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The Final thesis

Coronary Syndrome in Children with Inflammatory Heart Disease

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List of abbreviations

CAD	Coronary artery disease
CALs	Coronary artery lesions
CAAs	Coronary artery aneurysms
KD	Kawasaki Disease
iKD	Incomplete Kawasaki Disease
cKD	Complete Kawasaki Disease
IVIG	Intravenous immunoglobulin

Background

Coronary artery syndrome in children and adolescents is a rare condition, that might develop due to acute inflammation of the coronary arteries or due to anomalous origin of the left coronary artery (LCA). Early diagnosis and on time treatment initiation might be vital in some cases, especially among high-risk patients. Patients with chest pain, ECG abnormalities, and elevated troponin should be evaluated for coronary artery abnormalities. Coronary artery problems in children usually have a significant impact on both short-term and long-term outcomes. Early and accurate diagnosis, therefore, is crucial but technically challenging due to the small size of the coronary artery, high heart rates, and limited cooperation of children [1].

Inflammatory illnesses, such as rheumatic fever, Kawasaki disease, and viral myocarditis, can cause substantial acute cardiovascular damage and lead to long- standing complications in children. The acute presentations of these conditions are variable and can range from mild, nonspecific symptoms to life-threatening cardiovascular collapse [2]. Aforementioned pediatric inflammatory heart conditions, Kawasaki disease is a leading cause of acquired coronary artery disease.

Kawasaki Disease is a multisystem vasculitis but its most significant difficulty is the susceptibility to coronary artery vasculitis resulting in aneurysms occurring in up to a quarter of patients that remain untreated [3]. Such impediments increase the vulnerability of coronary vessels to thrombosis and stenoses with consequent risk of death and myocardial infarction [4]. Additionally, the aforementioned thromboses act as centre for accelerated vasculopathy in Kawasaki disease, increasing the risk of cardiovascular diseases.

The aim of the systematic review is to highlight the cases of coronary artery syndrome following treatment of Kawasaki disease. The objectives of the study include identifying the consequences of Kawasaki disease treatment, the causes of coronary artery complications after Kawasaki disease treatment and the possible solutions to the risk factors. This systematic review will highlight the relation between coronary artery syndrome and Kawasaki disease among the pediatric population.

CORONARY ARTERY SYNDROME IN CHILDREN WITH KAWASAKI DISEASE: A SYSTEMATIC REVIEW

Abstract

Introduction

Kawasaki disease (KD) is the leading cause of acquired coronary artery disease in children, typically presents in children below the age of 5 years. The male gender is more prone to the disease than the females. The standard treatment method is intravenous immunoglobin. The treatment can have shortcomings, and the main one is the development of coronary artery disease.

Methods

A systematic search of online databases was helpful for the systematic review. The databases include Cochrane Central Register of Control, PubMed, Science Direct, Web of Science, and EMBASE. Scrutiny was through thorough eligibility criteria that did not comprise the publishing year. The study included articles from different years.

Results

The search produced 940 articles which included various meta-analyses and systematic reviews. After going through the eligibility criteria, the appropriate Randomized Controlled Trials were forty. The other articles discussed non-relevant issues, and others were duplicates. The result of the systematic review indicates that IVIG resistant patients are at a higher risk for developing coronary lesions and aneurysms.

Conclusion

Intravenous immunoglobulin (IVIG) therapy is the main treatment principle for Kawasaki condition. In some patients, IVIG may lead to the development of coronary artery lesions, which might be associated with IVIG therapy resistance. There is subsequent research to curb the shortcoming by combining different treatment methods.

Keywords

Kawasaki disease, Echocardiography, Corticosteroids, Coronary artery disease, Aspirin, Intravenous immune globulin, Aneurysm.

Introduction

Kawasaki disease (KD) is also referred to as mucocutaneous lymph node syndrome.

The risk population is mostly infants and children below five years [5]. The disease is most common in children of Asian descent and is more is predominant among the male gender. In the early stages of the disease, the symptoms include joint pain, peeling skin, red eyes, swollen glands, swollen hands and legs, cracked and red lips, irritability, diarrhea, vomiting, fast heart rate, rashes, and fever [6]. The symptoms become complicated when the disease progresses, with the main development being blood vessel inflammation. Despite the life-threatening aspects of Kawasaki disease, it is treatable. The treatment is according to varying factors like the stage of the disease and the child's age, symptoms, and general health conditionn [7]. Although the inflammatory response is found in small and medium vessels of the body, the most common sites of inflammation and end-organ damage are the coronary arteries [8]. The severity of the condition is also a determining factor. Early discovery of Kawasaki disease translates to the appropriate treatment method. Research has influenced how people handle Kawasaki disease making the condition manageable.

