

Identification and Diagnosis of Risk Factors and Symptoms for Rheumatic Heart Disease

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ABSTRACT

Rheumatic heart disease (RHD) is one of the common heart disease acquired in children in many regions of the world, mainly in developing and underprivileged countries. This heart condition occurs following rheumatic fever caused by streptococcal infection. It affects the functionality of heart valves. When untreated it may lead to medical complications and even death. The disease mainly targeting children and young adults is responsible for cardiovascular morbidity and mortality in people. Prevention and treatment of acute rheumatic fever plays an important role in controlling the disease. Diagnosis of the disease is critically important because misdiagnosis of acute rheumatic fever can lead to worsening of damage caused to heart valves and may also lead to premature death. This being a preventable problem, it can be managed through surgeries to repair functions of cardiac valves. Alcohol consumption and tobacco smoking has shown synergistic effect which may prove detrimental to cardiovascular health.

Key words: Rheumatic Heart Disease, Streptococcus, Diagnosis, Morbidity and Mortality, Prevention and Treatment.

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INTRODUCTION

RHD is a chronic heart condition caused by rheumatic fever that can be prevented and controlled. Rheumatic fever is caused by a preceding group A streptococcal infection (Figure 1). Rheumatic heart disease (RHD) causes damage to heart valves that occurs after an episode of acute rheumatic fever (ARF).¹ It is caused by an episode or recurrent episodes of ARF, where the heart has become inflamed.² The normal blood flow is interrupted through damaged valves and the heart valves may be stretched and/or scarred, stretched valves that do not close properly and may cause backward blood flow, or scarred valves may not opening properly due to blockage. Untreated, RHD causes heart failure and those affected are at risk of arrhythmias, stroke, endocarditis and complications of pregnancy. These conditions cause progressive disability, reduce quality of life and can cause premature death in young adults. Heart surgery can prolong life and manage symptoms but does not cure RHD. Rheumatic heart disease is a chronic, disabling and sometimes fatal disease. It is 100% preventable. Acute rheumatic fever (ARF) primarily affects the heart, joints and central nervous system, heart failure and death.

Risk factor

Family history, Strep bacteria, Environmental conditions such as unclean water, overcrowding, and improper sanitation are some of the risk factors. The decline of rheumatic fever in developed countries is believed to be the result of improved living conditions and availability of antibiotics for treatment of group A streptococcal infection. Overcrowding, poor housing conditions, under nutrition and lack of access to healthcare play a role in the persistence of this disease in developing countries.² Besides these, genetic susceptibility of certain individuals has also been implicated in the etiology of acute rheumatic fever.

The global burden

Rheumatic fever and RHD mainly affects children and young adults (affected more) living in countries with low income and is responsible for about 233,000 deaths annually (Figure 2). At least 15.6 million people are estimated to be currently affected by RHD with a significant number of them requiring repeated hospitalization and often unaffordable heart surgery in the next five to twenty years.¹ Up to 1 per cent of all school children in

