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Epidemic profile of COVID-19 child deaths in Sri Lanka: a retrospective nationwide analysis

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Abstract

Introduction Understanding the impact of the COVID-19 pandemic on child survival is crucial. Analysing COVID-19-related child deaths, even years after the pandemic, is critical for informing future pandemic preparedness and response efforts.

Methods We conducted an analysis of all "SARS-CoV-2/COVID-19 positive deaths" among children and adolescents (aged < 18 years) recorded through a purposefully designed Child Death Surveillance and Response System (CDSRS) from October 2020 to September 2022. It included all deaths with a positive SARS-CoV-2. The analysis involved a thorough review of documents (bedhead tickets, field/institutional investigation and postmortem examination reports, and compiled case scenarios). Multivariable backward logistic regression was conducted to identify risk factors associated with deaths attributed to COVID-19 infection. Additionally, a comparison of socio-demographic characteristics was conducted between deaths due to all causes and those attributed to COVID-19 infection.

Results A total of 111 deaths with a positive SARS-CoV-2 test were analyzed. Among these, 81 deaths (73%) were categorized as directly attributed to COVID-19 infection. Fourteen children (17.2%) had Multisystem Inflammatory Syndrome. Cardiovascular disease was the most common comorbidity (28.4%). The odds of deaths attributed to COVID-19 infection were eleven times higher with chronic diseases compared to incidental SARS-CoV-2 positive test (OR:11.22, 95% CI:1.735, 72.496). Tamil ethnicity appeared to be protective when compared to the Sinhalese (OR:0.07, 95% CI: 0.008, 0.598). The model explained 44.8% of the variance. When compared to national all-cause mortality data, females ($p = 0.03$), post-neonatal infants ($p < 0.001$), and > 5–18 years ($p = 0.005$) were identified as being at higher risk of death due to COVID-19 infection.

Conclusion The proportion of COVID-19-positive deaths during the study period was higher than that reported in high-income countries, with most deaths directly attributed to SARS-CoV-2. Higher mortality rates were observed among post-neonatal infants, children over five years, females, those with Sinhalese ethnicity, and pre-existing chronic medical conditions, particularly cardiovascular disease.

Keywords Children, Comorbidity, COVID-19, Mortality, Sri Lanka

Introduction

Sri Lanka has been one of the South Asian countries most severely affected by COVID-19 [1]. An estimated 667,671 children and adults were infected with SARS-CoV-2 from October 2020 to September 2022. The total number of deaths (all ages) related to COVID-19 during this period in Sri Lanka was approximately 16,768 [2],

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which included 111 deaths among children and adolescents (< 18 years).

Previous reports consistently indicate that the severity of COVID-19 infection is typically lower in children than in adults, and many infected children exhibited no symptoms [3, 4]. In England, data from March 2020 to February 2021 revealed that almost all children and young people (99.995%) with a positive SARS-CoV-2 test survived [5]. In contrast, a multicenter study from Southeast Asia, Japan, and China reported a higher death rate among children (2.3%) [6]. As the pandemic progressed globally, severe and life-threatening manifestations of the disease emerged in children, including multisystem inflammatory syndrome (MIS-C) [7]. These findings underscore the diverse picture of the COVID-19 pandemic and the importance of continued monitoring and research, particularly regarding its impact on the child populations.

Limited studies have investigated clinical manifestations and risk factors for severe COVID-19 disease among children globally. The presence of pneumonia, thrombocytopenia, raised serum C-reactive protein, obesity, hypertension, immunosuppression, diabetes, chronic lung disease, renal disease, and admission to the intensive care unit (ICU) are some of the reported risk factors for mortality [8, 9]. In the absence of effective therapy, the ability to minimise mortality depends on a better understanding of the factors related to the severity of the disease.

Analysing disaggregated data at the country level is crucial for understanding the pandemic's effects on child survival. No review has analysed the disease burden among children, their clinical characteristics, and risk factors for mortality in Sri Lanka. Analysing COVID-19 child deaths, even years after the pandemic, is critical for informing future pandemic preparedness and response efforts. By comprehensively understanding the factors that contributed to pediatric fatalities, more effective strategies to protect children during future outbreaks of COVID-19 or other infectious diseases can be developed.

Therefore, this analysis aimed to quantify the number of deaths attributed to COVID-19 infection and those who died from an alternative cause but had a positive SARS-CoV-2/COVID-19 test. Additionally, the clinical profile, comorbidities, access to intensive care facility, and place of death of all children whose deaths were attributed to COVID-19 infection were assessed.

Methods

The Ministry of Health of Sri Lanka has implemented a national Child Death Surveillance and Response System (CDSRS) since 2016. Based on that, during the pandemic, a special surveillance mechanism for COVID-19 child deaths was initiated in the country under the guidance of the Family Health Bureau (FHB), the maternal and child health arm of the Ministry of Health. Both hospital and field health institutions were instructed to notify all probable COVID-19 child deaths. This enabled us to analyse all "SARS-CoV-2/COVID-19 positive deaths" among children and adolescents (aged < 18 years) using these records from October 2020 to September 2022. We included all deaths with a positive antigen or quantitative RT-PCR test for SARS-CoV-2. The documents, bedhead tickets, field/institutional investigation and postmortem examination reports, and compiled case scenarios of COVID-19-positive deaths were reviewed individually by a panel of experts (paediatricians, neonatologists, intensivists and community physicians). The case management was reviewed based on national guidelines for managing COVID-19 infection in children [10]. The local guideline for diagnosing and managing Multisystem Inflammatory Syndrome in Children (MIS-C) was adapted from the World Health Organization's 2020 guideline [11].

Clinical records of all eligible deaths were reviewed to determine whether COVID-19 infection contributed or unlikely contributed to the death. In Sri Lanka, the cause of death is categorised as immediate, antecedent/underlying, and contributory [12]. If the death certificate listed COVID-19 infection as the direct cause of death and the clinical course supported this, the death was classified as death attributed to COVID-19. If the contribution of COVID-19 infection needed to be clarified, the records were reviewed by a three-member panel with expertise relevant to the case. These cases were then categorised as either attributed to COVID-19 or unlikely to be due to COVID-19. The flow chart for this process is shown in Fig. 1.

