A Bibliometric Analysis of Research Productivity on Kawasaki Disease in Southeast Asia: Trend and Socioeconomic Drivers

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ABSTRACT

Objectives. The increasing prevalence of Kawasaki disease in Southeast Asia (SEA) and its potential relation with Coronavirus Disease 2019 (COVID-19) infection resulted in heightened interest in KD in the region, thus, this paper aimed to determine the trend and the socioeconomic facilitators of scientific productivity of KD research within the region. Specifically, this article determined the number of publication and citations related to KD per country, institution, and journal. We also explored the networks of countries within the region to the rest of the world and the keywords mostly associated with KD research in the region. Lastly, correlation of these bibliometric indices with socioeconomic factors in the region was analyzed.

Methods. A literature search of KD papers in SEA was performed using Scopus database. We obtained bibliographic data from the available literature and visualized network of existing collaborations and keywords using VOSviewer software.

Results. A total of 196 papers were included in the study. Bibliometric analysis showed a rising trend in publication within the region, most of which were from institutions in Singapore and Thailand. The most common topics on KD studies included clinical features, complications, treatment, and comorbidities.

Country characteristics such as gross domestic product (GDP) per capita, research and development (R&D) expenditure (% GDP), and number of physician and R&D researchers were positively correlated with bibliometric indices of KD research in SEA. Moreover, number of international linkages was significantly associated with KD research productivity in the region.

Conclusion. In summary, we showed an increasing trend of KD research in SEA. Funding allocation and capacity building are necessary to strengthen research productivity within the region.

Keywords: bibliometric analysis, Southeast Asia, Kawasaki disease research productivity, socioeconomic drivers

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INTRODUCTION

Kawasaki Disease (KD) is one of the leading causes of pediatric-acquired heart disease in developed regions, predominantly affecting young children less than five years old worldwide.[1] It is a rare, systemic inflammatory vascular disorder with potentially life-threatening complications, including coronary artery aneurysms (CAA) and subsequent coronary thrombosis.[2-4] The prevalence rate varies in different nations globally with Japanese having the highest incidence at 219/100,000 children less than five years old.[4,5] Epidemiologic report by Kim and colleagues in 2019 showed that Northeast Asian countries, including Japan, South Korea, China, and Taiwan have continuously increasing

incidence that is 10-30 times higher than in the United States (US) and Europe, where values remain stationary.[6] Moreover, a growing number of cases in developing countries was also reported. However, there are still no comprehensive studies discussing the current situation of KD in Southeast Asia (SEA).

Diagnosis of KD is through clinical signs and symptoms. According to the American Heart Association, a suspected case of KD presents with persistent fever for 5 days, and at least four of associated signs and symptoms including redness and edema of the hands and feet, redness of the conjunctiva, lips, and mouth, having strawberry tongue, cervical lymphadenopathy, and/or coronary disease detected by 2-dimensional echocardiography or coronary angiography.[7,8] However, not all patients fulfill this criterion. Delayed diagnosis and therefore treatment, poses as the most important prognosticating factors for CAA development which affect 25% of reported cases.[8,9] Current guidelines recommend administering a single dose of intravenous immunoglobulin (IVIG) (2g/kg) with aspirin (80-100 mg/kg/day in divided doses every 6 hours) within 10 days of illness.[1] Nevertheless, incomplete understanding of the etiology of KD and its pathophysiology hampers urgent diagnosis and management of patients.

KD ensues greater social and economic burden to populations of low socioeconomic status (SES). Dionne and colleagues reported that patients with lower SES are being treated later than patients with greater SES.[9] In general, patients from lower SES have prolonged length of stay and have increased risk of developing giant CAA. Therefore, further research on KD especially in regions of lower SES is vital to the development of cost-effective preventive, diagnostic, and therapeutic modalities to mitigate potential complications and subsequent financial burden to patients.

The use of bibliographic studies could shed light to the current research trends in KD to address possible gaps. Unfortunately, there has only been several systematic and bibliographic studies discussing the KD updates worldwide. A recent association of KD with Coronavirus disease 2019 (COVID-19) renewed interest on this condition. Specifically, limited bibliographic studies have been published in the Asian region. To our knowledge, there is no systematic analysis of research trends in KD in SEA. Hence, we evaluated country characteristics and trends of published research in KD in the region and identified the factors that could impact research productivity on KD within the region.

