



Current Real-World Outcomes of Recurrent Kawasaki Disease

Toshimasa Nakada

Department of Pediatrics, Aomori Prefectural Central Hospital 〒030-8553 Higashi-tukurimito 2-1-1, Aomori City, Aomori Prefecture, Japan

Email: toshimasanakada@yahoo.co.jp

Article History

Received: September 9, 2020

Revised: October 25, 2020

Accepted: October 27, 2020

Published: October 30, 2020

Abstract

Studies have shown that recurrent Kawasaki disease (KD) is a risk factor for resistance to initial intravenous immunoglobulin (IVIG) therapy and development of coronary artery lesions (CALs). However, current real-world outcomes of recurrent KD patients remain unclear. The objective of this retrospective study was to elucidate the outcomes of recurrent KD patients in the era of 2 g/kg IVIG therapy. Data were included from 201 KD patients who underwent acute-phase treatment from January 2009 to September 2020, with 184 (91.5%) receiving 2 g/kg IVIG therapy. The patients were divided into 7 with (recurrent group) and 194 without (nonrecurrent group) recurrent KD. At the first onset, the rates of initial IVIG therapy resistance (28.6% vs. 21.5%, $P = 1.000$), rescue therapy (14.3% vs. 14.4%, $P = 1.000$), and CALs (0.0% vs. 2.6%, $P = 1.000$) were similar between the recurrent and nonrecurrent groups. The rates of initial IVIG therapy resistance (14.3% vs. 21.5%, $P = 1.000$), rescue therapy (14.3% vs. 14.4%, $P = 1.000$), and CALs (0.0% vs. 2.6%, $P = 1.000$) were also similar between the recurrent group at the second onset and the nonrecurrent group at the first onset. KD recurrence may no longer be a risk factor for developing CALs in the era of 2 g/kg IVIG therapy, unless CALs appear at the initial episode.

Keywords: Coronary artery lesions; Intravenous immunoglobulin therapy; Kawasaki disease; Outcomes; Recurrence.

1. Introduction

Kawasaki disease (KD) is a form of acute febrile systemic vasculitis that primarily affects children younger than 5 years [1]. Coronary artery lesions (CALs) are a severe complication of KD.

Recurrent KD is defined as a recurring presentation of another episode after 2 months from the first one [2, 3]. The incidence of recurrence is high among those with cardiac sequelae during the first episode [2, 3]. Compared with patients who do not experience recurrence, patients with recurrent KD are more likely to be older, fulfill the atypical KD case definition, and develop CALs despite intravenous immunoglobulin (IVIG) treatment [4, 5].

Studies have shown that recurrent KD is a risk factor for CAL development [2-7]. However, an epidemiological study suggested that KD recurrence is no longer a risk factor for developing cardiac complications, unless cardiac sequelae appear at the initial episode [8].

The objective of this study was to elucidate the real-world outcomes of recurrent KD in the era of 2 g/kg IVIG therapy.

2. Participants and Methods

Our institutional ethics committee approved the study protocol and waived the requirement of patient consent due to the retrospective nature of the study.

This study included data from 215 patients who underwent acute-phase treatment for KD between January 2009 and September 2020 (Fig. 1). KD was diagnosed based on the criteria (Japanese, fifth edition) mentioned in the diagnostic guidelines for KD until August 2019 and on the revised criteria (Japanese, sixth edition) from September 2019 [9, 10]. A total of 14 patients with complications before initial therapy or with follow-up periods of < 2 months were excluded (Fig. 1). Six patients with complications before initial therapy had no KD recurrence.

The remaining patients were divided into two groups: those with (recurrent group, $n = 7$) and those without (nonrecurrent group, $n = 194$) recurrent KD (Fig. 1). The outcomes included the rates of IVIG resistance, rescue therapy, and CALs.

