Cardiology in the Young

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Global incidence of Kawasaki disease: a systematic review

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Original Article

Cite this article: Kang CR, Lee JS, and Choe YJ (2025) Global incidence of Kawasaki disease: a systematic review. *Cardiology in the Young* **35**: 1028–1039. doi: 10.1017/S104795112500191X

Received: 7 November 2024
Revised: 15 February 2025
Accepted: 25 March 2025
First published online: 8 May 2025

Keywords:
Mucocutaneous lymph node syndrome (Kawasaki disease); incidence; global health; epidemiologic studies; review literature as topic

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Abstract

Background: Kawasaki disease is a systemic vasculitis that primarily affects young children and represents a major cause of acquired heart disease in children in developed countries. The incidence of Kawasaki disease exhibits significant global variation, and the worldwide burden remains limited. *Methods:* A systematic review was conducted to investigate the global incidence of Kawasaki disease in children under 5 years of age. A comprehensive literature search was performed in PubMed, Embase, and KoreaMed up to July 15, 2024. Studies reporting population-level Kawasaki disease incidence were included. Data extraction and quality assessment were performed independently by two reviewers. *Results:* The search yielded 3,197 articles, of which 105 met the inclusion criteria. These studies examined Kawasaki disease incidence in children under 5 years of age across 34 countries, with the majority focusing on the Western Pacific Region and the Region of the Americas. The results demonstrated a wide range of Kawasaki disease incidence globally, with significant geographic variations. The highest incidence rates were observed in Japan, Korea, and Taiwan, with a trend of gradual increase over time. *Conclusions:* This study represents the most comprehensive review of global Kawasaki disease incidence to date. The substantial variation in incidence underscores the need to understand the factors influencing regional differences.

Introduction

Kawasaki disease is an acute systemic vasculitis of unknown aetiology that predominantly affects young children.[1] The disease's hallmark feature is inflammation of medium-sized arteries, with a particular predilection for the coronary arteries.[2] This can lead to coronary artery aneurysms and other cardiovascular complications, making Kawasaki disease the leading cause of acquired heart disease in children in developed countries.[3] While timely treatment with intravenous immunoglobulin and aspirin significantly reduces the risk of coronary artery involvement, a subset of patients remains unresponsive or develop complications despite treatment.[4]

The global epidemiology of Kawasaki disease has been characterised by marked geographic and temporal variations, with the highest incidence consistently reported in East Asia, particularly Japan and Korea.[5,6] However, a comprehensive understanding of the global burden of Kawasaki disease remains elusive, hindering the development of targeted prevention strategies, optimal allocation of healthcare resources, and a deeper understanding of the disease's aetiology.

To address this knowledge gap, we conducted a systematic review to investigate the global incidence of Kawasaki disease. By synthesising data from diverse populations and geographic regions, we aim to provide a more comprehensive picture of the worldwide burden of Kawasaki disease, which could inform clinical practice, public health initiatives, and future research directions.

Methods

Search strategy and data sources

A comprehensive literature search was conducted in PubMed, Embase, and KoreaMed by a trained medical librarian (Eun-Ji Kang) from inception up to July 15, 2024. The search strategy, developed initially for MEDLINE using the keywords and MeSH terms, was adapted for other databases. The exact search strategies for PubMed, Embase, and KoreaMed are outlined in Table S1. There were no language restrictions. Reference lists of included articles and relevant literature identified through manual searches were also screened for additional publications. The study protocol has been registered and published with PROSPERO.[7] This study was exempt from Institutional Review Board approval as a systematic review.

Study selection

Titles and abstracts of identified articles were screened according to the inclusion and exclusion criteria by two reviewers (CRK, YJC). Full-text review was conducted by the same reviewers for all identified articles. Two authors independently reviewed articles for inclusion, resolving disagreements by consensus. Inclusion criteria for selecting articles include studies whose aim is to describe Kawasaki disease incidence in children under 5 years of age in any country or area of a country, including original papers of observational studies, cross-sectional studies, case–control studies, and prospective and retrospective studies. Studies based on Kawasaki disease-relevant ICD-9/ICD-10 codes or guidelines for the diagnosis of Kawasaki disease were included. The exclusion criteria were a) duplicate studies; b) systematic review ± meta-analysis; c) non-original studies including reviews, comments, editorials, case reports, guidelines, and book chapters; d) intervention studies (randomized and clinical controlled trials); e) selected populations of participants with other basic diseases; f) no population-level incidence data of Kawasaki disease; and g) no data available for children under 5 years of age.

