RESEARCH



Kawasaki disease in the pre- and post-COVID-19 era: shifts in patterns and outcomes from a multi-center study

Maryam Alfalasi¹ · Rania Snobar² · Ikram Shaalan³ · Aisha Alkhaaldi² · Khulood Khawaja⁴ · Huda Aldhanhani¹ · Ghassan Ghatasheh⁵ · Kamran Mahmood³ · Najla Aljaberi^{5,6}

Received: 15 March 2025 / Revised: 3 May 2025 / Accepted: 18 May 2025 © The Author(s) 2025

Abstract

Purpose Kawasaki disease (KD) is an acute vasculitis of childhood, with potential complications such as coronary artery aneurysms (CAAs). The COVID-19 pandemic introduced challenges in KD diagnosis and management due to its overlap with multisystem inflammatory syndrome in children (MIS-C). This study aims to compare the clinical presentation, laboratory findings, treatment approaches, and outcomes of KD before and after the COVID-19 pandemic across four centers in the United Arab Emirates (UAE).

Methods This retrospective study analyzed pediatric KD cases (classified per the American Heart Association "AHA" criteria) from four tertiary hospitals in the UAE. Patients were categorized into group 1 (pre-COVID-19: January 2017–January 2020) and group 2 (post-COVID-19: February 2020–January 2023). Patients not meeting the AHA criteria and those with MIS-C were excluded. Data collection included demographics, clinical and laboratory features, and echocardiograms, with coronary artery abnormalities assessed per AHA guidelines.

Results Among 138 included patients (67 in group 1, 71 in group 2), incomplete KD was significantly more common post-COVID-19 (45% vs. 25%, p=0.020). Lower occurrence of cervical lymphadenopathy (72% vs. 50%, p=0.009) and strawberry tongue (90% vs. 70%, p=0.006) were noted. Compared to group 1, group 2 had higher use of steroids (40.8% vs. 12.5%, p=<0.001) and biologics (8% vs. 1.5%, p=0.502). Although not statistically significant, CAAs were more frequent in group 2 (21% vs. 10%, p=0.139), with trends toward increased giant CAAs.

Conclusions: Our study highlights shifts in the patterns of KD in the post-COVID-19 era. We observed a higher prevalence of incomplete KD cases over the 3 years following the pandemic.

What is Known:

- Post-COVID-19 pandemic era demonstrated the emergence of multi-system inflammatory syndrome in children (MIS-C) which overlaps with Kawasaki disease (KD).
- While most studies of KD and COVID-19 compare KD with MIS-C, very few describe changes in KD well after the peak of the pandemic.

What is New:

- This study combines data from four healthcare centers of KD patients classified per the American Heart Association (AHA) criteria with the exclusion of MIS-C patients to provide direct comparison of KD before and after COVID-19.
- Compared to the pre-COVID-19 era, KD cases post-COVID-19 tend to present in an incomplete form with less occurrence of cervical lymphadenopathy and strawberry tongue.

Communicated by Tobias Tenenbaum

Maryam Alfalasi and Rania Snobar contributed equally to this work.

 Najla Aljaberi najla.aljaberi@uaeu.ac.ae

Published online: 29 May 2025

- Department of Pediatrics, Sheikh Khalifa Medical City, Abu Dhabi, UAE
- Department of Pediatrics, Al Qassimi Women's & Children's Hospital, Sharjah, UAE
- Pediatric Rheumatology Division, Department of Pediatrics, Sheikh Shakhbout Medical City, Abu Dhabi, UAE
- ⁴ University Hospitals of Leicester NHS Trust, Leicester, UK
- Department of Pediatrics, Tawam Hospital, Al Ain, UAE
- Department of Pediatrics, College of Medicine & Health Sciences, UAE University, Al Ain, UAE



367 Page 2 of 9 European Journal of Pediatrics (2025) 184:367

Keywords Kawasaki disease · Vasculitis · COVID-19

Abbreviations

AHA American Heart Association
CAAs Coronary artery aneurysms
CDC Centers for Disease Control and

Prevention

CRP C-reactive protein
CMV Cytomegalovirus
EBV Epstein-Barr virus

ESR Erythrocyte sedimentation rate

ICD-10 International Classification of Diseases-10

IRB Institutional review board IVIG Intravenous immunoglobulin

KD Kawasaki disease

KDSS Kawasaki disease shock syndrome

MIS-C Multi-system inflammatory syndrome in

children

MRA Magnetic resonance angiography

PA Peripheral angiography

SARS-CoV-2 Severe acute respiratory syndrome

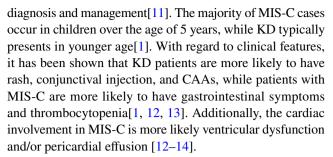
coronavirus

UAE United Arab Emirates

Introduction

Kawasaki disease (KD), an acute vasculitis primarily affecting children, continues to pose a significant public health concern due to its potential for causing coronary artery aneurysms (CAAs). While advancements in diagnosis and management have improved outcomes, understanding the disease's evolvement, particularly in the context of global health disruptions, is crucial. It has been hypothesized that the COVID-19 pandemic has affected KD in terms of presentation, laboratory workup, management, and outcomes[1]. Evidence shows that viruses like Epstein-Barr virus (EBV) and cytomegalovirus (CMV) increase the risk of autoimmunity, and severe acute respiratory syndrome coronavirus (SARS-CoV-2) may have a similar effect[2]. Viral infections are believed to induce autoinflammatory reactions involving molecular mimicry and bystander activation, raising the risk of autoimmunity[3–5]. Studies indicate an increased incidence of certain autoimmune disorders, including type 1 diabetes mellitus, ulcerative colitis, psoriasis, and autoimmune thyroiditis[6–8].

