



AN OVERVIEW OF KAWASAKI DISEASE DIAGNOSIS AND MANAGEMENT APPROACH: LITERATURE REVIEW

Rawan Hamdan Alenazy^{1*}, Taif Shayish Alanazi¹, Marium Mostafa Salama², Mona Theyab Alanazi¹, Raghad Aladham K Alanazi¹, Aseel Abdulkarim Alfahhad³, Almajd Metab Alanazi¹, Nazmi Maher Al-Qutub², Fatimah Khalil Almindil⁴, Faisal Abdulmoein Shaker Almosbahi⁵

1. Faculty of Medicine, Northern Border University, Arar, KSA.
2. Faculty of Medicine, Alfaisal University, Riyadh, KSA.
3. Faculty of Medicine, Imam Mohammad ibn Saud Islamic University, Riyadh, KSA.
4. Faculty of Medicine, Jouf University, Aljouf, KSA.
5. Faculty of Medicine, University of Jeddah, Jeddah, KSA.

ARTICLE INFO

Received:
23 Jun 2020
Received in revised form:
12 Oct 2020
Accepted:
17 Oct 2020
Available online:
28 Oct 2020

Keywords: Kawasaki Disease, Diagnosis, Management.

ABSTRACT.

Background: Kawasaki disease (KD) is a febrile vasculitis disorder that is considered a life-threatening disease if left untreated. It is the most common cause of acquired cardiac diseases in pediatric patients in developed countries. Several debates have been discussed in the literature regarding diagnosing and treating cases of KD. **Objective:** To review the published literature that discussed KD's diagnosis and management to provide adequate coverage of the important aspects of KD. **Conclusion:** There is no specific diagnostic test for proper KD diagnosis. Therefore, the clinical features and laboratory findings should be combined to reach the diagnosis. Regarding management, combined Intravenous Immunoglobulins (IVIG) with aspirin is the recommended treatment for acute KD. However, corticosteroids are the recommended alternatives in treating severe KD in cases of IVIG resistance. Regarding the proper regimens of the different options, the proper dosage and duration vary from region to region and institution to institution.

Copyright © 2013 - All Rights Reserved - Pharmacophore

To Cite This Article: Rawan Hamdan Alenazy, Taif Shayish Alanazi, Marium Mostafa Salama, Mona Theyab Alanazi, Raghad Aladham K Alanazi, Aseel Abdulkarim Alfahhad and *et al.*, (2020), "An Overview of Kawasaki Disease Diagnosis and Management Approach: Literature Review", *Pharmacophore*, **11(5)**, 163-167.

Introduction

Kawasaki disease (KD) is a form of vasculitis that affects mostly medium-sized arteries. It is considered a self-limiting inflammatory disease. It mostly affects the coronary arteries but it also affects the skin, mucous membranes, and conjunctiva [1].

Kawasaki disease (KD) is the most common cause of acquired cardiac diseases in pediatric patients in developed countries. It may lead to devastating complications in cases of missed diagnosis, late intervention, or refractory cases such as aneurysms, infarctions, and even sudden death [2].

It is important to have proper knowledge about KD, its epidemiology, etiopathogenesis, diagnostic criteria, and therapeutic options to conduct appropriate evaluation and management of such disease [3-5]. Therefore, we aim to review the published literature that discussed KD and provide a general evaluation of this disorder.

Methods:

PubMed database was used for articles selection, and the following keys were used in the mesh ((“Kawasaki disease”[Mesh]) AND (“management” [Mesh]) OR (“evaluation”[Mesh])).

In regards to the inclusion criteria, the articles were selected based on the inclusion of one of the following topics: Kawasaki disease, evaluation, and management.

Exclusion criteria were all other articles, which did not have one of these topics as their primary endpoint.

Corresponding Author: Rawan Hamdan Alenazy, Faculty of Medicine, Northern Border University, Arar, KSA. Email: rawanhamdan2625@gmail.com

Discussion:

Kawasaki disease (KD), which is also called mucocutaneous lymph node syndrome, is a febrile vasculitis disorder that is considered a life-threatening disease if left untreated [6]. The nomenclature, Kawasaki disease, was adopted after this form of vasculitis was described by the Japanese pediatrician Dr. Tomakisu Kawasaki in 1967 [7].

