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Rheumatic Heart Disease in Indian Paediatrics: A Review

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Authors' contributions

All the authors have equally contributed to this review. Author KC formulated the hypothesis. Authors VB and NCK has done the data collection, performed analysis. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Rheumatic heart disease (RHD) is a condition in which the valves of the heart are damaged, it is mainly caused by Group A *Streptococcus*, it mainly affects the paediatrics and young adults. Inflammation occurs in the joints, heart and blood vessels due to group A *streptococcus*. The exact pathogenesis of rheumatic heart disease is unknown. It is manifested as fatigue, chest pain and shortness of breath; pulmonary hypertension, heart failure are some of the complications of the disease. Endocarditis, viral myocarditis and prolapse of the mitral valve are the differential diagnosis of rheumatic heart disease. It is diagnosed by revised Jones and World Heart Federation criteria. Benzylpenicillin is the first-line drug for rheumatic heart disease, followed by oral Penicillin V, Erythromycin can be recommended. Paediatrics who are allergic to Penicillin Azithromycin, Erythromycin can be recommended based on Indian paediatrics and World Health Organization guidelines. It is prevented by reducing the exposure to infection in high-risk regions; treat with appropriate antibiotics; prevent recurrence of infections and complications. The aim of this review is to highlight rheumatic heart disease in paediatric population.

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Keywords: Acute rheumatic fever; rheumatic heart disease; jones criteria; WHF criteria; paediatrics; treatment of RHD; India.

ABBREVIATIONS

ARF : Acute Rheumatic Fever
RHD : Rheumatic Heart Disease
MBL : Mannose binding lectin
GAS : Group A Streptococcus
ESR : Erythrocyte Sedimentation Rate
CRP : C: Reactive Protein
MR : Mitral Regurgitation
AV : Atrial Regurgitation
MS : Mitral Stenosis
MV : Mitral Valve
ACEI : Angiotensin Converting Enzyme Inhibitors
BMV : Balloon Mitral Valvuloplasty
MRI : Magnetic Resonance Imaging
AHA : American Heart Association
WHF : World Heart Federation
WHO : World Health Organization

1. INTRODUCTION

Acute Rheumatic fever (ARF) is mainly developed by an autoimmune reaction which develops sequelae of pharyngitis mainly caused by Group A *Streptococcus*; the inflammation mainly occurs in the heart, joints and blood vessels due to rheumatic fever. Recurrence of infections with *Streptococcus pyogenes* leads to rheumatic heart disease (RHD) [1,2]. It is defined as a cardiac condition where the valves get damaged permanently in the heart by *Streptococcus species.* Paediatric's and adults with < 25 years of age living in poor hygiene areas are highly infected with rheumatic heart disease [3].

Since rheumatic heart disease is common in paediatric's, our review aim is to highlight the pathology and the management in paediatric's.

2. EPIDEMIOLOGY

Countries like Southeast Asia, Africa, Australia, India, Fiji, and New Zealand have high prevalence rates [2].

In developing countries, RHD accounts for about around 2,00,000-2,50,000 premature deaths every year in paediatric's [4].

The incidence rate is about 50 cases per 1 lakh populations in paediatric's and 2% of death occurred every year in the world [4].

In 2015 the estimated prevalence is about 0.4% in endemic regions; 0.0034% in non-endemic regions. 0.15 deaths were reported among 1 lakh population in paediatric's between the ages 5 – 9 years [5].

India, China and Pakistan are the countries that have the highest numbers of deaths reported in 2015 [5].

A study was conducted by ICMR from 1972 – 2010 in multiple regions of schooling going paediatrics in India and the criteria were the same for all the regions to include the paediatrics in the study. The prevalence rate was varied in different regions. The average prevalence was found to be 3.4 and 4.2 per 1000 people; prevalence is about 2 per 1000 people among the age groups [6].

In India, Kerala the prevalence is about 1to 12 per 1 lakhs population [6]. About 13 million cases in the year 2015 and nearly 1 lakhs death every year due to rheumatic heart disease among paediatric with the age group of 5 – 14 years in India [7].