With the emergence of autoimmunity, a new inflammatory disorder emerged related to COVID-19 multisystem inflammatory syndrome in children (MIS-C)[9]. The diagnostic criteria as per the Centers for Disease Control and Prevention (CDC) involve clinical and laboratory workup in addition to exposure to a COVID-19 to define MIS-C[10]. The overlap between KD and MIS-C causes difficulties in the



Several reports outline that KD has changed in pattern after COVID-19[15–18]. While the abovementioned overlapping features between KD and MIS-C influence this conclusion, there may be discernible shifts in how classic KD has changed after the pandemic. This study aims to address this knowledge gap by comparing the patterns and outcomes of complete and incomplete KD before and well after the peak of the COVID-19 pandemic, across four tertiary hospitals in the United Arab Emirates (UAE).

Methods

Ethical approvals

The data was collected from various tertiary hospitals across the UAE using the International Classification of Diseases-10 (ICD-10) coding. The institutional review board (IRB) approval was obtained from the respective hospitals under the Department of Health for multi-center projects (reference number: DOH/CVDC/2023/1092). The hospitals that were included were Sheikh Khalifa Medical City (SKMC) in Abu Dhabi, Sheikh Shakhbout Medical City (SSMC) in Abu Dhabi, Tawam Hospital in Al Ain, and Al-Qassimi Women's & Children's Hospital (AQWCH) in Sharjah. Informed consent was waived as per the standard for retrospective studies.

Study design, patients, and data collection

This research was conducted as a retrospective descriptive study. It included all pediatric patients in four tertiary hospitals across the UAE, who were less than 16 years old and have been diagnosed with KD based on the American Heart Association (AHA) criteria[19]. Patients were classified as typical or complete KD upon having a fever of at least 5 days with the presence of at least four of the following five clinical signs: rash (maculopapular, or erythemamultiforme), cervical lymphadenopathy (at least 1.5 cm in diameter), usually unilateral, bilateral bulbar conjunctival injection without exudate, erythema and crackling of the lips, strawberry tongue, and/or oral and pharyngeal mucosal



European Journal of Pediatrics (2025) 184:367 Page 3 of 9 367

erythema, erythema and edema of the hands and feet in the acute phase and/or periungual desquamation in the subacute phase. Patients were classified as incomplete KD if they had a fever for more than 5 days in addition to 2–3 of the above five mentioned clinical signs along with at least 3 of the 6 supportive laboratory criteria (albumin \leq 3.0 g/dL, anemia for age, elevated ALT, platelets \geq 450,000/mm³, WBC \geq 15,000/mm³, urine WBC \geq 10/high-power field), or a positive echocardiogram as per AHA guidelines.

As per the AHA criteria, the presence of a coronary artery aneurysm with a Z-score of 2.5 or above despite the absence of other criteria features confirmed the diagnosis of KD[19]. The updated MIS-C definition published in 2022[20] included patients under 21 years of age, presenting with fever (without a duration specified), CRP more than 30 mg/L, and new onset of at least 2 of the following: cardiac involvement, mucocutaneous involvement, shock, gastrointestinal involvement, and hematological involvement, with laboratory or epidemiological findings confirming SARS-CoV2. Patients who had overlapping symptoms of KD and MIS-C were also subject to the application of the AHA criteria for complete and incomplete KD. Those who met the AHA guidelines and had negative epidemiological evidence of SARS-CoV2 infection were considered to have KD (complete or incomplete). Finally, any patients not fulfilling the above-mentioned criteria or considered likely to have MIS-C were excluded.

Collected data included demographics, clinical features, laboratory values, and imaging results at onset and at follow-up. Laboratory values were taken at the peak or nadir of the specified test during the acute phase to be representative. If fewer than 10 patients had a specific laboratory value, these values were removed from the analysis; this includes interleukin-6 (IL-6), pro-BNP, and troponin levels, which were seldom done pre-COVID-19. Echocardiogram data were collected at predefined time points: 1 month, 6 months, and 1 year after the initial echocardiogram. The definitions of CAAs, including giant CAA, were used as per the AHA guidelines[19]. For those patients who exhibited giant CAAs, we collected echocardiogram data up to 2 years after discharge.

Finally, patients were categorized per their time of KD presentation into pre-COVID-19 group or "Group 1" (January 2017–January 2020) or post-COVID-19 group or "Group 2" (February 2020–January 2023).

