

Most common findings of carditis in children with rheumatic fever: a literature review.

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Abstract: Rheumatic Fever (RF) is an autoimmune disease triggered by *Streptococcus pyogenes*, primarily affecting children and young adults. Its most severe complication, carditis, leads to Rheumatic Heart Disease (RHD), impacting over 15 million individuals globally, with 500,000 new RF cases annually. Cardiac involvement occurs in some cases of RF patients, characterized by pancarditis and heart valve damage due to molecular mimicry. Contrary to literature expectations, male patients exhibited in this research a higher incidence of rheumatic carditis. This study reveals mitral regurgitation (90%) and aortic regurgitation (85%) as prevalent manifestations of rheumatic carditis, while Erythema marginatum and Chorea are less frequent.

Keywords: Carditis; Rheumatic fever; Children.

1. Introduction

Rheumatic fever (RF) is an acute disease characterized by an autoimmune response resulting from pharyngotonsillitis caused by *Streptococcus pyogenes*, also known as Group A streptococcus (GAS). RF primarily affects children and young adults. One of its most serious complications is carditis, which is responsible for chronic and often disabling sequelae.

Around the world, there are over 15 million people with chronic heart disease because of RF, with approximately 500,000 new cases of RF occurring annually.(1)

Cardiac involvement, the most severe complication of Rheumatic Fever (RF), occurs in 30 to 45% of patients. Typically, this involvement manifests as pancarditis, leading to irreversible damage to heart valves, a condition referred to as Rheumatic Heart Disease (RHD). RHD is the result of immune responses involving cross-reactions between streptococcal antigens and proteins found in human heart tissue, a phenomenon known as molecular mimicry.(2-4)

It is known that there is still a high number of misdiagnoses of carditis caused by rheumatic fever due to the lack of specific clinical signs, which poses a diagnostic challenge.(5)

The pronounced symptoms seen in chronic rheumatic heart disease stem from the formation of fibrous tissue within the heart's connective framework, especially affecting its valves.(6,7)

Notably, female gender has traditionally been considered a significant risk factor for Acute Rheumatic Fever (ARF) and Rheumatic Heart Disease (RHD), primarily due to access to healthcare,

especially preventive medicine, and genetically mediated immunological factors that predispose women to autoimmune diseases. (1,2)

This article offers a literature review on the presentation of carditis in pediatric patients after rheumatic fever infection, drawing insights from various studies. Additionally, it provides an overview of the anatomical and physiological aspects associated with the manifestation of rheumatic carditis.

2. Material and methods

Carditis was defined as the presence of pathological murmur upon physical examination and the identification of pathological valve regurgitation through echocardiography, in accordance with the criteria established by the World Heart Organization. Silent carditis, on the other hand, was defined as the presence of positive echocardiographic findings in the absence of clinical symptoms or features.(4,8,9)

The patients without clinical evidence or valvular regurgitation murmur but with echocardiographic findings of carditis were diagnosed as silent carditis.

A selection of articles addressing the subject of this study was conducted. To extract scientific articles, the PubMed and Elsevier databases were chosen, with no restrictions on dates or article types. The following descriptors were used: "Rheumatic fever", "Carditis", "Myocarditis", "Children", "Child", "Childhood", "Infantile", "Infant", "Pediatric", "Adolescent" and "Juvenile." Duplicate articles or those deemed impractical to assess were excluded.

A total of 207 studies were initially identified. Subsequently, a criterion of relevance to the pathophysiological findings commonly observed in children with rheumatic fever was applied, and their

abstracts were thoroughly reviewed. 150 studies were excluded for not meeting the eligibility criteria, leaving 37 for comprehensive evaluation. Ultimately, 20 papers were included in this literature review.

All data from the selected articles were meticulously recorded and analyzed in an Excel spreadsheet. They were categorized according to the most prevalent findings associated with rheumatic carditis, which included fever, arthritis, erythema marginatum, chorea, subcutaneous nodules, ECG abnormalities, mitral regurgitation, and aortic regurgitation.

To determine the manifestation of findings by gender (male and female), an average was calculated based on the values extracted from each of the 20 articles reviewed.

Formatting the main text. The findings of those patients studied in these articles were summarized in Table 1.