Data extraction and quality assessment

Two reviewers (CRK, YJC) independently extracted data on study details, such as first author, publication year, country, study period, study design, data source, and incidence (including incidence rate and admission rate) per 100,000 children under 5 years of age. Discrepancies were resolved through discussion. Studies that met the inclusion criteria were assessed for the risk of bias tool established by Hoy et al.[8]

Results

Study selection

In a systematic search of sources, 3,197 articles were identified. A total of 677 articles were duplicated, and 2,373 were excluded after screening the title and abstract of the articles. After reviewing full-text articles, 42 articles were excluded. Finally, 105 studies were included in the systematic review. Figure 1 shows the identified and retrieved articles in the study.

Study characteristics

The major characteristics of the studies are listed in Table 1. Eligible studies examined Kawasaki disease incidence in children under 5 years of age in 34 countries (Fig 2). A total of 105 studies were published from 1986-2024, mainly concentrated in 2011–2024. The studies were conducted between 1976 and 2021. Dividing the studies by WHO regions, 28 (26.7%) were from the Region of the Americas,[9–36] 22 (21.0%) from the European Region,[37–58] 2 (1.9%) from the Eastern Mediterranean Region,[59,60] 2 (1.9%) from the South-East Asia Region,[61,62] and 51 (48.6%) from the Western Pacific Region.[63–113] The majority of studies focused on countries in the Western Pacific Region and the Region of the Americas, and most studies were from the United States (n = 19, 18.1%),[11,12,14–19,21–26,28–30,34,36] Japan (n = 18, 17.1%),[63–65,78,89–91,93–96,103,106–111] Korea (n = 10, 9.5%),[72,79–82,84,98–101] and Taiwan (n = 7, 6.7%).[67,75–77,85,87,88] Regarding the methodology, of the total 105 studies, 4 were prospective and 101 were retrospective studies. Among the 101 retrospective studies, 3 were conducted with additional prospective studies, and 29 were conducted together with cross-sectional studies. The quality assessment of each study is shown in Table S2.

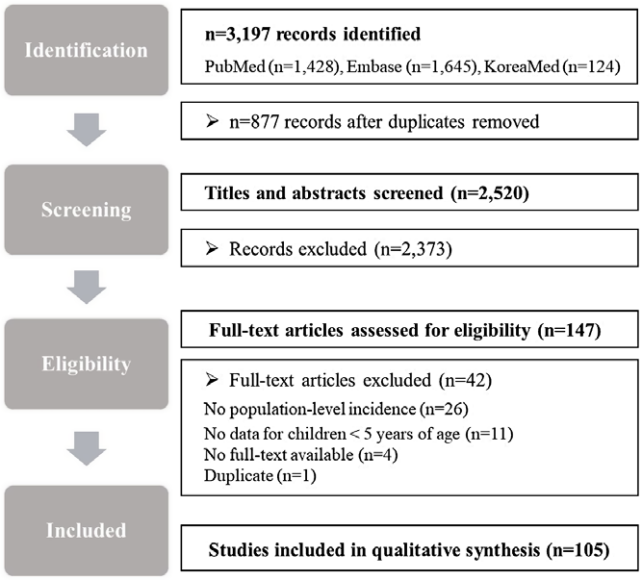

Figure 1. PRISMA flow diagram.

Incidence of Kawasaki disease in the world

The recent Kawasaki disease incidence in Japan and Korea is the highest worldwide (> 200 per 100,000 children <5 years old). Kawasaki disease incidence is also high in Taiwan and a province (Beijing) of China (> 50 per 1000,000 children <5 years old). For time trends of Kawasaki disease incidence in included studies, the incidence gradually increased in Australia, China, Hong Kong, Japan, Korea, New Zealand, Malaysia, and Taiwan, which are included in the WPR. However, during the COVID-19 pandemic, Kawasaki disease incidence tended to decrease in Japan and Korea.[65,98] In the United States, Kawasaki disease incidence differed by administrative region, the incidence in Hawaii was relatively high. There was a slight increase in Kawasaki disease incidence in Canada, Chile, Peru, and the United States, which are included in the AMR. Kawasaki disease incidence in countries included in the European Region, EMR, and South-East Asia Region is nearly constant with low incidence.