METHODS

Search Strategy and Selection Criteria

A systematic review of available literature was performed using the Scopus database. We used the search term: TITLE-ABS-KEY (Kawasaki syndrom* OR mucocutaneous lymph node syndrom* OR Kawasaki diseas*) lifted from PubMed MeSH database. The search was limited only to Southeast Asian countries based on the regional division of the United Nations Organization. Publications under the following countries were included: Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, Thailand, Timor-Leste, and Vietnam. Documents categorized as original article, review, letter, note, short survey, conference paper, and data paper were extracted. Documents published from 1979 to 2024, written in English, and at the final stage of publication were included in the analysis. Removal of duplicates was performed after extraction of the whole document list from the Scopus database. All electronic searches were performed on September 11, 2024.

Data Collection

A total of 196 articles and documents were obtained from our search in the Scopus database. The following information was obtained for each article: authors, year of publication, title, journal, institution, country, keywords, citation frequency, source of funding, type, publication stage, and subject area of the KD studies.

Statistical Analysis

Correlations between country-specific characteristics and bibliometric indices were determined using Spearman's rank-order correlation. The information on the population, gross domestic product (GDP), GDP per capita, research and development expenditure (%GDP), physician-to-population ratio, and researcher-to-population ratio were obtained from the World Bank.[10] The Spearman's correlation coefficient (ρ) was considered significant if the p-value was less than 0.05. This statistical analysis was done using GraphPad Prism software version 8 (GraphPad Software, San Diego, CA). The visualization of collaboration networks of countries and keywords used for KD research in SEA was conducted using VOS viewer version 1.6.16 (Leiden University, Leiden, Netherlands).[11]

Ethical Review

This paper was applied for and granted exemption from ethical review by the Research Ethics Board of the University of the Philippines Manila.

RESULTS

Annual Number of Kawasaki Disease Publications

There were a total of 196 published researches related to KD in SEA from 1979 to 2024. Surge of KD research outputs started in 2018 (Figure 1). Despite this, publications from the region paled in comparison with the rest of the globe. Scientific papers from SEA only accounted for 1.7% of the total worldwide outputs on KD.

Kawasaki Disease Publications by Country

The total publications, total citation (TC), citation per publication (CPP), and *h*-index of SEA countries for

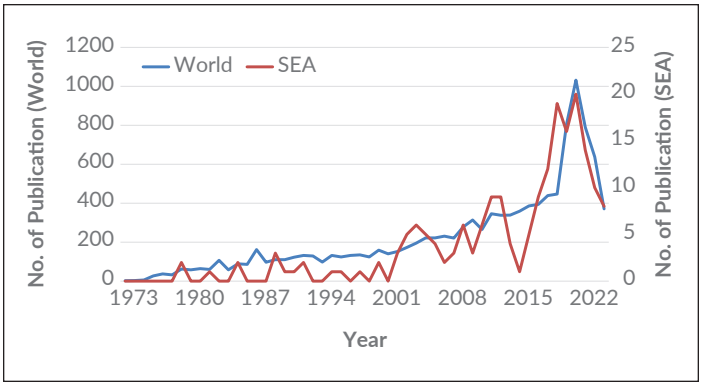

Figure 1. Comparison of the yearly publication related to Kawasaki disease in the World and in Southeast Asia (SEA) from 1973 to 2024.

Table 1. Citation Analysis of Kawasaki Disease Research Published per Country in SEA

Country*	TP	TC	CPP	*h*-index
Singapore	85	2263	26.62	23
Thailand	51	756	14.82	14
Malaysia	39	188	4.82	8
Indonesia	13	166	12.77	5
Vietnam	5	50	10.00	2
Philippines	5	33	6.60	2
Cambodia	1	14	14.00	1
Laos	1	0	0	0

TP – Total Papers, TC – Total Citations, CPP – Citations Per Paper

** Myanmar, Brunei Darussalam, and Timor-Leste (East Timor) have no registered publications on KD in Scopus on September 11, 2024.*

KD research outputs were presented in Table 1. Singapore had the highest number of KD research outputs and total citations among the SEA countries. Thailand and Malaysia also produced a significant number of publications on KD. Noticeably, Myanmar, Brunei Darussalam, and Timor-Leste (East Timor) had not contributed any scientific papers on KD in the Scopus database.

