

Serum Levels of Syndecan-1 in Patients With Kawasaki Disease

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Background: Kawasaki disease (KD) is an acute systemic vasculitis with coronary artery lesions (CALs) being the major concern. Syndecan-1 (SDC-1) is a major core protein expressed on the glycocalyx of endothelial cells. Shed SDC-1 in serum is regarded as a biomarker for endothelial activation or damage.

Methods: In this study, we aimed to determine the serum levels of SDC-1 and evaluate the relationship between serum levels of SDC-1 and the CALs in the acute phase of KD. Serum SDC-1 levels were measured in 119 children with KD and in 43 healthy children as normal controls and in 40 children with febrile disease. All KD patients were administered a single dose of intravenous immunoglobulin and aspirin per os within 10 days of KD onset.

Results: Serum levels of SDC-1, in addition to albumin and hemoglobin, were significantly increased in patients with KD than in healthy controls and febrile controls. Furthermore, the serum levels of SDC-1, albumin and hemoglobin were significantly elevated in KD patients with CALs than those without CALs. Additionally, serum levels of SDC-1 were significantly correlated with levels of hemoglobin and serum albumin in patients with KD. After intravenous immunoglobulin therapy, serum levels of interleukin-6, soluble cell adhesion molecules-1 and resistin were reduced while serum levels of SDC-1 were significantly increased in KD patients.

Conclusions: SDC-1 serum levels may mirror vascular endothelial damage and inflammation in KD. This might be utilized as a potential novel target for coronary artery protection in KD patients.

Key Words: syndecan-1, Kawasaki disease, coronary artery lesions

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Kawasaki disease (KD) is an acute, systemic vasculitis that mainly occurs in infants and young children.¹ Coronary artery lesions (CALs) are the most significant complications of this disease, which could induce myocardial infarction and death in adult-

hood.² KD has replaced rheumatic fever as the leading cause of acquired cardiac disease in children in developed countries.²

KD vasculopathy primarily involves muscular arteries and is associated with 3 processes: necrotizing arteritis, subacute/chronic vasculitis and luminal myofibroblastic proliferation. The cause of KD remains unknown; however, the activation of circulating neutrophils, T cells, interleukin (IL)-1, IL-6 and tumor necrosis factor (TNF) signaling pathways are all known to be involved in the pathogenesis of the disease.³ Our previous research has also demonstrated the association of elevated resistin and decreased hemoglobin (Hb) levels with the development of coronary aneurysm in KD.⁴

Endothelial cell damage is associated with immune activation in the acute phase of KD because of large numbers of circulating cytokines and inflammatory mediators observed in small-to-medium-sized arteries. This damage has been shown to persist even years after treatment with intravenous immunoglobulin (IVIG) therapy.^{5–7} The endothelial glycocalyx covers the luminal surface of the vascular endothelium which serves as a protective barrier.⁸ Syndecan-1 (SDC-1) is expressed on the glycocalyx of epithelial cells, endothelial cells and plasma cells and is the most prominent of 4 subtypes of syndecan. SDC-1 presents as a major transmembrane heparan sulfate proteoglycan whose core protein primarily consists of 3 domains: an ectodomain, a single transmembrane domain and a short cytoplasmic domain.^{9,10} The ectodomain of SDC-1 can be shed from the cell surface and released into serum by matrix metalloproteinase (MMP)-7, MMP-2, MMP-9, growth factors, chemokines and oxidative stress.¹¹ Released SDC-1 in serum has been historically used as a biomarker of endothelial activation and damage in trauma,¹² acute coronary syndrome,¹³ nephrotic syndrome,¹⁴ cardiogenic shock,¹⁵ acute myocardial infarction,¹⁶ systemic lupus erythematosus,¹⁷ inflammatory bowel disease,¹⁸ Crohn disease,¹⁹ severe sepsis²⁰ and cardiac fibrosis.¹¹

KD is a systemic vasculitis with increased IL-1 β , IL-6, TNF- α , MMP-9, soluble cell adhesion molecules-1 (sICAM-1) and resistin.^{3,21,22} It is unknown whether SDC-1 plays an important role in KD and if SDC-1 serum levels could be used as a biomarker to predict the development of CALs in patients during the acute phase. In this study, we aimed to ascertain the serum levels of SDC-1 in the acute phase of KD and elucidate whether there is a connection between serum levels of SDC-1 and CALs.

