Brief Review

Secondary prophylaxis to control rheumatic heart disease in developing countries: Put into a cage if can't be killed

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ABSTRACT

A significant socioeconomic inequality is the main barrier to achieve primordial prevention of rheumatic heart disease (RHD) in the developing countries. An effective vaccine with affordable cost against *Streptococcus* yet to be identified. The subclinical nature of rheumatic fever (RF) is the main hurdle for effective primary prevention of RHD. When RF and RHD are recognized at the earliest, treated adequately and SP with penicillin is strictly followed, then this disease can be kept under control though cannot be eradicated.

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1. Introduction

The prevalence of rheumatic heart disease (RHD) continues to be high in the developing countries.[1] Most of the developed countries have zero prevalence of rheumatic fever (RF) and RHD by 1980 because of significant improvement in socioeconomic growth, healthy lifestyle and timely use of penicillin in streptococcal pharyngitis.[2] In A recent study shows the echocardiographic prevalence of rheumatic heart disease in Indian school children using World Heart Federation (WHF), 2012 criteria is 7.7% which significantly high.[3] Even though the before study is recent and utilizes echocardiocardioghraghic evaluation to estimate the incidence and prevalence of RF and RHD, the study focuses on school children like most of the studies, therefore more likely suffer under reporting when all the age group is considered.[4] There are several strategies to control this disease in the developing countries like primordial, primary and secondary level of prevention. This review looks into the pros and cons of different strategies and highlights which major is the best strategy to control this disease in the developing countries like India, still having significantly high prevalence of RHD.[5]

2. Methods

This review has gone through the history of RF and RHD over last 50 years to find out which strategy is helpful to control or eradicate this disease. The study has used the search engines like Google Scholar, PubMed, Medline, Mendeley, Scopus and Cochrane data base. Original articles, reviews, meta-analysis and relevant book chapters have been included in this review to find out an appropriate strategy to control or eradicate rheumatic fever and rheumatic heart disease in developing countries like India. The review follows the PRISMA guideline preparing this review.

3. Result

Though rheumatic fever affects the age group of 5–15 years of age. RHD has a long natural history spanning over an over period of five decades or more. The natural history is quite eventful, which includes recurrent rheumatic activity, worsening of valvular damage, heart failure, atrial fibrillation and thromboembolism and death. It is considered as a major cause of cardiovascular death after coronary artery disease in the developing countries like India and other countries even though it is an entirely preventable and treatable disease.[6–10] The valvular damage progresses rapidly in the absence of secondary prevention resulting in crippling and killing the most contributing age group in the nation building i.e. young and middle age group of people. The gap in prevalence of RHD is declining around the globe but still there lies a significant gradient in the prevalence and incidence of RHD between developed and developing nations.[11,12] The morbidity and mortality related to RHD are worst in developing countries mostly due to poor infrastructure to care this scourge at all the level of its prevention to treatment.[13,14] Farther is the industrialization, the worse is the incidence and prevalence of RF and RHD.[6] The incidence and prevalence of this disease truly under reported because of poor infrastructure in the health sectors in the developing countries. A large and rapidly rising in population

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growth, rising in number of urban slums, lack of uniform socioeconomic growth and sanitary condition are the major hurdles to eradicate this disease from Indian subcontinent even through the initial desire to eradicate this disease dates to 1960 in India and guideline to prevent and treat this disease was formed by WHO dates back 1960.[15–17] RHD causes significant additional financial burden by crippling and killing the most contributing age group i.e. young and middle age group people irrespective of gender. The affected county spends a lot on prevention, catheter-based intervention and cardiac surgery for valvular damage. Neither the everyone with significant valvular heart disease has access to cardiac surgery and intervention in their local area nor every affected person can afford the cost of travel and surgery because cardiac surgery is not available in the most of the rural, semi-urban and most of the urban areas of India. As this disease has very long natural history and needs active follow up even after surgery, it is difficult for financially challenged people to afford the regular travel and treatment.

Like most of the infectious diseases which are linked to poor socioeconomic status and poor sanitary condition, RHD is 100% preventable. However, this disease still endemic in India[18] because of several issues which are associated with management are summarized in Fig. 1 and Table 1. The primordial prevention target is not reachable in near future in the Indian subcontinent because most of the areas are densely populated, rapid population growth rate, rising number of urban slums, poor living condition and poor health infrastructure.[19] Because of the subclinical nature of this disease and poor health infrastructure, early diagnosis of the streptococcal pharyngitis supported by throat culture or streptococcal antigen test is not feasible because of unavailability issues in remote areas from the city. Overnight improvement in the socioeconomic condition and health infrastructure of this vast subcontinent is a daydream. A ray of hope lies in the secondary prevention of rheumatic heart disease though it can't eradicate but can control this disease to the significant extent as early echocardiographic diagnosis followed by secondary prophylaxis with penicillin is one of the effective strategies in the developing countries and also financially affordable.[20] Secondary prophylaxis is effective only when it started in the very early part of disease before significant structural damage is occurred and continued over a long period of time.[21–23] However, the issues associated with sustaining secondary prophylaxis are as follows

1. Early diagnosis of rheumatic fever and rheumatic heart disease is must which needs echocardiographic evaluation as suggested by WHF,2012 criteria.[24] In the remote areas where there is no higher echocardiography machine is not available a portable echo machine or even a hand held echo probe would be quite useful to prick rheumatic heart disease in its very early stage.

