions, coughing and sneezing etiquette, self-isolation, and quarantine.[12] However, these efforts have not significantly reduced the number of COVID-19 cases in East Java.

Several studies have been conducted on COVID-19 to assess treatment-related risk factors and the clinical features of COVID-19 have become clearer in identifying the virus that causes COVID-19 and acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[13–16] The impact of COVID-19 on patients is clinically complex; outcomes may range from asymptomatic respiratory failure to death.[17] In a pandemic, community resilience must be considered, especially for vulnerable groups.[18] A previous study showed that the elderly were the most vulnerable population at risk, especially those with heart disease, respiratory disease, diabetes, or other autoimmune diseases.[19] Although children appear to have milder symptoms and a better prognosis than adults,[15,20,21] the number of cases in children is growing rapidly.[22] It may also contribute to community transmission.[23] Moreover, the potential harm caused by COVID-19 in children remains largely unknown, especially in neonates and infants.[24] Previous studies have shown that several factors contribute to the fatality rate of children, such as those age ≥ 10 years, severe illness, poor oxygen ratio, and chronic underlying disease.[25–27] Although several studies have analysed the predictors of mortality, most of the studies have focused on adults and the elderly, leading to difficulty in generalization. In this context, this study aimed to examine predictors of mortality among patients with COVID-19, especially in children.

Materials and Methods

Data Source

This study was a secondary data study using provincial COVID-19 data in Indonesia particularly in East Java province. The children dataset used for this study contains information about children aged less than 18 years and their health data related to COVID-19. East Java province COVID-19 platform pooled all of data from April 2020 to May 2021 through an online platform. The researcher applied for dataset access permission the East Java COVID-19 task force to obtain research data. The data were obtained from all health facilities in East Java that served all cities or regency within East Java province. Each health facilities were obliged to report all the cases to the data platform.

Subjects

This study involved paediatric patients with COVID-19 in East Java. The purposive sampling method was used to select a sample of 6441 children. The sampling technique allows selected respondents in population to be included in sampling due to certain criteria. The inclusion criteria in this study were children aged less than 18 years, either outpatient or inpatient. The definition of children following the guideline from the Government of Indonesia.[28]

Variables

The dependent variable in this study was survival status, namely, alive and dead. The time point started from the first-time admission to the health facilities until they discharged (dead or alive). Alive and dead is the current status when conducting data collection in May 2021 on health care status in outpatient and inpatient patients. Independent variables included sex, case definition, treatment status, severity of illness, travel history, and exposure to a person with a suspected/confirmed case of COVID-19. Sex was divided into two categories: male and female. In this study, the case definition category is divided into confirmed and suspected. Confirmed cases can be defined as positive cases of COVID-19 infection as evidenced by polymerase chain reaction (PCR) tests. Meanwhile, suspected cases were defined as cases that showed COVID-19-like symptoms with inconclusive results using PCR or any other type of testing.[12] Treatment status was divided into three categories: non-hospitalized (isolation), hospitalized, and hospitalized with a ventilator. The severity of illness was divided into mild, medium, and severe based on reference to the Decree of

the Minister of Health of the Republic of Indonesia. Mild symptoms include fever, cough, fatigue, anorexia, shortness of breath, myalgias, or other unspecified symptoms without evidence of viral pneumonia or without hypoxia. Moderate symptoms are characterized by the presence of clinical signs of pneumonia (fever, cough, shortness of breath, rapid breathing) without signs of severe pneumonia. Meanwhile, severe symptoms are characterized by clinical signs of pneumonia coupled with a respiratory rate > 30 x/minute or severe respiratory distress.[29] Travelling history and exposure to a person with a suspected/confirmed case of COVID-19 was divided into two categories: yes and no.

Data Analysis

SPSS version 25 was used for data analysis in this study. The data that were obtained were analysed using chi-square and logistic regression to examine the determinants of survival status in children with COVID-19. To determine the strength of the relationship between the dependent and independent variables, it was assessed using an odds ratio and 95% confidence interval (CI) ($p<0.05$). We adjusted for any variables known to be associated with the independent variables. All the missing data were excluded from this analysis.

Ethical Approval

The datasets used in this study are available upon request after all individual-level identification variables were removed. It was not possible to identify the residence of any of the subjects. Therefore, ethical approval was not required for the study. This study confirmed that informed consent was obtained from all participants and performed according to the Declarations of Helsinki ethical principles for medical research involving human subjects.[30]

Results

Out of 6441 children, 3496 children with COVID-19 in East Java were male (54.3%) and categorized as having a suspected case of COVID-19 (65.4%). Based on treatment status, as of 60% children were hospitalized (60.0%) and a few were hospitalized with a ventilator (1.2%). Higher percentage of the children with COVID-19 had mild cases (86.4%), no travel history (58.8%) and were exposed to a person with a suspected/confirmed case of COVID-19 (63.2%) (Table 1). Table 1 also describes a bivariate analysis of the survival status of paediatric patients with COVID-19, with 177 children (2.7%) dead and 6246 children (97.3%) alive. From the analysis results, several factors related to mortality among children with COVID-19 including treatment, severity of illness, and travel history.

