

# Subclinical rheumatic heart disease: A single center experience

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## ABSTRACT

**OBJECTIVE:** Rheumatic heart disease (RHD) is still a major cause of morbidity and mortality in developing countries. The aim of this study is to investigate asymptomatic RHD cases diagnosed by echocardiography without any acute rheumatic fever history, and to present follow-up results.

**METHODS:** Children who had been admitted to pediatric cardiology department between 2011- 2017 with various reasons (sport participation, palpitation etc) and diagnosed with RHD by echocardiography without a history of acute rheumatic fever were included the study. Echocardiographic findings of the patients were evaluated retrospectively.

**RESULTS:** A total of 75 patients, 55 girls and 20 boys, were included in the study. The median age of the cases was 13.6 years (minimum 5, maximum 18 years). The median follow-up period was 19.2 months, while the longest follow-up period was 66 months. At the time of admission, pathologic valvular insufficiency was present only in mitral valve in 69 (89.3%), only in aortic valve in 2 cases (2.7%), and both in aortic and mitral valve in 6 cases (8%). Forty (60%) cases were diagnosed as borderline RHD at the time of admission and 30 cases (40%) as definite RHD according to World Heart Federation criteria. Eighty- eight percent of the cases remained the same as borderline RHD, the findings of 2 patients improved from definite to borderline RHD. RHD of 4 patients deteriorated from borderline to definite RHD and in 2 patients valvar insufficiency completely resolved during the follow-up period. None of the cases needed valvar replacement.

**CONCLUSION:** RHD is still a serious health problem in our country. The sensitivity of echocardiography in detecting subclinical mild or asymptomatic cases is well known. For this reason, although it is not yet applied as a routine study, it is important to give a start to the nationwide echocardiographic screening program.

*Keywords:* Asymptomatic; children; echocardiography; rheumatic heart disease.

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Acute rheumatic fever (ARF) is an important public health problem in developing countries including Turkey [1–3]. Although ARA and RKH are considered to be parts of the same whole, their evaluation per se provides benefit. Indeed in some ARA patients, cardiac involvement is not seen at all, and in the medical history of nearly 50% of cases with RHD diagnosis of ARF is not encountered because of silent progression of ARA or unmade diagnosis This condition is termed as subclinical

carditis and is considered to be the major finding in both low and moderate and high-risk populations according to Jones criteria, which were lastly readjusted in 2015 [4].

Diagnosis of cases with definite ARA story and bearing morphological and functional features of RCC is easy to make. In certain cases with a definite history of ARA having any valvar structural/functional impairment is RHD unless proven otherwise [5]. However, the sub-clinical course leads to delayed diagnosis, and onset of

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**TABLE 1.** World Heart Association echocardiographic diagnostic criteria of RHD for patients aged  $\leq 20$  years

	Morphological changes	Pathological valvular insufficiency
Mitral valve RHD	Thickening of anterior mitral valve leaflet ( $\geq 3$ mm, age-specific) Thickening of chordae tendineae Reduced leaflet mobility Extensive mobility of the leaflet tip during systole	It should be observed in two different views  Insufficiency jet length should be $\geq 2$ cm in at least one view The velocity in one complete envelope should be $\geq 3$ m/sec Insufficiency jet should be pansystolic in at least one envelope
Aortic valve RHD	Irregular or focal consolidation Coaptation defect Reduced leaflet mobility Prolapsus	It should be observed in two different views Insufficiency jet length should be $\geq 1$ cm in at least one view Velocity should be $\geq 3$ m/sec in early diastole Insufficiency jet should be pansystolic in at least one envelope
Definite RHD (A, B, C or D)		
A. Pathological MR and presence of at least two morphological features of RHD of mitral valve		
B. Mitral stenosis (mean pressure gradient $\geq 4$ mmHg)		
C. Pathological AI, and presence of at least two morphological features of RHD of aortic valve		
D. Concomitant presence of borderline rheumatic involvement of both mitral and aortic valves		
Borderline RHD (A, B or C)		
A. Presence of at least two morphological features of rheumatic involvement of mitral valve without pathological MS or MR		
B. Pathological MR		
C. Pathological AI		

AI: Aortic insufficiency; MR: Mitral regurgitation; MS: Mitral stenosis.

secondary prophylaxis at baseline, resulting in increased morbidity and mortality due to RHD.

Echocardiography is the most appropriate tool for early diagnosis of subclinical RHD. In recent years, echocardiographic screening programs have been implemented in some countries in the light of an increasing number of publications [6–8]. A guide was issued by the World Heart Federation (WHF) for the rapid identification of RHD in patients without ARA to be used in these screening programs [9]. Table 1 summarizes the criteria found in this guideline.

Knowing the diagnostic criteria for RHD is also very important in terms of our country. However, there is no new study to determine the prevalence of RHD in our country, also a national echocardiographic screening program is not available.

The aim of this study is to analyze echocardiographically detected cases with RHD without ARF in the light of the current diagnostic criteria of RHD, and to share follow-up results of these cases.