Discussion

This systematic review identified 105 studies examining Kawasaki disease incidence in children under 5 years of age from 34 countries. Our review provides the most comprehensive assessment of the global incidence of Kawasaki disease to date. Study findings reveal considerable variation in Kawasaki disease incidence in children under 5 years of age across different populations and geographic regions. The Kawasaki disease incidence in the world reveals substantial variations, highlighting the need for a nuanced understanding of the global burden of Kawasaki disease. The elevated incidence of Kawasaki disease in Japan and Korea, as evidenced in this review, points towards a complex interplay of factors that may contribute to this phenomenon. The prevailing hypothesis suggests a combination of genetic predisposition, environmental influences, and diagnostic practices may be at play. The higher prevalence of certain

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Table 1. Summary of the characteristics of studies included

WHO region	First author	Publication year	Country	Study period	Incidence per 100,000 children <5 years of age	Study design	Data source characteristics
Region of the Americas (AMR)	Robinson	2021	Canada (Ontario)	1995–2017	18.4 (1995–2001), 25.0 (2002-2016)	retrospective	Ontario health administrative data
	Gorrab	2016	Canada (Quebec, Maghrebi origin)	1996–2013	18.49	retrospective, cross-sectional	Medical records
	Alkanhal	2023	Canada (Nova Scotia)	2007–2018	29.6	retrospective	Medical records
	Borzutzky	2012	Chile	2001–2007	6.3 (2001–2004), 9.3 (2005–2007)	retrospective	National hospital discharge databases
	Hoyos-Bachiloglu	2016	Chile	2001–2011	5.9 (2001–2003), 10.4 (2009–2011)	retrospective	National hospital discharge databases
	Schonhaut	2001	Chile (Santiago)	1987–1999	3.9	retrospective	Medical records
	Pierre	2000	Jamaica	1986–1998	2.7	retrospective	Medical records
	Tourneux	2005	Guadeloupe (French West Indies)	1995–2000	25.4	retrospective	Medical records
	Atamari-Anahui	2023	Peru	2015–2019	0.52 (2015), 1.34 (2016), 2.12 (2017), 2.38 (2018), 2.28 (2019)	retrospective	Hospitalization registry
	Belay	2003	USA	1997–1999	10.2	retrospective	Solucient Hospital discharge database
	Holman	2003	USA	1997–2000	17.1	retrospective	Kids' Inpatient Database
	Holman	2010	USA	1997–2007	17.5 (1997), 17.1 (2000), 19.6 (2003), 20.8 (2006)	retrospective	Kids' Inpatient Database
	Okubo	2017	USA	2003–2012	19.6 (2003), 20.8 (2006), 19.1 (2009), 18.0 (2012)	retrospective	Kids' Inpatient Database
	Vasudeva	2022	USA	2008–2017	17.1 (<1 yo), 16.2 (1–4 years old)	retrospective	National Inpatient Sample (NIS) database
	Holman	1999	USA (American Indian & Alaska Native)	1980–1995	4.3	retrospective	Indian Health Service (IHS) data
	Belay	2000	USA (West Coast HMOs)	1993–1996	9.0 ~ 19.1 (by HMOs)	retrospective	HMO (Health maintenance organization) data
	Chang	2002	USA (California)	1995–1999	15.3	retrospective	OSHPD (Office of Statewide Health Planning and Development) database
	Callinan	2014	USA (California)	2003–2010	20.5 (2003), 24.7 (2010)	retrospective	California State Inpatient Database
	Bronstein	2000	USA (San Diego, California)	1994–1998	8.0 ~ 15.4	retrospective	Medical records
	Taslakian	2021	USA (Olmsted County, Minnesota)	1979-2016	21.4	retrospective	Medical records

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Table 1. (*Continued*)