Covariates and definitions

The socio-demographic information included age, sex, ethnicity, socioeconomic status, parents' education, and resident district. Total household income was categorised by taking the estimated median value of the total household income of a family in Sri Lanka [13]. Education level was categorised as primary or less (No education or grade 1–5), secondary/collegiate (Grade 6–12) and tertiary [14]. Clinical data included symptom onset (defined as the day when the first symptom or sign occurred), day of hospital admission, SARS-CoV-2 testing (antigen/PCR or antibody testing) and death (time and place of death). Signs and symptoms at presentation (fever, cough, respiratory distress including oxygen saturation, gastrointestinal symptoms, etc.) and comorbidities were also noted. Also, respiratory support, admission to an intensive care unit, resuscitation, pharmacotherapies, and laboratory results were documented.

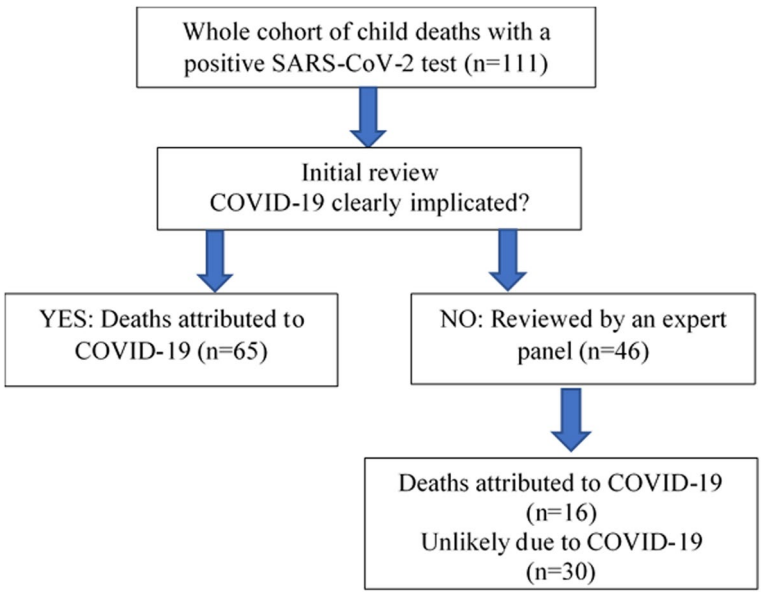

Fig. 1 Flow charts for review of case records

Based on the Chronic Condition Indicator Refined (CCIR) for ICD-10-CM, chronic diseases [15] were classified. A condition that lasts 12 months or longer and meets one or both of the following criteria: (1) The condition results in the need for ongoing intervention with medical products, treatment, services, and special equipment; (2) The condition places limitations on self-care, independent living, and social interactions were included. Life-limiting conditions were identified per the Directory of Life-Limiting Conditions (DLCC) [16].

Data analysis

We used SPSS version 22 for data analysis. Frequencies and proportions were computed for the categorical variables. Imputation was not done for missing data. We could not calculate the case fatality rate since the number of children < 18 years infected with SARS-CoV-2 in Sri Lanka during the same period was not available. However, the number of COVID-19 deaths in children < 18 years was calculated as a proportion of all deaths. Chi-squared and Fisher's exact tests were used to compare categorical variables between deaths attributed to COVID-19 infection and deaths with incidental SARS-CoV-2 positivity.

Multivariable backward logistic regression was conducted to identify risk factors associated with deaths attributed to COVID-19 infection. The dependent variable categorized deaths as either deaths attributed to COVID-19 infection or with incidental SARS-CoV-2 positive test. Independent variables with a p-value < 0.25 in univariate analysis were included in the multivariable model [17], with age added due to its clinical significance. To address multicollinearity, correlated variables ($r > 0.5$) were excluded; for example, only the chronic disease variable was retained after identifying collinearity with cardiovascular disease. Variables with fewer than ten observations, such as genetic disorders and respiratory disorders, were omitted from the analysis [18]. Additionally, variables with over 10% missing data, including fever, cough, and difficulty breathing, were excluded. Finally, the following variables were included in the analysis: age, gender, ethnicity, number of living children, oxygen saturation on admission, chronic disease, and life threatening/life limiting conditions. Dummy variables were created for age (Reference: > 12–18 yrs) and ethnicity (Reference: Sinhalese) to ensure proper inclusion in the analysis.

Additionally, a comparison of socio-demographic characteristics was conducted between deaths due to all causes and those specifically attributed to COVID-19 infection in 2021 [19]. However, this analysis could not be extended to other factors, such as chronic diseases or comorbidities, due to the unavailability of relevant data. Furthermore, deaths from 2020 and 2022 were excluded from the comparison because of the lack of published mortality data for these years.

Results

A total of 111 records were analysed. All had a positive SARS-CoV-2 test. The proportion of COVID-19-positive deaths out of all deaths among children in Sri Lanka during the study period was 0.7% (111/16768). Among them,

Table 1 Demographic and household characteristics of children who had a positive test for COVID-19 infection categorised by the likely cause of death

