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REVIEW ARTICLE

Rheumatic Heart Disease: Pathophysiology and Management

Abdel Salam Elsaid Hussein Sherif, Mohammad Gouda Mohamed, Ilham Saeid Hasan Ahmeedah *, Mohamed Salah Abdelbasit
Cardiology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt

***Corresponding author:**
Ilham Saeid Hasan Ahmeedah
Email:
alhamahmydh2@gmail.com

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ABSTRACT

Background: Rheumatic heart disease, which is frequently disregarded by the media and decision-makers, is a significant burden in poor nations where it accounts for the majority of youth cardiovascular morbidity and mortality, resulting in around 250,000 deaths annually globally. An aberrant autoimmune reaction to a group A streptococcal infection in a genetically vulnerable host causes the disease. The antecedent of rheumatic heart disease, acute rheumatic fever, can damage several organs and cause irreversible valve damage as well as heart failure. Penicillin works well to prevent the disease, but treating cases that have progressed requires a lot of resources, which makes managing disease particularly difficult in developing countries. Antibiotic prophylaxis against recurring episodes of acute rheumatic fever has thus been stressed in guidelines, and it appears to be a practical and cost-effective treatment.

Conclusions: Screening populations at risk for rheumatic heart disease in endemic areas may enable early detection and focused therapy. Active surveillance using echocardiography-based screening may become crucial in this situation.

Keywords: Rheumatic Heart Disease; Atrial fibrillation; Endocarditis.

INTRODUCTION

The most prevalent and serious side effect of ARF is rheumatic heart disease (RHD). It is a reaction of the systemic immune system to pharyngeal beta-hemolytic streptococcal infection. Pancarditis is a chronic illness caused by rheumatic fever that affects all layers of the heart and is characterized by heart valve distortion and scarring [1].RHD is the most prevalent cause of acquired valvular disease worldwide and often manifests 10 to 20 years after the initial sickness [2].

Compared to the aortic valve, the mitral valve is affected more frequently. Twenty-five percent of patients with chronic RHD have mitral stenosis, and forty percent of those patients also have mitral insufficiency. Progressive fibrosis, or the thickening and calcification of the valve, occurs over time and causes the left atrium to grow and forms mural thrombosis in that chamber. The stenotic valve resembles a fish mouth and is funnel-shaped. The first cardiac sound (s1) is audible upon auscultation and becomes less prominent as the leaflets thicken. As pulmonary hypertension progresses, the pulmonary component of the second heart sound (p2) becomes more prominent, and the splitting of the second heart sound (s2) becomes less noticeable. At the apex, where the diastolic filling murmur is also audible, the mitral valve frequently opens snappily [3].

Aortic insufficiency is commonly linked to chronic rheumatic heart disease-related aortic stenosis. The valve orifice shrinks to a round or triangular shape, and the commissures and cusps fuse together. Because the aortic leaflets are static and do not provide an aortic closure sound, auscultation may reveal that s2 is single. The base of the heart is where the systolic and diastolic murmurs of aortic valve stenosis and insufficiency are most audible [4].

Epidemiology

The most prevalent acquired cardiac condition affecting children and young people in developing nations is rheumatic heart disease (RHD). In endemic areas, RHD accounts for 15–20 percent of all heart failure patients [5].

According to a study on cases of rheumatic heart disease, there were 33.4 million RHD cases worldwide in 2015, 10.5 million RHD-adjusted life years, and 319400 RHD-related deaths.South Asia, central sub-Saharan Africa, and Oceania have the greatest rates of rheumatic heart disease. In nonendemic nations, there were reported to be 3.4 cases per 100,000 people in 2015, while in endemic countries, there were 444 cases per 100,000 people [6].

The majority of people with rheumatic heart disease are impoverished, have limited access to healthcare, and have an uncontrolled exposure to group A streptococcus. Seven to eight times greater than the rate of clinically apparent disease (2.7 per 1000 people) was determined by a systematic review and meta-analysis. the incidence of clinically silent RHD to be at 21.1 per 1000 individuals. From 4.7 per 1000 children at age 5 to 21.0 per 1000 children at age 16, the prevalence of rheumatic heart disease rises with age [7].

