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ORIGINAL RESEARCH

Age-Specific Cardiovascular and Platelet Dynamics in Kawasaki Disease

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Objective: To characterise age-specific differences in clinical manifestations, treatment response and platelet dynamics in Kawasaki disease (KD).

Methods: A retrospective analysis was conducted on 221 patients with KD who were admitted to the cardiology department of Suzhou Children's Hospital between June 2015 and May 2016. Patients were divided into three groups based on age: the infant group (≤12 months), the toddler group (>12 months to ≤36 months) and the child group (>36 months to ≤10 years). Clinical symptoms, signs, echocardiography (ECHO) findings, treatment characteristics and platelet counts were compared among the groups. Multivariate logistic regression was performed to identify independent predictors of severe cardiovascular damage. A *P*-value of <0.05 was considered significant.

Results: Major symptoms, such as lymph node enlargement and finger (toe) peeling, were significantly more pronounced in the toddler and child groups ($P < 0.05$). The overall incidence of cardiovascular damage was 56.1%, with 31.7% experiencing intravenous immunoglobulin (IVIG) resistance. Treatment delay (≥10 days from fever onset) occurred in 18.6% of cases and was associated with increased cardiovascular severity (adjusted odds ratio [aOR] = 2.45, 95% confidence interval [CI] 1.32–4.56, $P = 0.004$). Platelet counts and plateletcrit increased significantly during the acute and subacute phases, with the infant group exhibiting significantly higher platelet responses than the toddler and child groups (all $P < 0.05$). Multivariate analysis revealed that elevated platelet distribution width was independently associated with moderate-to-severe coronary artery lesions (aOR = 1.38, 95% CI 1.09–1.74, $P = 0.007$).

Conclusion: The clinical characteristics, ECHO findings, treatment patterns and platelet changes in patients with KD exhibit partial age-related differences. Treatment delay and IVIG resistance significantly impact cardiovascular outcomes. Clinicians are advised to incorporate age-specific diagnostic and treatment strategies, paying particular attention to timely intervention and platelet monitoring to facilitate early recognition and optimise clinical outcomes.

Keywords: Kawasaki disease, symptom, sign, platelet change, cardiovascular damage, echocardiography, IVIG resistance, treatment delay

Introduction

Kawasaki disease (KD), an acute systemic vasculitis predominantly affecting children under 5 years,[1,2] is the leading cause of acquired heart disease in developed nations.[3–6] In countries such as China, Japan and the United States, KD has replaced rheumatic fever as the most common cause of acquired heart disease in children and is recognised as a risk factor for ischemic heart disease in adulthood.[7–9] Despite standardised treatment with intravenous immunoglobulin (IVIG) and aspirin, 15–25% of untreated and 2–5% of treated patients develop coronary artery aneurysms (CAA), which can precipitate myocardial infarction or lifelong cardiovascular morbidity.[10,11]

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The pathophysiology of KD remains enigmatic, though dysregulated immune activation and vascular inflammation are hallmarks. Platelets, beyond their thrombotic functions, have emerged as pivotal mediators of vascular injury and immune dysregulation in KD.[12] Recent evidence underscores their role in instigating endothelial damage via cytokine release, leukocyte aggregation and transfer of non-coding RNAs to vascular cells.[13] For instance, reduced platelet miR-223 in KD patients impedes vascular smooth muscle cell regulation, accelerating coronary pathology,[14] while platelet–monocyte aggregates amplify inflammation through TGF-β/NF-κB signalling, driving CAA formation.[15] These mechanisms highlight platelets as central players in KD vasculopathy and potential therapeutic targets.

Clinically, the typical manifestations of KD include persistent high fever (≥5 days), bilateral lymph node enlargement, changes in oral mucosa (eg strawberry tongue, cracked lips), rash and extremity symptoms (eg redness and swelling of the palms and soles, as well as desquamation).[16] These symptoms are related to the immune response triggered by KD, and their incidence and presentation may vary among children of different age groups.[17] Infants ≤12 months exhibit higher IVIG resistance and CAA risk but often lack classic symptoms such as lymphadenopathy or extremity changes, delaying diagnosis.[18] Conversely, older children (>36 months) show more pronounced desquamation and coronary dilation.[19] Platelet responses also vary age-dependently: infants demonstrate heightened thrombocytosis and plateletcrit (PCT) during acute KD phases, suggesting intensified platelet activation.[20] Ricke's hypothesis posits that immune-complex-activated platelets release serotonin, inducing coronary capillary vasoconstriction and pressure-driven CAA formation,[21] consistent with epidemiologic associations. While the immune-complex hypothesis remains speculative, it underscores the need to explore platelet activation pathways in age-stratified KD cohorts. This age-stratified heterogeneity complicates clinical management and underscores the need for tailored prognostic tools.

The importance of timely treatment in KD cannot be overstated. Studies have consistently shown that delayed administration of IVIG beyond 10 days from fever onset is associated with increased risk of CAA.[22] Furthermore, approximately 10–20% of patients demonstrate IVIG resistance, requiring second-line therapies such as corticosteroids, infliximab or cyclosporine to control inflammation and prevent cardiovascular sequelae.[23] These treatment-related factors significantly influence disease outcomes and should be considered when evaluating patient prognosis.

This study comprehensively investigated the relationships among clinical symptoms, signs, electrocardiogram findings and platelet changes in patients with KD across various age groups. The systematic analysis could hopefully unveil the distinct characteristics of KD in different age groups and provide more effective diagnostic and therapeutic guidance for clinicians. We hypothesise that infants exhibit exaggerated platelet activation, driving severe vascular pathology despite subtler clinical presentations. By clarifying these age-platelet interactions, we aim to advance risk stratification and therapeutic targeting.