In a multivariate analysis using logistic regression, it was found that age, case definition, treatment status, severity of illness, and travel history had a significant relationship with survival status in children with COVID-19 in East Java. Based on the analysis results, as the child's age increases, the risk of death will decrease by 0.94 times [AOR=0.94; 95% CI=0.91–0.97]. Children with a suspected case of COVID-19 have a higher risk of death than children with a confirmed

Table 1 Sociodemographic Data of Patients with COVID-19 (n=6441)

Characteristics	Total		Survival Status (n=6441)					
			Alive		Dead			
	n	%	n	%	n	%	X2	p value
Sex							2.308	0.13
Male	3496	54.3	3390	97.0	106	3.0		
Female	2945	45.7	2874	97.6	71	2.4		
Case Definition							0.35	0.55
Suspected	4210	65.4	4098	97.3	112	2.7		
Confirmed	2231	34.6	2166	97.1	65	2.9		

(*Continued*)

Table 1 (Continued).

Characteristics	Total		Survival Status (n=6441)					
			Alive		Dead			
	n	%	n	%	n	%	X2	p value
Treatment							158.88	0.00*
Nonhospitalized	2497	38.8	2493	99.8	4	0.2		
Hospitalized	3866	60.0	3705	95.8	161	4.2		
Hospitalized with Ventilator	78	1.2	66	84.6	12	15.4		
Severity of Illness							470.37	0.00*
Mild	5568	86.4	5470	98.2	98	1.8		
Medium	832	12.9	775	93.1	57	6.9		
Severe	41	0.7	19	46.3	22	53.7		
Travel history							12.73	0.00*
Yes	2655	41.2	2559	96.4	96	3.6		
No	3786	58.8	3705	97.9	81	2.1		
Exposed to person with a suspected/confirmed case of COVID-19							2.97	0.08
Yes	4072	63.2	3971	97.5	101	2.5		
No	2369	36.8	2293	96.8	76	3.2		
Total	6441	100.0	6264	97.3	177	2.7		

Note: *p value<0.001. X^2=chi-square test.

case of COVID-19 [AOR=2.12; 95% CI=1.48–3.04]. Meanwhile, children hospitalized with ventilators had the highest risk of death, reaching 22 times that of isolated children [AOR=22.25; 95% CI=5.73–86.42]. The survival status of children with severe cases was 47 times more likely to die than those with mild cases [AOR=46.76; 95% CI=22.69–100.80]. The risk of death in children increased almost twice in children with a travel history compared to children without a history of travel [AOR=1.78; 95% CI=1.22–2.60] (Table 2).

Table 2 Multivariate Analysis of Survival Status in Children with COVID-19 (n=6441)

Variables	Unadjusted		Adjusted			
	OR	Sig.	OR	Sig.	95% CI	
					Lower	Upper
Age	0.90	0.00*	0.94	0.00*	0.91	0.97
Sex						
Male	1.27	0.13	1.06	0.71	0.77	1.46
Female	–					

(*Continued*)

Table 2 (Continued).

Variables	Unadjusted		Adjusted			
	OR	Sig.	OR	Sig.	95% CI	
					Lower	Upper
Case Definition						
Suspected	0.91	0.55	2.12	0.00*	1.48	3.04
Confirmed	–					
Treatment						
Nonhospitalized	–					
Hospitalized	27.08	0.00*	14.52	0.00*	5.23	40.30
Hospitalized with Ventilator	113.32	0.00*	22.25	0.00*	5.73	86.42
Severity of Illness						
Mild	–					
Moderate	4.10	0.00*	2.84	0.00*	1.89	4.23
Severe	64.63	0.00*	46.76	0.00*	21.69	100.80
Travel History						
Yes	1.72	0.00*	1.78	0.00*	1.22	2.60
No	–					

Notes: *p value<0.001. Adjusted for all independent variables.

Discussion

The results showed several factors related to mortality among children with COVID-19 in East Java. As the child's age increases, they are less likely to die of COVID-19. This result is in line with a previous study showing that the most significant proportion of severe and critical cases in children under one year of age was higher than that in older children, reaching 10.6%.[31] The authors argue that the health facilities in East Java do not support the most significant number of critical cases in children under one year of age. This increases the risk of death in younger children than that in older children. At first, neonates and infants were not prioritized in the first wave of the pandemic. In 2020, the government focused on the elderly group, and the capacity for paediatric care was limited.[32] This statement was also supported by data from online hospital applications that reported that the number of beds in the Neonatal Intensive Care Unit (NICU) and Paediatric Intensive Care Unit (PICU) in East Java were very limited in 2020.[8] Furthermore, these results can be used as supporting data to identify indicators of mortality in high-risk patients with COVID-19, such as the risk associated with the child's age.