Estimates based on this data suggest that the burden of RHD may grow by up to double that of the Global Burden of Disease research. It is possible that between 50 and 80 million people globally are currently afflicted with RHD, given that children in sub-Saharan Africa account for 6 to 7 percent of the global RHD burden [8].

Pathophysiology

Streptococcus pyogenes is a group A streptococcus that causes acute rheumatic fever. An aberrant immune response to this infection can damage valves, leading to rheumatic heart disease [9]. Three weeks following group A streptococcal pharyngitis, acute rheumatic fever can strike, affecting the joints, skin, brain, and heart [10].

Rheumatic valvular heart disease can arise from gradual fibrosis of the heart valves following several episodes of rheumatic fever. Heart failure or death could result from untreated valvular heart disease. It is unclear exactly how the pathophysiology works. MacCallum plaques and Aschoff nodules are signs of rheumatic carditis. Nodules in rheumatic fever-affected hearts exhibit Aschoff bodies. They are the outcome of cardiac muscle inflammation. In the left atrium, MacCallum plaques can be observed on the valves and subendocardium [11].

Valvular endothelial activation

In about 30–45% of cases, ARF made RHD more difficult. Following bacterial infection of the throat, an autoimmune reaction causes the release of cytokines and other inflammatory chemicals onto the tissues of the heart. imitation This response is mostly mediated by macrophages and CD4+ T cells, a subspecies of T lymphocytes. VCAM-1 and other chemicals facilitate the cells' response to the valves. RHD requires a genetic vulnerability in order to manifest. The T-cell molecular pathway is the fundamental cause of RHD. Consequently, the antigenson group Following their activation by streptococci, CD4+ T lymphocytes cross-react with related peptides found in cardiac tissue. The tissue being attacked—in this case, the endocardium of the heart valve—is naturally destroyed as a result of the antigen-T cell response. Peripheral blood monocytes in ARF overproduce other soluble molecules like TNF-α, IL-1, and IL-2. These cytokines stimulate both acute and chronic inflammatory reactions, which appear to persist as a chronic process long after the infectious pathogen has vanished. The lesion, known as the Aschoff nodule, is a cluster of granuloma cells that is indicative of a RHD lesion. It contains a range of immune cells and goes through several stages [10, 12].

Risk factors

Children and teenagers in low- and middle-income nations are primarily affected by rheumatic fever; factors such as poverty, overcrowding, low family education, and restricted access to healthcare are major contributors. Rheumatic heart disease can be avoided by putting an end to recurring ARF episodes. Once acute rheumatic fever (ARF) has been identified, subsequent ARF episodes can be avoided to prevent the disease's progression. In addition to managing symptoms, treatment lowers the chance of complications. The disease is still common in sub-Saharan Africa, the Middle East, Central and South Asia, the South Pacific, and among immigrants and older adults in high-income countries, particularly among indigenous peoples, even though it has been eradicated in many other parts of the world[13].

Symptoms of rheumatic heart disease

The diagnosis of rheumatic heart disease depends on a recent history of strep infection or rheumatic fever. Rheumatic fever symptoms might appear anywhere from one to six weeks following a strep throat episode. In certain instances, the infection might not have been detected or could have disappeared by the time the patient saw a physician.

Most cases RHD asymptomatic. When it does, symptoms may include: breathlessness during exertion, breathing difficulties when lying down (orthopnoea), waking up during the night and having to sit or stand up (paroxysmal nocturnal dyspnoea), fluid retention (oedema), syncope, stroke and fever linked to infection of damaged heart valves.