MATERIALS AND METHODS

Subjects and Data Collection

One hundred and twenty children with acute-phase KD [72 males and 48 females with a median age of 24.0 months (range: 13.0–39.0)] and 43 sex and age-similar healthy controls (HCs) and 40 sex and age-similar febrile controls (FC) with acute febrile disease such as bronchopneumonia (n = 32) and acute upper respiratory infection (n = 8) from Children' Hospital of Chongqing Medical University, Chongqing, China, were enrolled in the study. All patients met the American Heart Association diagnostic criteria,³ and the protocol for this study was approved by the Ethics Committee of Chongqing Medicine University. All patients with KD received a single dose of IVIG (2.0 g/kg) and 30–50 mg/kg/d of aspirin per os within 10 days of KD onset. If the diagnosis was confirmed beyond 10 days of KD onset, these treatments started as soon as possible after diagnosis.

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Upon admission, medical, demographic and laboratory data were collected. The laboratory data collected are as follows: levels of total protein (TP), albumin (ALB), alanine aminotransferase (ALT), aspartate aminotransferase, lactic dehydrogenase (LDH), γ -glutamyl transpeptidase (GGT), total bilirubin (TB), direct bilirubin (DB), potassium, sodium, white blood cells (WBCs), platelet (PLT), red blood cells counts (RBC), Hb, red cell distribution width (RDW), hematocrit (Hct) and C-reactive protein (CRP). To assess CALs, an echocardiography was obtained either within 2 weeks of onset of KD or before administration of IVIG. KD patients were divided in 2 groups: KD with CALs (KD-CALs, $n = 56$) and KD without CALs (KD-NCALs, $n = 64$). Presence of CALs was based on internal lumen diameter as >2.5 mm in children less than 3 years of age, >3 mm in children between 3 and 9 years of age and >3.5 mm in children 9–14 years of age according to echocardiography parameters.²³

Measurements of Serum Levels of SDC-1, Resistin, IL-6 and sICAM-1

Blood samples were collected from HC, FC and patients with KD in acute-phase upon admission before IVIG treatment. In 18 KD patients, blood samples were additionally collected 3–5 days after IVIG treatment. Samples were centrifuged at $3000\times g$ for 10 minutes and the serum was collected and stored at -80°C . Serum concentrations of SDC-1 in all 3 groups, resistin, IL-6 and sICAM-1, were determined by enzyme-linked immunosorbent assay kits (RayBiotech, Norcross, GA) according to the manufacturer's instructions. Because the serum of some cases was inadequate, several parameters were not detected in all individuals.

Statistical Analysis

Summary statistics for nonnormally distributed continuous variables are presented as medians with interquartile range (IQR) and normally distributed continuous variables are presented as means with standard deviation. All the categorical variables are expressed as number and percentage. The assumption of normality was assessed by the use of the Kolmogorov–Smirnov test. Comparisons of frequencies between groups were analyzed by the use of χ^2 tests. Two-sample t tests or analysis of variance were performed to analyze the comparisons of normally distributed continuous variables between the 2 groups or among 3 groups, respectively. For nonnormally distributed continuous variables, Mann-Whitney U tests or Kruskal-Wallis tests were performed to assess the comparisons between the 2 groups or among 3 groups, respectively. Comparisons of parameters before and after IVIG treatment in KD patients were performed with Wilcoxon paired signed rank test. Associations between continuous variables were performed with the use of Spearman rank order correlation analysis (ρ). All statistical analyses were conducted using statistical package for social science statistical software version 20.0. To compare the power of predicting CALs based on serum SDC-1 and other clinical characteristics, receiver-operating characteristic curves were plotted and areas under the curves (AUC) were calculated. The predictive accuracy of the 2 models was compared by DeLong test using MedCalc statistical software version 15.6.1. A 2-tailed $P < 0.05$ was considered statistically significant.

