

# 24 Are We Overlooking Rheumatic Heart Disease in the Conundrum of CAD-The Indian Scene

**Abstract:** Today the practice in cardiology has become synonymous with caring for patients of ischemic heart disease (IHD) right from diagnosis to interventions. This is because in the global scenario there is an increasing incidence of ischemic heart disease and a decreasing prevalence of rheumatic heart disease (RHD) so much so that the medical students in developed countries would not have ever seen a case of RHD in their whole career. In the developing countries like India the statistics for the incidence and prevalence of RHD are available since the past several decades but there is scant and unreliable statistics for IHD. Whereas, it is just the opposite in the developed countries where detailed data are available for IHD and its risk factors from every nook and corner of these nations.

*It is relatively easier to diagnose coronary artery disease (CAD) than RHD because any patient with chest pain is given the benefit of doubt and taken up for management of CAD, whilst any case of arthritis is not considered as rheumatic fever (RF) and most cases are diagnosed only after valvular heart disease has occurred. This is because the Jones criteria for diagnosis is rather complicated for the general practitioners to apply. If the diagnosis of RF and RHD was simplified and only migratory arthritis and / or carditis with history of sore throat were given sufficient importance to start early prophylaxis then certainly the incidence of RF and RHD can be made negligible in coming years.*

There is no specific set of symptoms, signs or laboratory test diagnostic of ARF. Jones criteria makes sense only when applied along with a strong clinical suspicion and judgment.

In a developing country like India, it is always better to over-diagnose RHD rather than under-diagnose by strict adherence to the Jones criteria. Proper and complete treatment of the initial attacks of RF and follow-up with prophylactic therapy are very important to prevent the potentially devastating complications, and curb the disease.

Each year more than 4 million patients are admitted with unstable angine/acute myocardial infarction all over the world, whereas according to WHO the number of children in the world, with RHD was 12 million in year 2000. The incidence of rheumatic fever ranges from 0.6 per 1000 in the US to as much as 11 per 1000 in some parts of India.<sup>1</sup>

In India there may be approximately 1.4 million patients of RHD. According to Dr Padmavati the incidence of RHD today is about an average of 5 per 1000 in India as compared to the low incidence of 0.5 per 1000 cases of RHD in the West.<sup>2</sup>

The Indian population has a very high incidence of Ischemic Heart Disease IHD/CAD, which goes hand in hand with abnormal lipid profile and widely prevalent risk factors that are different from those seen in the western population. Dietary patterns and anthropometric indices show wide racial and regional differences within the country. Hence, the wide variation in incidence and prevalence in the different regions of the country.

There have been epidemiological studies of CAD in India beginning as early as the 1960s, and continuing to date. Most of these studies are small and region-specific and unable to give country level analysis.

Anand (2000), based on various published sources in 1998, found that heart diseases had the highest prevalence (6.6 percent of the total population) along with respiratory illnesses in India.<sup>3</sup>

Bahl, et al (2001), reviewed studies on the prevalence of CAD in India. They looked at studies on urban population (Padmavati 1962, Gupta 1995, Beegom and Singh 1995), as well as rural population (Kutty, et al 1993, Jajoo, et al 1988) for estimating the prevalence of CAD and found that the rates varied across rural and urban populations quite substantially. They attributed the differences not only to the variation in the sample sizes, but also to genuine differences in demographic characteristics.<sup>3</sup>

Most of the studies on CAD in India have been community-based studies. The largest study that has looked into the prevalence of CAD is by Chaddha, et al (1990) among 13,500 urban dwellers in Delhi. The estimated prevalence rate was around 9.7 percent, and the estimates were based on clinical and ECG criteria. Reddy and Yusuf (1998), based on a cross-sectional survey of urban Delhi, found that the high prevalence of CAD in the urban sample was associated with the high levels of body mass index, blood pressure, fasting blood lipids (total cholesterol, ratio of cholesterol to HDL cholesterol, triglycerides), and diabetes.<sup>3</sup>

A body of evidence now exists to indicate that Kerala (an Indian state) may be on the brink of an epidemic of lifestyle diseases. The prevalence of risk factors is alarmingly high in the state, and CAD may be the major cause of cardiovascular diseases (CVDs) in Kerala. A survey based on integrated child development services (ICDS) data looked at the major causes of death in Varkala, Kerala, and found that about 21 percent of all deaths were due to heart attacks (Soman 2004). The same article mentions that a series of studies carried out in the state reveal significantly high risk factors for coronary heart disease in both urban and rural areas. The conclusion seems to be that everyday about 110 people die of heart attacks in Kerala, and about 1.5 lakhs of heart attacks occur every year in the state.