Prognosis

The reason why recurrences are important is that each one puts additional pressure and stress on the heart. The heart is extremely fortunate to survive the second or third fight, even if it is unlucky to survive the first attack. Still, the initial attack frequently involves the heart. It is widely accepted that children who have experienced multiple heart attacks are more likely to develop heart disease. Rheumatic recurrences account directly for most deaths from rheumatic heart disease. Relapses are rarely fatal, but practice makes perfect. always further heart damage, and many eventually pass away from new rheumatic attacks after a little period of time. Up to the age of 14, when it quickly declines along with the prevalence of recurrences, the death rate is significant. The child with rheumatoid arthritis's future rests on his capacity to endure the hardships of childhood and adolescence, when relapses are less common and resistance grows. Every year, rheumatic heart disease results in between 200000 and 250000 premature fatalities. It is also the leading cause of cardiovascular mortality in youth and young adults living in nations with inadequate access to healthcare. The patient might not appear until significant heart failure is evident, making surgery contraindicated, if the valvular disease is not serially monitored [14].

Complication

Until heart problems arise in late adulthood, rheumatic heart disease is typically dormant or quiet. The most frequent side effects from untreated severe valvular disease include atrial fibrillation, thrombosis, heart failure, pulmonary hypertension, and infectious endocarditis [15].

The most common cardiac condition among expectant mothers is rheumatic heart disease, which significantly increases morbidity and death in both the mother and the fetus. Due to increased blood volume placing additional strain on the heart valves during pregnancy, women with rheumatic heart disease are more likely to experience negative consequences, such as heart arrhythmias and heart failure. Women frequently do not become aware of their rheumatic heart condition until they become pregnant [16].

Subacute bacterial endocarditis

Subacute bacterial endocarditis (SBE) is a bacterial infection that typically results from viridans streptococci. Patients with rheumatic heart disease may have abnormalities in their mitral or aortic valves, which can lead to growths on the endocardium of damaged valves. If the SBE is detected early enough to get antibiotic treatment, it may be successful; if not, it can become lethal in six weeks to a year [17].

Since the germs that cause endocarditis typically originate in the mouth, maintaining proper dental hygiene is crucial for reducing the risk. In RHD, prophylactic antibiotic use prior to dental procedures reduces the risk of endocarditis.

Atrial fibrillation and stroke

Approximately 1 in 5 people with RHD symptoms are experiencing atrial fibrillation. the are usually linked to mitral valve disease-related persistent left ventricular enlargement [18].

Atrial fibrillation episodes are highly correlated with mitral valve dysfunction, particularly in cases of mitral stenosis. Atrial fibrillation affects 40–75% of people with mitral stenosis [19].

If the patient has had atrial fibrillation for less than six months, has mitral stenosis, and the left atrium is not noticeably enlarged, the likelihood of successfully cardioverting atrial fibrillation to sinus rhythm increases.Before cardioversion, the patient should be anticoagulated to reduce the risk of stroke or systemic embolize.

Heart failure

Heart failure, which occurs when the heart is too damaged to adequately pump blood throughout the body, is the primary cause of mortality from rheumatic heart disease. When the heart isn't working properly, fluid accumulates in the body and lungs, leading to symptoms including exhaustion, edema, and dyspnea. If treatment is not received, these symptoms often get worse over time [15].

When heart failure strikes a RHD patient, surgery may be necessary to either inflate the defective valve with a small balloon or replace it with an artificial one [20].

Pulmonary hypertension

A common cause of secondary pulmonary hypertension is mitral valve disease, which restricts the flow of blood from the atrium to the ventricle, raising left atrial pressure and causing pulmonary arterioles to constrict. These factors ultimately result in pulmonary vascular remodeling and pulmonary hypertension [21].

When pulmonary hypertension develops in mitral valve disease, it is thought to be a reason for an early surgical interval since it suggests a poor prognosis overall [22].

Management RHD

- **Atrial Fibrillation treatment**

Small, single-center randomized trials using either electric and pharmacological (usually amiodarone)

cardioversion or catheter ablation80 in addition to valvular interventions when indicated have demonstrated rhythm control over rate control with nondihydropyridine calcium channel blockers or β-blockers for treatment of symptomatic atrial fibrillation and maintenance of sinus rhythm. However, these strategies are not generalizable to all patients and may not be readily available or affordable in LMICs [23].