3. PATHOPHYSIOLOGY

The abnormality occurs in the immune system that results in RHD after exposure to *Streptococcus species* (Group A *Streptococcus*), mainly due to the recurrence of throat infection [4]. Bacteria contain M, T, R proteins on the cell surface which are involved in adhering to epithelial cells. *Streptococcus* species are highly specific to the M serotype, which is a high risk of developing rheumatic carditis and valvulitis [1,4]. In acute rheumatic fever, inflammatory proteins and cytokines (Mannose binding lectin (MBL) and Interleukin-1,6 and Tumor Necrosis Factor-α) production will be high that is used to eliminate GAS [1,8]. Recurrence of RF, fibrosis inflammations in the heart valves that lead to rheumatic valvular heart disease. In rheumatic heart disease, MBL binds to N-acetyl D-glucosamine to activate complement lectin to eliminate the bacteria [4]. Molecular mimicry occurred between the host antigen and GAS antigen. GAS binds to an antigenic peptide (HLA complexes) to activate T- cells that produce antigen antibodies. VCAM-1 protein which is present in rheumatic valves that mediates the binding of lymphocytes. Once VCAM-1 binds

with valvular endothelium there will be upregulation of proteins and GAS antigens that will result in the inflammation and infiltration of T-cells in rheumatic heart disease lesion [1].

4. CLINICAL MANIFESTATION, RISK FACTORS AND COMPLICATIONS

Rheumatic Heart disease is characterized by fatigue, breathlessness, headache, dizziness, chest discomfort, rapid or irregular heartbeat and swelling of the legs [9]. The risk factors for rheumatic heart disease paediatric with recurrence of rheumatic fever from low-income countries and environmental factors include poor sanitation, and living in overcrowded areas [1]. Atrial fibrillation, Pulmonary hypertension, Infective endocarditis, Rupture of the heart valve, and Heart failure are the complications of rheumatic heart disease [10].

5. DIAGNOSIS

5.1 Differential Diagnosis

Endocarditis, viral myocarditis, and mitral valve prolapse are the differential diagnoses of rheumatic heart disease [4].

5.2 Laboratory Test

Pharyngeal culture for GAS infection and elevation of C-RP, ESR and fibrinogen level during rheumatic heart disease [1].

Chest X-ray is used to check the lungs and heart; Electrocardiogram for abnormal rhythm monitoring and to get a proper idea of the heart valve and muscle cardiac MRI is used [9].

Echocardiography is used for the detection of subclinical carditis [6].

The diagnosis of Rheumatic fever and Rheumatic Heart Disease is based on criteria. Modified Jones Criteria for rheumatic fever and WHF Echocardiographic Diagnostic Criteria for rheumatic heart disease.

Diagnosis of rheumatic fever is based on AHA 2015 Modified Jones criteria which is divided into 3 parts (GAS infection based on population, Major criteria, Minor Criteria). In GAS infection: initial ARF consist of 2 major or 1 major + 2 minor manifestations; recurrent ARF: 1 or 2 major manifestations or 2 or 3 minor manifestations. Major criteria consist of carditis, arthritis, chorea, erythema marginatum and subcutaneous nodules. Minor criteria consist of polyarthralgia, fever, ESR or CRP prolongation of PR interval [11] is shown in Table 1.

Echocardiographic Diagnostic Criteria based on the 2012 World Heart Federation for RHD is categorized into 2 based on age(< 20 years and > 20 years of age). In echocardiographic criteria for paediatric's less than or equal to 20 years is divided into 3 sections definite, borderline and normal echocardiographic findings [12,13] is shown in Table 2.