WHO region	First author	Publication year	Country	Study period	Incidence per 100,000 children <5 years of age	Study design	Data source characteristics
	Davis	1995	USA (Washington)	1985–1989	6.5 (1985-1986), 15.2 (1987-1989)	retrospective	Statewide hospital data set
	Lin	2010	USA (New York)	1990–2009	14.6 (1990) ~ 22.5 (2002)	retrospective	Statewide Planning and Research Cooperative System (SPARCS) database
	Lin	2010	USA (Ontario)	1995–2006	14.4 (1995–1997), 20.4 (1998–2000), 24.1 (2001–2003), 26.2 (2004–2006)	retrospective, cross-sectional	Medical records
	Coustasse	2009	USA (Texas)	2004	13.8	retrospective	Texas Health Information Council
	Holman	2000	USA (Hawaii & Connecticut)	1994–1997	47.7 (Hawaii), 18.8 (Connecticut)	retrospective	Hawaii Health Information Corporation (HHIC), Connecticut Health Information Management and Exchange (CHIME)
	Holman	2005	USA (Hawaii)	1996–2001	45.2	retrospective	Hawaii State Inpatient Database
	Holman	2010	USA (Hawaii)	1996–2006	45.5 ~ 56.5	retrospective	Hawaii State Inpatient Database
	Dawson	2020	USA (Hawaii)	1996–2018	32	retrospective	Medical records
European Region (EUR)	Fischer	2007	Denmark	1981–2004	3.6	retrospective	Danish National Hospital Register
	Salo	1993	Finland	1982–1992	3.1 ~ 7.2	retrospective	Medical records
	Salo	2012	Finland, Norway, Sweden	1998–2009	11.4 (Finland), 5.4 (Norway), 7.4 (Sweden)	retrospective	Hospital discharge databases
	Juliusson	1999	Iceland	1979–1997	8.5	retrospective	Medical records
	Lynch	2003	Ireland	1996–2000	15.2 (9.6 ~ 19.3)	retrospective	Hospital In-Patient Enquiry (HIPE) database
	Olafsdottir	2012	Iceland	1996–2005	10.7	retrospective	Medical records
	Schiller	1995	Sweden	1990–1992	6.5	prospective	Medical records
	Grech	1999	Malta	1992–1997	3.2	retrospective	Medical records
	Bar-Meir	2011	Israel	1996–2009	6.4	retrospective	National Hospital Discharge Database
	Cimaz	2017	Italy	2008–2013	14.7 (2008–2013)	retrospective	National Hospital Discharge Record Database
	Mauro	2016	Italy (Emilia Romagna /Tuscany)	2008–2013	13.8/24.6 (2008–2010), 12.8/28.6 (2009–2011), 12.2/31.5 (2010–2012), 18.5/27.8 (2011–2013)	retrospective	Hospital discharge records database
	Pinto	2017	Portugal	2000–2011	6.5	retrospective	Hospital Discharge Records
	Tacke	2014	Netherlands	2008–2012	6.3 (2008), 5.5 (2009), 5.1 (2010), 6.2 (2011), 6.0 (2012)	retrospective	Dutch Pediatric Surveillance Unit
	Jakob	2016	Germany	2011–2012	7.2	prospective	National Surveillance: German Pediatric Surveillance Unit (ESPED)

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Table 1. (*Continued*)

WHO region	First author	Publication year	Country	Study period	Incidence per 100,000 children <5 years of age	Study design	Data source characteristics
	Riancho-Zarrabeitia	2018	Spain	2005–2015	11.7	retrospective	Hospital morbidity survey of the Spanish National Institute of Statistics (INE) database
	Sánchez-Manubens	2016	Spain (Catalonia)	2004–2014	8	retrospective (2004-2013), prospective (2014)	Medical records
	Sánchez-Manubens	2017	Spain (Catalonia)	2004–2014	8	retrospective (2004-2013), prospective (2013-2014)	Medical records
	Hall	2016	UK	2008–2012	9.1	retrospective	Health Improvement Network (THIN) database
	Harnden	2009	United Kingdom (England)	1998–2003	8.39	retrospective	Hospital Episode Statistics (HES)
	Odingo	2023	United Kingdom (England)	2006–2021	6.9 ~ 11.8	retrospective	National Disease Registries Directions
	Tulloh	2019	United Kingdom & Ireland	2013–2015	4.55	prospective	British Paediatric Surveillance Unit survey
	Gradoux	2022	Switzerland	2013–2017	8.4	retrospective	Swiss Paediatric Surveillance Unit
Eastern Mediterranean Region (EMR)	Shahbaznejad	2022	Iran	2015–2019	27.16	retrospective	National KD registration system
	Saffar	2005	Iran (East Mazandaran)	1997–2002	7.3	retrospective	Medical records
South-East Asia Region (SEAR)	Panamonta	2004	Thailand (northeast)	1991–2003	2.2	retrospective	Medical records
	Singh	2016	India (Chandigarh)	2009–2014	9.1 (2009), 3.02 (2010), 8.04 (2011), 1.00 (2012), 3.99 (2013), 6.97 (2014)	retrospective	Medical records
Western Pacific Region (WPR)	Royle	1998	Australia	1993–1995	3.7	retrospective, cross-sectional	Australian Paediatric Surveillance Unit (APSU)
	Lucas	2022	Australia	1993–2017	9.39 (1993–1997), 9.39 (1998–2002), 12.14 (2003–2007), 14.79 (2008–2012), 17.51 (2013–2017)	retrospective	National Hospital Morbidity Database
	Saundankar	2014	Australia (Western Australia)	1980–2009	2.82 (1980–1989), 7.96 (1990–1999), 9.34 (2000–2009)	retrospective	Medical records
	Ferreira	2021	Australia (Newcastle)	2015–2016	26.5 (2015), 22.4 (2016)	retrospective	Medical records
	Wang	2000	China (Jiangsu)	1993–1997	1.84 (1993), 2.64 (1994), 2.12 (1995), 2.66 (1996), 3.65 (1997)	retrospective	Medical records
	Du	2002	China (Beijing)	1995–1999	18.2 (1995), 21.1 (1996), 18.6 (1997), 30.6 (1998) and 27.8 (1999)	retrospective, cross-sectional	Medical records