2. Among the drugs used for secondary prophylaxis, the long-acting penicillin in the form of a depot injection or Mobile Injection Kiosks are effective than others like long-acting azithromycin, erythromycin or sulphonamide. The intramuscular injection of pennillion is associated with issues like round the year unavailability in local areas, fear to take injection because of allergy, local site pain and long duration injection on the 3–4 weekly basis.Though, once weekly long-acting oral azithromycin can be used as a substitute but less effective.[25]

The treatment of significant structural damage to heart valves complicated with heart failure, atrial fibrillation, infective endocarditis and thromboembolism is very difficult in the remote areas. The various reasons are 1 the lack of cardiothoracic surgery facility, financial challenge as the patient himself or herself can't earn though they are the earning member of the family, fear of death during surgery, prosthetic valve disease, lifelong medication and follow up even after surgery. Similar issues are also associated with a catheter-based intervention like valvuloplasty life.In either case, long life oral anticoagulation with monthly monitoring of coagulation profile is practically challenging for the people far from cities.

The candidate vaccine for RF is still in the developing stage to meet the criteria of its effectiveness against various strains of group A streptococcus and affordability to all the patients irrespective of their financial status and geographical territory.[26]
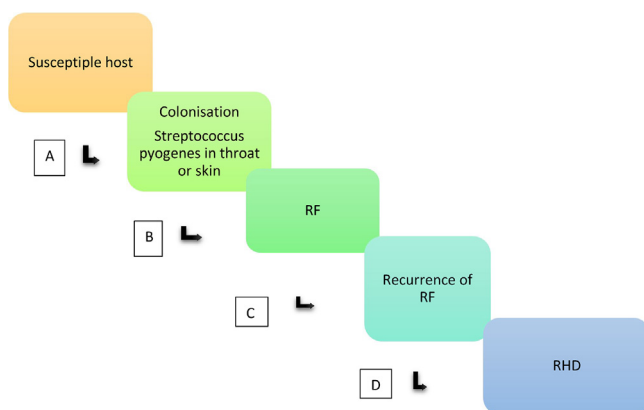
4. Conclusion

At present, the strategy which would be quite appropriate for developing countries is a national level initiative to ensure early diagnosis of all the cases rheumatic heart disease using world heart federation 2012 criteria followed by 100% coverage with secondary prophylaxis with long-acting intramuscular penicillin or its alternative till a nation achieve a uniform socioeconomic progress, hygienic life style and primary prophylaxis to streptococcal pharyngitis. As, the primordial and primary prevention can't be achieved in the near future, RHD can be put into a cage if can't be killed by ensuring 100% secondary prophylaxis to all the cases of rheumatic fever and rheumatic heart disease.

Conflict of interest

There is no conflict of interest.

Fig. 1. Level of intervention to prevent and treat rheumatic fever and rheumatic heart disease. A: Primordial prevention; B: Primary prevention;C: Secondary prevention; D: tertiary prevention (catheter-based intervention or surgery to repair the established structural damage).

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Table 1
The major strategies to reduce morbidity and mortality associated with rheumatic heart disease in developing countries.

Strategy	Advantage	Limitation
Primordial prevention: The reduction of risk factors for *S. pyogenes* exposure and infection in susceptible individuals.[27,28]	Incidence can be reduced to 90% or more by improving living conditions, hygiene, and the use of antibiotics[29] A successful antistreptococcal vaccine would eradicate RF.[11]	Need-based national level strategy, political commitments and international collaboration are needed to improve the socioeconomic status of people which is the pre-requisite for improving living condition.
Primary prevention: This strategy cures a sore throat caused by S. pyogenes, therefore prevent antibody-mediated structural damage to cardiac and other tissues.[30]	A ten-day course of oral penicillin or amoxicillin or a single injection of long-acting penicillin, commencing within nine days of the onset of the *S. pyogenes* infection almost stops cross infection and cures throat infection.[31,32]	At least one-third of ARF episodes occur in the setting of subclinical streptococcal infection. Asymptomatic recurrent GAS infection can trigger a recurrent attack and that an asymptomatic GAS pharyngitis can go undetected. Detection of streptococcal pharyngitis at the earliest phage is a formidable task at the community level in the developing countries.[33] Though some vaccine is available but whether the community can use it to affordably cost needs economical evaluation.[34]
Secondary prevention: A significant approach to prevent of recurrent GAS pharyngitis or pyoderma by continuous antimicrobial prophylaxis in those with previously diagnosed with ARF.[35]	It is the most successful approach to reduce the morbidity and mortality in the developing countries[20] as there are 3 to 10 subclinical RHD cases for every case of clinically diagnosed RHD, echocardiography criteria when used for diagnosis and follow up would increase adherence to SP.[36]	The allergy associated with penicillin and sulphonamide is a reasonable limitation. The use of oral penicillin V is an alternative regimen, but even with 100% adherence, it is not as protective as long-acting intra-muscular Penicillin.[37] Lifelong or long duration painful intramuscular injection leading to poor adherence. Non-availability in locality. There are not enough number of health professional in remote areas to give intramuscular injection of penicillin.
Tertiary Prevention: The provision of catheter-based and valve surgery to prevent morbidity and mortality from cardiac damage that has resulted from ARF.[38]	Improve survival Reduce morbidity.	Financial burden, infective endocarditis prophylaxis, prosthesis valve disease and Lifelong anticoagulation.[7]

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