Materials and Methods

General Data

A retrospective analysis was conducted on patients with KD who were admitted to the cardiology department of Suzhou Children's Hospital between June 2015 and May 2016. Based on the inclusion and exclusion criteria outlined below, a total of 221 eligible cases were identified, comprising 149 boys and 72 girls. The patients ranged in age from 57 days to 10 years and 3 months. Based on age distribution, the 221 patients were divided into three groups: the infant group (≤12 months, n = 67), the toddler group (>12 months to ≤36 months, n = 111) and the child group (36 months-10 years, n = 43) (Figure 1).

The inclusion criteria were as follows: patients (1) meeting the diagnostic criteria for KD, including persistent high fever (≥5 days) and other typical clinical manifestations (eg unilateral cervical lymphadenopathy ≥1.5 cm, mucosal changes in the oral cavity, rash and extremity changes varying by disease stage), based on the diagnostic guidelines of the American Heart Association;[24] (2) meeting the following age requirements: ≤12 months for the infant group, >12 months to ≤36 months for the toddler group and >36 months to ≤10 years for the child group; (3) undergoing echocardiographic (ECHO) examinations during hospitalisation, with complete clinical data and laboratory test results; and (4) with no other severe complications during the follow-up period after treatment.

The exclusion criteria included (1) children with other acute or chronic diseases (eg congenital heart disease, severe infections, systemic diseases) that could affect the cardiovascular system; (2) cases with other acute febrile illnesses with

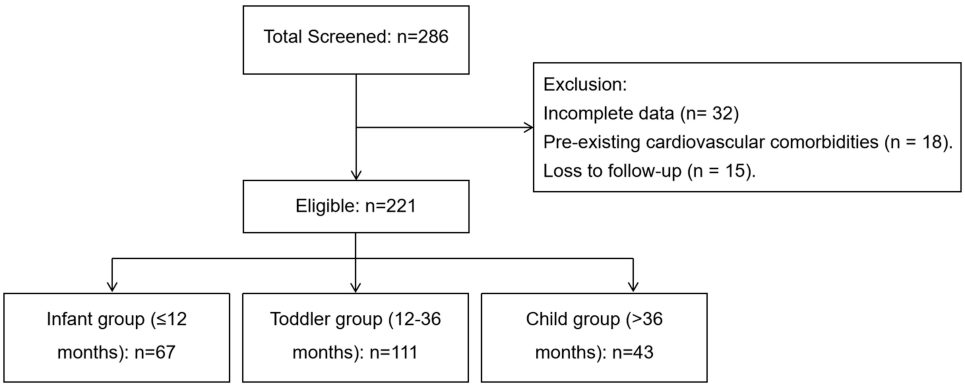

Figure 1 The flowchart of participant selection process.

skin rashes unrelated to KD, such as scarlet fever, sepsis, septicaemia, Epstein–Barr virus infection, measles, Stevens–Johnson syndrome, rheumatoid arthritis or drug allergies; (3) hospitalisations unrelated to KD (eg surgical procedures or trauma); and (4) patients with incomplete data or insufficient follow-up duration.

Methods

The participants' inpatient medical records were thoroughly reviewed, with detailed documentation of clinical symptoms and signs. The cardiac colour Doppler ultrasound examination employed a General Electric Healthcare Vivid™ 7 multifunctional Doppler ultrasound system (GE Healthcare, Milwaukee, WI, USA) with M4S and 5S cardiac probes (frequencies 1.5–4.3 and 2.4–5.0 MHz) to examine the patients' heart and blood vessels. For uncooperative or agitated patients, 10% chloral hydrate (0.5 mL/kg) was administered rectally for sedation. Interobserver variability (κ=0.89; 95% CI: 0.82–0.94) and intraobserver variability (κ=0.91; 95% CI: 0.85–0.96) were calculated using Cohen's κ, exceeding clinical reliability thresholds.

Treatment-Related Indicators

Treatment characteristics were systematically documented for all patients. IVIG resistance was defined as persistent or recrudescent fever ≥36 hours after completion of the initial IVIG infusion (2 g/kg). Treatment delay was defined as initiation of IVIG therapy ≥10 days from the onset of fever. The use of adjunctive therapies was recorded, including:

- Corticosteroids (methylprednisolone pulse therapy or oral prednisolone)
- Biological agents (infliximab, anakinra)
- Other immunosuppressive agents (cyclosporine, methotrexate)

The timing of treatment initiation, total duration of fever and time to defervescence after IVIG administration were documented for all cases.

Outcome Measures

(1) General data included age, sex and body weight. (2) Clinical symptoms and signs recorded included fever, conjunctival congestion, dry and cracked lips, Myrica tongue, cervical lymph node enlargement, erythema or induration of the hands and feet, finger (toe) peeling, rash and perianal skin redness or desquamation. Fever duration was defined as the total number of days from the onset of fever (as reported by the caregiver) to fever resolution, including both pre-admission and post-admission days. (3) Findings from the cardiac colour Doppler ultrasound included coronary artery intimal roughness, coronary artery dilation, coronary aneurysm, pericardial effusion, enlargement of the ventricles or atria, reduced ventricular or atrial systolic function and arrhythmia. Cardiovascular damage in patients with KD was classified as mild, moderate or severe based on coronary artery *Z-*score thresholds. Mild cases were characterised by