The main treatment for Kawasaki disease is the employment of aspirin and high-dose intravenous immunoglobulin. When aspirin and intravenous immune globulin treatment fails, the physician mostly prescribes other medicines, including corticosteroids [8]. Children with Kawasaki disease often improve health-wise, but there are exceptional conditions where serious complications can occur. Complications involving the heart include weakening of an individual's heart arteries, also known as coronary artery aneurysm, malfunctioning heart muscles or heart attack, malfunctioning heart valves, heart failure, and heart muscle inflammation, also called myocarditis, heart covering, also called pericarditis inflammation and endocarditis or heart lining inflammation [8].

During the acute phase of KD, tachycardia, a gallop rhythm, murmurs and decreased myocardial contractility secondary to myocarditis have been observed in the affect children. Electrocardiography (ECG) may reveal arrythmias, prolonged PR interval, ST segment depression or elevation and T-wave inversions. When a child develops a coronary artery aneurysm, they should undergo echocardiograms in several of the subsequent years following the illness. There are no defined guidelines for antiplatelet therapy for thrombosis prevention in children and infants. Therapeutic regimens used in patients with Kawasaki disease depend on the severity of coronary involvement and include antiplatelet therapy with aspirin, with or

without dipyridamole or clopidogrel; anticoagulant therapy with warfarin or low-molecular-weight heparin; or a combination of anticoagulant and antiplatelet therapy, usually warfarin plus aspirin [9]. Follow-up visits to the physician are essential despite the child's health doing well. Following coronary artery disease after Kawasaki treatment, the individual might suffer complications in the future like heart attacks [8]. Kawasaki condition is treatable, but an individual should have various follow-up sessions to ensure that they are safe from the shortcomings of the treatment forums.

Diagnosing Kawasaki translates to eliminating other possible conditions [10]. If a child has a five-day fever, they must entail four or five of the below symptoms to qualify as Kawasaki diseasese [11]. They include rash, red eyes, swollen lymph nodes, changes in the mouth lining, or skin changes in the feet or hands. The other recommended examinations include cardiac catheterization, lab tests, echocardiography, and electrocardiography [12]. The diagnosis is often based on the echocardiogram findings suggestive of coronary artery abnormalities. In patients with typical clinical presentation, initial echocardiography should be performed when the diagnosis of Kawasaki disease is considered. The treatment initiation should not be delayed.

In previous studies, intravenous immunoglobulin treatment has various shortcomings. Research highlights that 5% of infants or children with Kawasaki disease develop coronary aneurysms in the long run. 1% of the children who have Kawasaki disease suffer subsequent giant aneurysms [13]. Physicians state that for fast recovery, early detection and treatment are necessary. Failure to take quick action the risk of creation of aneurysms fastens fivefold. The coronary aneurysms evolution is fast and dynamic [14]. It can arrive at the peak in the initial six weeks following infection in some extreme conditions. In the subsequent 24 months, the development probability of myocardial infarction resulting from coronary artery thrombosis comprises a significant increase. The risk factors following the failure of early treatment initiation and diagnosis of Kawasaki disease among infants and children make the phenomenon vital. Therefore, identifying populations at a high risk of CAL is crucial to initiating early intervention. Otherwise, a large aneurysm can develop and lead to mortality and morbidity [5].

There have been rising cases of Kawasaki disease among children in various states, making the condition a lucrative research subject. There have been rising statistics in nations like Japan and the United States. Researchers do not view Kawasaki disease as a rare

development basis of an acute coronary syndrome. Present studies focus on applying corticosteroids for Kawasaki disease treatment among children and infants [19]. There is a shortcoming in the research related to Kawasaki condition treatment following conflicting results. Despite numerous evidence supporting the beneficial responsibility of the treatment, there are many mysterious elements related to corticosteroid application involving the best patient treatment group and the most effective structure [19]. Different professionals apply intravenous immune globulin as the major treatment protocol and corticosteroids as the following treatment option following the failure of the second intravenous immune globulin dose [19]. The shortcomings of the treatment modes have led to numerous research on the clinical elements of Kawasaki disease.

Methods

Literature Search

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to report the systematic review. Literature inclusion was not impacted by any influential or external factors hence minimal biases. It was difficult to follow the search protocol following persuasions from different factors which looked viable. However, the study strictly adhered to the protocol for proper insights on the coronary artery events in Kawasaki disease patients. A search was conducted on numerous online databases including PubMed, Cochrane, Google scholar, ScienceDirect, CINAHL, and Embase. The articles were selected according to their relevance to the topic of research, they were also authored in English language. The sources had no time limit to facilitate acquiring numerous information on the subject in different eras. The study designs included in the search for the systematic review included randomized controlled trials, Observational study designs, quasi-randomized, cross-over, cohort non-randomized controlled studies, controlled clinical trials, cluster-randomized and systematic reviews related to coronary artery syndrome in children with Kawasaki disease. The search was limited to scholarly works and peer-reviewed articles published under conventional channels. Therefore, all articles written in any language other than English, or irrelevant to the research topic coronary artery syndrome in children with Kawasaki disease were excluded.