2.1. Initial Therapy

During the study period, a single IVIG infusion of 2 g/kg/dose was given as initial therapy starting on day 5 of the illness, whenever possible [11]. Patients without inflammation or complications at presentation received acute-phase therapy without IVIG [11]. Between January 2009 and November 2017, anti-inflammatory drugs (aspirin or flurbiprofen) were initiated within 24 h after the initial IVIG infusion ended [12]. Aspirin and flurbiprofen were started at 30 and 3–5 mg/kg/day, respectively, and decreased to 5–10 and 3 mg/kg/day, respectively, once the patient

was afebrile [12]. Each treating physician chose aspirin or flurbiprofen after considering the patient's liver function and the risk of Reye syndrome during influenza season. After December 2017, low-dose aspirin (5 mg/kg/day) was begun on days 8–10 of illness after completion of IVIG infusion, including the second course of therapy [11].

2.2. Rescue Therapy

The decision to use rescue therapies in resistant patients was made 48 to 72 h after completion of the initial IVIG infusion. Physicians made this decision using comprehensive clinical parameters, including body temperature, major KD symptoms, general condition, and laboratory data [11]. Course 2 of therapy comprised rescue IVIG infusion at 2 g/kg/dose, and course 3 was an ulinastatin infusion, third course of IVIG therapy, or plasma exchange [11].

2.3. Diagnosis of CAL

CALs were diagnosed using echocardiography based on the Japanese criteria reported by Kobayashi, *et al.* [13]. A CAL was diagnosed if any examination showed an internal lumen diameter of ≥ 3 mm in a patient younger than 5 years or a diameter of ≥ 4 mm in a patient older than 5 years if the internal diameter of a segment was at least 1.5 times that of an adjacent segment or if the lumen appeared irregular. A transient CAL was defined as the disappearance of a CAL within 30 days of the illness.

2.4. Statistical Analysis

Statistical analyses were conducted using Stat Flex Version 6 for Windows (Artech Co., Ltd., Osaka, Japan). Chi-square, Fisher exact, and Mann–Whitney U tests were used as appropriate, with sample size considerations. $P < 0.05$ was considered statistically significant.

3. Results

The recurrent group included 7 patients (2 males and 5 females) (Table 1). A total 7 of 201 (3.5%) patients had KD recurrence. Age at the first KD onset was < 3 years in 6 of 7 patients (Table 1). Six of the seven patients had two onsets of KD, and one patient (patient number 1) had three onsets of KD (Table 1). The median interval from the first to the second onset was 4 months (range: 3 months–2 years and 5 months), and 6 of 7 patients (85.7%) had an interval of < 2 years between the first and second onset (Table 1). No patients in the recurrent group had incomplete KD (Table 1). Six of seven patients in the recurrent group had a negative family history of KD. One patient (patient number 7) had a positive family history of KD regarding her older brother.

All 7 patients in the recurrent group received 2 g/kg/dose IVIG therapy on days 5–7 of illness, and 5 of them (71.4%) responded at the first onset (Table 2). Six of seven patients (85.7%) responded at the second onset (Table 2). One patient (patient number 5) received acute-phase treatment including 2 g/kg IVIG therapy with concomitant use of medium-dose aspirin at the second onset in another hospital (Table 2). No patients in the recurrent group had CAL at < 1 or 1 month after KD onset (Tables 2 and 3).

The rates of initial IVIG therapy resistance (28.6% vs. 21.5%, $P = 1.000$), rescue therapy (14.3% vs. 14.4%, $P = 1.000$), and CALs (0.0% vs. 2.6%, $P = 1.000$) were similar between the recurrent and nonrecurrent groups at the first onset (Table III). The rates of initial IVIG therapy resistance (14.3% vs. 21.5%, $P = 1.000$), rescue therapy (14.3% vs. 14.4%, $P = 1.000$), and CALs (0.0% vs. 2.6%, $P = 1.000$) were also similar between those of the recurrent group at the second onset and the nonrecurrent group at the first onset.

4. Discussion

The main findings of this study were that no patients with recurrent KD had CALs at both initial onset and relapse, and the rates of CALs were similar between the recurrent and nonrecurrent groups (Tables 2 and 3). KD recurrence may no longer be a risk factor for developing CALs, unless CALs appear at the initial episode.