coronary artery intimal roughness or slight coronary artery dilation, defined as a Z score of ≥2.5 to <5. Non-coronary findings, such as ventricular or atrial enlargement, minor reductions in systolic function or small pericardial effusion, were recorded separately and not included in the grading unless accompanied by coronary changes. Moderate cases were classified as dilation of the left coronary artery or right coronary artery (Z score of ≥5 to <10). Severe cases involved dilation of both coronary arteries or coronary aneurysms (Z score of ≥10 or absolute internal diameter ≥8 mm). (4) Platelet counts and related parameters, including mean platelet volume (MPV), platelet distribution width (PDW) and PCT, were recorded for all three groups. All haematological parameters were measured using a Sysmex XN-9100 automated haematology analyser (Sysmex Corporation, Kobe, Japan) in the hospital's clinical laboratory. The electrical impedance method was used for detection.

Statistical Analysis

Statistical analyses were performed using SPSS 23.0 software (IBM, Armonk, NY, USA). A post hoc power analysis was performed using the platelet count data in the acute phase across the three age groups. The estimated power for detecting group differences using one-way analysis of variance (ANOVA) exceeded 0.95 at a significance level of 0.05, confirming sufficient statistical power for this analysis. The normality of continuous data was assessed using the Shapiro–Wilk test. Normally distributed measurement data were represented by mean ± standard deviation ($\bar{X} \pm s$). For homogeneous variances, one-way ANOVA and the t-test were used for comparisons among the three groups, and the Student–Newman–Keuls test was applied for pairwise comparisons between groups. If variances were not homogeneous, the Kruskal–Wallis rank sum test was used for comparisons among the three groups, with rank sum tests used for pairwise comparisons. Non-normally distributed measurement data were expressed as median (quartiles) (M[P25, P75]). Comparisons among the three groups and pairwise comparisons between groups were conducted using the rank sum test. Categorical data were represented by rates. Comparisons among the three groups were performed using the chi-square (χ^2) test in contingency tables, and pairwise comparisons between groups were conducted using four-cell χ^2-tests. For ordinal categorical variables (severity of cardiovascular damage), the Cochran–Armitage trend test was employed to assess linear trends across age groups.

Multivariate logistic regression analysis was performed to identify independent predictors of moderate-to-severe cardiovascular damage. Variables with $P < 0.10$ in univariate analysis were included in the multivariate model. These included age group, sex, IVIG resistance, treatment delay, use of adjunctive therapies and platelet parameters (MPV, PDW, PCT). Collinearity was assessed using variance inflation factors (VIF), with VIF >5 indicating significant collinearity. Model fit was evaluated using the Hosmer–Lemeshow goodness-of-fit test and McFadden's pseudo-R^2. Adjusted odds ratios (aOR) with 95% confidence intervals (CI) were calculated. A P-value of <0.05 was considered to indicate statistical significance. Effect sizes were calculated to complement P-values and quantify the magnitude of group differences. Cohen's d was used for pairwise comparisons of continuous variables. Cohen's f and Eta^2 were used for one-way ANOVA, with Cramer's V applied for categorical variables.

Results

General Data

A total of 221 patients with KD were included in this study, comprising 149 boys (67.42%) and 72 girls (32.58%). The patients were aged between 57 days and 10 years and 3 months, with a median age of 18.00 months (11.00, 32.00). The median body weight was 11.00 kg (9.50, 14.00). Based on age, the 221 patients were categorised into the following groups: (1) the infant group (≤12 months): 67 cases (30.32%), including 46 boys (68.66%) and 21 girls (31.34%); (2) the toddler group (>12 months to ≤36 months): 111 cases (50.23%), including 75 boys (67.57%) and 36 girls (32.43%); and (3) the child group (>36 months to ≤10 years): 43 cases (19.46%), including 28 boys (65.12%) and 15 girls (34.88%). A comparison of the gender distribution among the three groups showed no statistically significant differences (P = 0.927). As expected, height, body weight, and BMI increased significantly across the infant, toddler, and child groups, reflecting normal physiological growth patterns (all $P < 0.05$). Heart rate demonstrated a predictable decline with increasing age (P = 0.001). Inflammatory markers, including CRP and ESR, were elevated in all groups, with the highest

Table 1 Anthropometric and Clinical Characteristics

Parameter	Infant Group (n=67)	Toddler Group (n=111)	Child Group (n=43)	P-value
Male (n, %)	46 (68.66)	75 (67.57)	28 (65.12)	0.927
Height (cm)	68.2 ± 4.1	86.5 ± 5.3	112.7 ± 8.9	<0.001
BMI (kg/m²)	15.8 ± 1.2	16.2 ± 1.4	16.9 ± 1.6	0.003
Heart rate (bpm)	148 ± 12	132 ± 14	118 ± 11	0.001
CRP (mg/L)	98.6 ± 32.4	82.1 ± 29.8	64.2 ± 28.7	0.008
ESR (mm/hr)	68.5 ± 18.2	58.7 ± 16.4	49.3 ± 15.1	0.002

levels observed in infants (all $P < 0.05$), suggesting a more pronounced acute phase response in younger patients. These findings align with the systemic inflammatory nature of Kawasaki disease and highlight age-related variations in baseline clinical and laboratory parameters. (see Table 1).