Statistical analysis

Descriptive analysis was completed for all collected data. Comparisons were made between group 1 and group 2 with regard to clinical manifestations, laboratory markers, treatment patterns, and echocardiographic outcomes using the chi-square test (Fisher's exact test when appropriate) and independent *t*-test. IBM SPSS Statistics software, version 29.0.0.0 (241), was used to perform the statistical analyses.

Results

Figure 1 demonstrates a flowchart of patient inclusion and categorization into groups. A total of 430 patients with ICD-10 codes consistent with KD were identified. After applying the inclusion and exclusion criteria, 138 patients were included in the final analysis. Of those, 67 cases belonged to group 1 (pre-COVID-19) and 71 cases belonged to group 2 (post-COVID-19). The two groups had near equal proportions of males (60% vs. 66%, p= 0.539). Between the two groups, the mean age at diagnosis was 35 months in group 1, and 31 months in group 2, which was not statistically different (p= 0.341).

The direct comparison between group 1 and group 2 is outlined in Table 1. The clinical presentation between the two groups was mostly similar, with the exception of cervical lymphadenopathy (72% in group 1 vs. 50% in group 2, p = 0.009) and strawberry tongue (90% in group 1 vs. 70% in group 2, p = 0.006). The majority of the primary clinical features of KD, however, remained similar with the application of the inclusion and exclusion criteria. This minor shift in clinical features is also reflected strongly in the proportion of incomplete KD in the two groups. Of the 67 cases in group 1, 17 cases (25%) presented as incomplete KD. Of the 71 cases in group 2, 32 cases (45%) presented as incomplete KD. This shows a significantly higher number of incomplete KD post-COVID-19 (p = 0.02) even after applying the known KD diagnostic criteria and after removing MIS-C cases. The distribution of KD cases, including the proportion of incomplete KD each year, is demonstrated in Fig. 2.

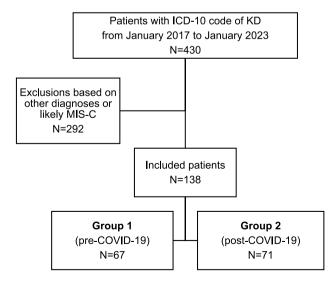


Fig. 1 Flowchart of included patients and the main categories of comparison



There were certain differences in laboratory parameters between the groups. Notably, group 1 patients exhibited higher levels of inflammatory markers, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), ferritin, and procalcitonin. Blood cell counts were equivalent between the

two groups aside from a significant reduction of hemoglobin in group 2 (p = 0.028). There were no differences in liver enzymes, albumin, or coagulation markers (data not shown).

The management of KD cases showed significant changes between the two periods (Table 1). Intravenous

Table 1 Detailed description of the clinical, laboratory, treatment, and outcome differences between patients with KD before and after COVID-19 (group 1 vs. group 2)

Parameter	Group 1 (<i>N</i> = 67)	Group 2 (<i>N</i> = 71)	<i>p</i> -value
Fever for 5 days	67 (100%)	68 (96%)	0.654
Cervical lymphadenopathy	48 (72%)	35 (50%)	0.009
Bilateral conjunctival injection	54 (81%)	59 (83%)	0.826
Rash	59 (88%)	58 (82)	0.348
Peripheral extremity changes	47 (69%)	43 (61%)	0.375
Strawberry tongue and/or cracked lips	60 (90%)	50 (70%)	0.006
Neurologic involvement	5 (8%)	7 (10%)	0.844
Incomplete KD	17 (25%)	32 (45%)	0.020
Laboratory values			
Hemoglobin (g/dL)	74.5 (40)	58.7 (43)	0.028
Lymphocytes ($\times 10^9/L$)	3.6 (3)	3.9 (3.7)	0.703
Neutrophils ($\times 10^9/L$)	10.7 (5.9)	9.57 (6.9)	0.323
Platelets ($\times 10^9/L$)	542 (285)	619 (337)	0.151
Creatinine (mg/dL)	38 (33)	31 (13)	0.095
ESR (mm/h)	74 (45)	60 (31)	0.034
CRP (mg/L)	162 (108)	126 (80)	0.027
Procalcitonin (ng/mL)	23.5 (38)	4.7 (10)	< 0.001
Management			
IVIG given	65 (97.0%)	71 (100.0%)	0.451
More than one IVIG Dose	18 (28%)	12 (17%)	0.151
IVIG adverse reactions*	0 (0%)	3 (4.4%)	0.264
Aspirin	61 (91%)	70 (99%)	0.103
Steroids	8 (12.5%)	29 (40.8%)	< 0.001
Steroid dose			0.705
Pulse ($\geq 10 \text{ mg/kg}$)	4 (50%)	10 (35%)	
High dose (> 2 mg/kg)	1 (13%)	6 (21%)	
Low dose (0.5–1 mg/kg)	3 (38%)	13 (45%)	
Any biologics	1 (1.5%)	6 (8%)	0.502
Complications			
Shock	3 (5%)	4 (6%)	1.000
Coronary artery aneurysm	7 (10%)	15 (21%)	0.139
Giant artery aneurysm	1 (14%)	3 (20%)	0.987
Decreased LVF	0 (0%)	2 (2.8%)	0.502
Prognosis			
Abnormal Z-score at 1 month of discharge	5 (9%)	7 (14%)	0.549
2	N = 54	N=51	
Abnormal Z-score at 6 months of discharge	2 (7%) N= 29	5 (15%) N = 33	0.433
Abnormal Z-score at 1 year of discharge	2 (13%) N = 16	3 (21%) N= 14	0.191

Values are described as mean (SD) for numeric variables and frequency (%) for categorical variables. Bolded values indicate statistically significant differences (p < 0.05).