Kawasaki disease (KD) has a higher prevalence in Asian countries compared to non-Asian countries with a significant difference [8]. In Japan, the annual incidence is more than 200 cases per 100,000 children [9]. In Korea, Kawasaki-diagnosed cases per year are 134 out of 100,000 children under 5 years old while the number in Taiwan is 66 per 100,000 [10, 11]. However, in non-Asian countries, the risk is significantly lower whereas 8.39 per 100,000 children under 5 years of age have the disease in England and 9.34 per 100,000 in Australia [12, 13].

Genetics:

Kawasaki disease (KD) is considered a complicated disease in which its onset can be triggered by a variety of infections or environmental agents in individuals who are genetically susceptible [14, 15]. Moreover, several identified susceptibility genes are linked with KD for example Caspase-3 calcium release-activated calcium modulator 1 (ORAI1), inositol 1,4,5-trisphosphate 3-kinase C (ITPKC), and CD 40 [16-18].

Studying and identifying the susceptibility genes are important to have better knowledge about the pathophysiology of the disease. It is believed that different genes are associated with different risks of complications for instance the development of coronary artery aneurysms in KD patients is associated with transforming growth factor (TGF)- β variants [14, 19].

Diagnosis:

Regarding the diagnosis of KD, there is no specific diagnostic test. Therefore, the clinical features and laboratory findings should be combined to reach the diagnosis [20].

There are criteria for diagnosing KD which rely primarily on clinical features. Kawasaki disease (KD) can be diagnosed when there is fever lasting for more than 5 days and 4 of the 5 following features: conjunctivitis, lymphadenopathy, rash, changes in oral mucosa, changes in the extremities. The conjunctivitis is mostly bilateral, non-suppurative, and bulbar. The lymphadenopathy is mostly cervical and more than 1.5 cm in size. The rash is polymorphous with no vesicles nor crusts. Examples of the changes in lips and oral mucosa include red cracked lips, strawberry tongue, and diffuse erythema of the oropharynx. The extremities change range from erythema or edema of the palms and soles to peeling off the fingertip's skin. Moreover, in the case of detected coronary artery abnormalities, fewer than 4 features can confirm the diagnosis of KD [21]. Erythema is one of the commonest signs that develop in KD. Besides, induration can appear at the location of previous Bacillus Calmette–Guérin (BCG) immunization. It has been thought that the pathophysiology behind it is because of the cross-reactivity of T cells between human heat shock proteins and specific mycobacterial epitopes in KD patients [22, 23].

Nevertheless, some KD patients may not complete all the criteria but they are or they will be at risk of coronary artery aneurysm. Therefore, high suspicion of the index is recommended when a child presents with some KD features especially if there is some evidence of systemic inflammation in laboratory findings for example high white blood cells (WBCs) count, elevated erythrocyte sedimentation rate (ESR), or high C-reactive protein (CRP) levels. So, it is recommended to conduct echocardiography to see if there is evidence of coronary vasculitis, which can be a diagnostic criterion for the confirmation of KD. However, absent evidence of coronary vasculitis cannot rule out KD [21, 22, 24]. Aseptic meningitis, arthritis, gastroenteritis, otitis, uveitis, pneumonitis, and dysuria and meatitis can also be present in cases of KD. Irritability is also a common symptom of KD despite it is not a part of the diagnostic criteria. The underlying pathology behind irritability is still unknown but it has been suggested that it is due to the possible presence of aseptic meningitis [22, 25]. Other complications include gastrointestinal ischemia, renal impairment, cranial nerve palsy, conclusions, and ataxia [20, 22, 24].

Management:

Combined IVIG with aspirin is the recommended treatment for acute KD by the American Heart Association and the American Academy of Pediatrics [6, 21].

The exact IVIG mechanism of action is still uncertain. However, several suggestions can be the reason behind the effectiveness of IVIG in treating KD such as reducing the release of cytokines and inflammatory mediators, suppression of TNF- α , neutralizing the infectious antigens, and the pathogenic autoantibodies [26, 27]. If IVIG therapy is started within the first 10 days of the onset of symptoms, there will be an increase in the success rate. Administering IVIG for patients who present after 10 days of the disease onset is not associated with high efficacy in reducing the risk of coronary artery aneurysm. Therefore, it is not recommended unless there are signs of active inflammations such as persistent fever, high ESR, and CRP [28]. However, approximately 1% of children who receive appropriate IVIG treatment develop coronary artery aneurysms [26, 29]. The recommended dose is 2 g per kg as a single dose infused for over 12 hours [27]. Other dosages and regimens have been suggested such as 400 mg per kg for 4-5 days but they were less effective in treating KD and preventing its complications especially coronary artery aneurysm [30, 31].