Table 1. AHA 2015 Modified Jones Criteria

Group A *Streptococcus* Infection – Based on Population	
Diagnosis: initial ARF	**Diagnosis: recurrent ARF**
2 major manifestation or 1 major plus 2 minor manifestation	1 or 2 major manifestations and 2 or 3 minor manifestations
Major Criteria	
Population at low risk	**Population at Moderate and High risk**
Carditis	Carditis
Arthritis – mainly polyarthritis	Arthritis - Monoarthritis or Polyarthritis
Chorea	Polyarthralgia
Erythema marginatum	Chorea
Subcutaneous nodules	Erythema marginatum
	Subcutaneous nodules
Minor Criteria	
Population at low risk	**Population at Moderate and High risk**
Polyarthralgia	Monoarthralgia
Fever (≥ 101.3ºF)	Fever (≥101.3ºF)
ESR ≥ 60 mm / hr and/or CRP ≥ 3.0 mg/dL	ESR ≥ 30 mm/hr and/or CRP ≥ 3.0 mg/dL
Prolonged PR interval, after accounting for age variability (unless carditis is a major criterion)	Prolonged PR interval, after accounting for age variability (unless carditis is a major criterion)

Table 2. Echocardiographic Diagnostic Criteria - 2012 World Heart Federation for RHD

Echocardiographic Criteria : less than or equal to 20 years
Definite RHD(either A,B, C or D) A) Pathological MR and 2 morphological features of MV B) MS mean gradient ≥4 mmHg C) Pathological AR and 2 morphological features of AV D) Borderline disease of both the AV and MV
Borderline RHD(either A, B, or C) A) 2 morphological features of RHD of the MV without pathological MR or MS B) Pathological MR C)Pathological AR
Normal echocardiographic findings (all A to D) A) MR that does not meet all four Doppler echocardiographic criteria (physiological MR) B) AR that does not meet all four Doppler echocardiographic criteria (physiological AR) C) An isolated morphological feature of RHD of the MV D) Morphological feature of RHD of the AV without any associated pathological stenosis or regurgitation
Echocardiographic Criteria : more than 20 years
Definite RHD (either A, B, C, or D) A) Pathological MR and 2 morphological features of MV B) MS mean gradient ≥4 mmHg C) Pathological AR and 2 morphological features of AV, only in individuals aged <35years D) Pathological AR and 2 morphological features of MV

Table 3. Pathological Regurgitation and Morphological features of RHD

Pathological Regurgitation	**Doppler Echocardiographic Criteria : All 4 should be include**
Mitral Regurgitation	1. 2 Views 2. Jet length ≥2cm 3. Velocity ≥3m/s 4. Pan-systolic jet
Atrial Regurgitation	1. 2 Views 2. Jet length ≥1cm 3. Velocity ≥3m/s in diastole 4. Pan-diastolic jet
Morphological Features	**Doppler Echocardiographic Criteria : All 4 should be include**
Mitral Valve	1. Anterior Mitral Valve leaflet (AMVL)thickening ≥3mm 2. Chordal thickening 3. Leaflet motion restricted 4. Excess leaflet tip motion – during systole condition
Atrial Valve	1. Irregular or focal thickening 2. Coaptation defect 3. Leaflet motion restricted 4. Prolapse

Pathological Regurgitation and Morphological features are classified based on doppler echocardiographic [12,13] is shown in Table 3.

6. MANAGEMENT

To treat acute rheumatic fever and rheumatic heart disease goal should be prepared initially

6.1 Goals

1. To treat *Streptococcus* pharyngitis and clinical manifestations of the disease
2. Recurrences of disease to be prevented
3. Providing education to the family and patient

Table 4. Management of RF and RHD for primary and secondary prophylaxis

Name of the Guidelines	**Benzathine penicillin G**	**Penicillin V**	**Azithromycin**	**Cephalexin**	**Erythromycin**
Indian Paediatric Guidelines	<27 kg: 0.6 million units ≥27kg: 1.2 million units Duration : Single dose ROA : IM	250 mg QID Duration : 10 days ROA : oral	12.5 mg/kg/day Duration : 05 days ROA : oral	15 -20 mg/kg BD Duration : 10 days ROA : oral	20 mg/kg/dose max.500mg BD ROA : oral
WHO Guidelines	≥30kg: 1.2 million units <30kg: 0.6 million units Duration : Single dose 3 – 4 weeks ROA : IM	250 mg BD ROA : oral	-	-	250 mg BD ROA : oral
Secondary Prophylaxis					
Name of the Guidelines	Benzathine penicillin G	Penicillin V	Erythromycin	Sulphonamide (penicillin allergy)	
Indian Paediatric Guidelines	<27kg: 0.6 million unit every 2 weeks ≥27kg: 1.2 million unit every 3 weeks	250 mg BD	20 mg/kg (max 500 mg) BD	-	
WHO Guidelines	<20kg: 0.6 million unit ≥20kg: 1.2 million unit every 4 weeks	250 mg twice BD	20 mg/kg (max 500 mg) BD	<30kg: 500mg daily ≥30kg: 1g daily	