3. Results

Sixty percent of the individuals studied were male; however, plausible reasons justifying this higher incidence in the literature were not identified. Regarding age, due to the substantial variation in criteria among the articles, there was no common age range across all of them, with a higher incidence observed among individuals aged 3-15 years. Additionally, a prevalence of mitral regurgitation (90%) and aortic regurgitation (85%) manifestations was identified in a significant portion of the analysed articles. Chorea (40%), Erythema marginatum (35%), and subcutaneous nodules (45%) were mentioned in nearly half of the studies. However, in almost all these studies, incidence rates greater than 5% were not observed, as highlighted in the literature(4,8,10-15). Even though these manifestations are highly specific to rheumatic fever, they are infrequently reported compared to more common symptoms such as fever and arthritis.

Contrary to what was expected based on the literature(1,5), a higher incidence of rheumatic carditis was observed in male patients, a trend that persisted across nearly all the studies examined.

The most significant finding in rheumatic carditis is the presence of mitral and aortic valve insufficiency, which can occasionally manifest without clinical symptoms, a condition known as silent carditis. The Jones criteria alone may be insufficient for diagnosing silent carditis; hence, Doppler echocardiography is recommended to detect valvular insufficiencies during both the acute and chronic phases of the disease. (6)

The most common echocardiographic findings were mitral regurgitation, aortic regurgitation, dilated left atrium, dilated left ventricle, and left ventricular dysfunction. (8,16-18)

The screening of manifestations associated with rheumatic carditis was conducted, as indicated in the table, based on the presence or absence of symptoms,

without considering the incidence rates. Therefore, the rates presented in the table do not directly indicate the incidence of these manifestations in the individuals studied but rather the incidence of these findings in the selected articles. Thus, the frequency of citation of these findings does not necessarily determine their incidence in the studied groups.

There is a lack of information regarding patients who underwent valve replacement surgery. None of the patients in the study exhibited signs of infective endocarditis.

In this research, the average age of patients diagnosed with Acute Rheumatic Fever (ARF) aligns with the frequently reported age range for individuals with streptococcal pharyngitis, consistent with recently published research findings.

Tab. 1 – Clinical parameters in patients with rheumatic carditis in the 20 studies.

Characteristics	N	Findings
Age	20	5-18
Male/female (%)	20	60/40
Arthritis (%)	20	70
Erythema marginatum (%)	20	35
Chorea (%)	20	40
Subcutaneous nodules (%)	20	45
Fever (%)	20	70
Mitral regurgitation (%)	20	90
Aortic regurgitation (%)	20	85
ECG abnormalities (%)	20	70

N: Quantity of studies. ECG abnormalities include sinus tachycardia, prolonged PR interval, ST segment elevation and T-wave changes, development of pathologic Q waves, ventricular arrhythmias, and AV conduction defects.

In the context of abnormalities observed in the electrocardiograms of patients, a notable percentage of studies involving patients with rheumatic carditis revealed alterations in the ECG, most commonly the prolongation of the PR interval, a characteristic finding indicative of electrical conduction block between the atria and ventricles.

At the cellular level, cytokines produced by activated lymphocytes and macrophages following antigenic stimulation can play a significant role in the pathogenesis of acute Rheumatic Fever (RF). Some studies(2,19) have identified a significant correlation between IL-6, TNF, ESR, and CRP levels in patients with rheumatic carditis.

4. Limitations

The selection and analysis of the chosen articles were based on the presence of rheumatic carditis. However, due to the challenge of establishing direct correlations between carditis and other common findings, the extraction of findings was determined by their presence or absence in the studies that confirmed the manifestation of carditis. Therefore, it is possible that individuals who developed carditis without necessarily exhibiting some of these common findings were subjects of this research.

5. Conclusion

The most prevalent findings observed in studies of rheumatic carditis were Mitral regurgitation (90%) and Aortic regurgitation (85%). In contrast, Erythema marginatum and Chorea occurred significantly less frequently than Mitral and Aortic regurgitation.

The study of findings associated with carditis also demonstrated a lower incidence of Erythema marginatum, Chorea, and Subcutaneous nodules, consistent with previously published research on the subject.

The noteworthy incidence of misdiagnoses among children with Acute Rheumatic Fever (ARF) needs to be resolved. A revised edition of the Jones criteria (2015) for ARF diagnosis holds the potential to enhance the identification of carditis.

6. References

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