	All deaths with SARS-CoV-2 positive test (*n* = 111)	Deaths attributed to COVID-19 infection (*n* = 81)	Deaths with incidental SARS-CoV-2 positive test (*n* = 30)	p value
Age (Categorical)				
< 1 month	25 (22.5)	15 (18.5)	10 (30)	0.1
One month – < 1 yr	38 (34.2)	31 (38.3)	07 (23.3)	0.05
1–5 yrs	16 (14.4)	11 (13.6)	05 (16.6)	0.7
> 5–12 yrs	32 (14.4)	23 (14..8)	09 (13.3)	0.9
Gender				
Male	52 (46.8)	33 (40.7)	19 (63.3)	0.06
Female	58 (52.3)	47 (58)	11 (36.7)	
Unconfirmed	01 (0.9)	00 (00)		
Ethnicity				
Sinhalese	73 (65.8)	55 (67.9)	18 (60)	0.3
Tamil	19 (17.1)	11 (13.6)	08 (26.7)	
Muslim	19 (17.1)	15 (18.5)	04 (13.3)	
[a]Father's educational level (*n* = 101)				
Primary or less	03 (2.9)	03 (4.1)	00 (00)	0.4
Junior Secondary	68 (67.3)	48 (64.9)	20 (66.7)	
Senior Secondary/Collegiate	22 (21.8)	18 (24,3)	04 (13.3)	
Tertiary	08 (07.9)	06 (8.1)	02 (6.7)	
[a]Mother's educational level (*n* = 100)				
Primary or less	04 (04)	03 (4.1)	01 (3.3)	0.4
Junior Secondary	62 (62)	42 (56.8)	20 (66.7)	
Senior Secondary/Collegiate	23 (23)	18 (24.3)	05 (16.6)	
Tertiary	11 (11)	09 (12,2)	02 (6.7)	
Mother's employment (*n* = 104)				
Homemaker	78 (75)	55 (71.4)	23 (76.7)	0.5
Income generating activity	26 (25)	20 (26)	06 (20)	
Household income (LKR)				
< Median	73 (65.8)	51 (63)	22 (73.3)	0.27
≥ Median	38 (34.3)	30 (37)	08 (26.7)	
Number of living children				
None	31 (27.9)	20 (25)	11 (36.7)	0.2
≥ 1	80 (72.1)	61 (75.3)	19 (63.3)	

[a] Percentages are calculated from the available data, excluding missing values

COVID-19 infection clearly contributed to 65 (58.6%). The remaining deaths (*n* = 46) were categorised as either attributed to COVID-19 (*n* = 16) or unlikely to be due to COVID-19 (*n* = 30). Finally, 81 deaths (73%) were categorised as attributed to COVID-19 (Fig. 1).

Socio-demographic and household characteristics of deaths attributed to COVID-19

Out of all the deaths attributed to COVID-19, more than half were less than one-year-old (*n* = 46, 57%) (Table 1). The female-to-male ratio was 1.4:1. Most (68%) children were of Sinhalese ethnicity. The percentage of Muslims was 18.5%. Most deaths, 25% (*n* = 28), were from the capital city (Colombo) in the Western province (Fig. 2). In terms of educational attainment, the majority of mothers (*n* = 45, 62.5%) and fathers (*n* = 51, 68%) had attained only junior secondary level or less (≤ Grade 11). Most mothers (*n* = 55/75, 73%) were homemakers. The household income was less than the median in most (*n* = 51/81, 63%) families.

Clinical characteristics of deaths attributed to COVID-19

Missing data limited the comprehensive analysis of the clinical features of the children who died due to COVID-19 infection. Thus, the percentage for each variable is calculated, excluding missing data. According to

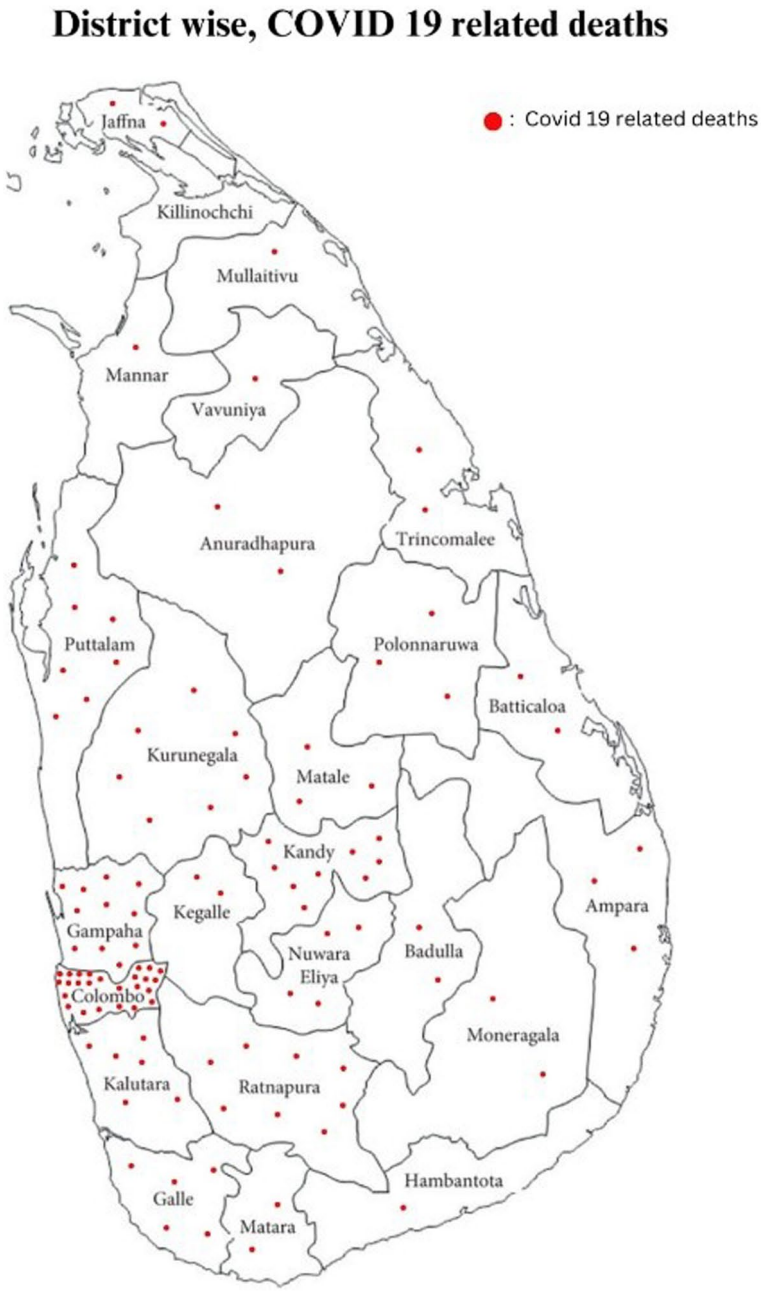

Fig. 2 Distribution of COVID-19-related deaths in Sri Lanka (2020 – 2022)

the available information, most had fever, cough, and tachypnea upon admission to the hospital (Table 2). Thirteen children (16%) had seizures on admission, and most (n-47, 58%) had saturation in air less than 92% on admission.