^{*}Adverse reactions from IVIG: allergic reaction or anaphylaxis.

European Journal of Pediatrics (2025) 184:367 Page 5 of 9 367

immunoglobulin (IVIG) was administered to almost all patients in both groups (two patients in group 1 declined IVIG treatment and had normal coronary arteries). While analyzing IVIG dosing patterns, some cases were not given the classic 2 g/kg dose at once; therefore, we compared the frequency of having more than one IVIG between the two groups, indicating possible repeat dosing and refractoriness of the typical 2 g/kg dose. The portion of patients who received multiple doses of IVIG (> 2 g/kg total) was not significantly different between the groups (28% in group 1 vs. 17% in group 2, p = 0.151). Steroid use was notably higher in group 2, with 40% of patients given steroids as compared to 12% of patients in group 1. Pulse steroid and high-dose steroids were also more prevalent in group 2. The use of biologics remained infrequent in both groups, but with trends towards using more biologics in group 2.

The two groups were compared with regard to complications and outcomes of their KD presentation. When hypotension and poor perfusion present with KD, it is termed as Kawasaki disease Shock syndrome (KDSS)[21]. In our included patients, 4.5% had KDSS in group 1 and 5.6% in group 2 without statistical significance. Despite having small numbers in this cohort, CAAs were more prevalent in group 2, with a higher proportion of giant CAAs. On the other hand, the incidence of ventricular dysfunction was also higher in group 2. Those cases were not frequent enough to show statistical significance. Regarding long-term outcomes, as measured by Z-scores through echocardiography, there was a trend towards more abnormal Z-scores in group 2, particularly at the 1-year follow-up. However, this difference did not reach statistical significance.

Upon closer look at the four cases of giant CAAs in our cohort, we found that all presented in infancy (< 12 months of age). Out of those, two patients were incidentally found to have systemic arterial aneurysms (SAAs). The affected vessels included internal and external carotid arteries, brachial, axillary, vertebral, abdominal aorta, renal, splenic, inferior mesenteric, and internal iliac arteries. The first patient presented at 8 weeks of age with fever, loose stools,

Fig. 2 Number of KD cases per year (total number is above each bar) including the percentage of incomplete KD cases each year (lighter top part of the graph). Data collection extended to January 2023 (N = 2 cases), but this is not included in the graph as the data does not represent a whole year

a protracted fever with echocardiogram showing giant CAAs leading to the diagnosis of KD. He also had SAA in addition and was treated aggressively with a similar regiment of anti-inflammatory treatment. Interestingly, he also developed erythema nodosum, which is a feature of small to medium-vessel vasculitis and is part of systemic vasculitides[22]. He underwent whole-exome sequencing given his atypical presentation, and it was negative for variants of interest including ADA2 gene mutations. After the initial KD treatment, his acute symptoms resolved including the erythema nodosum. Follow-up showed resolution of his CAAs and SAAs. The other two patients were not investigated for SAA. The third patient was a previously healthy 7-month-old boy who presented with complete KD. He developed giant left coronary and right coronary aneurysm with left coronary artery thrombus. The thrombus was large enough to occlude the left coronary artery, leading to cardiac arrest needing resuscitation and initiation of extra-corporeal membrane oxygenation. He required pulse steroids, thrombolytic therapy for cardiac thrombus, plasmapheresis, heparin, inotropes, aspirin, clopidogrel, infliximab, and anakinra. Unfortunately, with all the therapies, and after 4 months in the PICU, he was discharged to a long-term facility with complications of hypoxic ischemic encephalopathy and acquired cardiomyopathy. The fourth 37 Complete KD Incomplete KD 43% 21 18 17% 52% 11 36%

and unilateral lymph node enlargement. Labs were signifi-

cant for transaminitis, coagulopathy, and hyperbilirubine-

mia. He was treated initially as a case of MIS-C, but due

to persistent fever, an echocardiogram was obtained which

revealed giant aneurysms. Given his age and CAA pres-

entation, he was labeled as KD. After anti-inflammatory

treatment with high-dose steroids, IVIG, high-dose aspirin,

anakinra, and infliximab, he was maintained on an anti-

coagulation regimen with warfarin, low-dose aspirin, and

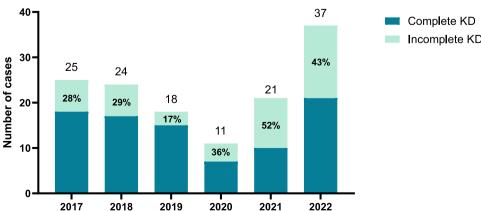
clopidogrel. At 2 years of follow-up, he continues on anti-

coagulation therapy and cardiac monitoring with improve-

ment in some coronaries but remaining giant CAA. The

second patient presented at 8 months of age with fever,

diarrhea, rash, and peripheral limb edema. He also had





patient had the most favorable outcome; he was a 4-monthold boy who presented at day 14 of fever and met the criteria for complete KD. The largest aneurysm was at the left anterior descending artery with a Z-score of 14. He received one dose of IVIG, aspirin, and clopidogrel. He was discharged after 6 days in the regular ward. His clopidogrel was discontinued after 14 months. Echocardiogram at age 6 years revealed the largest aneurysm in the proximal right coronary artery with a Z-score of 4.5. He is growing well and continuing to follow up with cardiology while being maintained on aspirin.