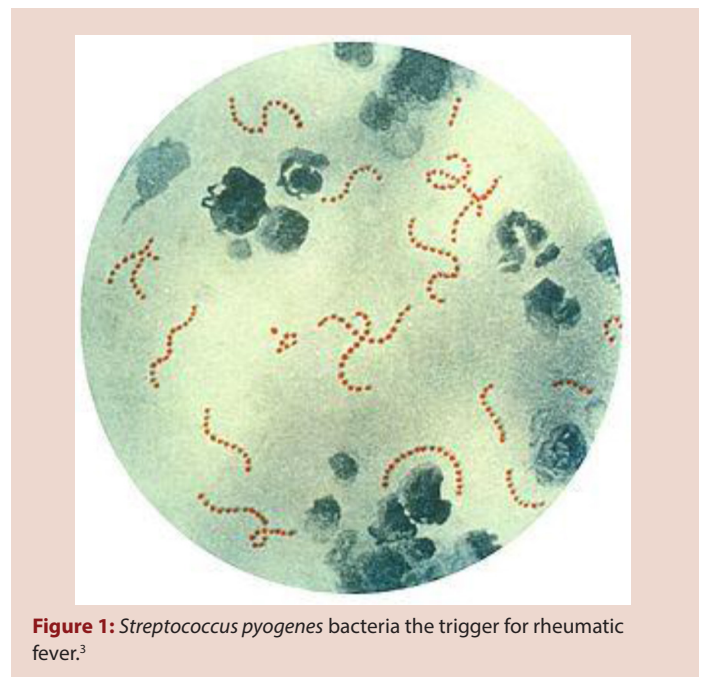
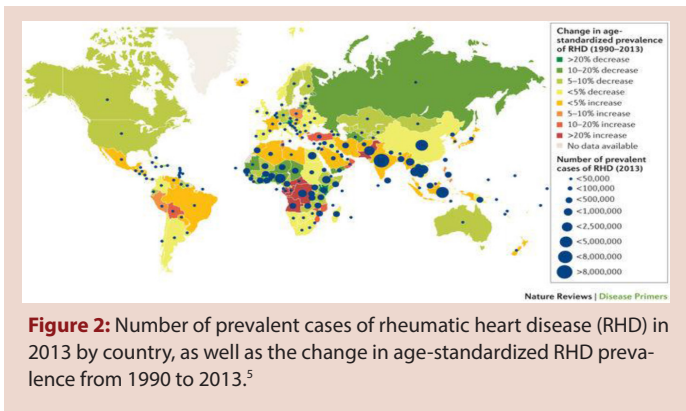


Figure 1: *Streptococcus pyogenes* bacteria the trigger for rheumatic fever.³

Africa, Asia, the Eastern Mediterranean region, and Latin America show signs of the disease.⁴

Signs and Symptoms

Potential symptoms and signs of ARF are classified into two categories: major and minor. Major signs and symptoms are strongly associated with ARF and include carditis (swelling of the heart), arthritis (pain, redness and swelling of one or more joints), Sydenham's chorea (strange movements that occur in the body and face), erythema marginatum (skin pigmentation which is painless), subcutaneous nodules (small lumps under the skin). Minor signs and symptoms are used to help support the diagnosis. These include fever, arthralgia (generalized joint aches), blood tests that suggest general illness, and changes seen on heart electrocardiogram. Positive test for group A streptococcus infection along with sign and symptoms are required to confirm ARF diagnosis (Figure 3).



Diagnosis^{2, 4-5}

An accurate diagnosis is important because

- Mistakenly confirming a diagnosis in a person who does not have ARF will result in years of unnecessary treatment
- Missing a diagnosis in a person who does have ARF may result in development or worsening of heart valve damage and the need for future heart surgery and/or premature death.

The diagnostic tests can be considered as those meant for (i) diagnosis of RF, (ii) presence of active vs. inactive RF in recurrences, and (iii) identification of carditis and valve damage in RHD. (Table 1)

Diagnosis of RF^{2, 4-5}

- 1) The diagnosis of RF is dependent on some laboratory tests included as minor criteria and consist of the following:
 - Acute phase reactants (leukocytosis, elevated sedimentation rate and presence of C reactive protein CRP).
 - Prolonged PR interval in the electrocardiogram.
- 2) The diagnosis requires presence of essential criteria in the form of evidence for recent GAS infection and consists of:
 - (i) elevated anti-streptococcal antibodies
 - (ii) positive throat culture for GAS, and
 - (iii) evidence for recent scarlet fever- rare in India
- 3) *Presence of active vs. inactive RF in recurrences:* Two investigations have been tried to assess the presence or absence of active RF in patients with recurrences besides ESR, CRP and evidence for recent GAS infection.
- 4) (i) *Induced subcutaneous nodules (SCN):* The test offers the advantage of being cheap and easily available everywhere. The potential utility of the test lies in identifying active RF. However, additional validation studies are perhaps needed.
- 5) (ii) *Myocardial biopsy:* A study of myocardial histology to identify active vs. inactive RF was utilized in patients of RF. Myocardial biopsies were performed in 89 patients of active RF and chronic RHD to identify active carditis. Myocardial biopsies failed to improve on clinically assessed presence of active RF. Myocardial biopsy was felt to be insensitive for identifying presence of active carditis (Figure 4).