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Table 1. (*Continued*)

WHO region	First author	Publication year	Country	Study period	Incidence per 100,000 children <5 years of age	Study design	Data source characteristics
	Du	2007	China (Beijing)	2000–2004	40.9 (2000), 50.5 (2001), 47.5 (2002), 53.3 (2003), 55.1 (2004)	retrospective, cross-sectional	Medical records
	Li	2008	China (Sichuan)	1997–2001	4.26 (1997), 5.21 (1998), 8.57 (1999), 7.70 (2000), 9.81 (2001)	retrospective, cross-sectional	Medical records
	Huang	2005	China (Shanghai)	1998–2002	16.79 (1998), 25.65 (1999), 28.16 (2000), 28.05 (2001), and 36.76 (2002)	retrospective, cross-sectional	Medical records
	Zhang	2012	China (Jilin)	1999–2008	1.39 (1999), 0.93 (2000), 2.14 (2001), 2.28 (2002), 3.35 (2003), 4.87 (2004), 6.65 (2005), 8.34 (2006), 11.61 (2007), 11.07 (2008)	retrospective	Medical records
	Ng	2005	Hong Kong	1994–2000	26 (1994–1997), 39 (1997–2000)	retrospective (1994-1997), prospective (1997-2000)	Medical records
	Zhang	2016	China (Inner Mongolia)	2001–2013	3.55	retrospective, cross-sectional	Medical records
	Yanagawa	1988	Japan	1985–1986	102 (1985), 172.2 (1986)	retrospective	Medical records
	Yanagawa	1995	Japan	1991–1992	90	retrospective, cross-sectional	Medical records
	Yanagawa	1996	Japan	1993–1994	95.1	retrospective, cross-sectional	Medical records
	Yanagawa	1998	Japan	1995–1996	102.6 (1995), 108.0 (1996)	retrospective, cross-sectional	Medical records
	Yanagawa	2001	Japan	1997–1998	108.0 (1997), 111.7 (1998)	retrospective, cross-sectional	Medical records
	Yanagawa	2006	Japan	1999–2002	119.6 (1999), 141.1 (2000), 138.8 (2001), 151.2 (2002)	retrospective, cross-sectional	Medical records
	Abrams	2018	Japan	1991–2004	89.5 (1991), 174.3 (2004)	retrospective, cross-sectional	Medical records
	Nakamura	2008	Japan	2003–2004	159.2 (2003), 174.0 (2004)	retrospective, cross-sectional	Medical records
	Nakamura	2008	Japan	2005–2006	184.6	retrospective, cross-sectional	Medical records
	Nakamura	2010	Japan	2007–2008	215.3 (2007), 218.6 (2008)	retrospective, cross-sectional	Medical records
	Nakamura	2012	Japan	2009–2010	206.2 (2009), 239.6 (2010)	retrospective, cross-sectional	Medical records
	Sano	2016	Japan	2007–2012	322.45	retrospective	Medical records
	Makino	2015	Japan	2011–2012	243.1 (2011), 264.8 (2012)	retrospective, cross-sectional	Medical records
	Makino	2018	Japan	2013–2014	302.5 (2013), 308.0 (2014)	retrospective, cross-sectional	Medical records

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Table 1. (*Continued*)