When atrial fibrillation or atrial flutter is present, anticoagulation with oral vitamin K antagonists, direct thrombin, or factor Xa inhibitors (direct-acting oral anticoagulants) is advised to prevent stroke [24].

- **Management of Heart Failure**

Often, the only course of action that can lead to symptomatic relief is pharmaceutical management. Diuretic medications (loop diuretic agents and spironolactone) and vasodilator therapy—most commonly angiotensin-converting enzyme inhibition and angiotensin II receptor blockers—as well as afterload reduction are part of the symptomatic medical care of moderate to severe multiple MR. Digoxin and β-blockade may also be taken into consideration. The diameter and volume of the left ventricle were significantly reduced after enalapril treatment [25].

- **Management pulmonary hypertention**

It is advised to use a variety of supportive therapies along with medicines. Diuretics can be used to relieve edema and fluid retention. It is possible to administer anticoagulants to stop blood clots from developing. It's possible that some people need a portable oxygen tank. A heart-lung, single-lung, or double-lung transplant may be advised in the most extreme circumstances. Exercise on a daily basis and pulmonary rehabilitation are also strongly advised to help people breathe easier and live better.

There are numerous choices for dental care. Antagonists of the endothelin receptor (ERAs) [26].

Evaluate heart valve function.

avoid blood vessel constriction and are frequently used to assist patients in engaging in physical activity. PDE 5 Inhibitors are phosphodiesterase inhibitors that widen blood arteries and relax the lungs. Lung blood arteries can relax thanks to soluble guanylate cyclase (sGC) stimulators, selective IP receptor antagonists, and prostacyclin analogs [27].

Surgical management of rheumatic heart disease

Indication of surgery

1-Aortic valve regurgitation

The recommendations on indications for surgery is recommended in symptomatic severe aortic regurgitation regardless to LV [28].

Surgery is recommended in asymptomatic patients with LVEF<50', LVESD>50mm and BSA >25mm/m2. Surgery should also be considered if significant changes in LV or aortic size occur during follow-up. TAVI may be considered in experienced centres for selected patients with aortic regurgitation and ineligible for SAVR [29].

2-Aortic stenosis

Intervention is recommended in symptomatic patients with high-gradient aortic stenosis regardless of LVEF. Intervention is recommended in asymptomatic patients with severe aortic stenosis and impaired LV function of no other cause [30] and those who are asymptomatic during normal activities but develop symptoms during exercise testing [31].

Mode of intervention

Must be performed in heart valve centres that declare their local expertise and out come date

- choice between surgical and transcatheter intervention must be based upon careful evaluation of clinical ,anatomical and procedures factor by heart team
- SAVR is recommended in yanger patient who are low risk of for surgery <75years [32].
- TAVI is recommended in older patients >75 [33].
- Ballon aortic valvotomymay be considered as bridge to SAVR or TAVI in haemdynamically in suitable patients and (if fisable) in this with severe stenosis who require urgent high risk NCS.

3- Mitral regurgitation

Surgery recommended in sever mitral regurgitation if was Symptomatic patient with LVEF >30% and LVESD <55 mm, asymptomatic patient with left ventricle no dysfunction with LVEF ≤60% or LVESD ≥45. Valve surgery/intervention is recommended only in patients with severe mitral regurgitation SMR who remain symptomatic despite GDMT(including CRT if indicated)and has to be decided by structured collaborative Team [34].

TEER transcatheter edg to edge repair should be considered in symptomatic patients not eligible for surgery [35].

4- Mitral stenosis

Clinically significant mitral stenosis is defined by a mitral valve area (MVA) ≤1.5 cm2. Commissural fusion with thickening of the posterior leaflet is the most important mechanism of stenosis. Valvular intervention by Percutaneouse mitral commissuratomy (PMC) is recommended in

symptomatic patients and contraindicated to surgery [36].

Mitral valve surgery is recommended in symptomatic patients who are not suitable for PMC in absence of futility. Surgery is recommended in patients with mild to moderate tricuspid regurgitation with dilated annulus >40mm or >21mm/m2 by 2D echocardiography [37].