Comparison of Fever Duration Among Different Age Groups

The comparison of fever duration among the three age groups revealed that the mean fever duration was 7.43 ± 1.91 days in the infant group, 7.85 ± 2.20 days in the toddler group and 7.93 ± 1.97 days in the child group, showing no significant differences among the groups ($P = 0.346$, $Eta^2 = 0.010$) (see Table 2). In terms of gender-specific fever duration within each group, the results were as follows. In the infant group, fever duration was 7.15 ± 2.07 days for boys versus 8.07 ± 1.36 days for girls ($P = 0.075$); in the toddler group, the duration was 7.72 ± 1.81 days for boys versus 8.11 ± 2.85 days for girls ($P = 0.382$); and in the child group, the duration was 8.04 ± 2.22 days for boys versus 7.73 ± 1.44 days for girls ($P = 0.637$). Although the difference in fever duration between male and female patients did not reach statistical significance ($P > 0.05$), we further calculated the effect size (Cohen's *d*) to evaluate the magnitude of difference. In the infant group, the effect size was −0.489, indicating a moderate difference, with female infants showing slightly longer fever duration. In the toddler and child groups, the effect sizes were −0.177 and 0.156, respectively, both indicating small differences (see Table 2).

Comparison of Clinical Symptoms Among Different Age Groups

The incidence rates of conjunctival hyperaemia, Myrica tongue, rash, dry lips and chapped lips were fairly similar across the age groups, showing no statistically significant differences (all $P > 0.05$). However, the following notable differences were observed. The incidence of lymph node enlargement was significantly higher in the child group (93.02%) compared with the toddler group (77.48%) and the infant group (70.15%) ($P = 0.017$, $V = 0.192$). The child group exhibited a significantly higher incidence of finger (toe) peeling (67.44%) compared with the infant group (38.81%) and the toddler group (54.05%) ($P = 0.011$, $V = 0.201$), suggesting a potential association between age and the manifestation of this symptom. Regarding reactions to Bacillus Calmette–Guérin (BCG) vaccination, the infant group had a significantly higher incidence (56.71%) compared with the toddler group (17.12%) and the child group (4.65%) ($P < 0.001$, $V = 0.460$). The observed increase in median body weight across the age groups, from 8.50 kg in the infant group to 11.00 kg

Table 2 Comparison of Fever Duration Between Male and Female Patients Within Age Groups

Group	Fever Duration (d)	Male (d)	Female (d)	*t*-value	*P*-value
Infant Group	7.43±1.91	7.15±2.07	8.07±1.36	−1.812	0.075
Toddler Group	7.85±2.20	7.72±1.81	8.11±2.85	−0.878	0.382
Child Group	7.93±1.97	8.04±2.22	7.73±1.44	0.476	0.637
F-value	1.067	–	–	–	–
P-value	0.346	–	–	–	–

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Table 3 Clinical Symptoms and Signs in Patients with KD of Different Ages

Parameter	Infants (n = 67)	Toddlers (n = 111)	Children (n = 43)	Statistic	P-value	Cramér's V/ε^2
Conjunctival hyperemia, n(%)	60 (89.55)	104 (93.69)	39 (90.69)	1.053	0.591	0.048
Myrica tongue, n(%)	54 (80.60)	88 (79.28)	41 (95.35)	5.666	0.059	0.164
Rash, n(%)	56 (83.58)	88 (79.28)	34 (79.07)	0.568	0.753	0.043
Lymph node enlargement, n(%)	47 (70.15)	86 (77.48)	40 (93.02)	8.145	0.017	0.192
Dry lips, n(%)	53 (79.10)	87 (78.40)	33 (76.70)	0.087	0.957	0.027
Chapped lips, n(%)	32 (47.76)	60 (54.05)	25 (58.14)	1.243	0.537	0.043
Hand/foot induration, n(%)	37 (55.22)	62 (55.86)	16 (37.14)	4.862	0.088	0.161
Finger (toe) peeling, n(%)	26 (38.81)	60 (54.05)	29 (67.44)	8.969	0.011	0.201
Perianal congestion, n(%)	31 (46.27)	33 (29.73)	12 (27.91)	5.465	0.065	0.166
Perianal desquamation, n(%)	13 (19.40)	31 (27.93)	15 (34.88)	3.380	0.185	0.098
BCG, n(%)	38 (56.71)	19 (17.12)	2 (4.65)	46.73	<0.001	0.460
Body weight (kg)	8.50 (7.50, 9.50)	11.00 (10.00, 13.00)	17.00 (15.00, 21.00)	80.06	<0.001	0.358

Table 4 Distribution of Cardiovascular Damage Severity Among Different Age Groups

Severity	Infant Group n(%)	Toddler Group n(%)	Child Group n(%)	Total n(%)
No damage	28 (41.8)	47 (42.3)	22 (51.2)	97 (43.9)
Mild	18 (26.9)	38 (34.2)	12 (27.9)	68 (30.8)
Moderate	7 (10.4)	16 (14.4)	4 (9.3)	38 (17.2)
Severe	14 (20.9)	10 (9.0)	5 (11.6)	18 (8.1)
Total with damage	39 (58.2)	64 (57.7)	21 (48.8)	124 (56.1)
χ^2 for trend	3.891			
P-value (trend test)	0.089			

in the toddler group and 17.00 kg in the child group ($P < 0.001$, $V = 0.358$)—reflects expected developmental growth patterns (see Table 3).—from 8.50 kg in infants to 11.00 kg in toddlers and 17.00 kg in children.

Treatment Characteristics Among Different Age Groups

Analysis of treatment patterns revealed significant variations across age groups (Table 4). Overall, 70 patients (31.7%) demonstrated IVIG resistance, with the highest proportion observed in the infant group (40.3%) compared to the toddler group (29.7%) and child group (23.3%) ($P = 0.041$, $V = 0.178$). Treatment delay (≥10 days from fever onset) occurred in 41 patients (18.6%), with no significant difference among age groups (infant: 20.9%; toddler: 18.0%; child: 16.3%; $P = 0.735$).