Guidelines and Selection Criteria

All studies relevant to Coronary artery syndrome in children with Kawasaki disease were included in the research. The sources which qualified to be part of the systematic review had specific qualities which ruled out the others. One criterion is that the population in question should be children from 5 years and below. The other qualification is that the population should be suffering from Kawasaki disease. The participants of the studies had acquired Kawasaki disease treatment. The treatment modes include IVIG, aspirin, or corticosteroids. The sources also discussed the shortcomings and risk factors of the treatment modes, including aneurysm. The systematic review also included investigations that did not major mainly on the treatment models for Kawasaki disease but on the repercussions which is coronary artery syndrome. The studies illustrated a retrospective and prospective nature for more information, leading to substantial conclusions. The study included database studies and clinical trials for compelling research results. The geographical location of the sources and the ethnicity and race of the populations were not elimination factors. The studies included African Americans, Asians, Latinos, Americans, and Europeans. Following initial selection of the articles, their abstracts and titles were skimmed to assess their relevance to the research topic. The exclusion criterion was on sources discussing specifically the treatment of Kawasaki condition. The other eliminated sources highlighted coronary artery syndrome from other conditions apart from Kawasaki disease and those whose population interest was not children below five years. The language also eliminated other sources which were not in English. The inclusion and exclusion criteria were essential for the systematic review in acquiring the appropriate sources.

Search String

Coronary Artery Syndrome in Kawasaki Disease Patients

Database	Search String
PubMed	((Intravenous Immune globin AND Kawasaki disease AND Coronary artery lesions))
PubMed Central	("risks" OR "shortcoming") AND ("Intravenous Immune globin OR "aspirin") AND ("Kawasaki disease" OR "mucocutaneous lymph node syndrome") AND ("coronary artery disease" OR "aneurysm")
Cochrane	("Corticosteroid) AND ("intravenous Immunoglobulin") AND ("Kawasaki disease") AND ("coronary artery disease" OR "aneurysm")
NCBI	((Intravenous Immune globin AND Corticosteroid AND Kawasaki disease AND coronary artery disease AND heart failure))

Data Extraction, Quality Assessment, and synthesis

The information recorded from the articles mean age of the participants, the study design, number of participants, treatment method, research conclusions, primary and secondary outcomes. The treatment options included intravenous immunoglobulin, aspirin, and corticosteroids. The Cochrane Revman Software was used to conduct a meta-analysis of the different sub-group data that was collected; a descriptive analysis of the collected data was also completed. All the information from the articles that passed the inclusion criteria and were fully eligible articles was collected, analyzed and tabulated into a preset extraction table that constituted diverse variables. The Research and Quality Scoring Method was used for the examination of the quality of the selected sources; the different articles were rated based on selected aspects. Ultimately, the final quality of the selected articles was measured depending on the collective score of every rating metric. Each article was rated from 0-9 depending on the combined quality. A collective score of 0-5 showed low quality articles while 6-9 showed high quality articles. Unfortunately, the combined quality does not in any way guarantee

faultlessness of the article. GRADE (Grading of Recommendations Assessment, Development, and Evaluation) was applied to assess the quality of the articles in addition to their confidence level. The risk-of-bias tool that was used for analysis of the reliability and transparency of the results was Cochrane Reveman Software. Any inconsistencies relating to any aspects of the selected articles were resolved during the process of data extraction.

Study Selection

The initial search in the online databases using the earlier mentioned keywords identified 940 studies. After removal of duplicates, only 336 studies were left. The abstracts and titles of the 336 studies were scanned to determine their relevance for the systematic review. After elimination, 46 articles remained; they were examined based on the eligibility criteria. Finally, 13 articles were identified which successfully passed the predefined eligibility criteria. The diagram below shows PRISMA diagram for the selection process.