Pathogenesis of Rheumatic fever^{2, 4-5}

Extensive reviews have been written about the pathogenesis of rheumatic fever and existing data have been exhaustively reviewed. The data supporting a role for the group A streptococcus as the triggering agent for development of rheumatic fever cannot be ignored. However, in concluding that currently available data are not sufficiently convincing about a role for

viruses in the pathogenesis of rheumatic fever, one must be careful not to be intolerant of new concepts.

It is clear that viruses may cause heart disease; viruses have been implicated in other forms of cardiovascular disease such as myocarditis and even atherosclerotic lesions to name only two. Autoimmune mechanisms have been postulated to account for cardiac damage. But there is little to directly associate these viruses with rheumatic fever.⁶

Historically there have been three major categories of hypotheses which have been promoted during the past five decades to explain a streptococcal pathogenesis for rheumatic fever.⁶

These include:

- (1) Direct infection (for example, by the group A streptococcus);
- (2) Effects of a streptococcal toxin (streptolysin O has been among the most commonly discussed); and (3) most feasibly, the concept of antigenic mimicry in association with an abnormal immune response.⁷

During the past half century, it is the concept of antigenic mimicry and/or an abnormal immune response to group A streptococcal extracellular or somatic antigens which has been most interesting. The issue was concisely summarized in a recent review by Cunningham who commented: “The disease is autoimmune in nature and most likely results in part from the production of autoreactive antibodies.⁸ Yet, although many candidate group A streptococcal antigenic moieties have been investigated, none has been unequivocally demonstrated to be the inciting “culprit” or to fully explain the disease process.⁹

Rheumatic heart disease surgical procedure

Balloon Mitral Valvotomy was introduced in 1985 is the standard approach for surgical management of valve disease. Mitral stenosis could be corrected surgically either by closed valvotomy, open commissurotomy or by valve replacement if the valve was calcified. Balloon valvotomy provides results as good as surgical valvotomy and has become the treatment of choice in spite of being more expensive. For mitral regurgitation the choice of treatment would be valve repair especially in younger patients to avoid long-term anticoagulant therapy. Most patients with mitral or aortic valve regurgitation end up with valve replacement. Balloon mitral valvotomy has been utilized in the paediatric patients below 12 years in age with acceptable results. It has been extended to patients of mitral stenosis with acute RF, without additional risk and acceptable results. In the presence of acute RF restenosis rate was, however, 40 per cent compared to 10 per cent in those without active RF.¹¹