RESULTS

Clinical Characteristics and Serum SDC-1 Levels in Subjects

There was no statistical difference in age and gender among HC, FC and KD groups. There were elevated SDC-1 serum levels in KD patients when compared with HC [5.3 ng/mL (IQR 4.6–7.1) vs.

2.8 ng/mL (IQR 2.2–3.8), respectively, $P < 0.001$] and to FC [4.7 ng/mL (IQR 3.5–5.7), $P < 0.001$], which is significant higher than that of HC. Compared with HC, there was also a significant increase in WBC, PLT, RDW, CRP, ALT, resistin, sICAM-1 and IL-6. In the KD group, there was a decrease in RBC, Hb, Hct, ALB, TP, LDH, potassium and sodium (Table, Supplemental Digital Content 1, <http://links.lww.com/INF/D99>). There were no significant differences of serum levels of SDC-1 in KD patients between IVIG resistance group ($n = 7$) and IVIG responsive group ($n = 112$) [4.9 ng/mL (IQR 4.2–7.3) vs. 5.4 ng/mL (IQR 4.6–7.1), respectively, $P < 0.941$].

Serum SDC-1 Levels in KD-CALs Group and KD-NCALs Group

There was no significant difference in age, gender, WBC, PLT, RDW, CRP, ALT, LDH, potassium, sodium, resistin, IL-6, sICAM-1 between KD-CALs and KD-NCALs. Alternately, there were significant increases in serum levels of SDC-1 and significant decreases in RBC, Hb, Hct, ALB and TP in KD-CALs when compared KD-NCALs (Table 1).

Correlations Between SDC-1 and Clinical Characteristics in Patients With KD

There were no significant associations between SDC-1 and aspartate aminotransferase, LDH, sodium, WBC, PLT or RDW. SDC-1 serum levels were significantly positively correlated with ALT, TB, DB, GGT, potassium, CRP, IL-6, resistin and sICAM-1. Moreover, serum SDC-1 levels were significantly negatively correlated with RBC, Hb, Hct, ALB and TP (Table 2).

Predicting CALs by SDC-1 and Other Clinical Characteristics

KD with CALs was predicted by receiver-operating characteristic curves analysis of SDC-1 levels in 119 cases through previously obtained laboratory datum. For the prediction of CALs, a SDC-1 cut-off value of 7.03 ng/mL yielded: a 40.0% sensitivity with 85.9% specificity, a positive predictive value of 71.0% and a negative predictive value of 62.5% with an AUC of 0.654 (95% confidence interval: 0.541–0.768; $P = 0.012$). Moreover, combining SDC-1, Hb and ALB did not result in a higher AUC than combining ALB and Hb (Fig. 1).

Comparison of Parameters Before and After IVIG Therapy

There were no significant differences in age, sex and other basic clinical characteristics between KD groups resampled and not resampled after IVIG therapy (data not shown). After IVIG therapy, serum levels of IL-6, sICAM-1 and resistin were reduced while serum levels of SDC-1 were significantly increased (Fig. 2).

DISCUSSION

We were able to demonstrate a significantly higher increase of serum SDC-1 in the KD group as compared with HC group and FC group, and in the KD-CALs as compared with KD-NCALs group. Serum SDC-1 levels were significantly positively correlated with CRP, IL-6, resistin, sICAM-1, TB, DB, LDH, GGT, potassium. Conversely, serum SDC-1 levels were significantly negatively correlated with RBC, Hb, Hct, ALB and TP. Serum SDC-1 levels remarkably increased after IVIG therapy in patients with KD while levels of IL-6, sICAM-1 and resistin decreased.