Network visualization was done to demonstrate partnerships outside of SEA (Figure 2). We noted that countries with higher KD research outputs had highest numbers of international collaborations. Singapore topped the ranking with 44 collaborators worldwide. Malaysia and Thailand followed with 25 global partners each. On the other hand, only four countries including Singapore, Thailand, Malaysia, and Philippines showed linkages with neighboring nations within the region.

Kawasaki Disease Publications by Institution

The top five institutions that recorded the highest output in terms of quantity and citation on KD research were in Singapore. The National University of Singapore contributed the greatest number of publications (38 papers) while A-Star, Genome Institute of Singapore topped the ranking based on total citations (Table 2).

Kawasaki Disease Publications by Journal

We noted that the top three journals that published KD research from the region were based locally. Singapore Medical Journal and Annals of the Academy of Medicine Singapore were from Singapore while Journal of the Medical Association of Thailand was based in Thailand. Despite this, majority belonged from international publishers. Furthermore, highest citation was recorded from PLoS, an international journal (Table 3).

Kawasaki Disease Research Trends in SEA

We determined the common topics associated with KD research in SEA through network visualization of keyword co-occurrence (Figure 3). The purple and yellow groups represented keywords related to coronary artery aneurysm, risk factors, and prevalence. The green group focused on registry, epidemiology, and SEA nations such as Singapore, Malaysia, Thailand, and the Philippines. On the other hand, red cluster included terms related to diagnosis (incomplete KD, echocardiography), coronary artery lesions, genetics, treatment [intravenous immunoglobulin (IVIG), methylprednisolone, off labeled indication], and multi-inflammatory syndrome-COVID 19 (MIS-C). Interestingly, blue cluster involved keywords about COVID-19 or multi-system inflammatory syndrome, vaccination, and adverse effects (Figure 3).

Country-specific Socioeconomic Factors and Correlation with Bibliometric Indices

We also performed a Spearman rank analysis to determine the socioeconomic factors that may affect research productivity in the region (Table 4). Gross domestic product per capita, number of Research & Development expenditure (% GDP), number of researchers in R&D, and physicians (per 1000 people) were positively correlated with research productivity in terms of total number of publications, citations, and *h*-index. Moreover, the number of research linkages worldwide positively influenced the total research output parameters (*h*-index, quantity of paper, and citation) in the region.

DISCUSSION

This bibliometric analysis showed the scene of KD research in SEA. Our results revealed a steady increase in the quantity of articles in the region, most of which were Singapore, Thailand, Malaysia, and Indonesia. The establishment of laws and publication requirements for scientific subsidy and as postdoctoral graduation in the late 2000s could have influenced the rise of research output in different countries within the region.[12,13] Moreover, the similarity of clinical

Table 2. Citation Analysis of Kawasaki Disease Research Published by Universities and Hospitals from SEA

Institution	TP	TC	CPP	*h*-index
National University of Singapore	38	1070	28.16	14
KK Women's and Children's Hospital	23	237	10.30	10
NUS Yong Loo Lin School of Medicine	23	574	24.96	10
A-Star, Genome Institute of Singapore	20	1338	66.90	15
National University Hospital	19	250	13.16	11
Mahidol University	18	426	23.67	8
National University Health System	13	79	6.08	4
Chiang Mai University	8	143	17.88	6
Prince of Songkla University	8	88	11.00	6
Chulalongkorn University	8	103	12.88	6

TP – Total Papers, TC – Total Citations, CPP – Citations Per Paper

Table 3. Top Journals that Published Kawasaki Disease Research from SEA Countries

Journal	TP	TC	CPP	*h*-index
Singapore Medical Journal	10	75	7.50	5
Journal of the Medical Association of Thailand	8	35	4.38	3
Annals of the Academy of Medicine Singapore	7	51	7.29	4
BMJ Case Reports	6	13	2.17	3
Journal of Paediatrics and Child Health	6	36	6.00	3
Medical Journal of Malaysia	6	9	1.50	2
Pediatrics International	6	45	7.50	3
Annals of Tropical Paediatrics	4	47	11.75	4
Pediatric Infectious Disease Journal	4	21	5.25	3
PLoS One	4	126	31.50	3

TP – Total Papers, TC – Total Citations, CPP – Citations Per Paper

Table 4. Correlation Analysis between Country-specific Characteristics and Bibliometric Indices for Kawasaki Disease Research in SEA