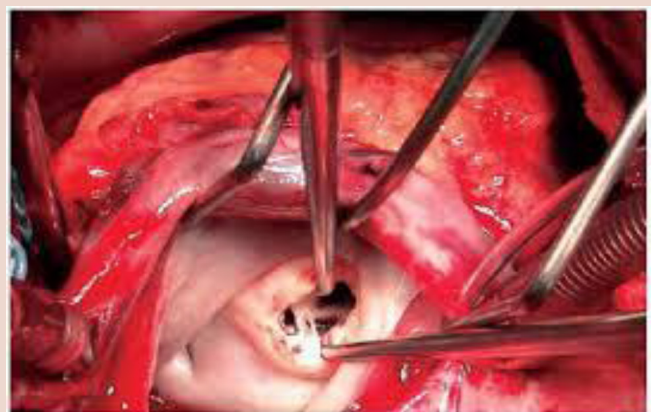


Figure 3: Surgical Repair of Mitral Valve Stenosis Due to Rheumatic Fever.¹⁰

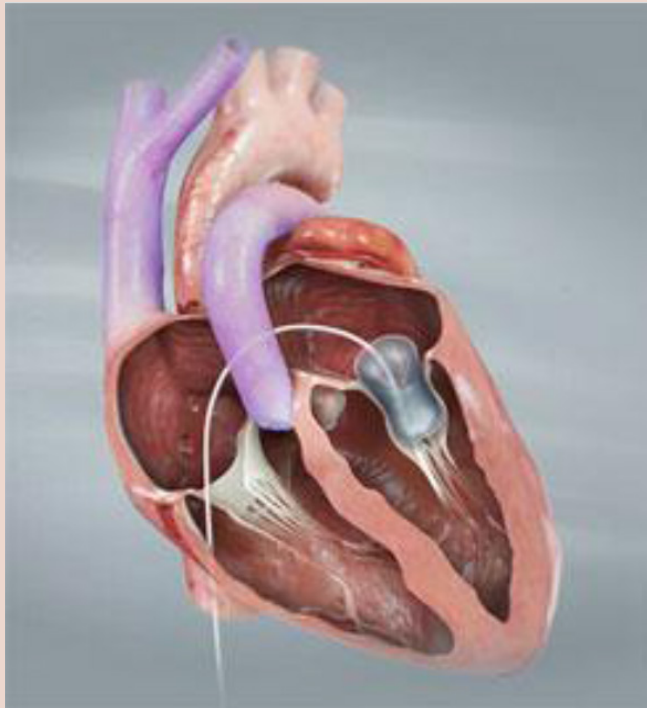


Figure 4: Balloon Mitral Valvuloplasty (BMV) for Rheumatic Heart Diseases.¹²

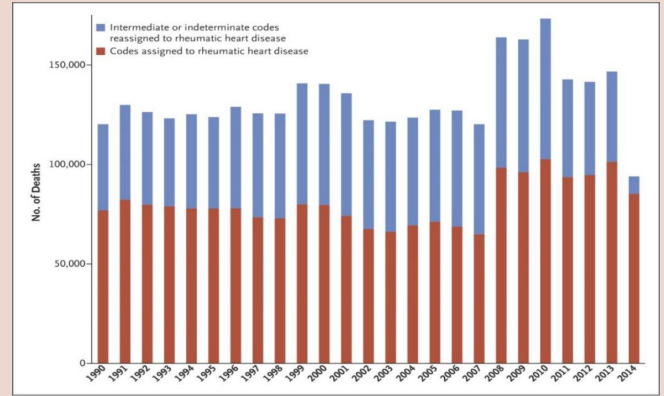


Figure 5: Total Reported Deaths Assigned to Rheumatic Heart Disease and Intermediate or Nonspecific Causes of Death Reassigned to Rheumatic Heart Disease, 1990–2014.⁸

Table 1: Affected valves and diseases.⁵

| Valve involved | Stenotic disease | Insufficiency/ regurgitation disease |
|-----------------|--------------------------|--|
| Aortic valve | Aortic valve stenosis | Aortic insufficiency/ regurgitation |
| Tricuspid valve | Tricuspid valve stenosis | Tricuspid insufficiency/ regurgitation |
| Mitral valve | Mitral valve stenosis | Mitral insufficiency/ regurgitation |
| Pulmonary valve | Pulmonary valve stenosis | Pulmonary insufficiency/ regurgitation |

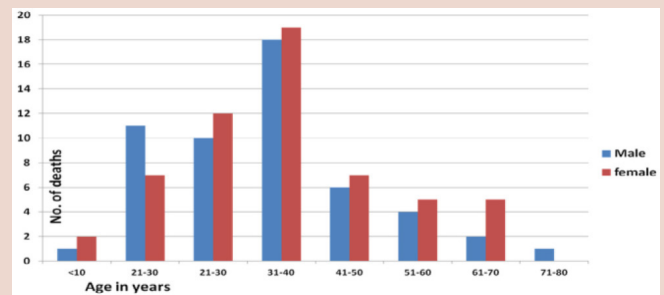


Figure 6: One-year mortality due to RHD in different age groups (N=120).¹⁴

Mortality and morbidity

One of the major causes of cardiovascular mortality and morbidity in developing and underdeveloped countries is Rheumatic heart disease (RHD). Its prevalence has significantly come down in developed countries, but this still remains an important cause of cardiovascular morbidity and mortality of younger age group in underprivileged world. The most important fact associated with this condition is, this is a preventable problem and a lot of morbidity and mortality can be avoided with proper preventive measures. There are many studies conducted to estimate the disease burden of rheumatic heart disease in different parts of the world. These show that the populations living in underdeveloped province are suffering more from the disease (Figure 5).