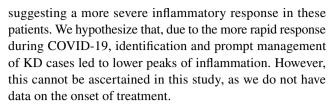
Discussion

This study investigated the impact of the COVID-19 pandemic on KD presentation and outcomes by comparing cases diagnosed before and after the COVID-19 pandemic across four tertiary pediatric hospitals in the UAE. While most clinical features remained consistent given the selective nature of this study, there was a significantly higher proportion of incomplete KD in the era post-COVID-19. Some of the first studies describing MIS-C in early 2020 as "Kawasaki-like disease" reported a high proportion of incomplete KD[9]. Many of those cases were later given the designation MIS-C after further charachterization[1, 12, 23]. In our study, we aimed to narrow the spectrum by eliminating cases that did not meet the AHA criteria for KD. The evolution of KD clinical patterns poses a diagnostic challenge and requires more focused efforts to raise the awareness of such atypical presentations. Regional and international collaboratives serve as major platforms to enhance the diagnostic process and inform the practicing physicians about the impact of early treatment[24–26].

We note a slightly younger age of presentation in our cohort after COVID-19, which has been demonstrated in other studies[18]. We do not report on the incidence of KD before and after COVID-19 in our study given the limited retrospective design. However, we do note the decline in reported cases in 2020 in line with other reports where it has been attributed to lower use of healthcare facilities and lower prevalence of common viral pathogens that would typically trigger KD[2, 27, 28].

In our population, KD has characteristically presented in an incomplete form more often after COVID-19. This is reflected by similar results in many centers internationally, where incomplete KD had a higher incidence rate in the post-pandemic as compared to the pre-pandemic[18, 26]. Similarly, a significant reduction in strawberry tongue and cervical lymphadenopathy was observed in our study and internationally[15, 29].

A notable finding was the elevated levels in inflammatory markers (ESR and CRP) in the pre-COVID group,



Patients in our study have received IVIG at the standard dose of 2 g/kg once or more in cases of refractory KD. This was less frequent in the post-COVID-19 group, which was associated with higher and more frequent doses of steroids as well as more frequent use of biologics. Receiving less IVIG post-COVID-19 in our cohort could be either due to successful response to the first dose or refractoriness and escalation of treatment with steroids and biologics. Refractoriness to first-dose IVIG was also noted in other reports during the pandemic period[30]. Given the parallel presence of MIS-C cases during the post-COVID-19 period, we believe that many physicians in our cohort simulated treatment patterns of MIS-C and applied them to KD. This pattern of treatment was encouraged in severe cases of MIS-C, where it has been recommended to use cytokine blockade after failure of a single dose of IVIG[23]. The same theory applies to the more frequent use of steroids and biologics in our post-COVID-19 cohort, where a more aggressive treatment approach was used due to perceived disease severity[30] or changes in treatment guidelines in response to the pandemic and the surge of MIS-C cases[23]. Analyzing the influence of those treatment patterns on overall outcomes and on CAAs is of incredible value but is limited, given the small sample size.

Several reports noted the higher number of CAAs and giant CAAs after COVID-19[31–33]. We note the same trend, although without statistical significance. We also identified incidental SAAs, which are infrequently reported in the literature. In one of the largest studies from China, high-risk patients were screened with full-body magnetic resonance angiography (MRA) or peripheral angiography (PA). They found that patients with SAA had a younger median age at onset (5 months) and a longer duration of fever. Notably, there was no difference with regard to the day at which IVIG was administered[34]. Most importantly, the regression rate of those SAAs is high, which is reassuring.

While our study provides valuable insights, it is limited by its retrospective design. The relatively short post-pandemic period may not fully capture the long-term impact of the pandemic on KD, but it is one of the few studies demonstrating data 3 years during and post-pandemic. The influence of concurrent pandemic-related factors, such as changes in healthcare-seeking behaviors, cannot be entirely discounted. Our study emphasized the application of the known AHA criteria to include cases of



European Journal of Pediatrics (2025) 184:367 Page 7 of 9 367

complete and incomplete KD, while cases of MIS-C were excluded to a high degree to provide as clear a distinction as possible and to understand the post-pandemic impact on KD while using the traditional criteria. Nonetheless, we recognize that some degree of diagnostic uncertainty is inherent, given the clinical overlap between KD and MIS-C, particularly in atypical presentations. This represents a potential limitation in interpreting our findings, despite our efforts to apply standardized definitions rigorously.