KD is systemic inflammatory response syndrome that associated with cytokines with an unknown cause.³ The long-term prognosis of KD is determined by the initial and current level of lesions that result in acute myocardial infarction.³ Several parameters including levels of vascular endothelial growth factor, B-type

TABLE 1. Clinical Characteristics of Patients of KD-CALs and KD-NCALs

	KD-NCAL	KD-CALs	P
n	64	56	
Male, n (%)	41 (64)	31 (55)	0.332
Age (mo)*	26.0 (16.0–43.75)	21.0 (12.0–38.0)	0.215
IL-6 (pg/mL)*	291.6 (87.6–565.3)	341.0 (148.6–925.5)	0.084
SDC-1 (ng/mL)*	5.2 (4.3–6.5)	5.9 (4.8–8.1)	0.006
Resistin (ng/mL)*	7.0 (4.9–12.9)	8.8 (4.0–14.5)	0.703
sICAM-1 (ng/mL)*	578.3 (434.0–825.9) (n = 62)	623.5 (475.0–1064.7)	0.066
Total protein (g/L)†	57.6 ± 5.8 (n = 62)	54.9 ± 6.5	0.023
Albumin (g/L)†	37.2 ± 4.4 (n = 62)	34.6 ± 4.7	0.002
ALT (U/L)*	29.1 (16.1–91.0) (n = 63)	38.7 (14.3–87.4)	0.853
LDH (U/L)*	100.0 (46.5–244.0) (n = 61)	231.3 (40.0–291.6)	0.152
Potassium (mmol/L)*	4.11 (3.8–4.5) (n = 62)	4.1 (3.6–4.6)	0.467
Sodium (mmol/L)†	137.9 ± 3.1 (n = 61)	137.7 ± 3.2	0.760
WBC (10 ⁹ /μL)†	15.3 ± 4.6	15.7 ± 6.4	0.713
Platelet (10 ⁹ /μL)†	376 ± 115	390 ± 144	0.563
RBC (10 ⁶ /μL)†	4.2 ± 0.4	4.0 ± 0.5	0.010
Hemoglobin (g/dL)†	109 ± 11	102 ± 12	0.001
Hematocrit (%)†	32.7 (31.0–35.1) (n = 63)	31.5 (28.2–33.3)	0.007
RDW (%)*	13.5 (12.9–14.3) (n = 63)	13.6 (13.3–14.6)	0.059
CRP (mg/L)*	59.5 (25.8–78.8)	57 (28.3–109.5)	0.251

KD-NCAL group: 1 case was missing in analyzing ALT, hematocrit, RDW. Two cases were missing in analyzing sICAM-1, total protein, albumin, potassium. Three cases were missing in analyzing LDH and sodium. KD-CALs group: 1 case was missing in analyzing IL-6, SDC-1, resistin. Two cases were missing in analyzing sICAM-1, ALT, potassium, sodium. Three cases were missing in analyzing total protein, albumin, LDH.

*Nonnormal distribution data are presented as medians with IQR and are analyzed by the use of Mann-Whitney *U* tests.

†Normal distribution data are presented as means and standard deviation (\bar{X} – SD) and are analyzed by the use of 2-sample *t* tests.

AST indicates aspartate aminotransferase; F, female; KD-NCAL, Kawasaki disease without coronary artery lesions; M, male.

TABLE 2. Spearman Correlation Between Serum SDC-1 Levels and Other Laboratory Data in All KD Patients