The first healthcare contact was a hospital outpatient department or an emergency unit in 77 out of 81 children who died of COVID-19 infection. The remaining four children were dead by the time they reached the hospital and were considered home deaths. Information on the onset of symptoms could not be retrieved in 20%; thus, the interval between the onset of symptoms and death was not analysed. Sixty-two per cent of children ($n=50$) were managed at an intensive care unit (ICU), with a delay in ICU admission noted among 14 deaths. Eighty per cent ($n=65$) of deaths due to COVID-19 infection occurred in a ward/ICU. Postmortem was conducted

Table 2 Clinical characteristics, hospitalisation and death of children who had a positive test for COVID-19 infection categorised by the likely cause of death

	All deaths with SARS-CoV-2 positive test	Deaths attributed to COVID-19 infection	Deaths with incidental SARS-CoV-2 positive test	p value
Symptoms on admission				
*Fever (Yes), *n* = 88	59 (67)	53/70 (75.7)	06 (33.3)	< 0.001
*Cough (Yes), *n* = 82	34 (41.5)	29/66 (43.9)	05 (31.2)	0.3
*Difficulty in breathing/tachypnea, (Yes), *n* = 88	65 (73.9)	55/76 (72.4)	10 (83.3)	0.4
Seizures (Yes)	18 (16.2)	13/81 (16.1)	05 (16.7)	0.9
Saturation on air < 92% (on admission)	57 (51.4)	47/81 (58)	10 (33.3)	0.1
Delay in getting an ICU facility	14 (12.6)	14 (17.3)	00	0.02
Place of death				
Hospital	100 (90)	77 (95)	23 (76.7)	0.004
Home	11 (10)	04 (05)	07 (23.3)	

Data is presented as n(%). The differences between groups were compared using the two-sided chi-squared test or Fisher's exact test if small numbers

*Variables with missing data

Table 3 Details of comorbid conditions

	COVID-19 positive deaths (*n* = 111)	Deaths attributed to COVID-19 infection (*n* = 81)	Deaths with incidental SARS-CoV-2 positive test (*n* = 30)	p value
Chronic disease	54 (48.6)	45 (55.6)	09 (30)	0.02
Life-threatening/Life-limiting condition	62 (55.9)	48 (59.3)	14 (46.6)	0.2
Comorbid conditions (one or more)	83 (74.8)	60 (74.1)	23 (76.7)	0.5
Comorbid conditions (one only)	65 (58.6)	46 (56.8)	19 (63.3)	0.5
Comorbid conditions (2 or more)	18 (16.2)	14 (17.3)	04 (13.3)	0.6

Data is presented as n (%). The differences between groups were compared using the two-sided chi-squared test

in 30 cases, and a verbal autopsy was carried out in 10 cases. None had received the COVID-19 vaccine.

Comorbidities in deaths attributed to COVID-19

Among deaths attributed to Covid-19 infection, 74% (*n* = 60) had one or more comorbid conditions (Table 3). Cardiovascular disease was the most common comorbidity (*n* = 23, 28.4%), with half being complex heart disease (*n* = 12) (Table 4). One child had infective endocarditis. Neurological conditions were present in 16 (19.8%) deaths attributed to COVID-19 infection; half of them had global development delay. One child had spinal muscular atrophy, and another had congenital muscular dystrophy. There were no children with isolated epilepsy. Diabetic ketoacidosis due to type 1 diabetes and biliary atresia in isolation were also reported among the deaths attributed to COVID-19 infection. Two children had isolated obesity, and one of them had non-alcoholic steatohepatitis. Only five children had chronic respiratory problems, including asthma (*n* = 1). Most deaths attributed to COVID-19 infection had one or more chronic conditions (55.6%) and life-limiting conditions (59.3%).

Comparison of socio-demography between deaths due to all causes compared to deaths attributed to covid-19 infection in 2021

In 2021, there were 98 SARS-CoV-2 positive deaths, 71 of that were attributed to COVID-19 infection. A comparison of these deaths attributed to COVID-19 infection with all-cause deaths during the same year revealed significant differences in death rates across age groups, particularly among neonates, post-neonatal children, and those older than 5 years (Table 5). Post-neonatal children and children over 5 years were at a higher risk of dying from COVID-19, whereas the all-cause neonatal death rate far exceeded that of COVID-19-related neonatal death rate. Additionally, females were observed to be more susceptible to COVID-19-related deaths compared to fatalities from other causes. (Table 6)

Risk factors associated with deaths attributed to COVID-19 infection

In the multivariable logistic regression analysis, the odds of mortality were eleven times higher for individuals with chronic diseases in COVID-19-related deaths compared to deaths with an incidental finding of a positive

Table 4 Comorbid conditions categorised

	COVID-19 positive deaths (*n* = 111)	Deaths attributed to COVID-19 infection (*n* = 81)	Deaths with incidental SARS-CoV-2 positive test (*n* = 30)	p value
Neurological	18 (16.2)	14 (17.3)	04 (10)	0.6
Prematurity	14 (12.6)	09 (11.3)	05 (20)	0.4
Malignancy	14 (12.6)	09 (11.3)	05 (20)	0.7
Cardiovascular	25 (22.5)	23 (28.8)	02 (10)	0.04
Genetic syndromes	06 (5.4)	05 (6.3)	01 (03)	0.6
Respiratory	08 (7.2)	03 (6.3)	05 (20)	0.02
Endocrine	05 (4.5)	05 (6.3)	00 (00)	0.2
GIT/Liver	06 (5.4)	05 (3.8)	01 (03)	0.6
Renal	02 (1.8)	02 (2.5)	00 (00)	0.9
Immune-deficiency	01 (0.9)	01 (1.3)	00 (00)	0.9
Other	04 (3.6)	02 (2.5)	02 (10)	0.3

Please note that some children had multiple comorbidities. Data is presented as n(%). The differences between groups were compared using the two-sided chi-squared test or Fisher's exact test if small numbers

SARS-CoV-2 test. Additionally, belonging to the Tamil ethnicity appeared to be protective against COVID-19 mortality when compared to the Sinhalese ethnicity. The model explained 44.8% (Nagelkerke R^2) of the variance.