Age and sex distribution of patients died due to RHD

The mean age at death was 41 years. Median age at death was 35 years. Minimum and maximum ages at death were 8 years and 73 years respectively. Maximum number of deaths were noted in females of age group

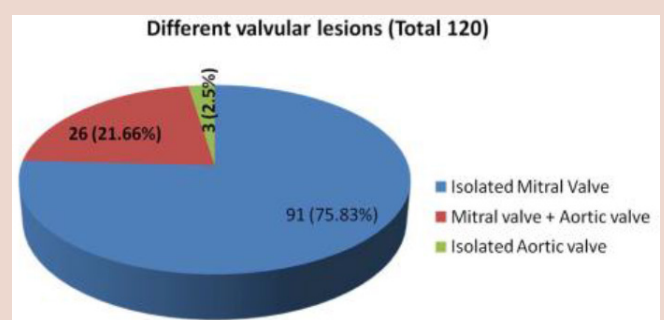


Figure 7: Distribution of different valvular lesion.¹⁵

31-40 years (19) followed by males (18) of the similar age group.¹³ Overall females outnumbered (67.56%) male (53.44 %) (Figure 6).¹³

Distribution of different valvular lesions¹⁵

Isolated Mitral valve affection was most common, found in 91 (75.83%) patients followed by Mitral valve and Aortic valve in combination. Tricuspid regurgitation secondary to pulmonary artery hypertension was not counted in this category (Figure 7).¹⁵

Treatment

Primary prevention of acute rheumatic fever (the prevention of initial attack) is achieved by treatment of acute throat infections caused by group A streptococcus. This is achieved by up to 10 days of an oral antibiotic (usually penicillin) or a single intramuscular penicillin injection. People who have had a previous attack of rheumatic fever are at high risk for recurrent attacks. Procaine Penicillin is the most commonly used antibiotics for secondary prophylaxis unless the patient is allergic to penicillin.¹ The management of rheumatic fever is geared toward the reduction of inflammation with anti-inflammatory medications such as aspirin or corticosteroids. Antibiotics should be administered to individuals with positive cultures for strep throat. Aspirin is the drug of choice and should be given at high dose.¹

Prevention

Primordial Prevention

- Primordial prevention aims to minimize risk factors for a disease in a population. Preventing streptococcus group A infections through managing factors like improvement to environment, economic, social and behavioral conditions that are known to increase the risk of infections. Examples include improved housing and reduced overcrowding.²

Primary Prevention

- Primary prevention aims to prevent complications from a known problem. In Australia, primary prevention includes early diagnosis of group A streptococcus throat infections in people most at risk of ARF (typically children aged 5–14 years), and treatment with antibiotics, commonly penicillin. This helps prevent spread of the streptococcal infection to others and helps prevent the infected person's body having an auto-immune reaction to the infection resulting in ARF.¹

Secondary Prevention

- Secondary Prevention refers to the early detection of disease and measures to prevent recurrent disease and worsening of the condition. Preventing reoccurring ARF which further prevents RHD or prevents worsening of RHD. Secondary prophylaxis with regular Benzathine Penicillin G (BPG) is the only RHD control strategy shown to be effective and cost-effective at both community and population levels. Secondary prevention mainly focuses on the strategies which aimed at improving the delivery of patient care and secondary prophylaxis, coordination of available health services, education provision and advocacy for necessary and appropriate resources.²

Tertiary Prevention

- Tertiary prevention aims to prevent complications once a disease is established. In the case of RHD, this means reducing symptoms to minimize disability and prevent premature death. Examples include heart valve surgery, medication to manage heart failure, and preventing stroke.

Vaccine

No vaccines are currently available to protect against *S. pyogenes* infection, although research is underway to develop one. Difficulties in developing a vaccine include the wide variety of strains of *S. pyogenes* present across the environment and the large amount of volunteer people and time that will be needed for required appropriate trials for safety and efficacy of the vaccine to be developed.