	SDC-1		
	ρ	P	N
IL-6 (pg/mL)	0.263	0.004	118
Resistin (ng/mL)	0.240	0.009	118
sICAM-1 (ng/mL)	0.224	0.016	115
TB (μmol/L)	0.262	0.005	113
DB (μmol/L)	0.444	<0.001	114
TP (g/L)	-0.413	<0.001	114
ALB (g/L)	-0.548	<0.001	114
ALT (U/L)	0.220	0.018	116
AST (U/L)	-0.033	0.725	116
GGT (U/L)	0.314	0.001	114
LDH (U/L)	0.052	0.585	113
Potassium (mmol/L)	0.192	0.040	115
Sodium (mmol/L)	-0.073	0.442	114
WBC (10 ⁹ /μL)	-0.060	0.514	119
PLT (10 ³ /μL)	-0.128	0.165	119
RBC (10 ⁶ /μL)	-0.279	0.002	119
Hb (g/dL)	-0.289	0.001	119
Hct (%)	-0.228	0.013	118
RDW (%)	0.075	0.422	118
CRP (mg/L)	0.340	<0.001	119

ρ is for Spearman correlation coefficient.
ALT indicates alanine aminotransferase.

natriuretic peptide, serum ALB, serum sodium, serum tenascin-C, CRP and inflammatory cytokines such as TNF- α and IL-6 have been reported to predict the development of CALs.²⁴ Due to the inaccuracy of these parameters, there is a high clinical need for novel biomarkers that predict the risk of CALs.

SDC-1 is the most important transmembrane heparin sulfate proteoglycan among 4 subtypes of syndecan, the ectodomain of which is shed from endothelium. Elevated serum levels of SDC-1 have been reported in patients with inflammatory diseases such as systemic lupus erythematosus,¹⁷ inflammatory bowel disease,¹⁸ Crohn disease,¹⁹ severe sepsis²⁰ and cardiovascular diseases such as acute coronary syndrome,¹⁵ cardiogenic shock,¹⁵ acute myocardial infarction,¹⁶ cardiac fibrosis¹¹ indicating the endothelium damage, but there are no available data on SDC-1 levels in KD.

In our present study, the serum levels of SDC-1 in FC is much higher than that in HC, which shows the shedding of SDC-1 might be promoted in other febrile diseases such as bronchopneumonia or acute upper respiratory infection. We demonstrated significantly elevated serum SDC-1 levels in patients with KD when compared with HC or FC. These levels were also remarkably higher in KD-CALs than in KD-NCALs. Additionally, SDC-1 levels were significantly and positively associated with inflammatory factors such as CRP, IL-6, sICAM-1 and resistin.

KD is a type of acute vasculitis that leads to endothelial cell damage individuated by SDC-1 shedding⁵⁻⁷ and consequently, serum levels of SDC-1 are increased. In our study, the results of serum SDC-1 levels indicate more remarkable SDC-1 shedding and endothelial cell damage in KD patients when compared with HC and FC. In KD children with CALs, there is more severe endothelial damage and serum levels of SDC-1 are much higher because of increased shedding.

An early study reported that increased serum MMP-9 levels in patients with CALs were higher than those without CALs.^{3,21,22} Lau et al²⁵ has demonstrated that inhibition of MMP-9 activity improves coronary outcome in an animal model of KD affirming that MMP-9 is crucial for the development of CALs in KD patients.^{26,27} Yang et al²⁹ showed that MMP-9 plays a crucial role in