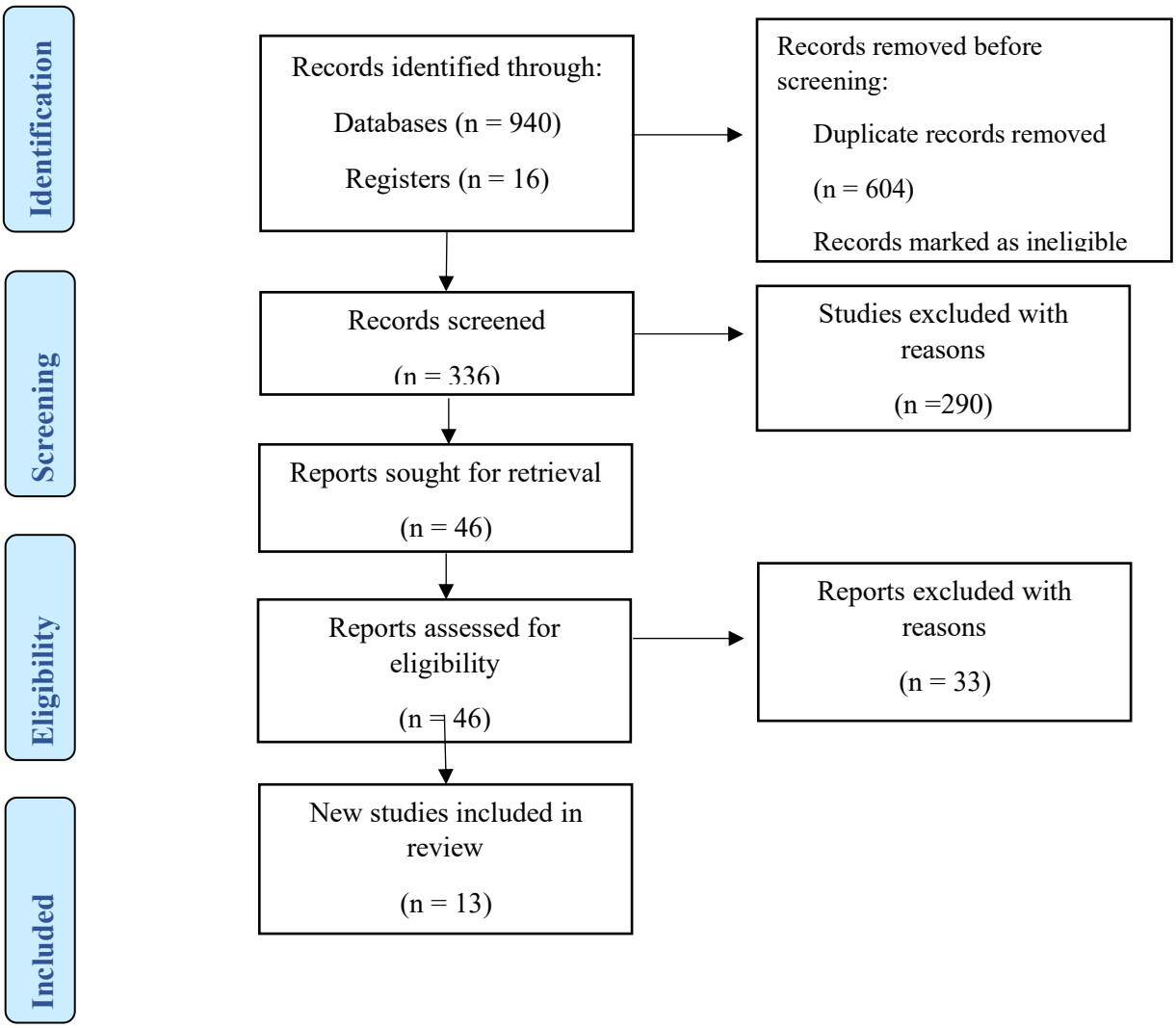

Figure 1. PRISMA flow chart for study selection process.

Results

Table 1. Basic characteristics of included studies

Serial No.	Author/Year	Type of study	Study Population	Data Collection	Method of Analysis
1.	Duan et al., 2020	RCTs	982	Clinical data	Univariate and multivariate logistic regression analyses
2.	Turkucar et al., 2020	Experimental	94	Clinical, laboratory, and echocardiographic data	SPSS
3.	Zhao et al., 2016	RCTs	2331	Clinical records	Multivariable logistic regression analysis
4.	Mossberg et al., 2021	Clinical trials	77	Clinical records	Multivariate analysis
5.	Kwak et al., 2014	Experimental	11	Clinical records	Qualitative visual analysis
6.	Jone et al., 2019	RCTs	69	Clinical records	R version 3.3.2

7.	Chang et al., 2020	Realist Evaluation	478	Clinical records	Multivariate logistic regression analysis
8.	Huang et al., 2022	RCTs	1293	Clinical records	least absolute shrinkage and selection operator
9.	Li et al., 2022	RCTs	635	Clinical records	Univariate analyses and binary logistic regression
10.	Piram et al., 2020	RCTs	465	Clinical records	Multivariate regression analysis
11.	Okada et al., 2003	RCTs	32	Clinical records	Multivariate analysis
12.	Kobayashi et al., 2012	Realist Evaluation	125	Clinical records	Intention to treat
13.	Kobayashi et al.,2009	Clinical trials	896	Clinical records	Univariate analysis

