

## RESEARCH PAPER

## Rheumatic Fever and Rheumatic Heart Disease among Clinically Suspected Patients with Joint Pain in a Specialized Hospital.

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### Abstract

**Background:** Rheumatic fever (RF) and rheumatic heart disease (RHD) are the leading causes of early cardiovascular morbidity and mortality especially in developing world. Recently more emphasis is given on the role of echocardiography for diagnosis of these diseases.

**Objective:** Recent and reliable data and studies on RF and RHD are very limited in Bangladesh. Therefore, this study was done to diagnose rheumatic fever and rheumatic heart disease among clinically suspected patients.

**Methods:** This cross-sectional study was conducted from February to June 2021 in National Center for Control of Rheumatic Fever and Heart Disease, Dhaka. A total of 250 patients irrespective of age and sex with complaints of joint pain and clinically suspected of RF and RHD were enrolled. Laboratory investigations including CBC with ESR, ASO titer, CRP, ECG and echocardiography were done.

**Results:** Among the suspected patients, acute rheumatic fever without carditis was diagnosed in 10 (4%) patients and 15 (6%) had rheumatic heart disease with recurrent RF and carditis. Rheumatic fever with carditis were diagnosed in 63 (25.2%) patients; among whom 19 (7.6%) had clinical carditis and 44 (17.6%) were diagnosed as subclinical carditis. Acute rheumatic fever was diagnosed only within 5-20 years of age patient and 60% patients of RHD were found in 21-30 age groups. About half (49.20%) of the patients of rheumatic fever with carditis were between 11 to 15 years of age. Several abnormalities of heart valves were detected by Echocardiography; 78.2% of the patients of RF and RHD had mitral regurgitation and all the mitral stenosis cases were detected in patients with RHD. Combination of mitral regurgitation with aortic regurgitation and mitral regurgitation with mitral stenosis was also present.

**Conclusion:** The findings of the study indicate that RF and RHD are not negligible in our country. Though the result does not indicate the prevalence or incidence; however, it highlights the need of systematic large-scale study with inclusion of echocardiography to find the prevalence of rheumatic fever and rheumatic heart disease in Bangladesh.

**Key words:** Echocardiography, joint pain, Revised Jones criteria 2015, rheumatic fever, rheumatic heart disease.

### Introduction

Rheumatic fever (RF) and its complication rheumatic heart disease (RHD) are important public health issues, because they are the leading causes of early

cardiovascular morbidity and mortality especially in developing world.<sup>1</sup> Rheumatic heart disease is a preventable and treatable form of cardiovascular disease, which is the most common acquired heart disease in young people that affects at least 34.2 million people around the world and claims over 340000 lives annually.<sup>2</sup> Although virtually eliminated from Europe and North America, the disease remains common in Central and South Asia, Africa, Middle East, the South Pacific.<sup>3</sup>

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Acute rheumatic fever (ARF) is a post-infectious sequel of pharyngeal infection with group-A  $\beta$ -haemolytic streptococcus.<sup>4</sup> Molecular mimicry and autoimmunity probably play the major role in pathogenesis of ARF and carditis.<sup>5</sup> RHD is characterized by fibrinous pericarditis and interstitial granuloma (Aschoff's nodule).<sup>6</sup> In endemic communities, approximately 60% of people with ARF subsequently develop RHD.<sup>7</sup>

ARF and RHD have been described as “diseases of poverty” because they are highly prevalent in socio-economic disadvantaged settings.<sup>8</sup> Bangladesh has most of the recognized risk factors making her a fertile soil for RF and RHD.<sup>1</sup> Prevalence of RF and RHD (data combined) among children in Bangladesh was reported to be 0.9 per 1000 children while prevalence of RF was found 1.2 in another study.<sup>9,10</sup> Classically, rheumatic fever affects the children and young adults; the disease reaches its peak by the end of first decade, and wanes with age thereafter.<sup>11</sup> ARF incidence is similar in male and female but the risk of RHD is 1.6-2 times greater in women.<sup>7,12</sup>