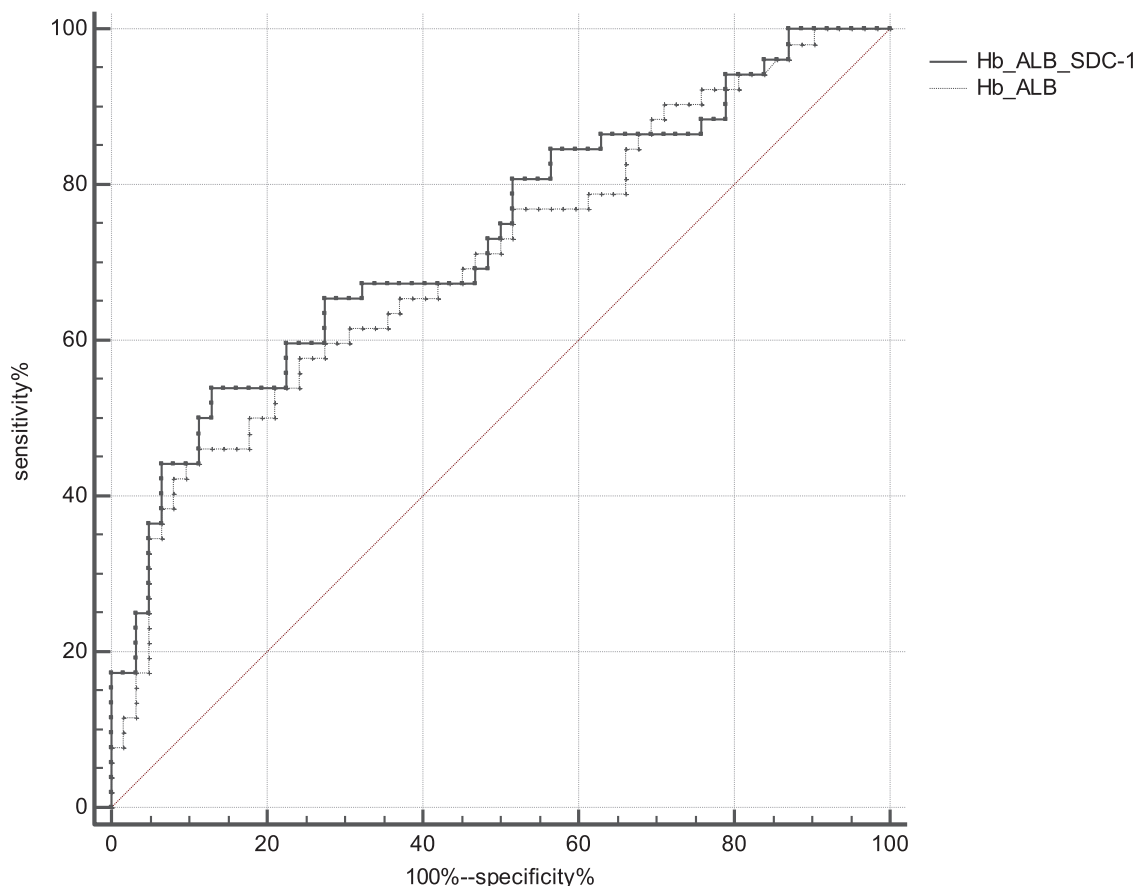


FIGURE 1. Diagnostic values of Hb-ALB and Hb-ALB-SDC-1 using area under the curve of the ROC plot. ROC curves exhibit comparable abilities of Hb-ALB and Hb-ALB-SDC-1 to distinguish KD patients with CAL from patients without CAL (Table 3). Hb-ALB indicates hemoglobin and albumin; Hb-ALB-SDC-1, syndecan-1, hemoglobin and albumin; ROC, receiver operating characteristics.

the shed ectodomain of SDC-1 *in vivo*.²⁸ In KD with CALs, there are higher levels of MMP-9 which leads to a more remarkable SDC-1 shed in coronary endothelial cells thereby resulting in more serious CALs and elevated levels of serum SDC-1. It is suggested that SDC-1 might behave as an endothelial damage marker reflecting the severity of CALs during the acute phase of KD.

Furthermore, TNF- α , IL-6 and IL-1 β play a role in induction of MMP-9 to enhance SDC-1 shedding.¹⁸ Our previous studies have shown higher levels of serum resistin in KD patients with coronary aneurysm, and resistin can promote the production of IL-1 β and TNF- α in human coronary artery endothelium cells.^{4,30} In this study, we found that elevated SDC-1 was significantly related to resistin in KD. Whether resistin directly or indirectly stimulates the release of MMP-9 and exerts a combined effect on SDC-1 shedding and CALs remains unclear. The underlying mechanisms need further elucidation.

