

# Rheumatic Fever and Rheumatic Heart Diseases in Bangladesh: Challenges and Remedies

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### Abstract

**Key words:**  
Rheumatic fever,  
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*In the 21<sup>st</sup> century, Rheumatic fever (RF) and Rheumatic heart disease (RHD) are neglected diseases of marginalized communities. Globally, RHD remains the most-common cardiovascular disease in young people aged <25 years. Although RF and RHD have been almost eradicated in areas with established economies, migration from low-income to high-income settings might be responsible for a new burden of RHD in high-income countries. Globally, the prevalence of rheumatic fever (RF) and rheumatic heart disease (RHD) has declined sharply but, in developing countries, RF is still a- leading cause of heart disease and, consequently, death in children and young adults. In 2005, it was estimated that over 2.4 million children aged 5-14 years were having RHD globally and 79% of all these cases were from less-developed countries.*

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### Introduction:

Globally, the prevalence of rheumatic fever (RF) and rheumatic heart disease (RHD) has declined sharply but, in developing countries, RF is still a- leading cause of heart disease and, consequently, death in children and young adults.<sup>1</sup> In 2005, it was estimated that over 2.4 million children aged 5-14 years were having RHD globally, and 79% of all these cases were from less-developed countries, such as Bangladesh.<sup>2</sup> The prevalence of RF defined by the revised Jones criteria among children aged 5-15 years in rural Bangladesh was 1.2.<sup>3</sup> These are conservative estimates, especially if echocardiographic screening is used; the actual figures are likely to be substantially higher.<sup>4</sup> Zaman *et al.* opined that protein energy malnutrition is likely to be associated with RF.<sup>5</sup>

Excluding the developed economies, the global burden of RHD in the 5-14 year old children has been estimated to be 0.8- 5.7/1000 with a median of 1.3/1000,<sup>6</sup> while the overall incidence of acute RF varies from 5 to 51/100,000 population with a mean of 19/100,000.<sup>7</sup> In a recent systematic review, the greatest burden of RF and RHD was found in sub-Saharan Africa, the lowest in North America, the highest mortality rates in the

indigenous populations of Australia (23.8/100,000), and among the countries with World Health Organization (WHO) vital registration data, the highest mortality was found in Mauritius (4.32/ 100,000).<sup>8</sup> The exact incidence and prevalence of RF and RHD in Bangladesh are not known. In the 2<sup>nd</sup> half of last century, RF and RHD constituted a significant proportion of admissions in general hospitals, and a lion's share of cardiovascular admissions.<sup>9</sup> Probably the community prevalence of RF and RHD was first reported in 1976, which was 7.5/1000 in general population.<sup>10</sup>

### Discussion:

Rheumatic fever is prevalent in many of the developing countries of the Indian subcontinent, the Arab countries of the Middle East, and the urban metropolises of Central and South America and Africa.<sup>11</sup> In developed countries, it has shown a decreasing trend for more than half a century and become almost absent nowadays. However, the trend in the developing countries remains almost unknown. It is extremely difficult to ascertain the exact trend in a developing country like Bangladesh.<sup>12</sup>

A community-based study was done on 5923 rural Bangladeshi children aged 5-15 years to

determine the prevalence of rheumatic fever (RF) and rheumatic heart disease (RHD). The prevalence was found to be 1.2 (95% confidence interval 0.3-2.1) per 1000 for RF defined by revised Jones criteria and 1.3 (0.4-2.2) per 1000 for Doppler echocardiography-confirmed RHD.<sup>13</sup>

### **Challenges and Remedies: Bangladesh Dealing with Controlling Rheumatic Fever and Rheumatic Heart Disease:**

Bangladesh is always vigilant to curb ARF and RHD with their sequels. Both Government and non government agencies working together in this field. There is a dedicated centre located at Dhaka known as National Center for Control of Rheumatic Fever and Heart Diseases (NCCRF&HD) to control RF and RHD. There is another centre known as National Institute of Cardiovascular Diseases (NICVD) for treatment of RF, RHD and to manage their complications specially Percutaneous transluminal mitral commissurotomy (PTMC), Closed mitral commissurotomy (CMC), Open mitral commissurotomy (OMC) and Valve replacement etc.