As known, low doses of aspirin have antiplatelet effects while high doses have anti-inflammatory activities. In treating KD cases, choosing whether to give high or low doses of aspirin is still controversial. Low-dose aspirin reduces prostaglandin and thromboxane production by preventing the release of cyclooxygenase enzymes. High-dose aspirin prevents I κ B kinase

(IKK) activity, which will inhibit the translocation of nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB). This will prevent the transduction of TNFα signals and affect the main pro-inflammatory cytokines regulation. Nevertheless, there is no significant difference regarding the coronary outcomes between high and low doses [32, 33]. Regarding the proper aspirin therapy in acute KD cases, the dosage and the duration vary from region to region and from institution to institution based on the present evidence. In North America, the usual prescribed dose of aspirin as an anti-inflammatory during KD is 80-100 mg/kg/day divided q6h. The usual prescribed dose in Japan is 20 mg/kg. Then, once the patient becomes afebrile for 2 to 3 days, the anti-inflammatory aspirin dose should be reduced to the antiplatelet dose only. Others recommend continuing high dose aspirin for 2 weeks regardless of the temperature. For antiplatelet aspirin, 3-5 mg/kg per day is the recommended dose. Low-dose aspirin should be continued for 6-8 weeks in patients who do not show evidence of coronary complications as well as fever and elevated inflammatory markers. However, low-dose aspirin must be continued for life in children with coronary artery damage [34].

In the case of IVIG resistance, corticosteroids are the recommended alternative in treating severe KD. The resistance rate can reach 20% of cases. Unfortunately, IVIG-resistant patients have a higher risk of developing coronary artery aneurysms in case they did not receive other appropriate treatment [21, 22, 24]. Regarding combining IVIG with corticosteroids, it has been suggested in several studies. Chen *et al.* [35] conducted a meta-analysis comparing IVIG therapy alone with IVIG plus corticosteroids as primary treatment of KD patients to evaluate the coronary artery aneurysm risk in both groups. They found that combination therapy has better outcomes regarding reducing the risk of coronary artery aneurysm in severe cases of KD than IVIG alone. Intravenous methylprednisolone or prednisolone was the used corticosteroids in the studies [35]. Nevertheless, other studies have suggested otherwise, in which corticosteroids were associated with similar or even increased risk of coronary artery aneurysm. It has been thought that this discrepancy in the results is due to the different agents, regimens, doses, and duration of corticosteroid treatments. Moreover, the benefits from the corticosteroids have been found in Japanese studies more than the American studies [36, 37]. Among these debates, the recommendations of using corticosteroids were to administer them in particular groups of patients. These include patients who are known as IVIG-resistant especially when there is ongoing fever, patients with persistent inflammatory signs for more than 2 days after administering an adequate dose of IVIG, patients with a high risk of developing severe complications, and patients who already developing coronary aneurysm especially when there is ongoing inflammation. Severe inflammation may appear as persistent high CRP despite IVIG, low albumin level, liver dysfunction, anemia, or shock [20, 38]. The most effective regimen of corticosteroids that have been suggested is prednisolone 2 mg/kg given intravenously for 1 week. Then, it is preferred to switch to oral prednisolone for 2 weeks [20, 35].

Regarding follow-up, it is recommended to start with baseline echocardiography at the presentation in order to evaluate the prognosis after 2 weeks and after 2 months as recommended [21]. However, more frequent echocardiography is recommended in severe and refractory cases. Regarding long-term follow-up, the reevaluation should be after 10 to 20 years in patients with a low risk of complications and did not develop any coronary abnormality. In patients who are at high risk of complications or developing coronary artery abnormalities, adequate cardiac evaluation, electrocardiogram, and echocardiogram are recommended to be performed twice yearly. In suspicious cases, coronary angiography is also recommended in order to have a proper assessment. Moreover, other medications can be added besides aspirin for long-term therapy, for example, beta-blockers and anticoagulants [8, 39].