Data analysis

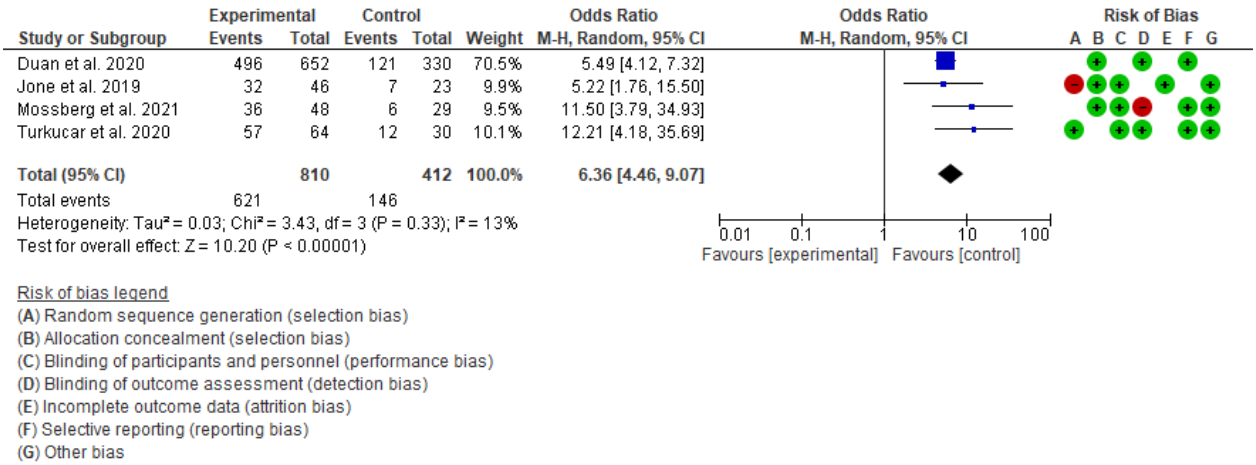

Figure 2: Forest plot indicating the relation between intravenous immunoglobulin (IVIG) and Coronary artery syndrome.

A random-effects model was applied for the subgroup analysis. The risk of coronary artery events among Kawasaki disease patients is 6.36 (95%CI, 4.46 to 9.07) on a 0.5 to 100 Visual Analogue Scale (VAS). The difference between the two events was 0.00001. The articles had high heterogeneity (P<0.33), and I^2 statistic is equal to 13%. The plot shows that Kawasaki disease patients are at a high risk of contracting coronary artery events.

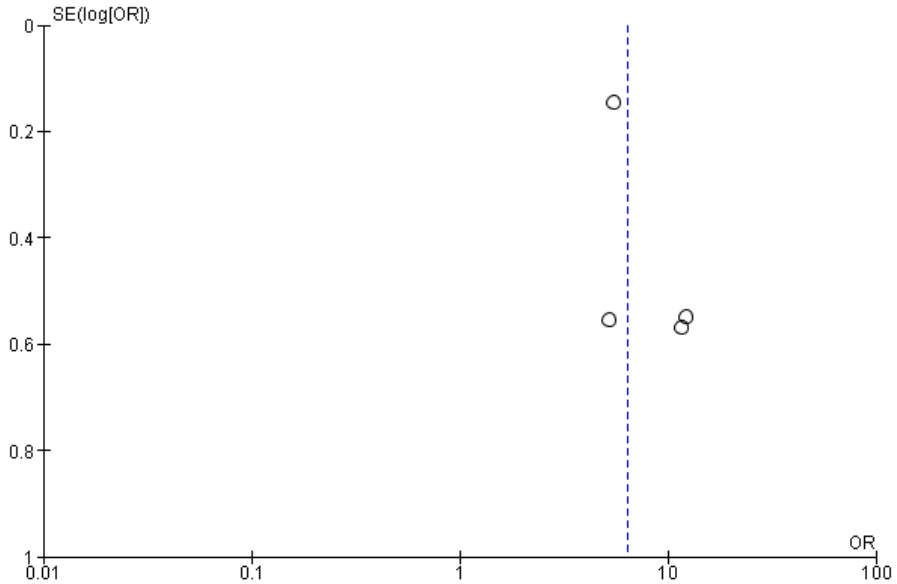

Figure 3: Funnel plot indicating the relation between intravenous immunoglobulin (IVIG) and Coronary artery syndrome.