Jones Criteria, the most widely used diagnostic criteria was modified in 2015.<sup>13</sup> There are several important changes made like the inclusion of echocardiography for diagnosis of carditis, two sets of criteria based on risk stratification.<sup>13</sup> It has given a high importance on echocardiography and provides specific diagnostic criteria for Subclinical carditis (SCC) which is now recognized as a manifestation of ARF.<sup>13</sup> Revision of some of the major criteria, as well as the determination of inflammation and fever rate parameters will help early diagnosis of rheumatic fever.<sup>14</sup> Echocardiography, a cornerstone in worldwide screening of prevalence of RHD, has evolved during last few decades. Therefore, consideration of Revised Jones criteria 2015 will be a better option for diagnosis of RF and RHD.

To ‘minimize the burden of RHD and eliminate RF’ the World Heart Federation (WHF) has launched a mission with the ambitious goal of achieving 25% reduction in premature death from ARF and RHD among individuals aged <25 years by 2025.<sup>15</sup> A major impediment is the lack of true burden of disease estimates on local, national, and international levels, which can be used for the implementation of existing evidence-based, cost-effective approaches for preventing ARF and treating RHD.<sup>13</sup>

Reliable studies and data on RF and RHD are very limited in Bangladesh and the last community-based

study was done 16 years ago.<sup>9</sup> Therefore, the prevalence of RF and RHD in Bangladesh estimated so far may not be accurate, and the true prevalence may be much higher.<sup>1</sup> The present study was designed to diagnose rheumatic fever and rheumatic heart diseases among clinically suspected patients with joint pain according to Revised Jones criteria 2015.

## Materials and Methods

This cross sectional study was conducted from February 2021 to June 2021 in National Center for Control of Rheumatic Fever and Heart Disease (NCCRF&HD), Dhaka. During the study period, total 2985 patients attended in the outpatient departments and among them 250 patients with joint pain clinically suspected of rheumatic fever and rheumatic heart disease were included in this study.

Considering the proportion of joint pain among patients of RF 35–88%, sample size was calculated.<sup>16,17</sup>

Study procedure: Patients irrespective of age and sex with the complaints of joint pain suspected of RF and RHD were enrolled in this study. Suspicion of RF and RHD was based on complaints of patients, clinical history and physical examination. Specialist physicians attended the patients and investigations including CBC with ESR, ASO titer, CRP, ECG were done and cardiologists performed echocardiography. With collaboration of clinical history, physical examination, investigation reports a confirmatory diagnosis was made according to the Revised Jones criteria 2015.

Laboratory investigations: Complete blood count (CBC) was done in automated cell counter machine (ERBA Lyse, Germany) and ESR was performed in automated ESR machine (VES mtrix 20). WBC count  $\geq 11,000$ /cmm in adult and  $\geq 11,500$ /cmm in children was considered as leukocytosis; ESR level  $\geq 30$  mm in first hour was considered as high level ESR.<sup>13</sup>

Quantitative ASO titer and semi-quantitative test of CRP was done in automated analyzer machine (ERBA Automated XL 200). ASO titer  $\geq 200$  International unit/ml and CRP  $\geq 3.0$  mg/dL were considered as significant.<sup>13</sup>

Echocardiography was done with a modern echocardiography machine (Philips, Affinity 30, Taiwan).

Case definition: Acute Rheumatic Fever: Two major or one major and two minor Jones criteria and an evidence of recent streptococcal infection.

Rheumatic heart disease: Disease of heart involving damage of one or more heart valves.

Clinical carditis: Detection of pathological cardiac murmur on clinical examination by auscultation that was not previously present.

Subclinical carditis: Pathological cardiac murmur detected on echocardiography that is not evident clinically on auscultation.

Data collection method: Data were collected using a preformed data collection form. Base line information was collected from the patient after exploration of different complaints. All information regarding clinical features was recorded.

Statistical analyses: All the relevant collected data were compiled on a master chart first and then statistical analysis was done using Microsoft Excel program.

## Results

A total of 250 patients with complaints of joint pain and clinically suspected of rheumatic fever and rheumatic heart disease were enrolled in this study.

Among 250 patients attended with joint pain female was predominant (53.20%) and male to female ratio was 0.88:1. Thirty-six percent patients were in 11-15 years of age group followed by 5-10 years of age group (28.40%). About 78% patients were between 5 to 20 years of age (Table-I).