COVID-19 and KD:

As we mentioned earlier, KD's onset can be triggered by a variety of infections or environmental agents in genetically susceptible individuals. There has been a recent increase in children who present with KD-like symptoms in different countries [40]. Nevertheless, these cases have similar symptoms and clinical features to COVID-19 and some of these children have confirmed SARS-CoV-2 infection. In Italy, severe KD cases have been seen with increased incidence in a recent COVID-19 cohort in Bergamo [41]. A link between these two conditions has been suggested but not defined yet. It has been thought that coronavirus infection can trigger KD in children who already have a history of KD. One of the reported cases has been treated with IVIG and aspirin which resulted in symptoms resolution [42]. Therefore, it is necessary to monitor KD patients for potential COVID-19 infection. In cases of positive coronavirus, the children should receive IVIG and get quarantined until the KD symptoms are completely resolved and the coronavirus test becomes negative [40].

Conclusion:

There is no specific diagnostic test for proper KD diagnosis. Therefore, the clinical features and laboratory findings should be combined in order to reach the diagnosis.

Regarding management, combined Intravenous Immunoglobulins (IVIG) with aspirin is the recommended treatment for acute KD. However, corticosteroids are the recommended alternative in treating severe KD in cases of IVIG resistance. Regarding the proper regimens of the different options, the proper dosage and duration vary from region to region and from institution to institution.