Clinical and laboratory characteristics of the deaths attributed to Multisystem Inflammatory Syndrome in Children (MIS-C)

Fourteen children had MIS-C, accounting for 17.2% of the total deaths attributed to COVID-19 infection in this cohort. In a sub-analysis of MIS-C cases ($n = 14$), 11 had a positive PCR test for COVID-19, and seven tested positive for antibodies. Four patients were older than 12 years, and the majority were females (9/14). Fever and lethargy were observed in 64% of cases, abdominal symptoms in 66%, and respiratory symptoms (cough, shortness of breath, or tachypnea) were universally present.

Rash was noted in 50% of MIS-C cases, while seizures occurred in two cases. Low blood pressure and poor peripheral perfusion were observed in five cases, and six presented with bleeding manifestations. One MIS-C case was associated with precocious puberty and obesity. Two had a history of prematurity, while all other cases were reported as previously healthy.

Laboratory findings revealed platelet counts below 150,000 in six MIS-C cases and neutropenia in two cases. C-reactive protein (CRP) was elevated in most cases, with marked elevation (> 100 mg/L) observed in six. The highest recorded D-dimer level was 15,165 ng/mL. Troponin was positive in 7 of the 9 cases tested, while data were either missing or the test was not performed in the remaining 5 cases.

Table 5 Age and gender distribution of deaths due to all causes compared to deaths attributed to covid-19 infection in 2021

	[a]Deaths due to all causes	Deaths attributed to COVID-19 infection	*p* value
Age (Categorical)			
<1 month	1499 (54.9)	13 (18.3)	<0.001
One month – <1 yr	555 (20.3)	26 (36.6)	<0.001
1–5 yrs	216 (07.9)	10 (14.1)	0.06
>5 yrs	457 (16.8)	21 (29.6)	0.005
Gender			
Male	1497 (46.8)	30 (40.7)	0.03
Female	1229 (52.3)	41 (58)	

[a] All-cause mortality as per national mortality and morbidity data 2021 [19]

Discussion

The present analysis describes COVID-19 child deaths from a lower middle-income country (LMIC), which has a well-structured healthcare system and impressive child mortality rates compared to the other countries in the South Asian region [20]. The Child Death Surveillance and Response System (CDSRS) in Sri Lanka, which was re-oriented to meet the information demands during the COVID-19 pandemic, helped to generate high-quality data. It captured information from both hospital and community levels. In addition, a desk review of all deaths by multiple experts enhanced the reliability of the information.

The number of deaths attributed to COVID-19 is frequently used as a key indicator and is considered essential for evaluating the severity of the pandemic. Among COVID-19 related deaths in Sri Lanka, 0.7% are child deaths with a positive SARS-CoV-2 test ($n = 111$). This proportion is higher than the reported global average (0.4%) and that of high-income countries (0.1%) but lower than that of low- and middle-income countries (0.9%) [2,

Table 6 Risk factors associated with deaths attributed to COVID-19 infection compared to deaths with incidental SARS-CoV-2 positive test

	B coefficient	Adjusted odds ratio	95% C.I		p value
Presence of chronic disease	2.42	11.22	1.735	72.496	0.01
Tamil vs. Sinhalese	−2.66	0.07	0.008	0.598	0.02
[a]Post-neonatal infants	2.13	8.43	0.770	92.411	0.08
Male	−1.45	0.24	0.051	1.078	0.06

[a] Reference: 1–5 years. $\chi 2(4) = 26.01$, $p < .002$. Nagelkerk R^2: 44.8%

21, 22]. Compared to other LMICs, the lower proportion of child deaths among all COVID-19-positive deaths in Sri Lanka can be credited to the country's well-structured healthcare system with better child and maternity care. Additionally, proactive preventive measures may have reduced the transmission risk to children [2, 23]. However, the mortality rate in Sri Lanka differs significantly from that of high-income countries such as Japan and New Zealand. The likely reasons could be linked to disparities in healthcare infrastructure, cultural differences and socioeconomic conditions [24].

To date, there are no standardised criteria to distinguish between deaths directly caused by COVID-19 and those where COVID-19 was a coincidental factor. Attributing COVID-19 as a cause of death presents significant challenges, primarily due to the complex interplay of comorbidities and the indirect effects of the pandemic on health behaviour. The proportion of child deaths directly attributed to COVID-19 among those who tested positive for SARS-CoV-2 varies across studies and regions. In the present analysis, COVID-19 infection was clearly implicated in 59% of cases and 27% of cases were considered coincidental. Compared to that, a study in England found that out of 185 children and young people who died within 100 days with a positive SARS-CoV-2 test, 43.8% were directly attributed to COVID-19 [25]. These differences may also be due to data collection variances and reporting standards.

The clinical manifestations of COVID-19 infection in our cohort matched the common symptoms observed globally. Many studies have documented fever, cough, and gastrointestinal (nausea and diarrhoea) as common symptoms in children hospitalised with COVID-19 [26, 27]. However, the incidence and presentation can vary slightly due to underlying health conditions and genetic predispositions [28, 29]. In our analysis, 11.7% had seizures, which is reported as a prevalent neurological manifestation in children with COVID-19, especially during the Omicron variant outbreak [30]. A study conducted in the USA showed that children with COVID-19 had a higher incidence of complex febrile seizures and longer seizure durations compared to those without the infection [31].

In our analysis, securing access to an intensive care unit was challenging, as 14 deaths attributed to COVID-19 infection were associated with delays in obtaining intensive care. Only four out of nine provinces in Sri Lanka have paediatric intensive care facilities. The overwhelming caseload exceeded the number of intensive care beds. Further, disrupted services due to supply chain issues, shortages of personal protective equipment, and reduced staffing added to the inability to provide optimal services [32, 33] Mitigating these effects is particularly challenging in resource-limited settings with higher health and financial needs and weaker health governance. This highlights the need for improvement in infrastructure, resources and preparedness for similar future crises.