Risk of Bias

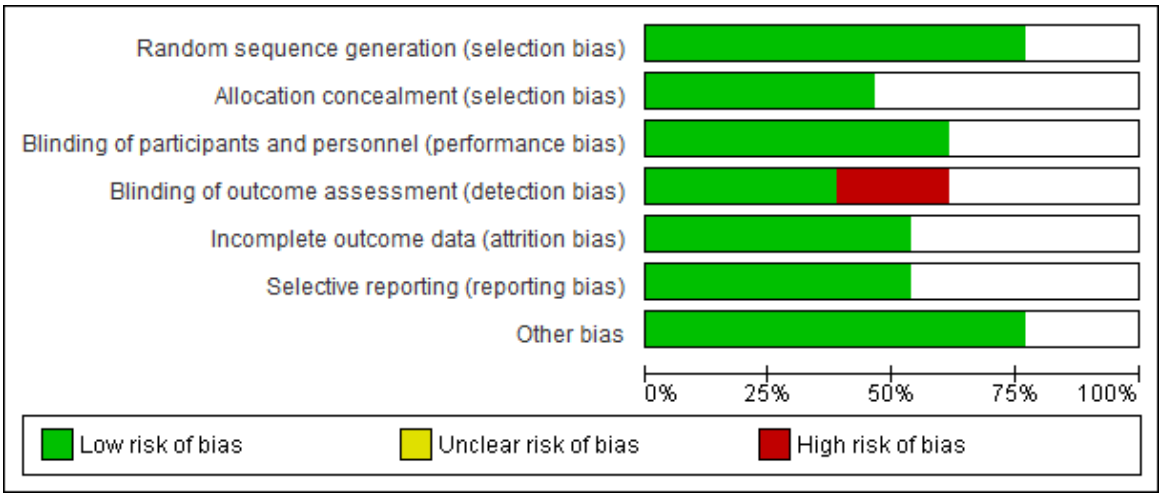

Figure 4: A risk of bias graph indicating the relation between IVIG and Coronary artery syndrome

The summary of the risk of bias was in Review Manager (RevMan 5.4.1), a Cochrane software. The results highlighted that the general risk of bias is averagely low. The allocation concealment selection bias, the blinding of participants, random sequence generation selection bias and personnel performance bias were generally low. There were no studies indicating unclear bias. The other risks that recorded a low bias risk include incomplete outcome data attrition bias and selective reporting bias. Other forms of risk of bias that were unmentioned in the graph recorded low risk. The blinding of outcome assessment detection bias also indicated high risk. The judgment in reviewing each risk of bias of various sources is properly presented in a summary and a graph as percentages in all the included studies in figures 4 and 5, respectively.

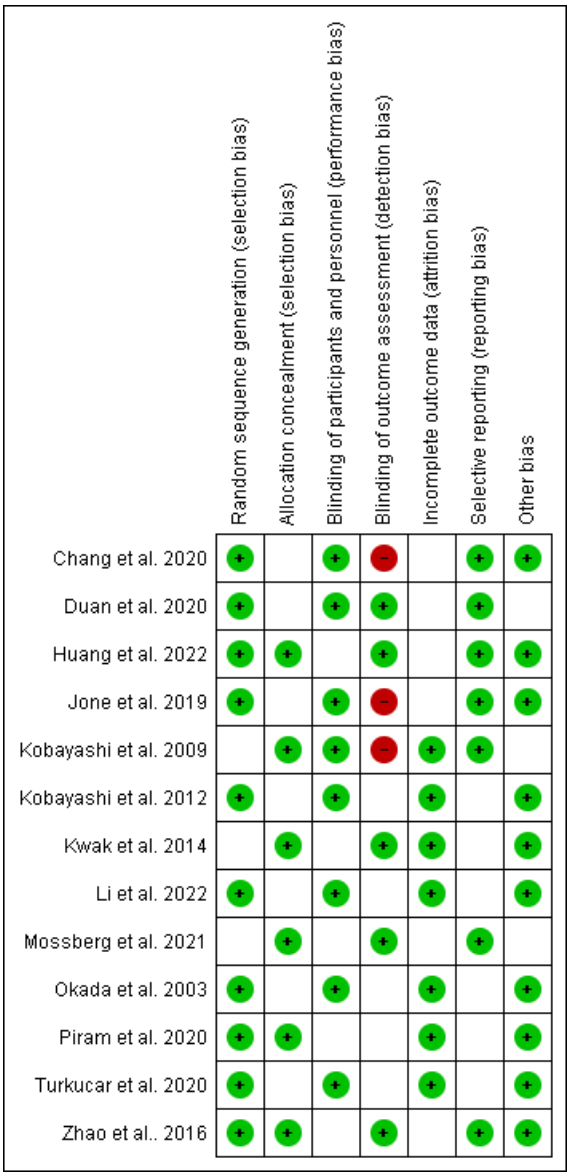

Figure 5: A risk of bias summary indicating the relation between IVIG and Coronary artery syndrome.