Previous studies have shown that KD recurrence was a risk factor for CAL development [2-7]. An epidemiological study in recurrent KD patients between 1989 and 1992 showed that 32 of 68 (47%) patients with cardiac sequelae after the initial onset and 78 of 491 (16%) patients without cardiac sequelae after the initial onset went on to suffer cardiac sequelae after the second onset, and that both proportions were higher than the proportions in all KD patients [6].

The main pathological finding of KD is systemic vasculitis [1]; therefore, two attacks of vasculitis damage the vascular wall more than only one attack [7]. This is considered as the main reason for the high prevalence of CALs in recurrent KD patients [7]. In fact, 2 of 5 patients (40%) with recurrent KD between 1991 and 2003 had medium-size CALs one month after both the first and second episodes in our department in a previous study [5]. During one patient's second onset of KD, a CAL recurred on the same portion of the coronary artery where an initial CAL had regressed after the first onset [5]. Additionally, no patients with recurrent KD had CALs both during the first onset and relapse of KD (Table 2).

The mainstay of current standard therapy in the acute-phase of KD is 2 g/kg IVIG, and evidence has established its efficacy in CAL suppression [14]. Conversely, 2 g/kg IVIG was not widespread as acute-phase standard therapy for KD before 2003. Of the 201 patients in this study, 184 (91.5%) received 2 g/kg IVIG therapy (Table 3). This may be a reason for the different outcomes in recurrent KD patients between previous studies and the present study. In fact, recent study regarding real-world outcomes of recurrent KD demonstrated similar rates of CALs among the first and second onsets of recurrent KD and single-onset KD [3].

Adding medium or high-dose aspirin to 2 g/kg IVIG therapy is controversial at present [15]. A randomized controlled trial on the effectiveness of IVIG monotherapy versus IVIG combined with high-dose aspirin in the acute KD stage is ongoing [16]. Studies suggested that aspirin may inhibit CAL prevention and that delayed use of aspirin (DUA) may be beneficial for the suppression of CALs and prevention of coronary artery stenosis in patients with KD [12], [17-19]. Furthermore, a recent study showed favorable medium-term outcomes of CALs in KD patients who received 2 g/kg IVIG with DUA [11]. The use of 2 g/kg IVIG therapy with DUA in the present study may be an additional reason for the favorable outcomes in patients with recurrent KD.

Between 1993 and 1994, the incidence of recurrent KD was high among patients with cardiac sequelae during the first KD episode [2]. However, an epidemiological study in patients between 2003 and 2012 showed that the presence of cardiac sequelae during the initial episode of KD did not affect the incidence of recurrence [20]. Widespread use of 2 g/kg IVIG therapy might have changed the incidence of recurrent KD among those with cardiac sequelae during the first episode.

An epidemiological study showed that risk factors for recurrent KD included male sex, age < 3 years, and initial IVIG therapy resistance [20]. In the present study, 6 of 7 patients (85.7%) with recurrent KD had their first KD onset under the age of 3 years (Table I). However, the age at first KD onset was similar between the recurrent and nonrecurrent groups (Table III). The rates of male gender and initial IVIG therapy resistance in patients with recurrent KD were 2 of 7 (28.6%), and these rates were similar between the recurrent and the nonrecurrent groups (Table III). One study showed a lower rate of male gender and similar rate of IVIG therapy resistance in recurrent KD patients compared with the nonrecurrent KD population [3].

A nationwide epidemiological survey of KD in Japan (2015–16) showed a 4.2% prevalence of KD recurrence [21]. Another epidemiological study showed that the incidence of recurrent KD has remained largely unchanged over the past 30 years [20]. The rate of KD recurrence in the present study and in the study conducted among KD patients in our department in 1991–2003 was 3.5% (7/201) and 3.6% (5/139), respectively [5]. These findings were consistent with those of the previously mentioned studies [20, 21].

One study showed that 21 of 22 (95.5%) recurrent KD patients during 2002–2010 had an interval of < 2 years between the first and recurrent episodes of KD, and the mean interval value was 12.0 months [3]. An epidemiological study demonstrated the average interval between two episodes in recurrent KD patients during 1989–1994 was 1.78 years [6]. In the present study, 6 of 7 (85.7%) recurrent patients had an interval of < 2 years between the first and recurrent episodes (Table I). The median interval between the first and second episodes among patients with recurrent KD in our department during 1991–2003 and 2009–2020 was 1 years and 3 months (range: 5 months–5 years and 10 months) and 4 months (range: 3 months–2 years and 5 months), respectively [5]. Although not statistically significant, the interval between the first and second episodes for recent patients with recurrent KD was shorter compared with that of patients during 1991–2003.