Among the clinically suspected patients, 10 (4%) patients were diagnosed as acute rheumatic fever without carditis and 15 (6%) had rheumatic heart

**Table-I:** Distribution of patients with joint pain according to age and sex (n=250).

Age (years)	Male n(%)	Female n(%)	Total n(%)
5-10	36 (14.4)	35 (14.0)	71 (28.4)
11-15	38 (15.2)	52 (20.8)	90 (36.0)
16-20	19 (7.6)	15 (6.0)	34 (13.6)
21-25	12 (4.8)	18 (7.2)	30 (12.0)
26-30	7 (2.8)	7 (2.8)	14 (5.6)
31-35	5 (2.0)	6 (2.4)	11 (4.4)
Total	117 (46.8)	133 (53.2)	250 (100)

disease with recurrent RF and carditis. Rheumatic fever with carditis were diagnosed in 63 (25.2%) patients among which 19 (7.6%) had clinical carditis and 44 (17.6%) were diagnosed as subclinical carditis. Acute rheumatic fever was found only among patients of 5-20 years of age. Maximum (60%) patients of rheumatic heart disease were diagnosed in 21-30 years group. About half (49.20%) of the patients having rheumatic fever with carditis were between 11 to 15 years, followed by 5-10 years group (31.75%) (Table-II).

Growing pain was the most common diagnosis other than RF and RHD, which was present in 36% of the total patients followed by Rheumatoid arthritis in 8.4% patients. There were few cases of osteoarthritis, Gout, SLE, septic arthritis and reactive arthritis (Figure-1).

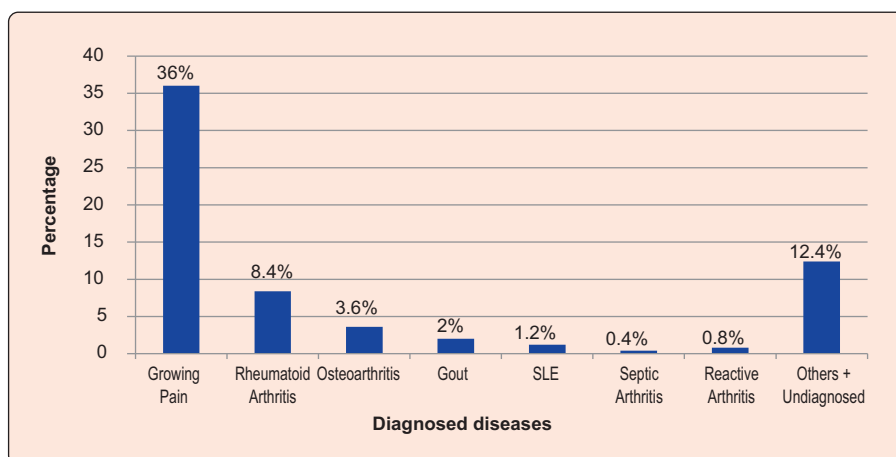
Presence of acute rheumatic fever without carditis was found 14.29% in male and 8.7% in female patients. Rheumatic heart disease was diagnosed in 16.67% male and 17.39% female patients. Rheumatic fever with carditis was diagnosed in 69.05% male and 73.91% female (Table-III).

Echocardiography detected mitral regurgitation in 78.2% patients of RF and RHD. Among other cardiac valvular abnormalities, aortic regurgitation and mitral stenosis was diagnosed in 3.85% and 2.56% patients respectively. Combination of mitral regurgitation with

**Table-II:** Distribution of rheumatic fever and rheumatic heart disease among clinically suspected patients.

Age(years)	ARF without carditis	RHD	RF with carditis		Total
			Clinical Carditis	SCC	
5-10	3	0	6	14	23
11 -15	5	1	9	22	37
16-20	2	3	2	3	10
21-25	0	5	1	1	7
26-30	0	4	1	3	8
31-35	0	2	0	1	3
Total	10(4.0%)	15(6.0%)	19(7.6%)	44(17.6%)	88(35.2%)