Discussion

The systematic review indicates that male Kawasaki patients record increasing erythrocyte sedimentation rate (ESR). The other outcome of review is that there are delaying cases of the use of IVIG [8]. Independent risk features for Kawasaki condition complicate coronary artery lesion (CAL) [1]. According to the results of the study, the CAL incidence rate is 10.6 % (104/982) Univariate analysis is instrumental in Kawasaki disease research, and in the study, it indicated that the two groups had substantially varying ESR, gender, fever duration, platelet count, and IVIG administration initiation time [11]. The male gender is at the risk of

contracting Kawasaki disease and forms the risk population for coronary artery disease from IVIG treatment.

The systematic review indicates that the IVIG resistant groups record a higher CALs rate than the IVIG responsive group. There is statistical significance in the risk factors which detect IVIG resistance in Kawasaki disease before the treatment [14]. The research develops a new risk-scoring structure to predict IVIG resistance among children with Kawasaki disease following the laboratory and clinical features. The information is useful for deciding the appropriate treatment for Kawasaki disease in preventing coronary artery involvement [8]. Early detection of the type of the Kawasaki condition ensures that there is an appropriate medication for the IVIG resisting population.

According to the results of the study, Kawasaki condition treatment has various CALs incidences, including coronary artery aneurysms and dilations. The coronary artery dilatations independent risk factors include incomplete Kawasaki disease, male patients, C-reactive proteins, and longer fever duration. Male, longer fever duration, incomplete Kawasaki disease, prolonged illness days at the commencement of the treatment, albumin <35 g/L corticosteroid therapy, and sodium ≤133 mmol/L are independent risk factors for coronary artery aneurysms (CAAs) according to the systematic review [11]. Risk factors for giant CAAs include albumin <35 g/L, corticosteroid therapy, and prolonged illness days at the initial treatment [15]. CALs have a strong relationship with longer fever duration, males, incomplete Kawasaki disease, corticosteroid therapy, prolonged days of illness at the initial treatment, albumin <35 g/L, CRP >100 mg/L, and sodium ≤133 mmol/L. For CAAs and giant CAAs, corticosteroid therapy is an independent risk factor [1]. Application of corticosteroids in treating Kawasaki Disease should be with caution following the CALs risk.

The systematic review states that there is an extremely high CAA frequency in infants and young children with Kawasaki disease. The relation between CAA risk and age is significant in children and infants presenting with incomplete Kawasaki disease (iKD). The cause of the CAA high frequency can result from treatment delays in the Kawasaki disease population [8]. Early treatment and detection are crucial when one suspects Kawasaki Disease in young children or infants with incomplete symptomatology which minimizes occurrences of coronary artery syndrome [14]. Complete Kawasaki Disease (cKD) and incomplete Kawasaki Disease (iKD) are different entities needing distinct therapeutic procedures [16]. There is a need for more research on the Western population as the Asian setup conclusions cannot

apply to them. The systematic review states that there should be an evaluation of the obstruction and collateral changes for Kawasaki disease patients to prevent myocardial infarction further [15]. Early detection and treatment of Kawasaki disease are crucial to sabotage shortcomings resulting from cKD and iKD treatment.

The systematic review highlights that IVIG is a powerful treatment strategy, but it cannot be self-sufficient in some circumstances. Research indicates that when combined with other therapy forms like infliximab, it can lead to better results while minimizing the shortcomings. Combining infliximab with IVIG as an initial therapy procedure minimizes the essence of additional therapy in Kawasaki disease patients with CALs. Intense initial therapy, entailing IVIG and infliximab, is the most appropriate for KD patients [16]. Identifying risk population children is essential for preventing the development of CAL. Independent risk factors contributing to CAL development include being of the male gender, IVIG resistance, CRP > 103 mg/L, and NLR > 3.5. IVIG is the primary KD treatment but combining it with other forms of therapy would lead to better results, including minimizing shortcomings.

According to the results of the systematic review, there was employment of a predictive nomogram developed using nine factors related to IVIG resistance in Kawasaki disease patients. The outcome is that it was a helpful tool for identifying patients who would likely be IVIG resistance. The nomogram has a likelihood of minimizing coronary artery lesions risk [6]. Previous studies have not indicated the IVIG resistance scoring structures recording good performance. In some countries like Eastern China, tools for predicting IVIG resistance risk are absent [6]. IVIG resistance risk factors in hospitalized Kawasaki disease patients include platelet count, percentage of neutrophils, serum sodium, incomplete Kawasaki disease, serum alkaline phosphatase levels, coronary artery damage, CRP, and serum albumin [15]. Researchers have established an easy-to-use nomogram for predicting the IVIG resistance risk factors for hospitalized children [14]. IVIG resistance is a major obstacle in treating Kawasaki disease, making it a major subject for numerous research.