Second-line therapies were required in 82 patients (37.1%). Corticosteroids were administered to 56 patients (25.3%), with methylprednisolone pulse therapy used in 38 cases and oral prednisolone in 18 cases. The use of corticosteroids was significantly higher in the infant group (35.8%) compared to the toddler (23.4%) and child groups (16.3%) ($P = 0.028$). Biological agents were used in 26 patients (11.8%), primarily infliximab (n = 20) and anakinra (n = 6). The median time from fever onset to IVIG administration was 6 days (IQR 5–8 days), with no significant difference among age groups ($P = 0.452$) (see Table 5).

Comparison of Cardiovascular Damage Among Different Age Groups of Patients with KD

Of the 221 patients with KD included in the study, 124 were diagnosed with cardiovascular damage (56.1%). When stratified by severity, 68 patients (30.8%) had mild damage, 38 (17.2%) had moderate damage and 18 (8.1%) had severe damage. The distribution of severity differed across age groups (Table 5). In the infant group, 39 cases (58.2%) had cardiovascular damage: 18 mild (26.9%), 7 moderate (10.4%) and 14 severe (20.9%). In the toddler group, 64 cases

Table 5 Treatment Characteristics Among Different Age Groups

Treatment Variable	Infant Group n(%)	Toddler Group n(%)	Child Group n(%)	Total n(%)	χ^2/H	P-value	Cramér's V
IVIG resistance	27 (40.3)	33 (29.7)	10 (23.3)	70 (31.7)	6.421	0.041	0.178
Treatment delay (≥10 days)	14 (20.9)	20 (18.0)	7 (16.3)	41 (18.6)	0.619	0.735	0.053
Second-line therapy (any)	29 (43.3)	39 (35.1)	14 (32.6)	82 (37.1)	2.142	0.343	0.099
Corticosteroids							
- Methylprednisolone pulse	15 (22.4)	17 (15.3)	6 (14.0)	38 (17.2)	2.186	0.335	0.099
- Oral prednisolone	9 (13.4)	7 (6.3)	2 (4.7)	18 (8.1)	3.872	0.144	0.132
- Any corticosteroid	24 (35.8)	26 (23.4)	7 (16.3)	56 (25.3)	7.156	0.028	0.180
Biological agents							
- Infliximab	8 (11.9)	9 (8.1)	3 (7.0)	20 (9.0)	1.093	0.579	0.070
- Anakinra	3 (4.5)	2 (1.8)	1 (2.3)	6 (2.7)	1.289	0.525	0.076
- Any biological	11 (16.4)	11 (9.9)	4 (9.3)	26 (11.8)	2.154	0.341	0.099
Days to IVIG (median, IQR)	6 (5–8)	6 (5–7)	7 (5–8)	6 (5–8)	1.576	0.452	-
Time to defervescence (h)	28 (20–42)	30 (22–44)	32 (24–46)	30 (22–44)	0.893	0.640	-

Abbreviations: IVIG, intravenous immunoglobulin; IQR, interquartile range.

(57.7%) had damage: 38 mild (34.2%), 16 moderate (14.4%) and 10 severe (9.0%). In the child group, 21 cases (48.8%) had damage: 12 mild (27.9%), 4 moderate (9.3%) and 5 severe (11.6%).

The Cochran–Armitage trend test revealed a marginally significant trend towards decreasing severity with increasing age ($P = 0.089$). When comparing moderate-to-severe damage specifically, infants showed a higher proportion (31.3%) compared to toddlers (23.4%) and children (20.9%), though this difference did not reach statistical significance ($P = 0.178$, $V = 0.114$).

Gender-specific analysis showed no significant differences in cardiovascular damage incidence between boys and girls within each age group (Table 6). Among boys, cardiovascular damage occurred in 58.7% of infants, 58.7% of toddlers and 46.4% of children ($P = 0.500$). Among girls, the rates were 57.1%, 55.6% and 53.3%, respectively ($P = 0.975$).

Table 6 Gender-Specific Comparison of Cardiovascular Damage Incidence

Group	Gender	Infant Group n(%)	Toddler Group n(%)	Child Group n(%)	χ^2	P-value	Cramér's V
With damage	Male	27 (58.7)	44 (58.7)	13 (46.4)	1.387	0.500[a]	0.057[a]
	Female	12 (57.1)	20 (55.6)	8 (53.3)	0.051	0.975[b]	0.022[b]
Without damage	Male	19 (41.3)	31 (41.3)	15 (53.6)			
	Female	9 (42.9)	16 (44.4)	7 (46.7)			
χ^2		0.014	0.096	0.181			
P-value		0.905[c]	0.756[c]	0.666[c]			
Cramér's V		0.000[c]	0.010[c]	0.017[c]			

Notes: [a]Comparison of cardiovascular damage incidence in males across the three groups. [b]Comparison of cardiovascular damage incidence in females across the three groups. [c]Gender-based comparison within each group.