### **Following are the stepwise approaches Bangladesh adopted to face the challenges of RF and RHD.**

1. Understanding of disease pathogenesis to improve management

A better understanding of ARF/RHD pathogenesis is critical to developing preventive and therapeutic interventions. Current approaches to diagnosis and treatment of ARF have their foundations in the mid-20<sup>th</sup> Century<sup>14</sup> The Jones Criteria have been revised and updated several times, and some countries have adapted them for their own circumstances,<sup>15</sup> but there continues to be cases of under- and over diagnosis, often with tragic consequences.<sup>16</sup>

#### **A. Immunology of the disease**

We need prospective, active recruitment of ARF cases with a view to using recent technologies to unravel the mysteries of the pathogenesis, particularly the immune response, of ARF. Using standardized data collection forms, each case would undergo thorough immune-phenotypic profiling, drawing on the latest understanding of other autoimmune diseases as well as the latest technologies.

#### **B. Genetics of this condition**

There is an inherited susceptibility to ARF,<sup>17</sup> but the basis for this susceptibility has yet to be clarified.<sup>18</sup> We have never sought genetic markers for ARF/RHD using modern techniques. We need to use these techniques to determine if there are areas of the human genome with polymorphisms highly associated with ARF/RHD, with a view to sequencing and further studying those areas of the genome to identify the nature of host susceptibility.

#### **2. Early Identification to Increase Chance of Success**

It is the unfortunate reality that most new patients entered onto ARF/RHD registers have already developed significant rheumatic valvular lesions. A major challenge, therefore, is to identify people with RHD early in the natural history of their illness, during a phase that often lasts many years when most cases are asymptomatic. The only way to identify asymptomatic cases is to conduct screening. We and others are increasingly demonstrating that echocardiographic screening is preferable to auscultation,<sup>19</sup> but many unanswered questions remain before this can be routinely advocated.

#### **A. Standardization by echocardiographic screening for rheumatic heart disease**

The aim is to share screening echocardiograms through a web-based interface, to compare interpretations by cardiologists and others around the world, with a view to making echo reading as objective as possible. The aim is for all echo readers to undergo training using a standard set of echocardiograms and agreed diagnostic criteria, with measurement of inter- and intra-observer variability before proceeding to read new screening echocardiograms.

#### **B. Evidence-based diagnostic criteria for rheumatic heart disease**

In 2005, a joint NIH-WHO working group developed standardized surveillance protocols for GAS diseases, which included a diagnostic definition of RHD on echocardiogram. This was a consensus definition based on opinion of an expert group, because of the absence of data.<sup>20</sup> The global collaboration needs to consolidate these data to develop evidence-based diagnostic criteria for RHD on echo.

### **C. Determining the significance of subclinical carditis**

There is concern that the extremely high rates of subclinical RHD being found in some studies—often ten times more than found by relying on the presence of a significant cardiac murmur—has not been proven to represent true RHD. Conversely, this may indeed represent a massive undetected burden of RHD, but we have no confirmation that these cases are truly part of the spectrum of clinical RHD, that they may potentially progress to clinical disease, and that they would benefit from secondary prophylaxis.

### **D. Determining the cost-effectiveness of screening, and making it justifiable**

All of this information needs to be compiled in an objective case for screening, complete with economic analysis. If screening is warranted, the challenge then is to make it practical and scalable in developing countries. In all countries, routine screening of school-aged children is not feasible if it relies on highly trained echocardiography technicians using expensive portable machines. The aim would be to generate guidelines for screening accompanied by training curricula for inexpert screening echocardiographers.

## **3. Search for an Effective Approach to Primary Prevention**

### **A. Vaccine for rheumatic fever**

In March 2010, the new Hilleman Institute (collaboration between the Wellcome Trust and Merck, having established an institute in India charged with developing vaccines for less-developed countries) convened a meeting to determine if their first priority vaccine would be for group A streptococcus (GAS). The meeting was a turning point for GAS disease control. It quickly became clear that GAS vaccines would not be chosen for several reasons. The current understanding of the immunopathogenesis of GAS diseases, particularly RF/RHD, is crude, and investigators have not taken advantage of the latest technologies.

### **The role of primary prophylaxis of streptococcal sore throat**

There is a disagreement internationally around the way in which primary prophylaxis should be incorporated into control strategies.<sup>21</sup> Everyone

seems to be in agreement that promotion of sore throat diagnosis and treatment within existing primary healthcare systems is important. Increasingly, there are calls to accept that microbiological diagnosis of GAS pharyngitis is not likely to be practical. So the ongoing debate to use oral or intramuscular penicillin continues.

### **B. The role of controlling skin infection**

There is circumstantial evidence from the Aboriginal population in Australia that skin infection may play a role in RF pathogenesis<sup>22</sup> which, in turn, raises the possibility that community-based programs to reduce rates of impetigo.<sup>23</sup> Streptococcal skin infection might, directly or indirectly, have a causative link with RF, or through intervention studies using either controlled trials or observational studies to map the rates of skin infections against rates of RF/RHD and monitoring changes over time.