In the risk analysis, post-neonatal infants and children older than 5 years were identified as being at greater risk compared to toddlers and preschoolers. This finding aligns with a systematic review of 83 studies conducted by Harwood et al. [34]. Notably, this review also found no gender differences in mortality rates, which contrasts with our findings [34]. Similar to the above review, higher case fatality rates among infants compared to children and adolescents aged 1 to 20 years have been reported in another systematic review [35], with rates of 0.07% versus 0.01% in high-income countries (HICs) and 1.3% versus 0.2% in low- and middle-income countries (LMICs). Neonatal deaths from other causes were significantly higher than deaths attributed to COVID-19 infection. Unlike other age groups, neonatal deaths are often multifactorial, indicating that the impact of acquired infections such as COVID-19 on neonatal mortality may be less pronounced.

High proportions of deaths were reported among females in our cohort when specifically compared to national mortality data. However, there is conflicting evidence. Some studies did not report a gender difference [34, 36, 37]. Conversely, most other studies have found that boys under 18 were more likely to die from the virus compared to girls of the same age group [38, 39]. Higher mortality among males is attributed to social, behavioural, genetic, and biological differences, such as stronger immune responses, which lead to higher cytokine storms [40].

In our study, we were unable to identify socioeconomic risk factors. However, global evidence indicates that individuals from low socioeconomic backgrounds are more vulnerable to COVID-19 [41]. Additionally, low education levels have been reported as a significant risk factor [41]. Within our cohort, the mortality rate among Muslims was disproportionately higher compared to their representation in Sri Lanka's overall population (18.5% vs. 9.3%), although it did not emerge as a risk factor in the regression model. Conversely, deaths among the Tamil ethnicity were comparatively lower than those among the Sinhalese in multivariable regression. These ethnic disparities in mortality may be influenced by biological factors and cultural practices.

comparisons were challenging. Nonetheless, our findings underscore that underlying chronic diseases are the primary risk factor for deaths attributed to COVID-19. Cardiovascular disease was significantly more prevalent among COVID-19-attributed deaths compared to deaths with incidental SARS-CoV-2 positive tests. In contrast, respiratory diseases were notably higher in non-COVID-attributed deaths within our cohort. While this observation is not readily explainable, Harwood et al. [34] reported that most comorbidities are associated with an increased risk of death due to COVID-19 infection, with asthma being a notable exception.

MIS-C is a post-infectious condition associated with COVID-19 that has been observed globally. In our analysis, 12.6% of cases were diagnosed with MIS-C. The proportion of MIS-C among children infected with SARS-CoV-2 varies by region. A study by the CDC in the United States found that 14% of the children who died from COVID-19 met the criteria for MIS-C [42]. A systematic review from 26 countries reported an incidence of 0.1% for MIS-C among all children with SARS-CoV-2 infection [43]. A study in India reported the temporal association between peaks in COVID-19 cases and subsequent increases in MIS-C [44]. We observed a strikingly lower number of MIS-C cases in the age group above 12 years, consistent with findings from a study conducted in Kerala, India [44]. Similar to other studies, the majority of children in our cohort had been previously healthy [44]. Among the neonates, two out of four were preterm. This aligns with findings from a study of 20 neonates with features consistent with MIS-C related to maternal SARS-CoV-2 in Kolhapur, India [45].

This analysis provides valuable insights into the unique vulnerabilities of children during a pandemic, guiding the development of tailored healthcare interventions, preventive measures, preparedness and critical gaps, such as delays in accessing intensive care. Additionally, quantifying the death toll, particularly deaths attributable to COVID-19, remains crucial, as this data has not yet been officially published. By leveraging this knowledge, we can strengthen healthcare infrastructure, enhance surveillance systems, and improve early detection and management of infectious diseases in children, ensuring a more resilient and proactive approach to safeguarding child health in the face of future pandemics. However, the following limitations should be considered when interpreting the analysis. Since it is a retrospective analysis, the accuracy of the extracted data relied upon the information entered in the hospital documents and postmortem analysis. Thus, even if we conducted a rigorous clinical review of all deaths, there may still have been a potential for misclassification of deaths attributed to COVID-19. As there is no diagnostic test for MIS-C, errors may have occurred due to the methods of diagnosis and reporting. Also, some actual COVID-19 deaths might have been underreported or misclassified due to the limitations in testing capacity. The mortality (child deaths as a proportion of all deaths) calculations were based on reported deaths to the Epidemiology Unit, the national focal institute for infectious diseases, and whether all deaths were correctly reported is uncertain. Nationwide data on deaths during the same period is crucial for comparison. However, of the available published data, only the age and sex distribution of deaths among children under 18 years in 2021 is accessible, with the remaining relevant data unavailable for comparison.

Conclusions

The proportion of COVID-19-positive deaths during the study period was higher than that reported in high-income countries, with most deaths (73%) directly attributed to SARS-CoV-2. Certain socio-demographic factors, compounded by existing comorbidities, likely contributed to this elevated mortality rate. Higher mortality rates were observed among post-neonatal infants, children over five years, females, individuals of Sinhalese ethnicity, and those with pre-existing chronic medical conditions, particularly cardiovascular disease.

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Authors' contributions

K.J. Conceptualization, Methodology, Data collection and Compilation, Writing—original draft, Writing—review & editing P.I. Data collection and Compilation, Writing-Reviewing, Editing S.W. Formal analysis, Writing-Reviewing, Editing D.H. Formal analysis, Writing-Reviewing, Editing C.S. Conceptualization, Writing-Reviewing, Editing G.L. Conceptualization, Methodology, Formal analysis, Writing—original draft, Writing—review & editing.

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Data availability
Data will be available from the corresponding author upon a reasonable request.