One patient (patient number 1) had a third onset of KD (Table 1). A previous study conducted in our department reported one other patient with a third onset of KD [5]. These two patients had an interval between the second and third onset of 3 and 6 years, respectively. Case reports also demonstrated two recurrent KD patients had a third onset of KD at 3 and 5 years, respectively, after the second onset [22, 23]. Physicians may need to be vigilant for a third onset more than 2 years after a recurrent KD patient's second onset.

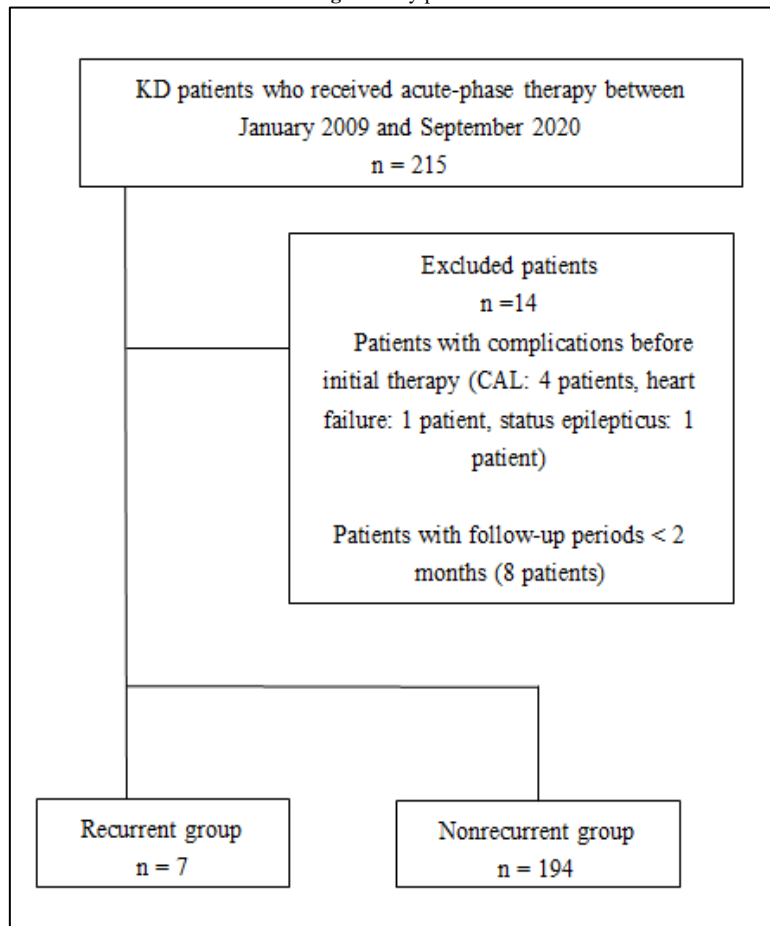
One study reported a child with recurrent KD and a positive family history of KD [22]. An epidemiological study showed that a positive family history of KD was a risk factor for KD recurrence [24]. However, a recent study regarding real-world outcomes of KD in families suggested that a positive family history of KD was not a risk factor for KD recurrence, and that further studies are warranted to elucidate the risk of KD in families in the era of 2 g/kg IVIG therapy [25]. In fact, in the present study, a total 6 of 7 patients (85.7%) in the recurrent group had a negative family history of KD.

The limitations of this study include the small sample size and the retrospective study design.

5. Conclusion

No patients with recurrent KD had CALs at both initial onset and relapse, and the rates of CALs were similar between the recurrent and nonrecurrent groups in the era of 2 g/kg IVIG therapy. KD recurrence may no longer be a risk factor for developing CALs in the era of 2 g/kg IVIG therapy, unless CALs appear at the initial episode. Appropriate acute-phase treatment utilizing 2 g/kg IVIG therapy at the first KD onset may lead to favorable outcomes in KD recurrence.