## **4. Execute what We Know Already into Practical RHD Control**

### **A. Improved rheumatic heart disease control strategies around the world**

It is universally accepted that the most cost-effective approach to RHD control is delivery of secondary prophylaxis and improved clinical care of ARF/RHD patients using register-based RHD control programs.<sup>[24]</sup> Yet, despite the WHO and the WHF recommending these strategies, there has yet to be established a sustained, national program in any developing country. There are examples of successful RHD control programs in some jurisdictions within countries (e.g. Cuba,<sup>24</sup> and around Chandigarh in northern India<sup>25</sup>).

### **Integrated planning for control programs with primary care and secondary care**

RHD control programs currently undertake little in the way of preplanned interactions with primary care staff. So far, nobody has outlined the most effective way that program staff can provide support to primary care staff that improves service delivery.

### **B. Rheumatic heart disease registers to assess disease outcomes**

With a few exceptions, the paucity of population-based RF/RHD data found in the previous

attempts at measuring the global disease burden persists today.<sup>26</sup> More widespread, and better used, RHD register data would allow us to construct sequential cohorts to track mortality, morbidity, and outcomes of valve surgery, analyzed by age group, presence of carditis or chorea at presentation and level of adherence to benzathine penicillin G.

### **C. Ways to improve delivery of secondary prophylaxis**

Although there is evidence that establishing register-based control programmes will, in itself, lead to improved adherence with secondary prophylaxis regimens, we are still largely ignorant of the specific ways to dramatically improve the proportion of scheduled benzathine penicillin G injections. There are remarkably few studies of this. Some subthemes here are as follows:

#### **D. Understanding factors of adherence**

We need qualitative and quantitative research to better understand perceptions and knowledge of patients, families, and health staff about ARF/RHD and secondary prophylaxis, and practices used by staff and local health systems to deliver care, beyond the small studies available to date.<sup>27</sup>

#### **E. New strategies to improve adherence**

Promising strategies from the above studies could then be trialed at the primary care level. There will likely be a range of designs, depending on the setting and level of health center. Some elements that, based on current knowledge, could be considered include (either stand-alone or in combination) implementation of continuous quality improvement approaches,<sup>28</sup> allocating responsibility for RHD care to particular primary health center staff, streamlining care in clinics so that people are not kept waiting for routine injections, implementing an active recall process and patient empowerment strategies.

#### **F. Effectiveness of comprehensive programs for rheumatic heart disease control**

Successful comprehensive strategies overseas have included registers, support to improve clinical care and delivery of secondary prophylaxis, emphasis on primary prevention (sore throat and skin sore treatment), raising

awareness of the symptoms of ARF and the need to seek medical care, improving knowledge of ARF/RHD, their management, and control among health staff, and broad awareness campaigns in the general community.<sup>29</sup>

### **The burden and economics of RHD and its control**

To date, there have been only two economic analyses of RHD control, both conducted by the same World Bank group, relying largely on data collected in the USA in the mid-20<sup>th</sup> century.<sup>30</sup> We need comprehensive disease burden estimates (using DALYs) and thorough analyses of the costs of ARF/RHD to model the cost-benefit and cost-effectiveness of different approaches to RF/RHD control.

### **G. The role of cardiac surgery for RHD in developing countries**

Middle-income countries such as South Africa, India, and Brazil have a growing capacity for cardiac surgery as well as capabilities to assist lower-income countries to operate on RHD patients. The availability of in-country cardiac surgery is increasing in some lower-income countries as well like Bangladesh. In addition, prosthetic valve replacement potentially carries with it significant morbidity and mortality, with devastating complications occurring due to infection, and hemorrhage or thrombosis related to difficulties in managing anticoagulant therapy.<sup>31</sup>

### **Conclusion:**

Being a third world country Bangladesh is fighting successfully against RF and RHD. Bangladesh can play the role model for those countries who are overburdened with RF and RHD and their sequels. Being a poor country Bangladesh is using its available resources to curb the incidence and prevalence of RF and RHD. Only appropriate planning and judicious implementation can reduce huge economic burden for diagnosis and management of such type of disease. Bangladesh needs more population based studies to get the exact information and inference. It is clear that with concerted efforts, strong links to clinical and

public health infrastructure and with strengthening advocacy and renewed international funding support, we have good prospects of controlling RF and minimizing the burden of RHD over the next decade.

### Competing Interests Statement

The authors declare no competing interests.

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