References

1. Hedrich, Christian M., Schnabel, A., Hospach, T. Kawasaki Disease. *Frontiers in Pediatrics*, 2018; 6:198-208. <https://doi.org/10.3389/fped.2018.00198>.
2. Naoe S, Takahashi K, Masuda H, Tanaka N. Kawasaki disease with particular emphasis on arterial lesions. *Pathology International*. 1991 Nov;41(11):785-97. <https://doi.org/10.1111/j.1440-1827.1991.tb01620.x>.
3. Arifin Z, Milanda T, Suwantika AA. Cost-effectivity of standardized-herbal medicine for DHF inpatients in a Primary Health Center. *J. Adv. Pharm. Educ. Res.* 2019;9(4):19-23.
4. Darkhor S, Estebansari F, Hosseini M, Charati JY, Vasli P. Effect of health promotion intervention on Nurses' healthy lifestyle and health-promoting behaviors: RCT study. *J. Adv. Pharm. Educ. Res.* 2018;8(1):108-114.
5. Ren-Zhang L, Chee-Lan L, Hui-Yin Y. The awareness and perception on Antimicrobial Stewardship among healthcare professionals in a tertiary teaching hospital Malaysia. *Arch. Pharm. Pract.* 2020;11(2):50-9.
6. Agarwal S, Agrawal DK. Kawasaki disease: etiopathogenesis and novel treatment strategies. Expert review of clinical immunology. 2017 Mar 4;13(3):247-58. <https://doi.org/10.1080/1744666x.2017.1232165>.
7. Kawasaki T. Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes in children. *Arerugi*. 1967;16:178-222.
8. Ramphul K, Mejias SG. Kawasaki disease: a comprehensive review. *Archives of medical sciences. Atherosclerotic diseases*. 2018;3:e41. <https://doi.org/10.5114/amsad.2018.74522>.
9. Harnden, A., Tulloh, R., Burgner, D. Kawasaki Disease. *Bmj* 349, no. sep17 3, 2014. <https://doi.org/10.1136/bmj.g5336>.
10. Kim GB, Han JW, Park YW, Song MS, Hong YM, Cha SH, Kim DS, Park S. Epidemiologic features of Kawasaki disease in South Korea: data from nationwide survey, 2009–2011. *The Pediatric infectious disease journal*. 2014 Jan 1;33(1):24-7. <https://doi.org/10.1097/inf.000000000000010>.
11. Lue HC, Chen LR, Lin MT, Chang LY, Wang JK, Lee CY, Wu MH. Epidemiological features of Kawasaki disease in Taiwan, 1976–2007: Results of five nationwide questionnaire hospital surveys. *Pediatrics & Neonatology*. 2014 Apr 1;55(2):92-6. <https://doi.org/10.1016/j.pedneo.2013.07.010>.
12. Harnden A, Mayon-White R, Perera R, Yeates D, Goldacre M, Burgner D. Kawasaki disease in England: ethnicity, deprivation, and respiratory pathogens. *The Pediatric infectious disease journal*. 2009 Jan 1;28(1):21-4. <https://doi.org/10.1097/inf.0b013e3181812ca4>.
13. Saundankar J, Yim D, Itoho B, Payne R, Maslin K, Jape G, Ramsay J, Kothari D, Cheng A, Burgner D. The epidemiology and clinical features of Kawasaki disease in Australia. *Pediatrics*. 2014 Apr 1;133(4):e1009-14. <https://doi.org/10.1542/peds.2013-2936>.
14. Pilania RK, Singh S. Kawasaki Disease. In *Periodic and Non-Periodic Fevers 2020* (pp. 45-63). Springer, Cham. https://doi.org/10.1007/978-3-030-19055-2_4.
15. Onouchi Y. Genetics of Kawasaki disease. *Circulation Journal*. 2012;CJ-12. <https://doi.org/10.1253/circj.12-0568>.
16. Onouchi Y. The genetics of Kawasaki disease. *International journal of rheumatic diseases*. 2018 Jan;21(1):26-30. <https://doi.org/10.1111/1756-185x.13218>.
17. Dietz SM, Van Stijn D, Burgner D, Levin M, Kuipers IM, Hutten BA, Kuijpers TW. Dissecting Kawasaki disease: a state-of-the-art review. *European journal of pediatrics*. 2017 Aug 1;176(8):995-1009. <https://doi.org/10.1007/s00431-017-2937-5>.
18. Onouchi Y, Fukazawa R, Yamamura K, Suzuki H, Kakimoto N, Suenaga T, Takeuchi T, Hamada H, Honda T, Yasukawa K, Terai M. Variations in ORAI1 gene associated with Kawasaki disease. *PloS one*. 2016 Jan 20;11(1):e0145486. <https://doi.org/10.1371/journal.pone.0145486>.
19. Shimizu C, Jain S, Davila S, Hibberd ML, Lin KO, Molkara D, Frazer JR, Sun S, Baker AL, Newburger JW, Rowley AH. Transforming growth factor- β signaling pathway in patients with Kawasaki disease. *Circulation: Cardiovascular Genetics*. 2011 Feb;4(1):16-25. <https://doi.org/10.1161/circgenetics.110.940858>.
20. Eleftheriou D, Levin M, Shingadia D, Tulloh R, Klein NJ, Brogan PA. Management of Kawasaki disease. *Archives of disease in childhood*. 2014 Jan 1;99(1):74-83. <https://doi.org/10.1136/archdischild-2012-302841>.
21. Newburger JW, Takahashi M, Gerber MA, Gewitz MH, Tani LY, Burns JC, Shulman ST, Bolger AF, Ferrieri P, Baltimore RS, Wilson WR. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. *Pediatrics*, 2004; 114(6): 1708–33. <https://doi.org/10.1542/peds.2004-2182>.
22. Brogan PA, Bose A, Burgner D, Shingadia D, Tulloh R, Michie C, Klein N, Booy R, Levin M, Dillon MJ. Kawasaki disease: an evidence based approach to diagnosis, treatment, and proposals for future research. *Archives of disease in childhood*. 2002 Apr 1;86(4):286-90. <https://doi.org/10.1136/adc.86.4.286>.
23. Sinha R, Balakumar TB. BCG reactivation: a useful diagnostic tool even for incomplete Kawasaki disease. *Archives of disease in childhood*. 2005 Sep 1;90(9):891-. <https://doi.org/10.1136/adc.2004.071332>.
24. Dillon MJ, Eleftheriou D, Brogan PA. Medium-size-vessel vasculitis. *Pediatric Nephrology*. 2010 Sep 1;25(9):1641-52. <https://doi.org/10.1007/s00467-009-1336-1>.