Surgery is recommend in sever regurgitation and who are symptomatic or have RV dilatation 'in absent RV or LV dysfunction and sever pulmonary vascular disease and hypertension [38].

Transcatheter is recommended in symptomatic and inoperable patient

5- Tricuspid stenosis

Surgery is recommended in symptomatic and severe tricuspid stenosis

Management of pulmonary hypertension

Pulmonary hypertension that occurs in RHD secondary to increase left atrial pressure due to mitral and aortic stenosis is pulmonary venous hypertension. The general treatment of PVH is directed toward the cause of left-sided heart disease. There is no specific medical therapy directed toward PVH itself, and none of the medications used for left-sided heart failure are contraindicated when PVH is present. In cases where PVH is due to mitral stenosis, correcting the valvular lesion with surgery or percutaneous valvuloplasty and can normalize pulmonary pressures immediately or in up to 6 months [39].

Preventation (antibiotic prophylaxis)

A full therapeutic course of antibiotics therapy should be given to patient with ARF to eradicate residual GAS, even if a throat culture is negative, prior to initiate of prophylaxis. Prophylactic antibiotic should be initiated immediately at the end of the therapeutic antibiotics course [40].

(1) Primary prevention

Relies on the proper treatment of streptococcal pharyngitis, that is, prevention of the first RF episode. The drug of choice is still phenoxymethylpenicillin orally at the following doses: adults and children with a body weight > 40 kg – 2–3 MIU/day in 2 divided doses every 12 hours for 10 days, children with a body weight < 40 kg – 100,000 to 200,000 IU/kg/day in 2 divided doses every 12 hours for 10 days. Benzylpenicillin, administered intramuscularly at a single dose (only in hospital settings), is acceptable, for adults and children with a body weight > 40 kg – 1.2 MIU, children with a body weight < 40 kg – 600,000 IU. In patients with hypersensitivity to penicillin (except for immediate-type reactions), first-generation cephalosporins (cefadroxil or cefalexin) are used. Cefadroxil: adults and children with a body weight > 40 kg – 1 g, children with a body weight < 40 kg – 30 mg/kg, in a single dose for 10 days. Cefalexin: adults 500 mg twice per day, children 25–50 mg/kg/day in 2 doses for 10 days. Macrolides should only be administered in patients with immediate-type hypersensitivity to beta-lactam antibiotics. The following can be used: erythromycin, clarithromycin and azithromycin [41].

- Erythromycin: adults and children with a body weight > 40 kg – 0.2–0.4 γ every 6–8 hours, children with a body weight < 40 kg – 30–50 mg/kg/day in 3–4 doses, for 10 days.
- Clarithromycin: adults and children with a body weight > 40 kg – 250–500 mg every 12 hours, children with a body weight < 40 kg – 15 mg/kg/day in 2 doses, for 10 days.
- Azithromycin: adults and children with a body weight > 40 kg – 500 mg on the first day, then 250 mg for three consecutive days, children with a body weight < 40 kg – a single daily dose of 12 mg/kg/day for 5 days or 20 mg/kg/day for 3 days [42].

(2) Secondary prevention

Is the prevention of subsequent rheumatic fever relapses through the chronic anti-streptococcaltreatment: phenoxymethylpenicillin or benzathine benzylpenicillin or possibly macrolides?

The duration of secondary prevention must be determined individually, depending on whether the patient has developed carditis and complications in the form of chronic valvular heart disease. Secondary prevention should be administered from 5 to 10 years from the last RF relapse, or up to 21 years of age (whichever is longer). In RF cases with carditis leading to chronic valvular heart disease, the prevention should be administered for 10 years or until 40 years of age. Secondary prevention makes use of benzathine benzylpenicillin, intramuscularly: in adults and children with a body weight > 20 kg – 1.2 MIU, in children with a body weight < 20 kg – 600,000 IU every 4 weeks. Phenoxymethylpenicillin is administered orally at a dose of 2 × 250 mg (i.e. 2 × 400,000 IU). [9].

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