Changes in Platelet and Leukocyte Levels at Different Stages Among Patients with KD in Different Age Groups

The analysis of white blood cell count, MPV and PDW among patients with KD in different age groups and stages of the disease showed no statistically significant differences (all $P > 0.05$). In all three groups, the platelet count and PCT increased progressively, peaking during the subacute phase and subsequently declining during the convalescent and sequelae phases. Compared with the toddler and child groups, the infant group showed a significantly higher platelet count and PCT in the acute, subacute and convalescent phases (all $P < 0.05$). During the sequelae phase, no significant differences were found between the infant group and the other two groups (all $P > 0.05$). Compared with the child group, the toddler group exhibited a significantly higher platelet count and PCT in the acute, subacute and convalescent phases (all $P < 0.05$). No significant differences were observed in the toddler group in the sequelae phase when compared with the child group (all $P > 0.05$) (see Table 7).

Table 7 Comparison of Platelet and White Blood Cell Counts in Patients with KD Across Different Phases

Parameter	Infants (n = 67)	Toddlers (n = 111)	Children (n = 43)	Statistic	P-value	Cramér's V/Cohen's f
Male, n(%)	46 (68.7)	75 (67.6)	28 (65.1)	0.152	0.927	0.026
WBC1 ($\times10^9$/L)	15.83±4.45	15.02±5.16	15.86±4.57	0.790	0.445	0.085
WBC2 ($\times10^9$/L)	9.79 (7.96, 13.01)	9.59 (6.71, 12.52)	8.85 (6.37, 14.12)	0.709	0.40	0.112
WBC3 ($\times10^9$/L)	8.34 (6.87, 9.68)	7.68 (6.47, 8.90)	6.87 (6.24, 10.19)	2.635	0.105	0.353
WBC4 ($\times10^9$/L)	7.55 (6.63, 9.35)	7.63 (6.53, 9.89)	7.62 (6.38, 10.34)	0.044	0.834	0.022
PLT1	374.36±13.21	338.30±8.00	300.11±10.38	9.170	0.000	0.818
PCT1	0.38±0.01	0.33±0.01	0.30±0.28	10.302	0.000	0.319
MPV1	10.96±1.02	10.01±0.08	12.02±1.89	1.288	0.278	0.411
PDW1	11.21±0.27	11.49±0.16	12.01±0.30	2.263	0.106	0.657
PLT2	587.36±17.75	519.24±42.76	419.11±16.67	3.338	0.037	0.742
PCT2	0.56±0.02	0.46±0.01	0.40±0.02	25.619	0.000	0.988
MPV2	9.39±0.11	9.37±0.11	9.13±0.32	0.568	0.568	0.158
PDW2	10.39±0.20	11.16±0.83	10.22±0.36	0.485	0.616	0.379
PLT3	397.85±14.11	326.83±13.33	284.81±21.19	10.571	0.000	0.756
PCT3	0.37±0.01	0.30±0.01	0.28±0.02	10.804	0.000	0.735
MPV3	9.06±0.22	8.43±0.28	8.12±0.52	1.761	0.174	0.463
PDW3	12.23±0.59	10.96±0.40	10.30±0.77	2.696	0.070	0.757
PLT4	265.78±16.88	286.89±39.17	237.70±21.26	0.406	0.667	0.296
PCT4	0.25±0.02	0.23±0.01	0.23±0.02	0.454	0.636	0.194
MPV4	8.00±0.45	7.62±0.37	7.54±0.61	0.258	0.773	0.252
PDW4	10.53±0.62	11.19±1.34	10.37±0.86	0.129	0.879	0.234

Abbreviations: PCT, plateletcrit; MPV, mean platelet volume; PDW, platelet distribution width; PLT, platelet; WBC, white blood cell. 1, acute phase; 2, subacute phase; 3, convalescent phase; 4, sequelae phase.

Table 8 Multivariate Logistic Regression Analysis of Factors Associated with Moderate-to-Severe Cardiovascular Damage

Variable	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P-value	aOR (95% CI)	P-value
Age group				
- Child (reference)	1.00	-	1.00	-
- Toddler	1.42 (0.78–2.59)	0.251	1.38 (0.74–2.57)	0.312
- Infant	2.01 (1.06–3.81)	0.032	1.82 (0.94–3.52)	0.074
Sex (male vs female)	1.18 (0.73–1.91)	0.497	1.09 (0.66–1.81)	0.734
Treatment delay (≥10 days)	2.78 (1.54–5.01)	0.001	2.45 (1.32–4.56)	0.004
IVIG resistance	2.31 (1.44–3.70)	<0.001	1.98 (1.21–3.24)	0.006
Corticosteroid use	1.89 (1.16–3.08)	0.011	1.31 (0.78–2.19)	0.309
Platelet parameters (acute phase)				
- PLT (per 100×10^9/L increase)	1.28 (0.94–1.74)	0.116	1.15 (0.82–1.61)	0.417
- MPV (per 1 fL increase)	1.21 (0.97–1.51)	0.089	1.12 (0.89–1.41)	0.341
- PDW (per 1% increase)	1.45 (1.16–1.81)	0.001	1.38 (1.09–1.74)	0.007
- PCT (per 0.1% increase)	1.31 (0.82–2.09)	0.256	1.24 (0.76–2.02)	0.389

Notes: Model fit statistics: Hosmer-Lemeshow test: χ^2 = 7.234, P = 0.412. McFadden's pseudo-R^2: 0.186. Area under ROC curve: 0.742 (95% CI: 0.684–0.800).
Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; IVIG, intravenous immunoglobulin; PLT, platelet count; MPV, mean platelet volume; PDW, platelet distribution width; PCT, plateletcrit.