Country-specific characteristics	Bibliometric indices	R	*p*-value
Gross domestic product (in USD, millions)	Total publications	0.6988	0.0627
	Total citations	0.6905	0.0694
	h-index	0.7066	0.0578
Gross domestic product per capita (in USD)	Total publications	0.9639	**0.0008**
	Total citations	0.9762	**0.0004**
	h-index	0.9701	**0.0005**
Research and development expenditure (% GDP)	Total publication	0.9157	**0.0034**
	Total citations	0.9286	**0.0022**
	h-index	0.9222	**0.0025**
Researchers in R&D (per million people)	Total publications	0.8916	**0.0054**
	Total citations	0.9286	**0.0022**
	h-index	0.8982	**0.0046**
Physicians (per 1000 people)	Total publications	0.897	**0.0046**
	Total citations	0.8743	**0.0074**
	h-index	0.8795	**0.0058**
International research collaborations	Total publications	0.9334	**0.0020**
	Total citations	0.9222	**0.0026**
	h-index	0.9518	**0.0010**

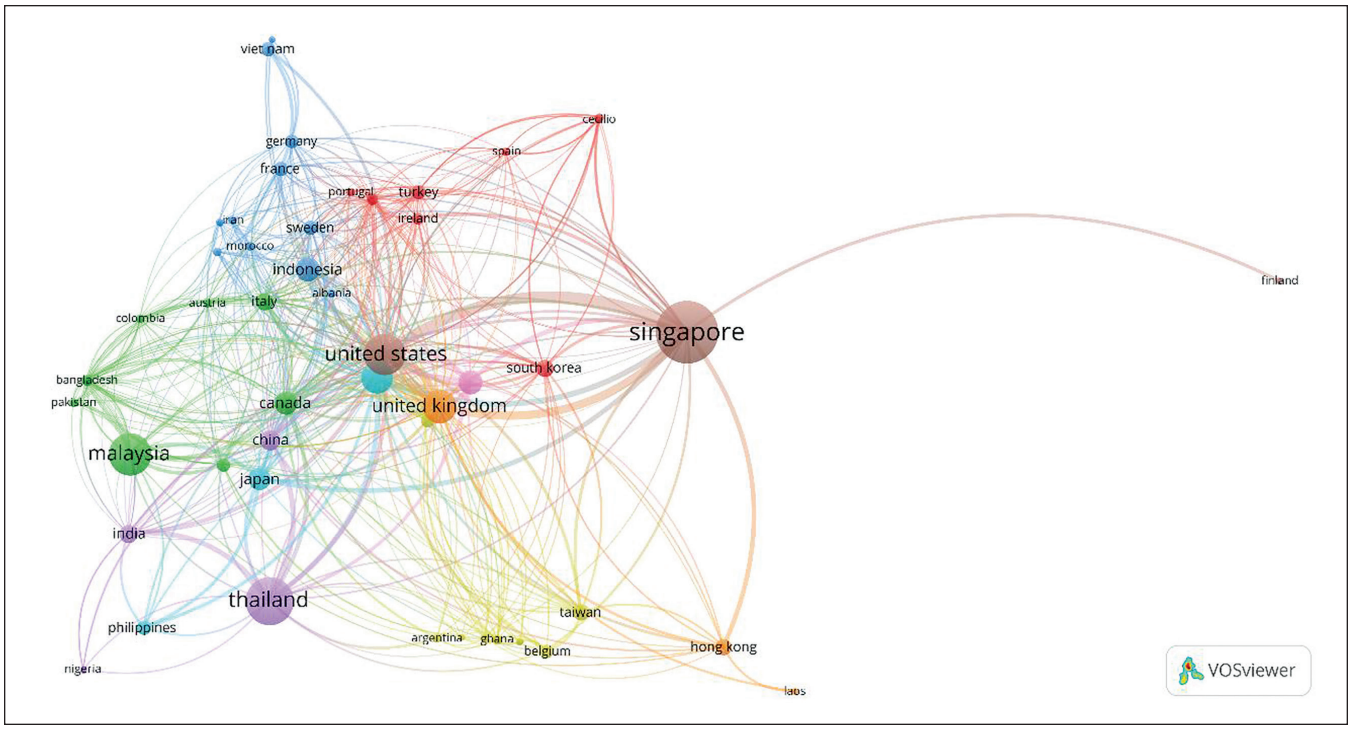

Figure 2. Network visualization of global partnership for Kawasaki disease research by Southeast Asian countries. Frame size is proportional to the number of collaborations of each country in the cooperation network. The thickness of the lines indicates the strength of the connection between countries.