The findings of this study highlight the need for continued surveillance and research to understand the long-term implications of the COVID-19 pandemic on KD. Longer follow-up periods with adjudicated KD cases meeting the traditional criteria would be of high value that could influence practice in the long run.

Conclusion

In conclusion, our study provides insights into the evolving landscape of KD following the COVID-19 pandemic. We found that KD patients presented more often with an incomplete presentation within the 3 years post-COVID-19. Features like cervical lymphadenopathy and strawberry tongue were lower in occurrence.

Author contributions Study conceptualization was performed by Najla Aljaberi, Maryam Alfalasi, Kamran Mahmood, Aisha Alkhaaldi, Ghassan Ghatasheh, Huda Aldhanhani and Khulood Khawaja. Data collection and analysis were performed by Maryam Alfalasi, Rania Snobar, Ikram Shaalan and Najla Aljaberi. The first draft of the manuscript was written by Maryam Alfalasi, Rania Snobar and Najla Aljaberi. All authors read, edited and approved the final manuscript.

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate The study was performed in accordance with the Declaration of Helsinki and was approved by the Department of Health (DOH) for multi-center projects (reference number: DOH/CVDC/2023/1092). Informed consent was waived as per the regulation for retrospective studies.

 $\label{lem:competing} \textbf{Competing interests} \ \ \text{The authors declare no competing interests}.$

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons

licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

References

- Sharma C, Ganigara M, Galeotti C, Burns J, Berganza FM, Hayes DA, Singh-Grewal D, Bharath S, Sajjan S, Bayry J (2021) Multisystem inflammatory syndrome in children and Kawasaki disease: a critical comparison. Nat Rev Rheumatol 17(12):731–748. https://doi.org/10.1038/s41584-021-00709-9
- Ishii T, Nawa N, Hosokawa S, Morio T, Fujiwara T (2024) Exploring viral infections' role in Kawasaki disease onset: a study during the COVID-19 pandemic. J Med Virol 96(5):e29660. https://doi.org/10.1002/jmv.29660
- Smatti MK, Cyprian FS, Nasrallah GK, Al Thani AA, Almishal RO, Yassine HM (2019) Viruses and autoimmunity: a review on the potential interaction and molecular mechanisms. Viruses 11(8):762
- Mobasheri L, Nasirpour MH, Masoumi E, Azarnaminy AF, Jafari M, Esmaeili S-A (2022) SARS-CoV-2 triggering autoimmune diseases. Cytokine 154:155873. https://doi.org/10.1016/j.cyto. 2022.155873
- Al-Beltagi M, Saeed NK, Bediwy AS (2022) COVID-19 disease and autoimmune disorders: a mutual pathway. World J Methodol 12(4):200–23. https://doi.org/10.5662/wjm.v12.i4.200
- Tesch F, Ehm F, Vivirito A, Wende D, Batram M, Loser F, Menzer S, Jacob J, Roessler M, Seifert M, Kind B, König C, Schulte C, Buschmann T, Hertle D, Ballesteros P, Baßler S, Bertele B, Bitterer T, Riederer C, Sobik F, Reitzle L, Scheidt-Nave C, Schmitt J (2023) Incident autoimmune diseases in association with SARS-CoV-2 infection: a matched cohort study. Clinical Rheumatol 42(10):2905–14. https://doi.org/10.1007/s10067-023-06670-0
- Hileman CO, Malakooti SK, Patil N, Singer NG, McComsey GA (2024) New-onset autoimmune disease after COVID-19. Front Immunol 15. https://doi.org/10.3389/fimmu.2024.1337406
- Chang R, Yen-Ting Chen T, Wang SI, Hung YM, Chen HY, Wei CJ (2023) Risk of autoimmune diseases in patients with COVID-19: a retrospective cohort study. EClinicalMedicine 56:101783. https://doi.org/10.1016/j.eclinm.2022.101783
- Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, Bonanomi E, D'Antiga L (2020) An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet 395(10239):1771–8. https://doi.org/10.1016/S0140-6736(20)31103-X
- Melgar M (2022) Council of State and Territorial Epidemiologists/CDC surveillance case definition for multisystem inflammatory syndrome in children associated with SARS-CoV-2 infection—United States. MMWR Recomm Rep 71:14
- Lin J, Harahsheh AS, Raghuveer G, Jain S, Chouieter NF, Garrido-Garcia LM, Dahdah N, Portman MA, Misra N, Khoury M.
 Emerging insights into the pathophysiology of multi-system inflammatory syndrome in children associated with COVID-19.
 Can J Cardiol 2023
- Alkan F, Bircan O, Bal A, Bayturan S, Zengin N, Coskun S (2024) Comparison of early characteristics of multisystemic inflammatory syndrome and Kawasaki disease in children and the course of Kawasaki disease in the pandemic. BMC Pediatr 24(1):485. https://doi.org/10.1186/s12887-024-04966-x
- Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, Ramnarayan P, Fraisse A, Miller O, Davies P, Kucera F, Brierley