Multivariate Analysis of Factors Associated with Cardiovascular Damage Severity

Multivariate logistic regression analysis was performed to identify independent predictors of moderate-to-severe cardiovascular damage (Table 8). After adjusting for potential confounders, the following factors were independently associated with increased risk: treatment delay ≥10 days (aOR = 2.45, 95% CI 1.32–4.56, P = 0.004), IVIG resistance (aOR = 1.98, 95% CI 1.21–3.24, P = 0.006) and elevated PDW in the acute phase (per 1-unit increase: aOR = 1.38, 95% CI 1.09–1.74, P = 0.007).

Age group showed a trend towards association, with infants having higher risk compared to children (aOR = 1.82, 95% CI 0.94–3.52, P = 0.074). Neither MPV (aOR = 1.12, 95% CI 0.89–1.41, P = 0.341) nor PCT (aOR = 1.24, 95% CI 0.76–2.02, P = 0.389) showed significant associations with cardiovascular severity. The use of adjunctive corticosteroid therapy was not independently associated with cardiovascular outcomes after adjusting for disease severity indicators (aOR = 1.31, 95% CI 0.78–2.19, P = 0.309). The final model showed good fit (Hosmer–Lemeshow P = 0.412, McFadden's pseudo-R^2 = 0.186).

Discussion

KD is a type of paediatric vasculitis characterised by inflammation of blood vessels. Although most cases have a favourable prognosis, cardiovascular damage remains one of the major complications of the disease.[25] The findings of this study reveal statistically significant differences in cardiovascular damage, treatment responses and clinical manifestations among patients with KD of different age groups, providing critical information for understanding the clinical characteristics and management of the disease.

In terms of gender distribution, boys accounted for 67.42% of all KD cases, consistent with the widely observed trend of higher prevalence in male patients.[2] This may be attributed to biological sex differences, warranting further investigation into how hormonal levels and genetic factors influence the development of KD.[26] However, the male-to-

female ratio in our cohort was 2.07:1, which is slightly higher than the widely reported epidemiological ratio of approximately 1.5:1. This discrepancy may reflect a degree of selection bias inherent in hospital-based retrospective studies.[27] Our sample primarily included children with moderate-to-severe disease who underwent ECHO evaluation, and male patients are known to have a higher risk of coronary involvement and hospitalisation. Additionally, regional demographic variation may also influence the observed sex distribution. Furthermore, when comparing fever duration across age groups, no significant differences were observed ($P = 0.346$), indicating that the fever presentation of KD is relatively consistent regardless of age. This may reflect an overall improvement in awareness and early recognition of KD by clinicians, enabling timely treatment regardless of age. In particular, it suggests that even in infants —who are often subject to such delays due to atypical presentations – current clinical protocols may be effective in avoiding such delays.[28] This underscores the limitation of relying solely on fever duration for diagnosing KD, highlighting the need for clinicians to consider other symptoms and laboratory findings in comprehensive assessments.

Our findings regarding treatment characteristics provide important insights into age-related differences in therapeutic response. The significantly higher rate of IVIG resistance in infants (40.3%) compared to older children aligns with previous studies suggesting that younger age is a risk factor for treatment failure.[29] This may be related to the immature immune system in infants, resulting in a more dysregulated inflammatory response that is less responsive to standard immunoglobulin therapy. The association between treatment delay and cardiovascular severity (aOR = 2.45) underscores the critical importance of early diagnosis and prompt treatment initiation, consistent with the established guidelines recommending IVIG administration within 10 days of fever onset.[30]

Regarding major clinical symptoms, the incidence of lymph node enlargement was significantly higher in the child group (93.02%) compared with the infant group (70.15%) and the toddler group (77.48%) ($P = 0.017$). This suggests that age may play an important role in the manifestation of this symptom. Lymph node enlargement is one of the major clinical manifestations of KD, and its variability across different age groups appears to be related to the maturity of the immune system.[31] The immune response to infections in older children may be more robust, potentially leading to higher incidences of lymph node swelling. This finding indicates that clinicians should pay particular attention to lymph node changes when managing patients with KD in different age groups, especially in older children. The incidence of finger (toe) peeling was significantly higher in the child group (67.44%) compared with the infant group (38.81%) and the toddler group (54.05%) ($P = 0.011$). This reveals a strong correlation between increasing age and the occurrence of finger (toe) peeling. Finger (toe) peeling typically occurs during the subacute phase of the disease, and it may be associated with the extent of systemic inflammatory responses and vascular damage.[32] The prominence of this symptom in the child group might reflect a comparatively stronger or more prolonged inflammatory response following KD.[33] Therefore, during treatment, particularly in the convalescent phase, special attention should be paid to the skin condition of children in this age group to manage related symptoms promptly.

The stratified analysis of cardiovascular damage severity provides novel insights into age-related disease patterns.[34] While the overall incidence of cardiovascular damage did not differ significantly among age groups, the severity distribution showed notable variations. The higher proportion of severe cardiovascular damage in infants (20.9%) compared to older children suggests that younger patients may be at greater risk of serious coronary complications, possibly due to delayed diagnosis, incomplete clinical presentations or age-related differences in vascular responsiveness to inflammation.[35] This finding has important implications for risk stratification and monitoring intensity in different age groups.

The multivariate analysis revealed that elevated PDW was independently associated with moderate-to-severe coronary artery lesions (aOR = 1.38, 95% CI 1.09–1.74). This finding is consistent with recent studies suggesting that PDW, as a marker of platelet activation and size heterogeneity, may reflect the degree of vascular inflammation and endothelial damage in KD.[36] The increased PDW may indicate enhanced platelet turnover and activation, contributing to the prothrombotic state observed in severe KD. This suggests that PDW could serve as a readily available biomarker for risk stratification and may guide decisions regarding antiplatelet therapy intensity.