The Economic Review (2004), for Kerala has identified cardiovascular diseases as a major cause of mortality and morbidity in Kerala. Krishnaswami (2004) based on his study found that the prevalence of heart ailments in Kerala state was around 6.85 per 1000. An earlier study by Kutty, et al (1993) in the rural areas of Trivandrum found the prevalence of coronary heart disease (CHD) to be 74 per 1000. Yet another study by Beegom and Singh (1995) in urban Kerala indicated a prevalence of CHD of around 139 per 1000.<sup>3</sup>

Today the practice in cardiology has become synonymous with caring for patients of IHD right from diagnosis to interventions. This is because in the global scenario there is an increasing incidence of ischemic heart disease and a decreasing prevalence of RHD so much so that the medical students in developed countries would not have ever seen a case of RHD in their whole career. In the developing countries like India the statistics for the incidence and prevalence of RHD are available since the past several decades but there is scant and unreliable statistics for IHD, whereas, it is just the opposite in the developed countries where detailed data are available for IHD and its risk factors from every nook and corner of the country.

It is relatively easier to diagnose CAD than RHD because any patient of chest pain is given the benefit of doubt and taken up for the management of CAD whilst any case of arthritis is not considered as rheumatic fever (RF) and most cases are diagnosed only after valvular heart disease has occurred. This is because the Jones criteria for diagnosis is rather complicated for the general practitioners to apply. If the diagnosis of RF and RHD was simplified and only migratory arthritis and/or carditis with history of sore throat were given sufficient importance to start early prophylaxis then certainly the incidence of RF and RHD can be made negligible in few years.

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There is no doubt that the incidence of CAD, hypertension and metabolic syndrome (MS) is showing a steep rise. But at the same time large outlay especially by the private sector, into the management, control and prevention of these diseases. On the other hand RF and RHD are definitely being ignored and in the coming years it is quite possible that there may be a resurgence of this disease resulting in great avoidable loss to the nation.

Several studies have confirmed that the diagnosis of carditis with valvular regurgitation increases with the use of echocardiography in patients of ARF and that echocardiography is an extremely useful tool for detection of RF and RHD (Saxena A, 2000).<sup>4</sup>

A study of 200 patients of RF by Lalchandani, et al showed that out of all the Jones criteria, only arthritis, arthralgia and carditis were present in the patients and no patient had chorea, erythema marginatum or subcutaneous nodules all of which are labeled as major Jones criteria ! Therefore, it was suggested by Lalchandani, et al to simplify the diagnosis of RF to include any patient with arthralgia/arthritis with or without carditis starting with or without sore throat and with or without echocardiographic evidence of RHD.<sup>5</sup>

There is an immense amount of work going on in the field of IHD from conservative management to interventions, surgery, and even stem cell therapy. But in the field of RHD we have not even worked out alternatives for dangerous and fatal drugs like intramuscular benzathine, penicillin and aspirin.

**Table 1:** Incidence of various factors of RHD in two decades (1981-2000)

Year	RF (n%)	RHD n(%)	RF and RHD n(%)	Total HD
1981-85	529 (9.1)	2163 (37.1)	2692 (46.2)	5833
1986-90	550 (9.2)	2295 (39.6)	2845 (47.8)	5949
1991 - 95	693 (9.4)	2681 (36.3)	3374 (45.7)	7384
1996-2000	2409	9798	12.207	26.585

Table by SN Routray<sup>7</sup> : IHJ 2003; 55: 152-157.

In India, the prevalence of RHD between 1940 and 1983 was 1.8 to 11 per 1000, and 1 to 3.9 per 1000 from 1984 to 1995. The prevalence of acute RF was 0.05 to 1.7 per 1000 from 1940 to 1983 and 0.18 to 3 per 1000 between 1984 and 1995.<sup>6</sup>

According to Dr SN Routray, over the past 20 years, there has been no significant decline in the rate of admission to a major government hospital of an under-developed state, Orissa. This was the conclusion from a study of hospital admissions from 1981 to 2000<sup>7</sup> (Table 1).