367 Page 8 of 9 European Journal of Pediatrics (2025) 184:367

- J, McDougall M, Carter M, Tremoulet A, Shimizu C, Herberg J, Burns JC, Lyall H, Levin M (2020) Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. JAMA 324(3):259–269. https://doi.org/10.1001/jama.2020.10369
- 14. Godfred-Cato S, Abrams JY, Balachandran N, Jaggi P, Jones K, Rostad CA, Lu AT, Fan L, Jabbar A, Anderson EJ, Kao CM, Hunstad DA, Rosenberg RB, Zafferani MJ, Ede KC, Ballan W, Laham FR, Beltran Y, Bryant B, Meng L, Hammett TA, Oster ME, Bamrah Morris S, Belay ED (2022) Distinguishing multisystem inflammatory syndrome in children from COVID-19, Kawasaki disease and toxic shock syndrome. Pediatr Infect Dis J 41(4):315–323. https://doi.org/10.1097/inf.000000000000003449
- Burney JA, Roberts SC, DeHaan LL, Shimizu C, Bainto EV, Newburger JW, Dominguez S, Jone PN, Jaggi P, Szmuszkovicz JR, Rowley AH, Samuy N, Scalici P, Tremoulet AH, Cayan DR, Burns JC, Investigators KS (2022) Epidemiological and clinical features of Kawasaki disease during the COVID-19 pandemic in the United States. JAMA Netw Open 5(6):e2217436. https://doi. org/10.1001/jamanetworkopen.2022.17436
- Yu H, Ni C, Xia Y, Li J, Hang B, Han C, Xu Z, Luo M, Rong X, Zhu J, Chu M (2022) Characteristics of Kawasaki disease before and after the COVID-19 pandemic in a large pediatric heart disease center. Front Pediatr 10:895408. https://doi.org/10.3389/fped.2022.895408
- Lin Y-H, Lin C-H, Lin M-C (2024) Declining incidence of Kawasaki disease during the COVID-19 pandemic: a time series analysis. Pediatr Infect Dis J 43(11):1021–1026. https://doi.org/10.1097/inf.00000000000004434
- Ae R, Makino N, Kuwabara M, Matsubara Y, Kosami K, Sasahara T, Nakamura Y (2022) Incidence of Kawasaki disease before and after the COVID-19 pandemic in Japan: results of the 26th nationwide survey, 2019 to 2020. JAMA Pediatr 176(12):1217–1224. https://doi.org/10.1001/jamapediatrics.2022.3756
- Jone P-N, Tremoulet A, Choueiter N, Dominguez SR, Harahsheh AS, Mitani Y, Zimmerman M, Lin M-T, Friedman KG, on behalf of the American Heart Association Rheumatic Fever EaKDCotCoL-CHDaHHitY, Council on Cardiovascular and Stroke N, Council on Cardiovascular Radiology and I, and Council on Clinical C (2024) Update on diagnosis and management of kawasaki disease: a scientific statement from the American Heart Association. Circulation 150(23):e481-e500. https://doi.org/10.1161/CIR.00000000000001295
- Melgar M, Lee EH, Miller AD, Lim S, Brown CM, Yousaf AR, Zambrano LD, Belay ED, Godfred-Cato S, Abrams JY, Oster ME, Campbell AP (2022) Council of state and territorial epidemiologists/CDC surveillance case definition for multisystem inflammatory syndrome in children associated with SARS-CoV-2 infection - United States. MMWR Recomm Rep. 71(4):1–14. https://doi. org/10.15585/mmwr.rr7104a1
- Nugud AA, Nugud A, Wafadari D, Abuhammour W (2019) Kawasaki shock syndrome in an Arab female: case report of a rare manifestation and review of literature. BMC Pediatr 19(1):295. https://doi.org/10.1186/s12887-019-1662-9
- Thurber S, Kohler S (2006) Histopathologic spectrum of erythema nodosum. J Cutan Pathol 33(1):18–26. https://doi.org/10.1111/j. 0303-6987.2006.00402.x
- 23. Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, Behrens EM, Kernan KF, Schulert GS, Seo P, Son MBF, Tremoulet AH, VanderPluym C, Yeung RSM, Mudano AS, Turner AS, Karp DR, Mehta JJ (2022) American College of Rheumatology clinical guidance for multisystem inflammatory syndrome in children associated with SARS-CoV-2 and hyperinflammation in pediatric COVID-19: version 3. Arthritis Rheumatol 74(4):e1–e20. https://doi.org/10.1002/art.42062
- Arab Y, Harahsheh AS, Dahdah N, El-Kholy N, Abed MY, Abu Al-Saoud SY, Agha HM, Alahmadi F, Alamer SR, Awadhi ZA, Ali S, Ali MT, Alrabte H, Al-Saloos H, Al-Senaidi KS, Alzyoud