Declarations

Ethics approval and consent to participate
The Ethics Review Committee of the Faculty of Medicine, University of Colombo, Sri Lanka, approved the protocol (EC-22–061) on 19.05.2022. The waiver was granted based on the retrospective data analysis of patient records. The data were de-identified prior to analysis, ensuring patient confidentiality, and the study was conducted by relevant ethical guidelines for retrospective research. Furthermore, this study was conducted in compliance with the ethical principles outlined in the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. The World Bank. Economic and poverty impact of COVID-19: Sri Lanka development update 2021. 2021. https://documents1.worldbank.org/curated/en/284901624350168752/pdf/Sri-Lanka-Development-Update-2021.pdf. Accessed 07 June 2024.
2. UNICEF, UNICEF Data website. https://data.unicef.org/resources/covid-19-confirmed-cases-and-deaths-dashboard/COVID-19 confirmed cases and deaths. Accessed 07 June 2024.
3. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiology of COVID-19 among children in China. Pediatrics. 2020;145(6):e20200702. https://doi.org/10.1542/peds.2020-0702.
4. Mantovani A, Rinaldi E, Zusi C, Beatrice G, Saccomani MD, Dalbeni A. Coronavirus disease (2019). (COVID-19) in children and/or adolescents: a meta-analysis. Pediatr Res. 2021;89(4):733–7. https://doi.org/10.1038/s41390-020-1015-2.
5. Smith C, Odd D, Harwood R, Ward J, Linney M, Clark M, et al. Deaths in children and young people in England after SARS-CoV-2 infection during the first pandemic year. Nat Med. 2022;28(1):185–92. https://doi.org/10.1038/s41591-021-01578-1.
6. Wong JJM, Abbas Q, Chuah SL, Malisie RF, Pon KM, Katsuta T, et al. PACCOVRA Investigators of the PACCMAN Research Group. Comparative analysis of pediatric COVID-19 infection in Southeast Asia, South Asia, Japan, and China. Am J Trop Med Hyg. 2021;105(2):413–20. https://doi.org/10.4269/ajtmh.21-0299.
7. Rafferty MS, Burrows H, Joseph JP, Leveille J, Nihtianova S, Amirian ES. Multisystem inflammatory syndrome in children (MIS-C) and the coronavirus pandemic: current knowledge and implications for public health. J Infect Public Health. 2021;14(4):484–94. https://doi.org/10.1016/j.jiph.2021.01.008.
8. Wong-Chew RM, Noyola DE, Villa AR. Características clínicas y factores de riesgo de mortalidad en menores de 18 años con COVID-19 en México y Ciudad de México [Clinical characteristics and mortality risk factors in patients aged less than 18 years with COVID-19 in Mexico and Mexico City]. An Pediatr (Barc). 2022;97(2):119–28. https://doi.org/10.1016/j.anpedi.2021.07.014. Spanish.
9. Sharma AG, Kumar V, Sodani R, Sapre A, Singh P, Saha A, et al. Predictors of mortality in children admitted with SARS-CoV-2 infection to a tertiary care hospital in North India. J Paediatr Child Health. 2022;58(3):432–9. https://doi.org/10.1111/jpc.15737.
10. Sri Lanka College of Paediatricians. Diagnosis and management of COVID-19 infection in children. 2021. https://slcp.lk/wp-content/uploads/Diagnosis-and-Management-of-COVID-19-Infection-in-Children.pdf. Accessed 07 April 2024.
11. World Health Organisation. Multisystem inflammatory syndrome in children and adolescents with COVID-19. 2020. https://iris.who.int/bitstream/handle/10665/332095/WHO-2019-nCoV-Sci_Brief-Multisystem_Syndrome_Children-2020.1-eng.pdf?sequence=1
12. Sri Lanka Medical Council. Guidelines for medical practitioners & dentist's medical & death certificates. April 2016. https://www.mc.lk/images/publications/MedicalAndDeathCertificate.pdf. Accessed February 2024.
13. Department of Census & Statistics. Household income and expenditure survey–2019. 2019. http://www.statistics.gov.lk/Resource/en/IncomeAndExpenditure/HouseholdIncomeandExpenditureSurvey2019FinalResults.pdf. Accessed 10 Feb 2024.
14. Liyanage IMK. Education system of Sri Lanka: strengths and weaknesses. https://www.ide.go.jp/library/Japanese/Publish/Reports/InterimReport/2013/pdf/C02_ch7.pdf. Accessed 10 Feb 2024.
15. Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project (HCUP). Chronic condition indicator refined (CCIR) for icd-10-cm diagnoses, v2023.1. 2022. https://hcup-us.ahrq.gov/toolssoftware/chronic_icd10/chronic_icd10.jsp. Accessed 10 Feb 2024.
16. Hain R, Devins M, Hastings R, Noyes J. Paediatric palliative care: development and pilot study of a "Directory" of life-limiting conditions. BMC Palliat Care. 2013;12(1):43. https://doi.org/10.1186/1472-684X-12-43.
17. Chowdhury MZI, Turin TC. Variable selection strategies and its importance in clinical prediction modelling. Fam Med Community Health. 2020;8(1):e000262. https://doi.org/10.1136/fmch-2019-000262.
18. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol. 1996;49(12):1373–9. https://doi.org/10.1016/s0895-4356(96)00236-3.
19. Ministry of Health, Sri Lanka. Annual health bulletin. 2021. https://www.health.gov.lk/annual-health-bulletin/.
20. Levels & trends of child mortality. United Nations Inter-agency Group for Child Mortality Estimation (UNIGME) 2023. https://childmortality.org/wp-content/uploads/2024/03/UNIGME-2023-Child-Mortality-Report.pdf.
21. UNICEF. Child mortality and COVID-19. 2023: https://data.unicef.org/topic/child-survival/covid-19/. Accessed 09 June 2024.
22. Max Planck Institute for Demographic Research (MPIDR). COVerAGE global demographic database of COVID-19. 2022. https://www.coverage-db.org/. Accessed 09 June 2024.
23. Health Promotion Bureau. COVID-19 situation report. Live updates on New Coronavirus (COVID-19) outbreak. 2022. https://www.hpb.health.gov.lk/en. Accessed 09 June 2024.
24. Worldometer. Corona virus pandemic. 2024. https://www.worldometers.info/coronavirus/. Accessed 09 June 2024.
25. Bertran M, Amin-Chowdhury Z, Davies HG, Allen H, Clare T, Davison C, et al. COVID-19 deaths in children and young people in England, March 2020 to December 2021: an active prospective national surveillance study. PLoS Med. 2022;19(11):e1004118. https://doi.org/10.1371/journal.pmed.1004118.
26. Cox D. What do we know about COVID-19 and children? BMJ. 2023;12(380):21. https://doi.org/10.1136/bmj.p21.
27. Madani S, Shahin S, Yoosefi M, Ahmadi N, Ghasemi E, Koolaji S, et al. Red flags of poor prognosis in pediatric cases of COVID-19: the first 6610 hospitalised children in Iran. BMC Pediatr. 2021;21(1):563. https://doi.org/10.1186/s12887-021-03030-2.
28. Pam, Stephen, Dung-Gwom., Chinemelum, Adaora, Onodugo., Ugochukwu, Anthony, Eze. (2) Rheumatic Manifestations of Covid-19. (2024). https://doi.org/10.9734/bpi/mono/978-81-973195-5-6/ch13
29. Muhammad, M., Qureshi., Ashok, Kumar., Anand, Dev., Sanam, Sanam., FNU, Anam., Lareb, Gul., Ugal, Kishore., Muhammad, Ayoob, Memon., FNU, Partab., Mohsin, Ali., Sakshi, Kumari. Cutaneous manifestations of covid-19. (2023). https://doi.org/10.53555/jptcp.v30i17.2645
30. Iijima H, Kubota M, Ogimi C. Change in seizure incidence in febrile children with Covid-19 in the era of Omicron variant of concern. J Pediatr Infect Dis Soc. 2022;11(11):514–7. https://doi.org/10.1093/jpids/piac085.
31. Antoon JW, Hall M, Howard LM, Herndon A, Freundlich KL, Grijalva CG, et al. Covid-19 and acute neurologic complications in children. Pediatrics. 2022;150(5): e2022058167. https://doi.org/10.1542/peds.2022-058167.
32. Pujolar G, Oliver-Anglès A, Vargas I, Vázquez ML. Changes in access to health services during the COVID-19 pandemic: a scoping review. Int J Environ Res Public Health. 2022;19(3):1749. https://doi.org/10.3390/ijerph19031749.