In school children of the Shimla hills of Northern India, prevalence was 2.98 to 9 per 1000 in a study by Dr Thakur in 1996.<sup>8</sup>

In a study by Jose, et al, out of 2,29,829 children aged 6 to 18 years, screened from 2001 to 2002 in rural district of Tamilnadu, Vellore, 374 children were found to have heart disease. Prevalence of RHD in these children was 0.68 per 1000 children. Prevalence of RHD varies from 1 to 5.4 per 1000 school children.<sup>9</sup> According to V Jacob Jose, this difference in prevalence is due to echocardiographic diagnosis being done in some studies<sup>9</sup> (Table 2).

In a study of prevalence of RHD in school children of district Kanpur, UP, by Lalchandani, et al in 2000, it was found that the total prevalence of RHD was 4.54 per 1000. In urban areas the prevalence was 2.56 per 1000 and in rural 7.42 per 1000. Total prevalence of RF was 0.75 per 1000; 1.20 per 1000 in rural and 0.42 per 1000 in urban school children.<sup>10</sup>

In a study by Lalchandani, et al in 2004 of rural children above age 15 years, RHD was found in 20 out of 4326 people and acute rheumatic activity was present in 2 people. The prevalence of RHD was 4.58 per 1000 and that of acute rheumatic activity was 0.47 per 1000.<sup>11</sup>

In spite of all these studies having been done all over the country confirmatory epidemiological data for RF, RHD and Streptococcal infections have not been compiled, and therefore, the magnitude of the problem is difficult to assess. RF and RHD continue to be a serious problem with great suffering to the whole family of the patient, huge morbidity and mortality resulting in immeasurable loss to the nation in terms of money and manpower.

It is indeed very sad that a disease like RF which has been so well studied and is easily treatable, preventable and controllable is still so widely prevalent in India. It is especially pathetic that a disease which can be prevented at a very low cost is allowed to simmer and flare up to a permanent damage of the valves, the cost of treatment of which then runs into lakhs of rupees.

RHD is a disease of the socio-economically weaker class who live in poor hygienic conditions, poorly ventilated and overcrowded houses. CAD is apparently more common in the affluent classes who have sedentary lifestyles and no dearth of food. Since the patients of IHD are more in numbers in the urban areas and belong more often to the affordable socioeconomic class, it is they who seek treatment right up to the level of revascularization. So, it is but natural that the doctors treating CAD patients will also belong to the creamy layer of their profession.

## PRESENT TEXT ON ETIOPATHOGENESIS OF RF AND RHD<sup>12</sup>

*Rheumatic fever* is acute or first presentation of infection by Streptococcus leading to sore throat, fever, arthritis and/or carditis.

*Rheumatic heart disease* refers to a chronic rheumatic infection leading to irreversible, permanent damage of heart valves.

### Etiology

Rheumatic fever is caused by group A beta hemolytic streptococcal infection.

The disease starts with upper respiratory tract infection, i.e. streptococcal sore throat. After a gap of a few months to a few years involvement of the heart occurs in the form of valvular heart disease.

**Table 2:** Prevalence rate of R fever

Author	Place	Year	Age (yrs)	Population studied	Prevalence (per 1000)
ICMR	Delhi	1982-90	5-15	13509	2.9
Padmavati	Delhi (Urban)	1984-1994	5-10	40000	3.9
Grover et al	Rajpurani	1988-1991	5-15	31200	2.1
Avasthi et al	Ludhiana	1987	6-16	6005	1.3
Patel et al	Anand	1986	8-18	11346	2.03
Lalchandani et al	Kanpur	2000	7-15	3969	4.54
Jose	Vellore	2001 - 2002	5-18	229829	0.68

Table by Jose<sup>9</sup>

### Age

Can occur at any age but typically occurs from 5 to 15 years.

### Epidemiology

Rheumatic fever is more common in:

- Poor (low socioeconomic status) people
- Families of affected individuals

- Poor housing conditions
- Overcrowding.

### Pathogenesis

After streptococcal infection of the throat, the development of rheumatic fever depends upon the immunity of the host, the virulence of the bacteria, individual resistance, serotype 1, 3, 5, 6, 18, abnormal immune response of the host, unique surface markers on non T lymphocytes.

The joints and heart valves are involved in RF and RHD by:

1. Direct infection
2. Toxic effect of extracellular products of bacteria
3. Abnormal immune response.

The theory of antigenic mimicry for rheumatic fever means that some antigens of the streptococci are similar to the host tissues and hence are destroyed by the antibodies produced by the host.