WHO region	First author	Publication year	Country	Study period	Incidence per 100,000 children <5 years of age	Study design	Data source characteristics
	Makino	2019	Japan	2015–2016	330.2 (2015), 309.0 (2016)	retrospective	Medical records
	Ae	2020	Japan	2017–2018	359 (2018)	retrospective, cross-sectional	Medical records
	Ae	2022	Japan	2019–2020	324.5 (2019), 219.8 (2020)	retrospective, cross-sectional	Medical records
	Iio	2021	Japan (Kobe)	2016–2020	315 (2016), 300 (2017), 353 (2018), 347 (2019), 188 (2020)	retrospective, cross-sectional	Medical records
	Park	2005	Korea	2000–2002	86.4	retrospective, cross-sectional	Medical records
	Park	2007	Korea	2003–2005	104.2 (2003), 106.4 (2004), 104.6 (2005)	retrospective, cross-sectional	Medical records
	Park	2011	Korea	2006–2008	108.7 (2006), 118.3 (2007), 112.5 (2008)	retrospective, cross-sectional	Medical records
	Ha	2016	Korea	2007–2014	139.1 (2007), 131.0 (2008), 143.0 (2009), 161.7 (2010), 163.6 (2011), 163.9 (2012), 178.8 (2013), 188.4 (2014)	retrospective	Health Insurance Review & Assessment Service (HIRA) claims
	Kim	2022	Korea	2008–2017	254.5 (2008), 266.8 (2009), 314.3 (2010), 294.4 (2011), 300.6 (2012), 351.8 (2013), 327.4 (2014), 328.3 (2015), 396.8 (2016), 374.5 (2017)	retrospective	National Health Insurance Service data
	Kim	2014	Korea	2009–2011	127.7	retrospective, cross-sectional	Medical records
	Kim	2017	Korea	2012–2014	170.9 (2012), 194.9 (2013), 194.7 (2014)	retrospective, cross-sectional	Medical records
	Kim	2020	Korea	2015–2017	202.2 (2015), 197.1 (2016), 191.0 (2017)	retrospective, cross-sectional	Medical records
	Lim	2021	Korea	2015–2018	172.4	retrospective	Health Insurance Review and Assessment (HIRA) Open Access Big Data Platform
	Oh	2024	Korea	2012–2020	201.7 (2012), 224.0 (2013), 236.9 (2014), 231.2 (2015), 222.0 (2016), 217.3 (2017), 238.9 (2018), 230.0 (2019), 141.2 (2020)	retrospective	National Health Insurance Service data
	Heaton	2006	New Zealand	2001–2002	8	prospective	New Zealand Paediatric Surveillance Unit (NZPSU) Reports
	Gee	2023	New Zealand	2000–2017	15.6 (2000), 23.1 (2017)	retrospective	National Minimum Dataset
	Mat Bah	2021	Malaysia (Johor)	2006–2019	5.7 (2006), 10.5 (2007), 8.9 (2008), 9 (2009), 10.1 (2010), 14.4 (2011), 20.7 (2012), 19 (2013), 19 (2014), 14 (2015), 16.2 (2016), 19.2 (2017), 21.1 (2018), 19.5 (2019)	retrospective	National Medical Research Register

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Table 1. (*Continued*)

WHO region	First author	Publication year	Country	Study period	Incidence per 100,000 children <5 years of age	Study design	Data source characteristics
	Celis-Seposo	2024	Philippines	2009–2019	16.3 (2009), 23.2 (2010), 20.3 (2011), 18.7 (2012), 17.8 (2013), 16.5 (2014), 18.5 (2015), 14.9 (2016), 22.0 (2017), 20.5 (2018), 19.9 (2019)	retrospective	Philippine Pediatric Society (PPS) disease registry
	Lue	2014	Taiwan	1976–2007	0.06 ~ 8.88 (1976-1985), 16.79 ~ 35.50 (1986-1995), 42.40 ~ 66.24 (1996-2007)	retrospective	National Health Insurance (NHI), medical records
	Chang	2004	Taiwan	1996–2002	66	retrospective	National Health Insurance (NHI)
	Lue	2014	Taiwan	1996–2007	59 (1996), 52 (1997), 72 (1998), 68 (1999), 69 (2000), 76 (2001), 71 (2002), 59.9 (2003), 66.9 (2004), 74.8 (2005), 77.1 (2006), 70 (2007)	retrospective	National Health Insurance (NHI)
	Lin	2015	Taiwan	1997–2010	48.46 ~ 57.56 (1997-2003), 65.52 ~ 82.77 (2004-2010)	retrospective	National Health Insurance Research Database (NHIRD)
	Huang	2019	Taiwan	1997–2011	29 ~ 44 (1997-2003), 32 ~ 65 (2004-2011)	retrospective	National Health Insurance Research Database (NHIRD)
	Huang	2009	Taiwan	2003–2006	69	retrospective	National Health Insurance (NHI)
	Huang	2013	Taiwan	2000–2010	61 (2000), 67 (2001), 63 (2002), 56 (2003), 62 (2004), 68 (2005), 71 (2006), 68 (2007), 76 (2008), 69 (2009), 79 (2010)	retrospective	National Health Insurance (NHI)

