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Research Article

Clinical Spectrum and Management Outcomes of Pediatric Kawasaki Disease in Resource-Limited Settings

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Abstract

This experimental prospective cohort study investigated the clinical spectrum and management outcomes of pediatric Kawasaki disease in a resource-limited tertiary centre over a two-year period. The objective was to characterize presentation patterns, timeliness of care, echocardiographic findings and response to intravenous immunoglobulin (IVIG) in a setting with constrained diagnostic and therapeutic resources. A total of 60 children aged 2 months to 8 years were enrolled after sample-size calculation (epi-info; power 80 %, alpha 0.05, expected coronary aneurysm frequency 20 %). Inclusion required ≥5 days fever plus ≥4 principal criteria or incomplete presentation supported by inflammatory markers; exclusion included alternative confirmed infections or chronic immunodeficiency. Verbal informed consent from guardians was obtained. Patients received IVIG 2 g/kg and aspirin; echocardiography at baseline, 2 and 8 weeks assessed coronary Z-scores. Primary outcomes included incidence of coronary artery abnormalities (≥Z 2.5), IVIG resistance (persistent fever >36 h post-infusion), inflammatory marker reduction, and hospital stay. Results revealed that 65 % presented with incomplete phenotype; mean fever duration prior to treatment was 9.2 ± 3.1 days; IVIG initiated at mean 10.5 ± 2.8 days. Coronary aneurysms occurred in 18 % (mean Z 3.1 ± 0.5), IVIG resistance in 22 %. C-reactive protein fell from 145 ± 38 to 62 ± 20 mg/L ($p < 0.001$). Age, delayed treatment, and incomplete presentation were significantly associated with aneurysm development ($p = 0.02–0.04$). These findings demonstrate a novel emphasis on high incomplete-presentation rates, delayed intervention and

resource constraints driving adverse outcomes. Early recognition and accessible IVIG remain critical to reducing coronary sequelae.

Keywords: Kawasaki disease; resource-limited; coronary artery aneurysm.

Introduction

Kawasaki disease (KD) is an acute systemic vasculitis of medium-sized vessels that primarily affects children under five years of age. Its etiology remains elusive, though an aberrant immune response to unidentified environmental or infectious triggers in genetically predisposed individuals is widely hypothesized. Global incidence is highest in East Asia, but recognition in low-resource regions remains limited. Untreated KD leads to coronary artery aneurysms in up to 25 % of cases and carries risk of long-term cardiovascular sequelae. Early diagnosis and administration of intravenous immunoglobulin (IVIG) within 10 days reliably reduce aneurysm risk to under 5 %.1-4.

In resource-constrained settings, multiple barriers inhibit optimal KD management. Delays in presentation and diagnosis are common, especially for incomplete KD forms that lack full diagnostic criteria. The limited availability and affordability of IVIG, scarcity of trained pediatric echocardiographers, and low awareness among caregivers and health workers contribute to poorer outcomes. Recent case series from Sub-Saharan Africa and South Asia report longer fever durations before presentation, high rates of thrombocytosis and elevated inflammatory markers, incomplete presentations, and limited echocardiographic follow-up owing to equipment or expertise constraints.5-7

Emerging observational data highlight that children in these settings present later and more often with atypical KD, leading to higher rates of coronary involvement. For instance, Kenyan cohorts demonstrated median fever durations over eight days and more incomplete KD presentations, with many lacking proper follow-up echocardiography. In Bangladesh case series, echocardiographic abnormalities persisted at two weeks in nearly 90 % before resolution by six weeks, with one mortality from thrombosis. Latin American registry data showed that a coronary artery Z-score ≥ 2.5 at presentation strongly predicts aneurysm risk, reinforcing the need for timely imaging even where resources are limited.8-10

Despite these insights, experimental prospective studies quantifying presentation patterns, timing of IVIG, laboratory response, and outcome relationships remain scarce in low-resource contexts. Such data are essential to define local disease behavior, prognostic markers, and to justify investments in early recognition, training, and affordable treatment access. The present study was therefore conducted in a tertiary centre with typical constraints to evaluate clinical phenotype distribution, diagnostic timelines, treatment patterns, echocardiographic evolution, and factors associated with coronary artery outcomes in pediatric KD. By integrating laboratory, clinical and imaging data and applying standard definitions and statistical analysis, the work seeks to provide rigorous evidence of how resource limitations affect disease trajectory and identify modifiable factors that could improve prognosis even where infrastructure is limited.

Methodology

A prospective cohort design was adopted in Ayub Teaching Complex, Abbottabad. Sample-size calculation using Epi-Info Version 7 assumed an expected coronary aneurysm frequency of 20 %, confidence level 95 %, power 80 %, yielding a required sample of 58; rounded to 60 to allow for potential losses. Children aged 2 months to 8 years fulfilling diagnostic criteria—≥5 days of fever plus ≥4 principal clinical features, or incomplete KD supported by elevated C-reactive protein (>100 mg/L) and thrombocytosis (>450 × 10^9/L)—were enrolled consecutively. Exclusions were confirmed alternative infections (e.g. dengue, bacterial sepsis), prior KD, immunodeficiency, or guardian refusal. Verbal informed consent was obtained from caregivers after explanation in local language; the process was documented.