ARF- Acute rheumatic fever, RHD- Rheumatic heart disease, SCC- Subclinical carditis



**Figure-1:** Pattern of other diseases diagnosed among patients with joint pain (n=162).

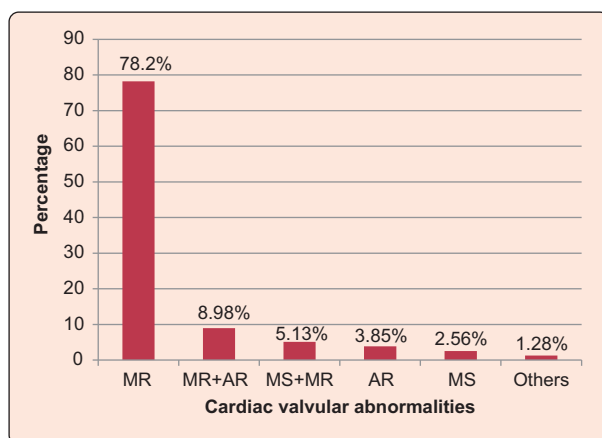
**Table-III:** Distribution of patients with rheumatic fever and rheumatic heart disease according to sex (n=88).

	Male	Female	p-value
ARF without carditis n(%)	6 (14.29)	4 (8.70)	p-value- 0.39321 <sup>S</sup>
RHD n(%)	7 (16.67)	8 (17.39)	p-value 0.99148 <sup>S</sup>
RF with carditis n(%)	Clinical Carditis	11 (23.91)	p-value- 0.88763 <sup>S</sup>
	SCC	23 (50.00)	
	Total	34 (73.91)	
<b>Total</b>	<b>42 (100)</b>	<b>46 (100)</b>	

ARF- Acute rheumatic fever, RHD- Rheumatic heart disease, SCC- Subclinical carditis

<sup>S</sup> -Not significant. The difference between occurrence of ARF without carditis, RHD and RF with carditis among male and female patients are not statistically significant (chi-square test; Significance level- 0.05).

aortic regurgitation was present in 8.98% and combination of mitral regurgitation plus mitral stenosis was present in 5.13% patients (Figure-2).



**Figure-2:** Cardiac valvular abnormalities in color Echocardiography among patients with rheumatic fever and rheumatic heart disease (n=78).

MR-mitral regurgitation, AR-aortic regurgitation, MS-mitral stenosis.

### Discussion

Communicable infectious diseases have decreased in our country; however, the number of patients with rheumatic fever and rheumatic heart disease are not negligible. Bangladesh is quite an endemic place for rheumatic fever with several possible risk factors prevailing here. During risk stratification according to the Revised Jones criteria 2015 children of Bangladesh were considered in ‘Moderate/ high risk population’ as they were ‘Children not clearly from a low-risk population’. As there is no recent study on prevalence of RF and RHD, the authors considered that children of Bangladesh were not clearly in low risk population.

All the patient with acute rheumatic fever in this study were between 5 to 20 years of age which is in accordance with the data in Bangladesh where it was reported that the disease affects mainly children and young adults, most common between 5 to 22 years of age.<sup>18</sup> Rheumatic heart disease may develop few years later among these people as a sequel of acute rheumatic fever.

Acute rheumatic fever without carditis was diagnosed among 4% clinically suspected cases and 6% patients had rheumatic heart disease with recurrent rheumatic fever and carditis. The most common finding in the study was rheumatic fever with carditis that comprised of subclinical carditis (without murmur but with echocardiographic evidence of valvulitis) and clinical carditis (with valvulitis murmur) which was found in 25.2% of total patients and three-fourth of patients with RF and RHD. Carditis, which is the most serious manifestation of rheumatic fever, might be due to undetected and untreated ARF among this study population. If not treated properly, carditis may turn into RHD with its attendant complications of atrial fibrillation, heart failure and even death.<sup>19</sup> Subclinical carditis detected by echocardiography without associated cardiac murmur on auscultation was more common than clinical carditis in this study. Many patients without a known history of ARF are now being diagnosed as SCC due to the introduction of echocardiography in the screening process. Starting of antibiotic in secondary prophylaxis at earlier stage among these patients can reduce morbidity and mortality due to RHD remarkably.<sup>20</sup>

Incidence of acute rheumatic fever was found higher in male than female patients (14.29% vs 8.70%). However, RHD and rheumatic fever with carditis were almost similar in male and female patients with joint pain. Incidence of ARF worldwide is found similar in male and female but in women the risk of RHD is 1.6-2 times greater, which did not coincide with the finding of this study.<sup>7,12</sup> The discrepancies may be due to the difference between the study populations; this study enrolled a small number of patients with joint pain whereas the other studies were done on general population.