### Diagnosis of RF

RF is diagnosed by application of Jones criteria updated in 1992.

There are 5 major criteria and few minor criteria plus supporting evidence of streptococcal infection.

### 5 Major Criteria

1. Carditis
2. Arthritis
3. Chorea
4. Subcutaneous nodules
5. Erythema marginatum.

**Table 3:** Prevalence of rheumatic fever and RHD 1982-2000

<i>Authors</i>	<i>Place</i>	<i>Year</i>	<i>Age (yrs)</i>	<i>Population studied</i>	<i>RHD prevalence (per 1000)</i>	<i>RF incidence (per 1000/year)</i>
ICMR	Ballabgarh	1982- 90	5-15	22729	1.0	-
ICMR	Varanasi	1982- 90	5-15	12190	5.4	-
ICMR	Vellore	1982- 90	5 - 15	13509	2.9	-
Padmavati	Delhi (Urban)	1984- 94	5-10	40000	3.9	0.384
Grover	Raipurani	1988- 91	5-15	31200	2.1	0.54
Awasthi	Ludhiana	1987	6-16	6005	1.3	0.70
Patel	Anand	1986	8-18	11346	2.03	0.176
Lalchandani	Kanpur	2000	7-15	3963	4.54	0.75

*Table by Grover et al<sup>16</sup>*

### Minor Criteria

1. Fever
2. Arthralgia
3. Increased ESR
4. Increased C-reactive protein
5. Increased PR interval
6. H/o RF, and H/o sore throat.

### *Essential Evidence*

- Positive throat culture for group B hemolytic streptococcus
- Positive rapid antigen detection tests
- Elevated streptococcal antibody titer ASO titer (anti-streptolysin O).

### Major Criteria

#### *Carditis*

There is pancarditis i.e. pericarditis, myocarditis, endocarditis.

*Pericarditis:* There is very little serious effusion like butter on bread (bread and butter appearance) and no constriction, pericardial friction rub.

*Myocarditis:* There is sinus tachycardia, mitral regurgitation, S3 gallop, MR, TR, increased PR interval, heart failure.

*Endocarditis:* There is inflammation of heart valves leading to murmur of mitral stenosis (Carey Coomb's murmur- blowing mid-diastolic murmur at the apex), murmur of aortic regurgitation, and mitral regurgitation.

#### **Arthritis**

- Arthritis is migratory, affecting the ankles, wrists, knees, and elbows.
- Usually the small joints of the hand and feet are not involved.
- Big joints like hip joints are not involved.
- The arthritis lasts for a few days in one joint and then occurs in another joint, even before it is cured in the first joint. When the joint is cured, there is no sequelae or residual deformity of the joint.
- Typically, the arthritis lasts for a day or two in one joint. It flits from one joint to another. This migrating polyarthritis lasts for a few days to weeks affecting one or two joints at a time.

The pain of rheumatic arthritis responds dramatically to 2 g of Aspirin given 4 times a day (3-4 tablets given 4-6 hourly).

#### **Chorea**

- Rheumatic chorea is called Sydenham's chorea or St. Vitus Dance.
- It occurs several months after the streptococcal infection.
- It is very rare.
- Arthritis and carditis are not present in patients of chorea.

In children the chorea starts with restlessness, change in handwriting, irritability, and later typical movements of the trunk and whole body.

#### **Subcutaneous Nodules**

These are small and found over extensor surface of joints in long-standing RHD. They may disappear in a few days.

#### **Erythema Marginatum**

These are transient macular eruptions with rounded borders. May be with irregular margins. Specially on the trunk. Pink in color, non pruritic (do not itch). They are very uncommon in Indians.

## **Evidence of Streptococcal Infection**

The organism – beta hemolytic Streptococcus may be grown on culture from throat swabs – 2 or 3 cultures may be done.

Rapid antigen test for Streptococcus may be done.

Group A streptococcal antibodies may be measured i.e. antistreptolysin O (ASO), anti-deoxyribonuclease B, anti DNase B, anti hyaluronidase, antistreptozyme test.

At least 80% of ARF patients will have raised ASO.

### *Diagnosis*

- At least 2 major or 1 major and 2 minor criteria plus essential evidence of Streptococcal infection is required to diagnose rheumatic fever.
- Usually arthritis and carditis do not occur together.
- Patients of RF may present with chronic valvular heart disease but without history of rheumatic arthritis.
- Patients of rheumatic chorea usually have no arthritis or carditis.
- Subcutaneous nodules and erythema marginatum are usually not present at initial diagnosis.
- Presence of multiple features of Jones criteria indicate active disease.