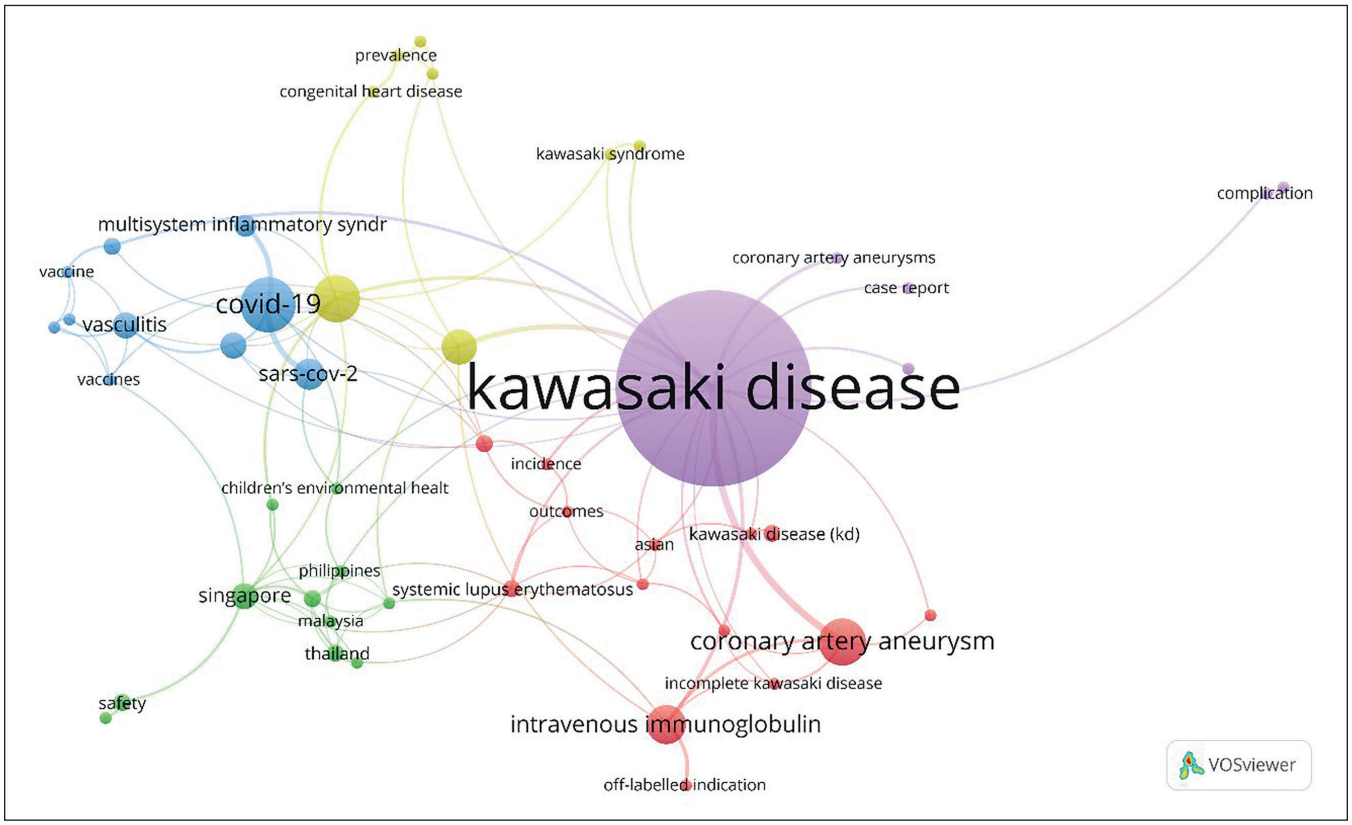

Figure 3. Keyword visualization of Kawasaki disease research in Southeast Asia.

symptoms of KD with the hyper-inflammatory state occurring in children infected with COVID-19 may have contributed to the upsurge of interest in KD from 2020 onwards.[14,15] Similar upward trajectory was reflected worldwide during the height of the COVID-19 pandemic. Despite this, KD publications from SEA countries still lag compared with other countries worldwide. Nations from within the region only contributed a mere 1.7% out of the total outputs globally. In addition, only eight out of eleven member nations in SEA were able to publish in Scopus-indexed journals.