The initial goal is to kill the group A *Streptococcus* organism, Benzathine Penicillin G shows sensitivity towards GAS organism and is more commonly administered with a dose of about 0.6 million units for paediatrics <26 kg as a single dose; if there is any allergic reactions occurred during penicillin therapy switch the therapy to Azithromycin, Erythromycin and Cephalexin . During carditis conditions bed rest and reduce the physical activity for 1.5 months. Paracetamol can be given for fever and to reduce pain [14].

In some patients recurrence of RF is high almost about 40-60% once they developed a single episode of acute rheumatic fever. To prevent recurrence of disease secondary prophylaxis antibiotics recommended for every 3 – 4 weeks [15].

If any inflammations occur in the rheumatic fever it should be treated with aspirin and naproxen for mild carditis and arthritis. Moderate to severe carditis prednisolone is used for 2 weeks followed by tapering, along aspirin was administered for 12 weeks [14].

Duration for secondary prophylaxis no carditis: 5 years / 18 years, mild - moderate carditis: 10years/ 25 years and severe carditis: Lifelong [14].

In chronic rheumatic heart disease conditions patients, should be on medical management. In moderate to severe Mitral Regurgitation diuretics is recommended; ACEI (Captopril 0.25mg/kg) is used to reduce the afterloads in MR condition [14,16]. In patients with acute failure who develops mitral stenosis during rheumatic fever, beta-blockers were recommended to improve the cardiac outputs [14].

Atrial Fibrillation Warfarin is used to prevent clot; digoxin, calcium channel, beta blockers which are used to maintain the pumping of the heart and Amiodarone for controlling the rhythm [17].

During pulmonary venous congestion, oxygen and diuretic therapy should be given initially. Patients who did not respond to therapy develop tachycardia, hypotension and hypoxia pulmonary vasodilator drugs should be discontinued [14].

6.2 In Valvular Heart Disease [18]

For mitral stenosis balloon mitral valvuloplasty (BMV) and valve replacement for patients not suitable for BMV. Mitral Regurgitation is mainly treated with surgery like the replacement of a valve. Aortic stenosis condition balloon procedure is not effective. For symptomatic patients, surgery is more effective. Prosthetic valve replacement for aortic regurgitation.

As per Indian Pediatric and WHO guidelines treatment of rheumatic fever and rheumatic heart disease Benzathine Penicillin G, Penicillin V, Azithromycin, Cephalexin and Erythromycin is recommended for primary prophylaxis. For secondary prophylaxis Benzathine Penicillin G; Penicillin V and Azithromycin is shown in Table 4.

7. CONCLUSION

Prevention of rheumatic heart disease is categorized into 4 types (Primordial, Primary, Secondary and Tertiary). Primordial prevention is to control the exposure to Group A *Streptococcus* in high-risk regions. Primary prevention is to control the infection of acute rheumatic fever in the initial stage with appropriate antibiotics; Secondary prevention is to control the recurrence of infection with antibiotic administration for a longer period; Tertiary prevention is to control the complications of rheumatic heart disease. Our review focuses on rheumatic heart disease in Indian paediatrics. This review helps to understand rheumatic heart disease in a detailed manner in the paediatric population. Since many cardiac problems occurring in paediatrics; our review focuses mainly on rheumatic heart disease in paediatrics is one of the limitations. In the future, more studies to be reviewed on other cardiac problems in paediatric populations.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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