### *Treatment*

- Antistreptococcal antibiotics
- Treatment of clinical manifestations
- Prophylaxis of RF.

## **Antistreptococcal Antibiotics**

Oral penicillin V 500 mg BD for 10 days.

If allergic to penicillin then erythromycin 250 mg 4 times daily for 10 days.

Or intramuscular benzathine penicillin G single dose – single intramuscular injection of 1.2 million units, after sensitivity test.

## **Treatment of Clinical Manifestations**

### *Arthritis*

- Salicylates 2 gm 4 times daily
- Other analgesics also give relief
- Prednisone should be avoided as anti-inflammatory
- Duration of anti-inflammatory drugs should be 4-6 weeks and then gradually tapered till ESR returns to normal.

### *Carditis*

- Salicylates and prednisone may have some anti-inflammatory effect.
- Digitalis, diuretics, ACE inhibitors may be used for LV dysfunction and heart failure.
- *Bed rest* at least for a few days is advised to all patient of carditis and patients of arthritis.

## **PROPHYLAXIS FOR RF**

Patients who have had an attack of RF are very prone to recurrence. Each attack of RF leads to increased damage to the heart valves. Therefore, all patients of RF must be given prophylaxis for at least 5 years or more from the last attack.

Prophylaxis consists of benzathine penicillin 1.2 million units (12 lacs) intramuscular after sensitivity test every 21 days.

If the patient is allergic to penicillin then erythromycin 250 mg BD or sulphadiazine 1 g daily is given for 5 years.

## **PROBLEMS IN MANAGEMENT AND PREVENTION OF RHD AND ITS SOLUTION**

Patients of RHD are more in the villages than in the cities as has been shown by various statistical data. Because of this, these patients first go to their family doctor or a PHC. Over a period of time and especially in the last 5 years the two main drugs required in the treatment and prophylaxis of RHD are difficult to procure and consume; these are benzathine penicillin injections and aspirin tablets. With increased cases of consumer litigations against doctors physicians shy away from giving penicillin injections. Also Aspirin in high doses if at all available is not tolerated by the patients. This may have already resulted in a small increase in the incidence of RHD which may be expected to become appreciable in a couple of years unless alternatives to these two drugs are given the green flag.

Two recent publications have suggested alternative treatment regimen for the management of acute RF, i.e. use of NSAIDs instead of aspirin (Aceclofenac and Nimesulide) and oral azithromycin 2 days in a week instead of intramuscular benzathine penicillin for prophylaxis of rheumatic fever.<sup>13,14,15</sup>

These new drugs have been found to be as effective as their old counterparts. The most important thing was that compliance was extremely good with the new drugs. So, if this infectious disease is to be curbed then the use of aceclofenac/nimesulide and azithromycin instead of aspirin and IM benzathine penicillin respectively, needs to be popularized.

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## Multiple Choice Questions

1. **Which of the following is minor criteria for diagnosis of rheumatic fever (Jones Criteria)?**
    - A. Fever
    - B. Arthralgia
    - C. Increased C - reactive protein
    - D. All of the above
  2. **Which of these is true?**
    - A. Rheumatic fever has no association with HLA
    - B. Only HLA DR 2 and HLA DR4 are associated with increased frequency of RF
    - C. It is not known if RF has any association with HLA
    - D. HLA DR2, HLADR4, HLADR1, DRW6, DR7, DW53, DQW2 all have been found to be associated with RF and RHD
  3. **Which of these is true?**
    - A. M Protein is responsible for virulence of group A Streptococcus
    - B. The capsule of streptococcus is responsible for virulence
    - C. Cell wall peptidoglycan is responsible for virulence
    - D. None of the above is responsible for the virulence of streptococcus
  4. **Molecular mimicry is :**
    - A. Molecular similarity of human tissues and the streptococcal organism
    - B. Similarity of antibodies of Streptococcus and other organisms
    - C. Similarity of affected tissues of the body like heart and joints
    - D. All of the above
  5. **Rheumatic fever may be treated by:**
    - A. IM Benzathine Penicillin G 12 lakhs once only
    - B. Penicillin - V oral 500 mg BD × 10 days
    - C. Both A and B
    - D. None of the above
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**1. D 2. D 3. A 4. A 5. C**