Growing pain which is a very common form of episodic childhood musculoskeletal pain was the most common finding in the young patients with arthralgia in this study among whom RF and RHD were not diagnosed. This was in accordance with several studies where it has been reported that discomfort of growing pain is experienced by up to one-third of children during early childhood.<sup>21,22</sup> Diagnosis of growing pain is based on typical clinical symptoms and exclusion criteria and there are no specific laboratory tests.<sup>23</sup>

Echocardiography is indispensable for assessment of valve lesions secondary to RHD and the gold standard comprehensive assessment.<sup>24</sup> Almost all

RHD cases in this study had mitral valve lesions and only few had additional aortic valve lesions. The most common lesion was mitral regurgitation and the result of this study coincides with report of Zu'hlke et al.<sup>24</sup> Mitral stenosis which is pathognomonic of RHD were detected only among cases of RHD. Coexistence of valve involvement like mitral stenosis with mitral regurgitation and aortic regurgitation with mitral stenosis were also found.

The number of patients with RF and RHD found in this study is much higher than the prevalence rate of these diseases among general population of Bangladesh. This higher rate of RF and RHD may be explained in the following ways. This study enrolled only suspected patients of RF and RHD with joint pain in a specialized hospital for this very disease after being clinically suspected by specialist physicians. In this study Revised Jones criteria 2015 adopted by WHF were followed during categorization and diagnosis. Prevalence of RHD was found over two times greater (26.1% vs 11.3%) in studies that employed WHF diagnostic criteria than those using WHO criteria.<sup>25</sup> This discrepancy in prevalence might be explained by the difference in definition for case detection and diagnostic criteria.<sup>26</sup>

Besides, in this study, echocardiography was used as a tool for diagnosis of carditis and RHD. Prevalence of RHD globally was reported more than three times greater (21.2% vs 6.4%) in studies that used echocardiography for both screening and confirmation compared to those studies which used auscultation for screening followed by echocardiography for confirmation.<sup>25</sup> Echocardiography is the most cost-effective tool for population screening and estimating the prevalence of RHD.<sup>27</sup> It is also advisable that echocardiography should be done by specialist cardiologist as sometimes it is difficult to detect subclinical carditis without the help of specialist cardiologist or sometimes it is over diagnosed.

During last few decades due to improvement of the several aspects of socio-economical condition of Bangladesh, disease like RF has much decreased. However, there are some risk factors like malnutrition, overcrowding, inadequate health care facilities, lack of knowledge and awareness, history of repeated pharyngeal infection present here especially among the underprivileged peoples. Even in some developed countries, population groups that live in poverty have high rates of ARF and RHD, like the indigenous

population of New Zealand and northern and central Australia.<sup>7</sup> In this study, history of repeated sore throat or pharyngitis was present in two-third of patients having RF and RHD. There are also some cases of non-adherence of treatment for secondary prophylaxis of rheumatic fever among people of Bangladesh.

### Conclusion

The findings of the study indicate that rheumatic fever and rheumatic heart disease is not uncommon in our country. NCCRF&HD is a specialized center for management of rheumatic fever and rheumatic heart disease and often many patients from all over the country are referred here. Therefore, patients enrolled in this study with joint pain and clinical suspicion of RF and RHD do not represent the general population of Bangladesh. However, results of this study arise the question and highlight the need of systematic large-scale nationwide study with the inclusion of echocardiography especially portable echocardiography and considering Revised Jones criteria 2015 to find the prevalence of rheumatic fever and rheumatic heart disease in Bangladesh and ultimately to reduce the morbidity due to those treatable diseases

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