In earlier studies circulating endothelial cells, endothelial microparticles, thrombomodulin, antithrombin, von Willebrand factor antigen and coagulation factor VIII activity were used as indicators of endothelial cell damage in KD.^{6,7,31} Although SDC-1 was a biomarker for glycocalyx damage indicating endothelial injury, there were no reports about the implication of SDC-1 in KD. We exhibited an increase of serum SDC-1 as a potential novel biomarker of activation and damage of endothelial cells in KD.

Many studies have shown that patients who are resistant to initial IVIG are at increased risk of developing CALs.³ However,

we did not find an elevated serum level of SDC-1 in IVIG resistance group. The small sample of IVIG resistance group might not reflect the whole real situation which needs further research.

Anemia is a common clinical feature in patients with KD and prior investigations have reported Hb to be a predictor for the development of CALs in KD.³²⁻³⁴ Xu et al³⁵ reported significantly higher RDW in patients with CALs than in those without. We noted similar results of Hb and additionally observed that it is significantly negatively associated with SDC-1.

Studies have reported that increased hepcidin can induce transient anemia in acute-phase KD.³² Anemia could be caused by prolonged active inflammation in KD,^{33,36} and decreased levels of Hb might be related to the suppression on bone marrow function by factors such as resistin⁴ although the underlying mechanism of anemia in KD patients remains unclear. SDC-1 is one kind of core protein of the glycocalyx layer which covers the vascular luminal surface which RBCs cannot pass through.⁸ Deeper penetration of RBCs into a damaged glycocalyx leads to variations in RDW³⁷; this may explain the mechanism of the RBC distribution width feature in KD with CALs.

Alternately, KD is characterized as endothelial injury in addition to the damage of the glycocalyx layer in which RBCs could penetrate the destroyed layer and be released in circulation causing a decreased Hb concentration. Our study may be the first attempt to address the mechanism of decreasing Hb levels caused by vascular endothelial damage in KD patients especially with the

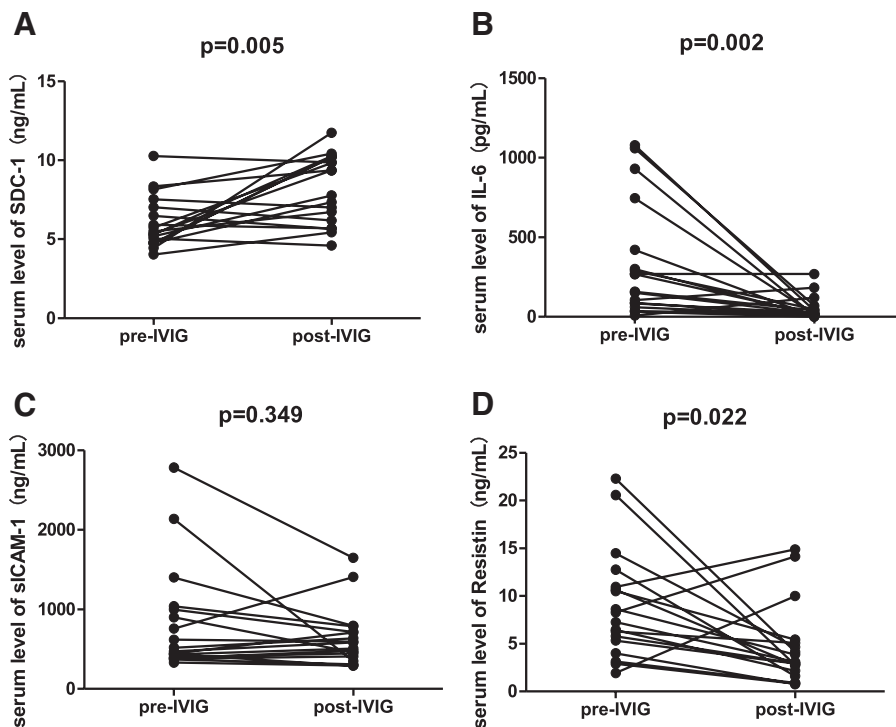


FIGURE 2. Changes in biochemical data before and after IVIG. Serial changes in biochemical data in KD patients (n = 18) before and after IVIG. A: serum levels of SDC-1 were significantly higher after IVIG than before treatment. B: Serum levels of IL-6 significantly decreased after IVIG therapy in the KD patients. C: Serum levels of sICAM-1 decreased after IVIG therapy in the KD patients. D: Serum levels of resistin significantly decreased after IVIG therapy in the KD patients. P value is for the comparison between KD patients before and after IVIG therapy.