Inflammation

While corticosteroids are often used, evidence to support this is poor. Salicylates are useful for pain. Steroids are reserved for cases where there is evidence of an involvement of the heart.

The use of steroids may prevent further scarring of tissue and may prevent the development of sequelae such as mitral stenosis.

Heart failure

Some patients develop significant carditis which manifests as congestive heart failure. This requires the usual treatment for heart failure: ACE inhibitors, diuretics, beta blockers, and digoxin. Unlike normal heart failure, rheumatic heart failure responds well to corticosteroids.

Rheumatoid heart disease with pregnancy

Issues that have to be addressed include the risks during pregnancy to the mother and the developing fetus by the presence of maternal valvular heart disease as an intercurrent disease in pregnancy. Valvular heart lesions associated with high maternal and fetal risk during pregnancy include:

1. Severe aortic stenosis with or without symptoms
2. Aortic regurgitation with NYHA functional class III-IV symptoms
3. Mitral stenosis with NYHA functional class II-IV symptoms
4. Mitral regurgitation with NYHA functional class III-IV symptoms
5. Aortic and/or mitral valve disease resulting in severe pulmonary hypertension (pulmonary pressure greater than 75% of systemic pressures)
6. Aortic and/or mitral valve disease with severe LV dysfunction (EF less than 0.40)
7. Mechanical prosthetic valve requiring anticoagulation
8. Marfan syndrome with or without aortic regurgitation.¹¹

Progression of disease, quality of life and outcome

Good health and well-being are the goal of medicine. However, medical and surgical treatment of severe rheumatic valvular disease are at best palliative, and these are neither accessible nor affordable to the majority of the affected patients who are poor and young. The age for repair of mitral valve was 20-30 years old. This being the productive and young age-group. Unfortunately, RHD has compromised their quality of life from a young age. In addition, amongst the adult patients who required rheumatic mitral valve repair or intervention, there was female preponderance. In an adult out-patient audit, 74.5% of the patients with RHD were female, of which 77.1% were in the reproductive age group of 15-45 years old. These patients require more medical care during their antenatal, intrapartum and postnatal period; and have higher rates of morbidity and mortality for both the mother and the baby. ARF recurrences cause progressive valvular damage and can lead to complications such as congestive cardiac failure, atrial fibrillation, stroke or infective endocarditis. About three quarter of patients undergoing rheumatic mitral valve surgery had congestive cardiac failure and a quarter had atrial fibrillation.¹¹

Recurrent attack of rheumatic fever and prevention

Secondary prevention of recurrent ARF with regular intramuscular benzathine penicillin injection to prevent recurrent streptococcal pharyngitis and progressive valvular damage, is an important and proven cost-effective measure to reduce the financial and medical burden of ARF and RHD on both the population and the healthcare system.¹¹

Effect of smoking and alcohol consumption

Consumption of alcohol and tobacco use have been associated with a wide range of cardiovascular diseases, which may be detrimental and (for moderate drinking) some potentially beneficial effects. Intake of three or more alcoholic drinks per day and smoking tobacco share additive, adverse effects on some forms of cardiovascular disease. Examples of these adverse effects include increases in blood pressure and levels of triglycerides in the blood and higher risks of stroke and congestive heart failure. Relatively little evidence is available that effects are worse when smoking and drinking occur together than from their independent effects alcohol and tobacco consumption act synergistically. In most cases, more moderate drinking does not share these risks and even has effects opposite those of cigarette smoking on HDL-C and blood clotting.¹⁶

Health education

Presently there is no any national health programme or health education programme related to control of RHD, in India. The knowledge and awareness regarding RHD may be spread to the community by posters, banners and television shows. Community level health workers may be educated that patients with joint pain or swelling should contact physician as this could lead to valvular heart disease. This approach can help to detect ARF in early stage. When such patients are brought to the physician they should undergo blood investigations and echocardiography as required.¹