- R, Awidat N, Bouayed K, Bouaziz A, Boukari R, El Ganzoury MM, Elmarsafawy HM, Elrugige N, Fitouri Z, Kotby A, Ladj MS, Bekkar M, Mouawad P, Salih AF, Suleiman M, Choueiter NF (2024) Kawarabi: administrative structuring of a multicenter research collaborative to study Kawasaki disease in the Arab Countries. World J Pediatr Congenit Heart Surg 15(2):177–83. https://doi.org/10.1177/21501351231205570
- 25. Alzyoud R, El-Kholy N, Arab Y, Choueiter N, Harahsheh AS, Aselan AS, Kotby A, Bouaziz A, Salih AF, Abushhaiwia A, Alahmadi F, Agha HM, Elmarsafawy HM, Alrabte H, Al-Saloos H, Boudiaf H, Hijazi I, Bouayed K, Al Senaidi KS, Boughammoura L, Jalal M, Ladj MS, Abu-Shukair ME, ElGanzoury MM, Hammadouche N, Elsamman N, Mouawad P, Boukari R, Benalikhoudja N, Jdour S, Abu Al-Saoud SY, Touri SN, Kammoun T, Fitouri Z, Dahdah N (2023) Access to care and therapy for Kawasaki disease in the Arab countries: a Kawasaki Disease Arab Initiative (Kawarabi) multicenter survey. Pediatr Cardiol 44(6):1277–84. https://doi.org/10.1007/s00246-023-03166-1
- 26. Harahsheh AS, Shah S, Dallaire F, Manlhiot C, Khoury M, Lee S, Fabi M, Mauriello D, Tierney ESS, Sabati AA, Dionne A, Dahdah N, Choueiter N, Thacker D, Giglia TM, Truong DT, Jain S, Portman M, Orr WB, Harris TH, Szmuszkovicz JR, Farid P, McCrindle BW, Alsalehi M, Ballweg JA, Barnes B, Braunlin E, Buffone A, Bustamante-Ogando JC, Chang AJ, Corral N, Dancey P, El-Ganzoury M, El-Samman N, Elias M, Fernandez-Cooke E, Friedman K, Garrido-Garcia LM, Garrido LM, Goldenberg GL, Grcic MM, Harris KC, Hicar MD, Hindt B, Jone P-N, Kajimoto H, Kaneta K, Khare M, Knutson S, Kutty S, Lanari M, Maksymiuk V. McHugh KE, Merves S, Misra N, Mohandas S, Mondal T, Norozi K, Nowlen T, Pagano JJ, Prasad D, Raghuveer G, Ravi P, Sundaram B, Sehgal A, Shah A, Vázquez BT, Tremoulet AH, Venkataraman A, Watelle L, Yamazaki-Naksahimada MA, Yetman AT (2024) Kawasaki disease in the time of COVID-19 and MIS-C: the International Kawasaki Disease Registry. Can J Cardiol 40(1):58-72. https://doi.org/10.1016/j.cjca.2023.06.001
- Kyohei I, Kousaku M, Chisato M, Kunitaka O, Rika Y, Junji E, Osamu M, Takahiro O, Ikuyo U, Masahiro N (2021) Incidence of Kawasaki disease before and during the COVID-19 pandemic: a retrospective cohort study in Japan. BMJ Paediatrics Open 5(1):e001034. https://doi.org/10.1136/bmjpo-2021-001034
- Nakata F, Matsubara K, Hamahata K, Miyakoshi C, Minamikawa S, Ota K, Okutani T, Yamaoka R, Eguchi J, Ueda I, Yokoyama N, Horinouchi T, Nukina S (2024) Resurgence of Kawasaki disease following relaxation of coronavirus disease 2019 pandemic restrictions in Japan. J Pediatr 275:114251. https://doi.org/10.1016/j.jpeds.2024.114251
- Fridman MD, Tsoukas P, Jeewa A, Yeung RSM, Gamulka BD, McCrindle BW (2023) Differentiation of COVID-19–associated multisystem inflammatory syndrome from Kawasaki disease with the use of cardiac biomarkers. Can J Cardiol 39(6):815–823. https://doi.org/10.1016/j.cjca.2022.11.012
- Ünlü AM, Holm M, Krusenstjerna-Hafstrøm T, Glarup M, Bjerre J, Herlin T (2023) Changes in Kawasaki disease incidence and phenotype during the COVID-19 pandemic. Dan Med J 70(6)
- Harrowell I, Webb R, Han DY, Best E, Mitchelson B, Wilson N, Ostring G (2024) Increasing incidence of Kawasaki disease and associated coronary aneurysm in Aotearoa New Zealand: a retrospective cohort study. Arch Dis Child 110:327772. https://doi.org/10.1136/archdischild-2024-327772
- Navaeifar MR, Shahbaznejad L, Sadeghi Lotfabadi A, Rezai MS (2021) COVID-19-associated multisystem inflammatory syndrome complicated with giant coronary artery aneurysm. Case Rep Pediatr 2021(1):8836403
- Richardson KL, Jain A, Evans J, Uzun O (2021) Giant coronary artery aneurysm as a feature of coronavirus-related inflammatory syndrome. BMJ Case Reports CP 14(7):e238740



European Journal of Pediatrics (2025) 184:367 Page 9 of 9 367

34. Zhao Q-M, Chu C, Wu L, Liang X-C, Sun S-N, He L, Zhao L, Wang F, Huang G-Y, Niu C, Liu F (2019) Systemic artery aneurysms and Kawasaki disease. Pediatrics 144(6):e20192254. https://doi.org/10.1542/peds.2019-2254

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