On admission, detailed history and physical examination were performed, and baseline labs drawn (complete blood count, CRP, ESR, liver enzymes, albumin). Echocardiography by available pediatric or trained general cardiologist was done at baseline, at 2 weeks and at 8 weeks; coronary artery dimensions were measured and indexed for body-surface-area to derive Z-scores. IVIG 2 g/kg single infusion over 10 hours was administered, along with aspirin (high-dose 80–100 mg/kg until defervescence, then low-dose 3–5 mg/kg). No corticosteroids were used, reflecting local practice. Persistent fever (>36 h post-IVIG) was defined as IVIG resistance. Hospital stay duration was recorded.

Primary outcomes were incidence of coronary aneurysm (Z-score ≥ 2.5), IVIG resistance, reduction in CRP and length of hospitalisation. Secondary analysis evaluated relationships of age, sex, fever duration before treatment, complete vs incomplete presentation with coronary outcomes. Statistical analysis used SPSS: continuous variables expressed as mean ± SD; categorical as counts and percentages. Independent-samples t-test compared means; chi-square tested proportions. Paired t-test assessed CRP change. Logistic regression tested predictors of aneurysm; significance set at $p < 0.05$.

Results

Table 1. Demographic and clinical features (n = 60)

Variable	Value
Mean age (years) ± SD	2.8 ± 1.6
Male sex, n (%)	38 (63 %)
Mean fever duration before admission (days) ± SD	9.2 ± 3.1
Incomplete presentation, n (%)	39 (65 %)
Mean CRP on admission (mg/L) ± SD	145 ± 38
Thrombocytosis at diagnosis (>450 × 10^9/L), n (%)	42 (70 %)

Table 2. Treatment timing and laboratory response

Variable	Value
Mean time to IVIG from fever onset (days) ± SD	10.5 ± 2.8
CRP before IVIG (mg/L) ± SD	145 ± 38
CRP at 48 h post-IVIG (mg/L) ± SD	62 ± 20
Mean hospital stay (days) ± SD	6.8 ± 2.2
CRP reduction p-value (paired t-test)	< 0.001

Table 3. Outcomes and predictors of coronary aneurysm

Outcome / Predictor	Value / Association
Coronary aneurysm ($Z \geq 2.5$), n (%)	11 (18 %)
IVIG resistance, n (%)	13 (22 %)
Mean Z-score among those with aneurysm ± SD	3.1 ± 0.5
Age (years) mean (aneurysm vs no aneurysm)	3.5 vs 2.6 (p = 0.03)
Fever duration (days) mean (aneurysm vs no)	11.2 vs 8.8 (p = 0.02)
Incomplete presentation (%) with aneurysm vs without	82 % vs 60 % (p = 0.04)

Explanatory note: The cohort had high rates of delayed presentation and incomplete phenotype. IVIG led to significant CRP reduction. Coronary aneurysms occurred in nearly one-fifth, associated with older age, longer fever duration, and incomplete presentation.

Discussion

First, the exceptionally high proportion of incomplete KD (65 %) in this cohort underscores diagnostic challenges in resource-constrained environments, aligning with recent African and South Asian studies reporting incomplete phenotypes in up to 55 % of patients and prolonged fever prior to diagnosis. Such presentations often delay initiation of treatment, increasing coronary risk.11-14

Second, mean fever duration before treatment exceeded nine days, and IVIG was typically administered at day 10.5. This delay contrasts sharply with high-income settings where treatment is often achieved by day 5–7. Such delays have been repeatedly associated with increased incidence of coronary involvement, as corroborated by registry data showing that initial coronary Z-score elevation (> 2.5) strongly predicts worse outcomes.15-17

Third, CRP reduction from 145 to 62 mg/L within 48 h reflects biochemical responsiveness to IVIG, even when administered late. This suggests that systemic inflammation remains modifiable, though some vascular injury may already be established by the time of therapy.18-20

Fourth, an 18 % aneurysm rate is substantially higher than the < 5 % typically achievable with early therapy, but mirrors findings from regional case series in Bangladesh and Iran where delayed care and incomplete diagnosis raised aneurysm rates to 15–25 %.

Fifth, statistically significant associations between aneurysm development and older age, longer fever duration, and incomplete presentation reinforce the importance of early recognition and timely intervention. These variables are modifiable at the system level through clinician training, public education, and investment in echocardiography access.

Sixth, IVIG resistance in 22 % of cases, while higher than typical 10–15 %, may reflect later administration and high baseline inflammatory burden. This suggests the potential utility of adjunctive therapies in such settings, pending resource availability.

Seventh, hospital stay averaged nearly seven days—prolonged relative to ideal scenarios—likely due to delayed presentation, laboratory monitoring, and follow-up echocardiography scheduling constraints. Even so, no mortality observed, suggesting that timely treatment, once initiated, remains life-saving.

Collectively, this study provides robust experimental evidence that in resource-limited settings, KD often manifests in incomplete form, is diagnosed late, and exhibits higher coronary aneurysm rates. However, administration of IVIG—even when delayed—achieves significant inflammation reduction and prevents death. The findings argue strongly for targeted strategies to improve early recognition, broaden echocardiographic access, and subsidize IVIG to reduce long-term cardiovascular harm.

Conclusion

This study highlights that delayed diagnosis and high rates of incomplete presentation in resource-limited settings significantly elevate coronary artery aneurysm risk in pediatric Kawasaki disease. Nevertheless, timely IVIG administration, even if delayed, reduces inflammation and prevents mortality. Strengthening early recognition and expanding access to affordable IVIG and echocardiography are critical to closing the outcome gap.

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