Fig-1. Study profile



KD: Kawasaki disease, CAL: coronary artery lesion.

Table-1. Baseline Characteristics of Patients with Recurrent Kawasaki Disease

Patient	Gender	Age	Interval from first onset	Major signs
Patient 1	Female	1 y and 3 m		6
First onset		1 y and 7 m	4 m	5
Second onset		5 y and 4 m	4 y and 1 m	6
Patient 2	Female	1 y and 7 m		6
First onset		4 y and 0 m	2 y and 5m	6
Patient 3	Female	4 y and 11 m		6
First onset		5 y and 2 m	3 m	6
Patient 4	Male	2 y and 0 m		6
First onset		2 y and 3 m	3 m	6
Patient 5	Male	2 y and 1 m		5
First onset		2 y and 11 m	10 m	5
Patient 6	Female	1 y and 7 m		5
First onset		1 y and 10 m	3 m	5
Patient 7	Female	2 y and 0 m		6
First onset		2 y and 5 m	5 m	5
Second onset				

Pt: patient, KD: Kawasaki disease, Age: age at KD onset, y: years, m: months, Interval: interval period of KD onset between the first and the second patient, Major signs: numbers of KD major signs.

Table-2. Treatment and Outcomes of Patients with Recurrent Kawasaki Disease

Patient	IVIG (start day of illness)	Aspirin/ flurbiprofen	CAL
Patient 1			
First onset	Nonresponder (5)	Flurbiprofen	None
Second onset	Responder (5)	Flurbiprofen	None
Third onset	Responder (5)	Medium-dose aspirin	None
Patient 2			
First onset	Responder (7)	Flurbiprofen	None
Second onset	Responder (5)	Medium-dose aspirin	None
Patient 3			
First onset	Responder (7)	Flurbiprofen	None
Second onset	Responder (5)	Flurbiprofen	None
Patient 4			
First onset	Nonresponder (5)	Medium-dose aspirin	None
Second onset	Responder (5)	Medium-dose aspirin	None
Patient 5			
First onset	Responder (5)	Low-dose aspirin	None
Second onset	Responder (5)	Medium-dose aspirin#	None
Patient 6			
First onset	Responder (6)	Low-dose aspirin	None
Second onset	Responder (6)	Low-dose aspirin	None
Patient 7			
First onset	Responder (6)	Low-dose aspirin	None
Second onset	Nonresponder (5)	Low-dose aspirin	None

Pt: patient, IVIG: intravenous immunoglobulin therapy,

CAL: coronary artery lesion.

#: concomitant use with IVIG.

Table-3. Comparison of Clinical Findings between Recurrent Group and Nonrecurrent Group at the First Onset

Variables	Recurrent group (n = 7)	Nonrecurrent group (n = 194)	P-value
Male gender	2 (28.6%)	97 (50.0%)	0.445
Age at KD onset (months)	24.0 (19.0–24.8)	27.5 (14.0–47.0)	0.699
Incomplete type	0 (0.0%)	39 (20.1%)	0.350
Low-dose aspirin/ medium-dose aspirin/ flurbiprofen	3 (42.9%)/ 1 (14.3%)/ 3 (42.9%)	37 (19.1%)/ 95 (49.0%)/ 62 (32.0%)	0.720
IVIG	7 (100.0%)	177 (91.2%)	0.643
Day of illness at initial IVIG therapy	6.0 (5.0–6.8)	5.0 (5.0–6.0)	0.320
Nonresponder	2 (28.6%)	38 (21.5%) (n = 177)	1.000
Rescue therapy	1 (14.3%)	28 (14.4%)	1.000
For nonresponder	1 (14.3%)	22 (11.3%)	1.000
For relapse	0 (0.0%)	5 (2.6%)	1.000
For responder	0 (0.0%)	1 (0.5%)	1.000
CAL	0 (0.0%)	5 (2.6%)	1.000
Less than one month after KD onset	0 (0.0%)	5 (2.6%)	1.000
One month after KD onset	0 (0.0%)	2 (1.0%)	1.000
Recurrence	7 (100.0%)	0 (0.0%)	< 0.001
Follow-up periods (months)	17.0 (7.8–86.8)	41.0 (14.0–61.0)	0.913

Data are presented as n (%) or median (interquartile range).