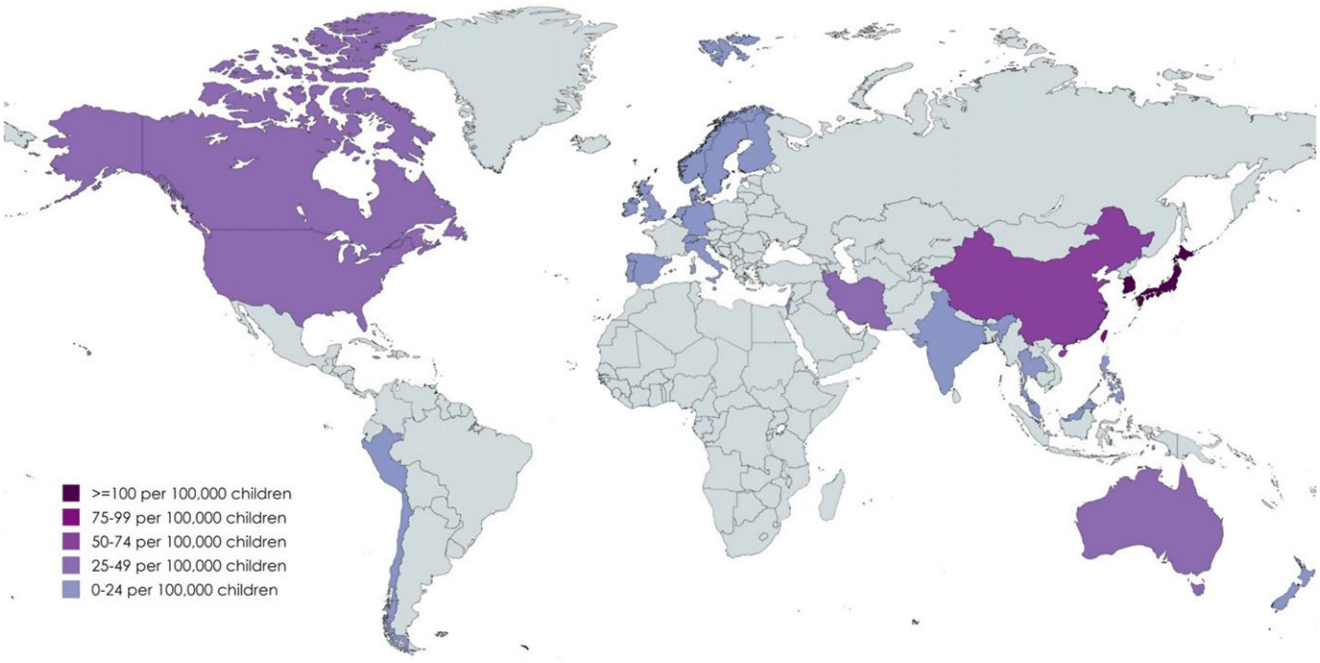

Figure 2. Global incidence of Kawasaki disease in children <5 years.

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genetic markers in these populations, particularly specific HLA alleles, suggests a genetic susceptibility to Kawasaki disease.[114] The notably higher incidence observed in studies from California and Hawaii, regions with a larger proportion of Asian populations within the United States of America, further suggests the potential influence of genetic factors in Kawasaki disease susceptibility.[15,23] The rapid industrialisation and improved sanitation in these countries align with the 'hygiene hypothesis,' which proposes that reduced exposure to infectious agents in early childhood may increase the risk of immune-mediated diseases like Kawasaki disease.[115] The well-established diagnostic criteria and heightened awareness of Kawasaki disease in Japan and Korea likely contribute to the higher reported incidence, as healthcare professionals in these countries may be more adept at recognising and diagnosing the disease.[116] The complex aetiology of Kawasaki disease necessitates further research to elucidate the precise contribution of each factor to the high incidence in Japan and Korea.