Case definition was significantly related to the survival status in children with COVID-19. Children with suspected status have a 2.12 higher risk of death than children with confirmed status. This study is similar to previous research in which there were more suspected cases in children than confirmed cases, reaching 65.9%.[33] A patients with a confirmed case of COVID-19 showed clinical signs and symptoms compared with patients with a suspected case.[34] Patients with a confirmed case, by definition, may experience severe symptoms such as difficulty breathing, loss of speech/mobility, confusion, and chest pain.[19] Based on this definition, the signs and symptoms and illness severity cause patients with confirmed cases of COVID-19 to have an increased risk of mortality. Although the clinical manifestations of children with COVID-19 are generally less severe than those of adults, they are more susceptible to infection.[33] We also assume

that children with confirmed status have rapid treatment and intervention compared with suspected cases. Thus, it can increase the risk of mortality among children with suspected cases.

Based on the results of this research, treatment factors were found to be significantly related to survival in children with COVID-19. Children who were hospitalized on a ventilator had 22 times higher risk of death than isolated children. This finding is consistent with studies conducted in Saudi Arabia showing that patients on mechanical ventilators (MVs) experience a high risk of death from COVID-19.[35] Additionally, another study showed that the risk of death in patients admitted to the intensive care unit was high among hospitalized patients with COVID-19.[36] Children and paediatric patients who required intensive care and those who died had different comorbidities with hydronephrosis, leukaemia, and intussusception.[37] This demonstrated that comorbidities might be one of the factors contributing to the survival status of patients with COVID-19, but our data did not analyse this issue. The survival probability among patients with COVID-19 is also associated with the length of hospital stay (LOS), in which the first 14 days of hospitalization have a higher survival probability than patients treated for 30 days.[35] Hospitalized children had a higher prevalence of symptoms, namely, fever, respiratory and gastrointestinal symptoms, and relatively lower haemoglobin and neutrophil levels.[38] Based on this finding, we think this remains important to assess symptoms in children with COVID-19 to determine indications for hospitalization and ventilator use to increase survival probability.

The present study demonstrated that the survival status of children was associated with the severity of illness. Children with severe cases were 47 times more likely to die than those with mild cases. This study is in line with previous research conducted in China showing that the severity of illness in the nonsurvival group was higher than that in the survivor group.[39] The mortality rate among patients with critical and severe cases increased to 17.6%. Decreases in arterial partial pressure of oxygen (PaO_2) and the fraction of inspired oxygen (FiO_2) were detected among nonsurviving patients with COVID-19, which mainly caused acute lung injury and death, especially in severely ill patients.[39] Another study also showed that severe COVID-19 causes approximately 20% of hospitalizations and causes acute respiratory distress syndrome (ARDS) and viral sepsis.[40] We suspect that although children have a risk of mild disease severity, infants and children with congenital (pre-existing) illnesses and various comorbidities, such as malignancy, could be a precipitating factor for increased disease severity, requiring ICU care, as described by previous studies.[37,41] This illustrates the urgent need for an early warning system to monitor the progression of COVID-19 in children.

The last factor related to the risk of death in children was travel history. Children with a travel history were more likely to die than children without a travel history. This finding is consistent with a previous study showing that the major risk factors for COVID-19 in children were related to having close contact with family members with COVID-19, travel history, and living in endemic areas.[37] A travel history is related to community mobility which has been believed to contribute to the increase of COVID-19 transmission.[42] We also suspected that community mobility among children increases the risk of COVID-19 exposure, which increases children's vulnerability to severe illness and death.

Limitations

Some limitations were identified in this study. First, the data were secondary and contained only certain variables. Therefore, researcher only select the available variables within the dataset. Second, the results of this study do not imply causality. Further the data were not reported the possibility of bias on the testing site and the cause of dead of the children. Despite these limitations, this study contributes to informing determinant factors of mortality among children with confirmed and suspected cases of COVID-19 in a specific population.

Conclusion

Mortality among children with COVID-19 was determined by several factors, including age, suspected status, hospitalization with ventilators, severe illness, and travel history. The key to reducing the risk of COVID-19-related mortality among children remains at the clinical and community levels. The promotion and prevention strategy should be deployed massively to reduce the risk of transmission at the community level. While at the clinical setting, resources should be utilized to prevent children getting severe condition. Therefore, initiatives to improve patient management like supportive care including provision of respiratory support, nutrition support, and family support at the clinical level should be implemented and prevention strategies

within the community should also be improved. At the community level, health education through face-to-face or virtual can be implemented to give supportive care and monitor the health status of children.

Data Sharing Statement

The datasets analysed during the current study available from the corresponding author on reasonable request.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was funded by Universitas Airlangga, Surabaya, Indonesia through "Hibah Riset Mandat Top Tier" (Top Tier Mandate Research Grant) grant number [768/UN3.15/PT/2021].

Disclosure

The authors report no conflicts of interest in this work.

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