Incomplete type: major signs of KD \leq 4, KD: Kawasaki disease,

IVIG: intravenous immunoglobulin, CAL: coronary artery lesion.

Acknowledgments

I would like to thank all of those who were involved in the medical management of the patients included in this study, and Enago (www.enago.jp) for the English language review.

References

- [1] Kawasaki, T., Kosaki, F., Okawa, S., Shigematsu, I., and Yanagawa, H., 1974. "A new infantile acute febrile mucocutaneous lymph node syndrome (MLNS) prevailing in Japan." *Pediatrics*, vol. 54, pp. 271-276.
- [2] Hirata, S., Nakamura, Y., and Yanagawa, H., 2001. "Incidence rate of recurrent Kawasaki disease and related risk factors: from the results of nationwide surveys of Kawasaki disease in Japan." *Acta Paediatr*, vol. 90, pp. 40-4. Available: <https://doi.org/10.1111/j.1651-2227.2001.tb00253.x>

- [3] Yang, H., Du, Z. D., and Fu, P., 2013. "Clinical features of recurrent Kawasaki disease and its risk factors." *Eur. J. Pediatr.*, vol. 172, pp. 1641-1647.
- [4] Maddox, R. A., Holman, R. C., Uehara, R., Callinan, L. S., Guest, J. L., and Schonberger, L. B., 2015. "Recurrent Kawasaki disease: USA and Japan." *Pediatr. Int.*, vol. 57, pp. 1116-1120. Available: <https://doi.org/10.1111/ped.12733>
- [5] Nakada, T., 2008. "Clinical features of patients with recurrent Kawasaki disease." *Nippon Rinsho*, vol. 66, pp. 296-300.
- [6] Nakamura, Y., Oki, I., Tanihara, S., Ojima, T., and Yanagawa, H., 1998. "Cardiac sequelae in recurrent cases of kawasaki disease: A comparison between the initial episode of the disease and a recurrence in the same patients." *Pediatrics*, vol. 102, pp. 1-5. Available: <http://www.pediatrics.org/cgi/content/full/102/6/e66>
- [7] Nakamura, Y., Yanagawa, H., Ojima, T., Kawasaki, T., and Kato, H., 1998. "Cardiac sequelae of Kawasaki disease among recurrent cases." *Arch Dis Child*, vol. 78, pp. 163-165.
- [8] Sudo, D., Makino, N., and Nakamura, Y., 2020. "Recurrent Kawasaki disease and cardiac complications: nationwide surveys in Japan." *Archives of Disease in Childhood*, vol. 105, pp. 848-852.
- [9] Ayusawa, M., Sonobe, T., Uemura, S., Ogawa, S., Nakamura, Y., and Kiyosawa, N., 2005. "Revision of diagnostic guidelines for Kawasaki disease." *Pediatr Int*, vol. 47, pp. 232-4. Available: <https://doi.org/10.1111/j.1442-200x.2005.02033>
- [10] Fukazawa, R., Kobayashi, J., Ayusawa, M., Hamada, H., Miura, M., and Mitani, Y., 2020. "JCS/JSCS 2020 guideline on diagnosis and management of cardiovascular sequelae in Kawasaki disease." *Circ. J.*, vol. 84, pp. 1348-1407.
- [11] Nakada, T., 2020. "Acute phase treatment and medium-term outcomes in Kawasaki disease." *European Journal of Medical and Health Sciences*, vol. 2, pp. 1-7. Available: <http://dx.doi.org/10.24018/ejmed.2020.2.4.419>
- [12] Nakada, T., 2015. "Effects of anti-inflammatory drugs on intravenous immunoglobulin therapy in the acute phase of Kawasaki disease." *Pediatr Cardiol*, vol. 36, pp. 335-9.
- [13] Kobayashi, T., Inoue, Y., Takeuchi, K., Okada, Y., Tamura, K., and Tomomasa, T., 2006. "Prediction of intravenous immunoglobulin unresponsiveness in patients with Kawasaki disease." *Circulation*, vol. 113, pp. 2606-12. Available: <http://www.circulationaha.org>