WHO register based project

A register based project for control of ARF/RHD was launched by WHO in 1972. This had shown a significant reduction in health costs. WHO then embarked upon a global programme and by 1990, ARF registers had been established in 16 countries and over 3000 cases of RHD or prior ARF detected. A later review highlighted improved compliance with secondary prophylaxis. Subsequently only a few countries expanded their programmes. In India also this approach of controlling RHD is lacking. In present scenario this could be very useful in ensuring secondary prophylaxis due the fast development of telecommunication in recent years. Today most of the people, even those residing in the remote villages are having the mobile phones.¹

If a registered RHD patient does not turn up for secondary prophylaxis he/she can be contacted and reminded through his/her registered phone number to get it done. Thus, a higher percentage of secondary prophylaxis can be ensured which will ultimately reduce overall prevalence of RHD and severe form of the disease in the society.¹

Future advancements in diagnosis

The use of the much cheaper hand-held portable echocardiography to detect RHD in children and adults with symptoms should be explored, as the image quality might be sufficient for screening purposes. Interestingly, the World Health Organization supported the development of a simple, affordable, solar-powered blood-pressure device. Support for other cheaper devices, as for cardiac ultrasound, would be laudable.¹⁷

World health federation

RHD Action is a global initiative that unites and empowers the rheumatic heart disease community. Led by a coalition of core organizations, RHD Action shares technical advice, advocacy support, and policy insights with partners and allies across the world. Together, we work to create positive change and better health outcomes for people living with RHD and their communities. Since co-founding **RHD Action** in 2015, the World Heart Federation's work to prevent and control RHD has been channeled through this initiative, whose other founding members include **RhEACH** and **Medtronic Philanthropy**.¹⁸⁻²⁰

CONCLUSION

Rheumatic heart disease (RHD) is one of the heart diseases acquired in adults and young children mainly in developing countries. Streptococcal infection leads to Rheumatic fever which in turn leads to heart condition. Heart valves functionality is majorly affected. It requires immediate medical attention or it may lead to medical complications. Today preventive cardiology is mainly focused upon the ischemic heart disease globally, but RHD is a significant problem in developing world which causes a lot of morbidity and premature deaths. It can be prevented and controlled with patient education, early case detection and regular secondary prophylaxis through patient registry system.¹ Lack of awareness about acute rheumatic fever and its effect on heart valves can lead to worsening of damage caused to heart valves and may also lead to premature death. The heart condition can be managed through surgeries. Currently there are no national health programme or health education programme related to control of RHD, in India. Awareness and knowledge sharing regarding rheumatic heart disease helps to control the incidence of the disease.²¹⁻²²

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CONFLICT OF INTEREST

There are no conflicts of interest.

ABBREVIATIONS

RHD: Rheumatic heart disease; **RF:** Rheumatic fever; **ARF:** Acute rheumatic fever; **CRP:** C reactive protein; **GAS** group A streptococcal; **SCN:** Induced subcutaneous nodules; **BMV:** Balloon Mitral Valvuloplasty; **BPG:** Benzathine penicillin G; **NYHA:** New York Heart Association; **LVEF:** Left ventricular ejection fraction; **HDL-C:** high-density lipoprotein-cholesterol; **WHO:** World Health Organization; **RhEACH:** Rheumatic heart disease. Evidence. Advocacy. Communication. Hope.

SUMMARY

Both RF and RHD are considered to be a neglected public health problem with respect to the Indian scenario. Keenness of a declining trend in RF and RHD through improving socioeconomic status as materialized in the developed countries. Whereas in India despite overwhelming evidence of the cost-effectiveness of registry-based prevention programs the country does not have any national program or effective policy for the control and treatment of RF and RHD. Furthermore inadequate understanding of the pathogenesis also disadvantaged research and development in the treatment of RF and RHD. In addition it happened the further development for research in production of an effective vaccine against RF and RHD. Though Indian Council of Medical Research has initiated a program in year 2000 named as Jai Vigyan Mission Mode Project on the prevention and control of RF and RHD. The program mainly deals with the epidemiological studies of streptococcal sore throat having registry-based surveillance of RHD and school-based surveys for prevalence of RHD. Likewise extensive health education based campaigns upsurge the awareness about disease symptoms, signs, mode of transmission and the treatment and management of RHD.

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