33. Ranzani OT, Bastos LSL, Gelli JGM, Marchesi JF, Baião F, Hamacher S, et al. Characterisation of the first 250,000 hospital admissions for COVID-19 in Brazil: a retrospective analysis of nationwide data. Lancet Respir Med. 2021;9(4):407–18. https://doi.org/10.1016/S2213-2600(20)30560-9.
34. Harwood R, Yan H, Talawila Da Camara N, Smith C, Ward J, et al. Which children and young people are at higher risk of severe disease and death after hospitalisation with SARS-CoV-2 infection in children and young people: a systematic review and individual patient meta-analysis. Clinical Medicine. 2022;44:101287. https://doi.org/10.1016/j.eclinm.2022.101287.
35. Kitano T, Kitano M, Krueger C, Jamal H, Al Rawahi H, Lee-Krueger R, et al. The differential impact of pediatric COVID-19 between high-income countries and low- and middle-income countries: a systematic review of fatality and ICU admission in children worldwide. PLoS ONE. 2021;16(1):e0246326. https://doi.org/10.1371/journal.pone.
36. Ortiz-Prado E, Izquierdo-Condoy JS, Fernandez-Naranjo R, Vasconez J, Dávila Rosero MG, Revelo-Bastidas D, et al. The deadly impact of COVID-19 among children from Latin America: the case of Ecuador. Front Pediatr. 2023;11:1060311. https://doi.org/10.3389/fped.2023.1060311.
37. Dewi R, Kaswandani N, Karyanti MR, Setyanto DB, Pudjiadi AH, Hendarto A, et al. Mortality in children with positive SARS-CoV-2 polymerase chain reaction test: lessons learned from a tertiary referral hospital in Indonesia. Int J Infect Dis. 2021;107:78–85. https://doi.org/10.1016/j.ijid.2021.04.019.
38. Kharroubi S, Diab-El-Harake M. (5) Sex differences in COVID-19 mortality: a large US-based cohort study (2020–2022). AIMS public health. 2024. https://doi.org/10.3934/publichealth.2024045.
39. Kini A, Anand M, Ranjan U. Sex-disaggregated analysis of risk factors of COVID-19 mortality rates in India. Open Public Health J. 2023;16(1). https://doi.org/10.2174/18749445-v16-e230517-2022-210.
40. Chegni H, Babaii H, Hassan ZM, Pourshaban M. Immune response and cytokine storm in SARS-CoV-2 infection: risk factors, ways of control and treatment. Eur J Inflamm. 2022;20. https://doi.org/10.1177/1721727X221098970.
41. Khanijahani A, Iezadi S, Gholipour K, Azami-Aghdash S, Naghibi D. A systematic review of racial/ethnic and socioeconomic disparities in COVID-19. Int J Equity Health. 2021;20(1):248. https://doi.org/10.1186/s12939-021-01582-4.
42. McCormick DW, Richardson LC, Young PR, Viens LJ, Gould CV, Kimball A, et al. Deaths in children and adolescents associated with COVID-19 and MIS-C in the United States. Pediatrics. 2021;148(5):e2021052273. https://doi.org/10.1542/peds.2021-052273.
43. Rubens JH, Akindele NP, Tschudy MM, Sick-Samuels AC. Acute covid-19 and multisystem inflammatory syndrome in children. BMJ. 2021;1(372):n385. https://doi.org/10.1136/bmj.n385.
44. Tiwari A, Balan S, Rauf A, et al. COVID-19 related multisystem inflammatory syndrome in children (MIS-C): a hospital-based prospective cohort study from Kerala. India BMJ Paediatrics Open. 2021;5:e001195. https://doi.org/10.1136/bmjpo-2021-001195.
45. Pawar R, Gavade V, Patil N, Mali V, Girwalkar A, Tarkasband V, et al. Neonatal Multisystem Inflammatory Syndrome (MIS-N) associated with prenatal maternal SARS-CoV-2: a case series. Children (Basel). 2021;8(7):572. https://doi.org/10.3390/children8070572.

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