- [14] Research Committee of the Japanese Society of Pediatric Cardiology; Cardiac Surgery Committee for Development of Guidelines for Medical Treatment of Acute Kawasaki Disease, 2014. "Guidelines for medical treatment of acute kawasaki disease: Report of the research committee of the japanese society of pediatric cardiology and cardiac surgery (2012 revised version)." *Pediatr. Int.*, vol. 56, pp. 135-58. Available: <https://doi.org/10.1111/ped.12317>
- [15] McCrindle, B. W. and Tierney, E. S. S., 2017. "Acute treatment for Kawasaki disease: challenges for current and future therapies." *J. Pediatr*, vol. 184, pp. 7-10.
- [16] Kuo, H. C., Guo, M. M., Lo, M. H., Hsieh, K. S., and Huang, Y. H., 2018. "Effectiveness of intravenous immunoglobulin alone and intravenous immunoglobulin combined with high-dose aspirin in the acute stage of Kawasaki disease: study protocol for a randomized controlled trial." *BMC Pediatr*, vol. 18, p. 200. Available: <https://doi.org/10.1186/s12887-018-1180-1>
- [17] Lau, A. C., Duong, T. T., Ito, S., and Yeung, R. S., 2009. "Intravenous immunoglobulin and salicylate differentially modulate pathogenic processes leading to vascular damage in a model of Kawasaki disease." *Arthritis Rheum*, vol. 60, pp. 2131-41. Available: <https://doi.org/10.1002/art.24660>
- [18] Cho, H. J., Bak, S. Y., Kim, S. Y., Yoo, R., Baek, H. S., and Yang, S., 2017. "High neutrophil: lymphocyte ratio is associated with refractory Kawasaki disease." *Pediatr Int.*, vol. 59, pp. 669-74. Available: <https://doi.org/10.1111/ped.13240>
- [19] Nakada, T., 2018. "Acute phase treatment for prevention of coronary artery stenosis caused in Kawasaki disease: a single center retrospective study." *Journal of Advanced Research in Medicine*, vol. 5, pp. 1-7. Available: <https://doi.org/10.24321/2349.7181.201818>
- [20] Sudo, D. and Nakamura, Y., 2017. "Nationwide surveys show that the incidence of recurrent Kawasaki disease in Japan has hardly changed over the last 30 years." *Acta Paediatrica*, vol. 106, pp. 796-800. Available: <https://doi.org/10.1111/apa.13773>
- [21] Makino, N., Nakamura, Y., Yashiro, M., Kosami, K., Matsubara, Y., and Ae, R., 2019. "Nationwide epidemiologic survey of Kawasaki disease in Japan, 2015-2016." *Pediatr Int.*, vol. 61, pp. 397-403. Available: <https://doi.org/10.1111/ped.13809>
- [22] Kraszewska-Glomba, B., Kuchar, E., and Szenborn, L., 2016. "Three episodes of Kawasaki disease including one after the Pneumo 23 vaccine in a child with a family history of Kawasaki disease." *Journal of the Formosan Medical Association*, Available: <http://dx.doi.org/10.1016/j.jfma.2016.04.005>
- [23] Goswami, N., Marzan, K., Oliveira, E. D., Wagner-Lees, S., and Szmuszkowicz, J., 2018. "Recurrent Kawasaki Disease: A Case Report of Three Separate Episodes at > 4-Year Intervals. Children." vol. 5, p. 115.
- [24] Uehara, R., Yashiro, M., Nakamura, Y., and Yanagawa, H., 2004. "Clinical features of patients with Kawasaki disease whose parents had the same disease." *Arch. Pediatr. Adolesc Med.*, vol. 158, pp. 1166-1169.
- [25] Nakada, T., 2020. "Outcomes of Kawasaki disease in families." *European Journal of Medical and Health Sciences*, vol. 2, pp. 1-5. Available: <http://dx.doi.org/10.24018/ejmed.2020.2.5.494>