TABLE 3. Area Under the Curve for Predicting CALs in Kawasaki Disease

	AUC	95% CI
Hb-ALB-SDC-1	0.730	0.639–0.809
Hb-ALB	0.707	0.612–0.786

P = 0.219. P value is the result of the statistical test comparing the AUC for prediction CAL using the Hb-ALB alone vs. using Hb-ALB-SDC-1

CI indicates confidence interval; Hb-ALB, hemoglobin and albumin; Hb-ALB-SDC-1, syndecan-1, hemoglobin and albumin.

complication of CALs where Hb may reflect endothelial damage indirectly.

Hypoalbuminemia is common and associated with more severe and prolonged acute disease of KD³ that may result from the increased vascular permeability accompanied with the vascular endothelium damage.³⁸ The glycocalyx and its principal core protein SDC-1 are degraded in vascular diseases leading to break down of the vascular permeability barrier.³⁹ Our study presented a significantly higher increase in SDC-1 serum levels of KD with CALs than in KD without CALs while the serum ALB levels were significantly, negatively associated with SDC-1. This suggests that hypoalbuminemia could reflect the extent of the vascular damage, and the shedding of SDC-1 in vascular endothelial cells might be the key mechanism of hypoalbuminemia in KD.

Also, in the present study, we have shown that serum SDC-1 levels alone have mild accuracy for predicting CALs. However, the combination of serum SDC-1 with Hb and ALB did not increase prediction accuracy significantly when compared with the combination of Hb and ALB. KD and CALs might have some impact on SDC-1 which mirrors the inflammation and vascular endothelial damage. However, there are not sufficient data to support the serum level of SDC-1 as a diagnostic marker for KD patients with CALs.

Mostafavi et al³¹ elucidated the persistence of vascular injury late after KD which increased the risk of atherosclerosis in

patients with a history of KD. Previous studies have shown that inflammation was ameliorated after IVIG treatment while endothelial damage may be prolonged.⁷

We discovered higher levels of serum SDC-1 after IVIG treatment which demonstrates the steadfastness of endothelial damage. It indicates that IVIG failed to alleviate the shedding of SDC-1 in vascular endothelial cells in the acute phase of KD and the endothelial damage might remain a long time even after IVIG. Moreover, our results suggest that preservation of endothelial cells from damage in KD is important to reach a better long-term prognosis. Nevertheless, protection against further shedding of SDC-1 might be a promising target for restoration of previously damaged vascular endothelium in KD and has the potential for considerable therapeutic value.

There are several limitations in the present study. Other biomarkers of inflammation should be measured in FC group to make the evidence stronger. The small number of KD patients repeated sampled after IVIG therapy might weaken the findings, besides long-term prognosis of SDC-1 shedding needs to be evaluated. Additionally, because of lack of the data of serum levels of SDC-1 at different time point of KD, we were unable to reveal the variation tendency of SDC-1 and analyze the restoration of endothelium damage after onset of KD.

CONCLUSIONS

These are foremost results which demonstrate elevated SDC-1 serum levels in the acute phase of KD and a maintained increase of SDC-1 levels after IVIG treatment. KD and CALs might have some impact on SDC-1 which mirrors the inflammation and vascular endothelial damage. However, SDC-1 as a diagnostic marker for CALs in KD, the data are not sufficient to make a final assessment. The mechanisms for anemia and hypoalbuminemia could echo vascular damage and may be explained by SDC-1 shedding in KD. SDC-1 might be a novel potential therapeutic target for the protection of coronary artery in KD patients.

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