Clinical pediatrics should have skills and expertise for early prediction and identification of IVIG-resistant Kawasaki disease patients according to the systematic review. Research has developed a useful, inexpensive, and easy-to-perform predictive scoring structure in various centers with an efficient predictive ability for IVIG-resistant Kawasaki disease cases [15]. The model would assist pediatricians in forecasting the IVIG-resistant Kawasaki Disease patients to provide reasonable therapeutic structures for Kawasaki disease in children [10].

Research continuously focuses on the solution programs for Kawasaki disease complications to ensure a full recovery.

In most Kawasaki disease patients according to the systematic review, the initial treatment is not enough. Most of them need the second-line treatment [18]. Secondary treatment predictors following the initial IVIG have hepatomegaly levels as greater than or equal to 30, with the treatment days being less than five days and the lymphocyte count being less than 2400 per millimeter squared [19]. Research has established proper IVIG resistance predictors while developing new scores with acceptable specificity and good sensitivity among different populations, especially the non-Asian, which is most risky [19]. Predicting IVIG-resistant patients will assure appropriate covering of the subsequent risks from the treatment like coronary artery syndrome.

The systematic review states that patients with Kawasaki disease have high interleukin pretreatment serum levels. Administering IVIG treatment alone can be ineffective but combining it with corticosteroids will result in exemplary results [16]. The other improvements in the patients' health include a shorter fever duration and a decreased C-reactive protein concentration [10]. Research highlights that corticosteroids quickly ameliorate symptoms by minimizing cytokine levels in Kawasaki disease patients [16]. Coronary artery abnormalities are lower when the doctors administer intravenous immunoglobulin and prednisolone [17]. The action improves patients' health with Kawasaki disease among different populations by minimizing the risks following the treatment procedure [18]. Combining IVIG with other therapy forms like corticosteroids minimizes the shortcomings of the treatment strategy.

Limitations

In this systematic review efforts were applied to limit and control the number of variables that would be used for analysis. The restrictions were applied through a sensitivity analysis of all the studies that passed the eligibility criteria. The possibility of bias exists owing to the diverse intrinsic differences between selected studies with different designs. Additionally, although the studies were varied with respect to their different respects including the type of corticosteroids used and other combinations of treatments, they were limited in their representation. For instance, most of the studies were authored in Asian countries such as China and Japan, where there are more cases of Kawasaki disease. However, it would be

advantageous to gain the perspective of research conducted in other parts of the world such as Europe, a new component that affects the treatment strategies may be discovered. Most included studies were conducted in Asian countries, where the high awareness of KD may lead to an earlier treatment than in other countries. It is therefore impossible to determine whether the results of the systematic review and apply to other regions as well.

There were some contradicting results in the studies that were focusing on the same variables. The contradictions may be due to different quantities of the measured variables including dosing quantities. For instance, the category of corticosteroids and the dosing varied significantly according to the study. Owing to the numerous differences, there were many inconsistencies especially during subgroup analysis. Therefore, the results of the analyses are subject to scrutiny, they are not an accurate representation of the true nature of use of the treatment. In some cases, subgroup analysis was not possible owing to the limited number of studies that passed the eligibility criteria for inclusion. The research should focus on more varied treatment options for Kawasaki disease including different categories of corticosteroids. Additionally, the follow-up period should be increased to assess any side effects or symptoms that may fail to appear short-term. The limitations also included a language where some articles with important information were eliminated as they were not in English. The aforementioned limitations negatively impacted the reliability of the data collected and the overall quality of the systematic review.

Conclusion

Kawasaki disease is a rampant illness among children below five years. The disease mostly affects boys, and the treatment method is either aspirin or intravenous immunoglobin. The treatment method has its shortcomings for the patients. Development of coronary artery complications, such as coronary lesions and aneurysm is the main shortcoming. Research has looked into the problem, and one of the solutions is combining two methods of treatment to curb the repercussions. Among the medications whose combination with intravenous immunoglobulin can curb the development of coronary artery disease is corticosteroids. Prednisolone is the other medication form that physicians often combine with intravenous immunoglobulin. In children with severe degree of coronary lesions, early diagnosis translates to early treatment hence curbing the risk of contracting coronary complications.

Recommendations

For patients especially children with Kawasaki disease that may be clinically considered to be at high risk for non-response to treatment using intravenous immunoglobulin, medical personnel may consider the application of primary corticosteroid treatment combined with intravenous immunoglobulin to diminish the risk of development of abnormalities such as Coronary artery lesions. Medical personnel should consider whether these results are relevant to their patient population. Heterogeneity in the dosage of corticosteroid across the different clinical trials included is a significant consideration. A significant percentage of the population that was included in the studies were high risk patients, some of them had a high risk of intravenous immunoglobulin resistance. It is impossible to determine whether the combined treatment could be effective in all patients with Kawasaki disease. Future researchers should consider the generality in the applicability of the treatment.

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