The observed temporal trends in Kawasaki disease incidence, as revealed in our systematic review, offer valuable insights into the evolving understanding and recognition of this disease. The general upward trajectory of Kawasaki disease incidence, particularly in the Americas and Europe, likely reflects improved diagnostic capabilities and heightened awareness among healthcare professionals. The increasing familiarity with Kawasaki disease's clinical presentation and the refinement of diagnostic criteria may have led to more accurate identification and reporting of cases, contributing to the observed rise in incidence.[117,118] For instance, the gradual increase in Kawasaki disease incidence in the United States, Canada, Chile, and Peru exemplifies this trend. The growing recognition of Kawasaki disease in these regions, coupled with improved diagnostic accuracy, likely plays a significant role in the upward trajectory. Furthermore, the admixture of populations and increased migration may have contributed to the rising incidence in certain regions.[119] The introduction of new genetic susceptibilities and environmental exposures through population mixing could potentially influence the occurrence of Kawasaki disease. The relatively high incidence observed in Hawaii, a region known for its diverse population, might be attributed, in part, to this phenomenon.[23,24,26] Conversely, the notable decline in Kawasaki disease incidence in Japan and Korea during the COVID-19 pandemic suggests the potential role of preceding infections in triggering Kawasaki disease.[65,98] The reduced circulation of common respiratory viruses during the pandemic might have contributed to this decrease, implying that exposure to certain infections may play a role in the development of Kawasaki disease. The decrease in incidence observed in these countries during the pandemic provides compelling evidence supporting this hypothesis. These temporal trends underscore the dynamic nature of Kawasaki disease epidemiology and highlight the importance of ongoing surveillance and research. The evolving understanding of Kawasaki disease, coupled with the potential influence of population dynamics and infectious triggers, necessitates continuous efforts to monitor and analyse incidence patterns. Such efforts will be crucial for developing effective prevention and treatment strategies and ultimately reducing the global burden of this disease.

This study is the first systematic review to assess the global incidence of Kawasaki disease comprehensively. However, several limitations warrant acknowledgement. Grey literature, which includes unpublished studies, conference abstracts, and reports, was excluded from our review due to the potential for publication bias and the difficulty in assessing the quality of these studies Additionally, the quality of included studies was variable, with quite a few studies demonstrating low methodological rigour. Future research should focus on identifying the specific factors driving the observed geographic and temporal variations in Kawasaki disease incidence. Large-scale, population-based studies with standardised diagnostic criteria and rigorous methodologies are needed to generate more precise estimates for specific populations. Investigations into genetic, environmental, and infectious triggers of Kawasaki disease are crucial for developing targeted prevention and treatment strategies.

Understanding the burden of Kawasaki disease has significant clinical implications. Comprehensive incidence data can inform the allocation of healthcare resources, guide public health interventions, and aid in the design of clinical trials for novel therapies. Recent evidence suggests that Kawasaki disease has surpassed rheumatic fever as the leading cause of acquired heart disease among children globally, not just in developed countries (Pilania RK, et al., Cardiology in the Young, In Press). This highlights the growing burden of Kawasaki disease worldwide and the need for increased awareness and research to address this evolving challenge. Our review highlights the need for further research on the incidence of Kawasaki disease in underrepresented regions, such as the Arab world. Also, scarcity of studies from the Eastern Mediterranean Region and the South-East Asia Region suggests that the true incidence of Kawasaki disease in these regions may be underestimated and warrants further investigation. Understanding the regional variations in Kawasaki disease incidence can help tailor diagnostic and treatment algorithms to specific populations, potentially improving patient outcomes.[120] Furthermore, recognising the geographic variability in Kawasaki disease incidence can help tailor diagnostic and treatment algorithms to specific populations, potentially improving patient outcomes.

This systematic review highlights the substantial global burden of Kawasaki disease and underscores the significant variation in incidence rates across different populations. It is crucial to recognise and address the regional variations in disease burden. Future research should prioritise elucidating the factors contributing to these variations, ultimately leading to more effective prevention, diagnosis, and management of Kawasaki disease worldwide.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S104795112500191X.

Data availability statement. The data that support the findings of this study are available on request from the corresponding author, YJC.

Acknowledgements. The authors thank Eun-Ji Kang from the Medical Library, Korea University, for searching abstracts and articles related to this study.

Author contributions. YJC conceived and designed the study. CRK gathered, processed, and cleaned the data. CRK analysed the data. CRK and YJC had full access to all the data in the study. JSL worked on project administration and methodology. CRK wrote the first draft of the manuscript followed by iterative revision with JSL. All authors substantially contributed to discussion of content and reviewed and edited the manuscript before submission. All authors were involved in the decision to submit and agreed to publish the paper.

Competing interests. All authors declare no competing interests.

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