Our findings reveal that a big portion of research papers and total citations arise from the top academic and/or research institutions in Singapore and Thailand. The four listed universities from Thailand are among the largest in the country. Our results are further corroborated by the study of Schoenfeld et al. which observed that research capacity is influenced by the size of the organization, with larger universities having more personnel to perform research projects.[16] Furthermore, it was noted that countries with the highest research outputs also have the broadest number of collaborators beyond the region. Our previous bibliometric study in SEA supported these data showing the influence of joint efforts in research productivity and scientific impact.[17] This further emphasizes the importance of institutional collaborations to the research productivity related to KD. Particularly, Singapore has its own research linkage program named Campus for Research Excellence and Technological Enterprise (CREATE), a program that establish connections with ten top ranking universities in different parts of the world including those in Switzerland, United States of America, and China.[18] Cocal et al. found that research organizations with external solid partnerships have a greater chance of producing scientific output compared to their counterparts.[19] Cooperation with countries that have better facilities and expertise in KD can assist other SEA nations to generate more data and research projects in their respective locality. Stronger partnerships will be useful in developing improved control and management of KD in the different countries within the region.

It is worth noting that despite having locally accredited papers occupying the highest ranks, international medical journals dominated the overall top ten list in terms of volume of KD publications. The preference to publish in international journals may be driven by using bibliometric indexes as parameters of global ranking of academic and research institutions. Often, international journals boast of higher impact factors and citation scores which subsequently perceived as greater visibility of one's work and prestige. Additionally, there are the rise of initiatives to include foreign publication as part of the career advancement scheme of faculty members, hence, compelling the universities and colleges to publish in internationally recognized databases.[20,21]

Despite the overall upward trend in the region, there are countries that have yet to contribute to the research outputs related to KD. The low research contributions may be due to limited published reports or unavailability of non-indexed publications in the Scopus database. Factors such as low English proficiency may shape the probability of getting accepted to Scopus-indexed journals. Non-native speakers of English may have lower acceptance rate into high-ranking international papers compared to their English-speaking neighbors. Previous study by Man et al. demonstrated that English proficiency increases the chance of publishing articles in international journals.[22] Aside from the abovementioned factors, our data showed that gross domestic product per capita, R&D expenditure, number of researchers in R&D, and physician (per 1000 people) are significantly associated with prolific KD research. Results revealed that Singapore, Thailand, and Malaysia which contributed the bulk of research papers and citations, are among the top countries with highest GDP per capita and number of personnel involved in R&D.[10] These findings suggest the importance of building human capacity and allotting funds for health research to increase research productivity in the region. Similarly, government-led initiatives that offer grants and incentives to prolific researchers are good predictors of self-efficacy and productivity in the field.[23-25]

Lastly, keyword visualization reflected in our study included clinical features, diagnostic test, disease complications (vasculitis, coronary artery aneurysms), treatment options including IVIG and methylprednisolone, risk factors, gene association, and COVID-19 infection. Recently, trend in KD research shifts globally due to heightened interest in its link with COVID-19.[26] It was observed that since the early phase of the COVID-19 pandemic, more articles discussed the occurrence of KD-like symptoms among pediatric COVID-19 patients. In fact, some of the articles covered in this analysis focus on the diagnostic dilemma of KD and KD-like disorders. Interestingly, etiologic agents are not part of the author's keywords among the articles mined in this region. The paucity of research tackling potential etiology of KD could lead to the misdiagnosis of this disease among at risk cohorts given that diagnostic criteria rely heavily on nonspecific early signs and symptoms. The existence of incomplete KD cases further aggravates the over or underdiagnosis of KD. The identification of a definite etiology could have established specific diagnostic criteria to detect KD at an early stage therefore preventing disease and/or complications among high-risk populations. Additionally, lack of priority in establishing comprehensive KD patient registry in the region may hamper efforts to clearly identify triggers of this condition. Multisystem inflammatory syndrome in children (MIS-C) also known as pediatric inflammatory multisystem syndrome (PIMS) and PIMS temporally associated with SARS-CoV-2 infection (PIMS-TS) share overlapping features with KD. Both diseases present with mucocutaneous symptoms including conjunctival injection (40%), mucositis (27.5%), cervical lymphadenopathy (4%), and edema of upper and lower extremities.[27,28] The presence of similar symptoms together with IgG against several coronavirus in KD patients