25. Amano S, Hazama F. Neural involvement in Kawasaki disease. *Pathology International*. 1980 May;30(3):365-73. <https://doi.org/10.1111/j.1440-1827.1980.tb01331.x>.
26. Alexoudi I, Kanakis M, Kapsimali V, Vaiopoulos G. Kawasaki disease: current aspects on aetiopathogenesis and therapeutic management. *Autoimmunity Reviews*. 2011 Jul 1;10(9):544-7. <https://doi.org/10.1016/j.autrev.2011.04.005>.
27. Bayers S, Shulman ST, Paller AS. Kawasaki disease: part I. Diagnosis, clinical features, and pathogenesis. *Journal of the American Academy of Dermatology*. 2013 Oct 1;69(4):501-e1. <https://doi.org/10.1016/j.jaad.2013.06.040>.
28. Kuo HC, Yang KD, Chang WC, Ger LP, Hsieh KS. Kawasaki disease: an update on diagnosis and treatment. *Pediatrics & Neonatology*. 2012 Feb 1;53(1):4-11. <https://doi.org/10.1016/j.pedneo.2011.11.003>.
29. Galeotti C, Bayry J, Kone-Paut I, Kaveri SV. Kawasaki disease: aetiopathogenesis and therapeutic utility of intravenous immunoglobulin. *Autoimmunity reviews*. 2010 Apr 1;9(6):441-8. <https://doi.org/10.1016/j.autrev.2009.12.004>.
30. Hsieh KS, Weng KP, Lin CC, Huang TC, Lee CL, Huang SM. Treatment of acute Kawasaki disease: aspirin's role in the febrile stage revisited. *Pediatrics*. 2004 Dec 1;114(6):e689-93. <https://doi.org/10.1542/peds.2004-1037>.
31. Shulman, Stanford T. Management of Kawasaki Disease. *The Journal of Pediatrics*, 1998; 113(6): 1116–17. [https://doi.org/10.1016/s0022-3476\(88\)80596-1](https://doi.org/10.1016/s0022-3476(88)80596-1).
32. Yin MJ, Yamamoto Y, Gaynor RB. The anti-inflammatory agents aspirin and salicylate inhibit the activity of I κ B kinase- β . *Nature*. 1998 Nov;396(6706):77-80. <https://doi.org/10.1038/23948>.
33. Vane JR. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. *Nature new biology*. 1971 Jun 23;231(25):232-5. <https://doi.org/10.1038/newbio231232a0>.
34. Yeung, Rae S. M. Kawasaki Disease. *Textbook of Clinical Pediatrics*, 2012, 1675–84. https://doi.org/10.1007/978-3-642-02202-9_165.
35. Chen S, Dong Y, Yin Y, Krucoff MW. Intravenous immunoglobulin plus corticosteroid to prevent coronary artery abnormalities in Kawasaki disease: a meta-analysis. *Heart*. 2013 Jan 15;99(2):76-82. <https://doi.org/10.1136/heartjnl-2012-302126>.
36. Kobayashi T, Saji T, Otani T, Takeuchi K, Nakamura T, Arakawa H, Kato T, Hara T, Hamaoka K, Ogawa S, Miura M. Efficacy of immunoglobulin plus prednisolone for prevention of coronary artery abnormalities in severe Kawasaki disease (RAISE study): a randomised, open-label, blinded-endpoints trial. *The Lancet*. 2012 Apr 28;379(9826):1613-20. [https://doi.org/10.1016/s0140-6736\(11\)61930-2](https://doi.org/10.1016/s0140-6736(11)61930-2).
37. Kato H, Koike S, Yokoyama T. Kawasaki disease: effect of treatment on coronary artery involvement. *Pediatrics*. 1979 Feb 1;63(2):175-9.
38. Lega JC, Bozio A, Cimaz R, Veyrier M, Floret D, Ducreux C, Reix P, Di Filippo S. Extracoronary echocardiographic findings as predictors of coronary artery lesions in the initial phase of Kawasaki disease. *Archives of disease in childhood*. 2013 Feb 1;98(2):97-102. <https://doi.org/10.1136/archdischild-2011-301256>.
39. Manlhiot C, Niedra E, McCrindle BW. Long-term management of Kawasaki disease: implications for the adult patient. *Pediatrics & Neonatology*. 2013 Feb 1;54(1):12-21. <https://doi.org/10.1016/j.pedneo.2012.12.013>.
40. Xu S, Chen M, Weng J. COVID-19 and Kawasaki disease in children. *Pharmacological Research*. 2020 Sep;159:104951. <https://doi.org/10.1016/j.phrs.2020.104951>.
41. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, Bonanomi E, D'Antiga L. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *The Lancet*. 2020 May 13. [https://doi.org/10.1016/s0140-6736\(20\)31103-x](https://doi.org/10.1016/s0140-6736(20)31103-x).
42. Jones VG, Mills M, Suarez D, Hogan CA, Yeh D, Segal JB, Nguyen EL, Barsh GR, Maskatia S, Mathew R. COVID-19 and Kawasaki disease: novel virus and novel case. *Hospital Pediatrics*. 2020 Jun 1;10(6):537-40. <https://doi.org/10.1542/hpeds.2020-0123>.