This study found that platelet count and PCT in patients with KD of different age groups gradually increased during the acute, subacute and recovery phases, peaking in the subacute phase before declining progressively. Notably, platelet count and PCT in the infant group were significantly higher during the acute and subacute phases compared with the

other age groups (all $P < 0.05$). This finding aligns with previous studies,[37] indicating that infants with KD may experience more pronounced platelet activation and proliferation during the early stages of the disease. Recent evidence highlights the pivotal role of platelets not only as markers of systemic inflammation in KD but also as active participants in vascular injury and immune dysregulation. Platelets interact with monocytes and neutrophils to form platelet–leukocyte aggregates, contributing to endothelial activation and interleukin (IL)-1β/IL-6 production. These mechanisms can exacerbate vasculitis and promote the development of CAA, especially in IVIG-resistant cases.[38] Moreover, clinical studies have reported that higher platelet counts during the subacute phase are positively associated with elevated levels of C-reactive protein and IL-6, and are independent predictors of coronary artery involvement.[39] Notably, Ciccone's cohort of adult vasculitis patients revealed that sustained platelet activation correlates with arterial remodelling – a mechanism analogous to KD-associated coronary aneurysm formation.[40] These findings underscore the importance of dynamic platelet monitoring in KD as both a prognostic indicator and a potential therapeutic target. This heightened platelet response in infants may reflect a stronger systemic inflammatory state and immature immune regulation, both of which can exacerbate platelet activation. Moreover, infants often present with incomplete KD, which can delay diagnosis and prolong the inflammatory process, thereby further increasing platelet counts. These findings suggest that platelet indices in infants may be useful for monitoring disease severity and guiding anti-inflammatory or antiplatelet therapy. These dynamic changes reflect the physiological characteristics of KD at different stages of development, underscoring the need for clinicians to monitor and manage these haematological parameters closely. Appropriate adjustments to treatment plans are essential to mitigate potential risks of cardiovascular damage.

During the sequelae phase, while platelet count and PCT gradually return to normal across all groups, an important issue arises: the long-term risk of sequelae in patients with KD requires ongoing attention. Previous studies have shown that patients with KD may face cardiovascular sequelae even following treatment. Therefore, systematic cardiac evaluations during follow-up are particularly necessary for children, ensuring timely identification and intervention for any related issues.

KD in different age groups presents varied clinical manifestations, treatment responses and laboratory features, which should be considered during diagnosis and management. Age-related differences in clinical presentation, treatment efficacy and platelet dynamics may have important implications for individualised care. For example, the significantly higher platelet counts and PCT in infants, combined with their increased rate of IVIG resistance, suggest an enhanced thrombotic tendency and inflammatory state, potentially requiring earlier or more intensive antiplatelet and anti-inflammatory therapy. In addition, infants often lack classical symptoms such as lymph node swelling and finger peeling, which may delay diagnosis and increase the risk of cardiovascular damage. Therefore, early identification and age-adapted treatment approaches are crucial to improving prognosis in KD.

In summary, this study reveals significant statistical insights into the clinical symptoms, treatment patterns and haematological changes in patients with KD across different age groups, highlighting the critical role of age in the manifestation and management of the disease. By fully leveraging these findings, we can more effectively identify high-risk patients and develop individualised treatment plans tailored to different age groups. Future studies should further explore the mechanisms of KD and its influencing factors across various age groups. In particular, longitudinal cohort studies are recommended to evaluate long-term cardiovascular outcomes and the trajectory of platelet-related parameters in patients across different age groups. Investigations into genetic, immunological and environmental factors that contribute to KD severity in younger patients will also provide valuable insights for early diagnosis and treatment.

However, this study has some limitations. First, generalisability may be limited by the single-centre cohort, and functional platelet assays were unavailable retrospectively. Second, the sample size for severe cardiovascular damage was relatively small, which may have limited the statistical power to detect some associations. Potential selection bias was mitigated through consecutive enrolment, strict exclusion criteria and multivariable adjustment for treatment timing. Nevertheless, prospective validation of age-specific platelet cutoffs remains essential. Future multi-centre prospective studies with larger sample sizes are needed to validate these findings.

Conclusions

The study results indicated that KD can occur across all age groups. Fever duration showed no significant differences between age groups or genders, suggesting that fever duration is fairly consistent. However, clinical symptoms such as lymph node enlargement, finger (toe) peeling and reactions to BCG vaccination exhibited significant differences among the age groups, indicating that age might influence symptom presentation. While the overall incidence of cardiovascular damage did not differ significantly among groups, severity patterns showed age-related variations, with infants experiencing more severe coronary lesions. Treatment delay and IVIG resistance were identified as significant independent risk factors for moderate-to-severe cardiovascular damage. Platelet count and PCT showed a marked upward trend during the acute phase of KD, with the most pronounced changes observed in the infant group. Additionally, elevated PDW was independently associated with cardiovascular severity, suggesting its potential as a biomarker for risk stratification. In conclusion, our findings may aid clinicians in the early diagnosis of atypical presentations in infants, as well as in the targeted cardiac evaluation and treatment optimisation of all age groups. These findings support age-specific risk stratification, timely therapeutic intervention and tailored follow-up strategies in clinical practice.

Data Sharing Statement

All data generated or analyzed during this study are included in the article.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Children's Hospital of Soochow University. Written informed consent was obtained from all parents/local guardians.

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Disclosure

None of the authors have any personal, financial, commercial, or academic conflicts of interest to declare for this work.

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