strengthen the possibility of a viral etiology of KD among genetically susceptible patients.[26,29,30] Coincidentally, a review of medical records of KD patients detect the presence of respiratory infection prior to the appearance of clinical symptoms and signs relevant to KD diagnosis.[31] Nevertheless, emerging evidence support the notion that MIS-C and KD are probably distinct disease entities despite numerous similarities. Firstly, KD usually affects children less than five years of age while MIS-C mostly occurs in adolescents with peaks among 7-11 and 18-21 years old. Gastrointestinal symptoms are also prominent in MIS-C but are rare in KD. In terms of treatment, MIS-C shares some parallelism with KD being treated as an inflammatory disorder, however, the former seems to require more aggressive management such as the use of inotropes and mechanical ventilation in 80% of patients. As in KD, IVIG by consensus is the first line of treatment with usual addition of glucocorticoids to prevent the fatal sequelae of severe cytokine storm.[27,28] But even with relatively good response of KD patients with IVIG, the presence of complications even among patients who were treated early in the course of their illness prompted the continued efforts to discover newer therapeutic targets.[27] Therefore, it is not surprising to see therapeutic options being repeatedly listed in the list of keywords in this study. New discoveries could improve clinical practice guidelines to better manage children of Asian descent who have shown greater risk for coronary aneurysm formation compared with their Caucasian peers. It is recommended that KD patients shall be given IVIG within 10 days after illness onset. Nevertheless, there are still cases of developing cardiovascular sequelae despite early intervention. In fact, Tremoulet and colleagues found that Filipino children (both parents are Filipinos) living in San Diego County show worse z-scores compared with their non-Asian peers even after early administration of IVIG.[4] Thus, it is not surprising to see therapeutic option repeatedly arise in the list of keywords. Sustaining the recent progress in KD research productivity within the region may generate further information on etiology and potential disease mechanisms that would eventually lead to better patient care.

We acknowledge that there are several limitations in this bibliometric study. For this analysis, we solely used research articles and published materials written in English, in the final stage of publication, and indexed in the Scopus database. In spite of restricting our search from one database, Scopus is recognized as one of the numerous databases with the largest collection of scientific articles. As for the type of papers covered in the analysis, majority of the documents were original articles comprising of at least 75% of the total publication, followed by reviews, letters, notes, editorial and survey. We recognized that papers categorized as reviews, letter, notes, editorial, and survey do not carry the same weight as original articles, however, they still provide valuable information to the growing knowledge on KD. These non-original articles include discussions on the epidemiology of KD cases and IVIG resistance in certain parts of the region, hypothesis on the host-pathogen interaction, pathogenetic mechanisms through genome-wide association studies, diagnostic and therapeutic gaps and opportunities especially on the utility of candidate biomarkers such as tumor necrosis factor and polymorphisms, case series/studies of disease sequelae, reviews on KD vasculitis as adverse event post-immunization, risk factors and outcomes of delayed diagnosis, case studies of atypical symptoms observed in affected children and possible mimicker of KD in both children and adult cohorts. All of these information were deemed important to the quest of understanding KD as a disorder. Moreover, socioeconomic factors gathered for analysis date back more than five years at the time of writing. This hinders the correlation of more recent status of country parameters to the bibliometric indices relevant to KD research. Despite this limitation, we were able to demonstrate the use of bibliometric analysis in mapping the progress and facilitators of research productivity of KD research in SEA.

CONCLUSION

In summary, this bibliometrics study showed an increasing trend of KD research in SEA. Highest research outputs in KD were from Singapore, Thailand, and Malaysia. Factors such as GDP per capita, number of personnel in R&D, R&D expenditure (%GDP) and strong international collaboration positively correlated with research productivity in KD study in the region. As of current, there is still no definite etiological agent attributed to KD and its mechanism is poorly understood. The continued efforts in discovering mechanistic pathways and novel therapeutic targets would be crucial in preventing life-threatening complications especially among high-risk patients. Hence, better funding and capacity building would be a tremendous boost in the field and could open opportunities to determine better strategies in curbing the prevalence of this condition in SEA.

Statement of Authorship

Both authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

Both authors declared no conflicts of interest.

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