## MATERIALS AND METHODS

Established cases with available echocardiographic evidence of pathologic valve insufficiency under our surveillance without any history of acute rheumatic fever who referred to Pediatric Cardiology Policlinic between 2011 and 2017 with different clinical indications (participation in sportive activities, palpitation) were included in the study. All patients underwent transthoracic echocardiography with a Vivid 3 Expert (General Electric Medical Systems, USA) device using 3 and 7 MHz probes by an experienced pediatric cardiologist. The mitral valve insufficiency jet was assessed throughout the systole in the apical four-chamber examination, and, aortic valve insufficiency jet was assessed in the apical five-chamber examination throughout the diastole.

For the echocardiographic diagnosis of the pathologic valve insufficiency, criteria previously defined, and then updated by WHF in 2012 were used [9]. According to these criteria, for the mitral valve insufficiency the following criteria should be present: insufficiency jet should be

**TABLE 2.** Characteristic features of the patients with rheumatic heart diseases (n=75)

Age (mean±SD)	13.6±3.3 years
Gender, % (female/male)	73.3 /26.7
BMI (kg/m <sup>2</sup> )	19.4±3.6
Complaints (%)	
Chest pain	36
Palpitation	10.7
Murmur	9.3
Syncope	6.7
Other	37.3
Murmur, % (yes/no)	26.7/73.3

SD: Standard deviation; BMI: Body mass index.

seen at least two different sections; jet length should be at least 2 cm, and peak flow rate should be at least 3 m/sec during systole; however criteria for aortic valve insufficiency were as follows; at least insufficiency jet should be seen at least two different sections; the length of the jet should be at least 1 cm, and the peak flow velocity along the diastole should be greater than 3 m/s.

The presence of borderline, and definite RHD was also assessed according to criteria including morphological valvar changes determined by WHF. The presence of mitral stenosis or at least two of the RHD morphologic criteria in addition to pathologic mitral regurgitation (MV) for the mitral valve was assessed to be sufficient for definitive diagnosis of rheumatic mitral valve disease. For the aortic valve insufficiency, the presence of at least two morphological criteria in the setting of pathologic aortic regurgitation (AR), which was sufficient for the diagnosis of definitive rheumatic aortic regurgitation (Table 1).

The data were analyzed using the SPSS 22.0 statistical package program (SPSS Inc., Chicago, Illinois, USA). The distribution pattern of the data was evaluated by the Shapiro-Wilk test. Qualitative variables are shown as numbers and percentages. Quantitative variables were expressed as mean±standard deviation for normally distributed data. Descriptive analysis was performed for the clinical findings of the patients such as age, gender and clinical features.

## RESULTS

During a six-year period, RHD was diagnosed echocardiographically in a total of 75 patients who were referred

**TABLE 3.** Characteristic features of valvular involvement (n=75)

	n	%
Valvular involvement		
Isolated MR	67	89.3
Isolated AI	2	2.7
MR+AI	6	8
Degree of valvular involvement		
Mild	65	86.7
Moderate	10	13.3
Severe	0	0
Types of RHD		
Borderline	45	60
Definite	30	40

AI: Aortic insufficiency; MR: Mitral regurgitation.

to us for different clinical indications. In only 26.7% of the cases physical examination detected heart murmurs. It was determined that the patients were mostly girls and that the most frequent cause of referrals was chest pain. Clinical and demographic characteristics of the patients are given in Table 1.

Echocardiographically, mostly pathologic isolated mitral regurgitation was detected in patients (89.3%). In any one of the patients, severe valve insufficiency was not observed. The characteristics of valvular deficiencies in patients are given in Table 2.

However, morphologic changes accompanying pathologic valvular insufficiencies were detected in 30 (40%) patients and 45 (60%) patients were diagnosed with RHD. There was no difference between the age of diagnosis between patients with definite, and borderline RHD.

Penicillin prophylaxis was initiated for all patients who met the criteria for borderline or definitive echocardiographic diagnosis. While 44 of the 75 patients were followed up for more than one year, and the median follow-up period was determined as 19.7 months. At the end of the follow-up period, echocardiographic improvement was not observed in the majority of the patients, and valvular insufficiency of 2 cases regressed completely. The findings of valve failure of the patients after the follow-up period are given in Table 3.

At the end of the follow-up period, 88% of the cases remained as borderline RHD at baseline and at the end

**TABLE 4.** Follow-up outcomes of the patients

	n	%
Follow-up period (months)	19.2±19.7	
Disappearance of valvular insufficiency	2	2.7
Improvement in valvular insufficiency	13	17.3
Worsening of valvular insufficiency	1	1.3
Unchanged valvular status	59	78.7

SD: Standard deviation.

of the follow-up period, while findings of 2 cases regressed from definite RHD to borderline RHD, 4 cases with borderline RHD progressed to definite RHD, and 2 cases were completely normalized. When the patients progressing to definite RCC were examined, it was determined that the shortest, and the longest follow-up periods were 6 and 66 months, respectively. In 3 of these patients, mitral valve thickening and prolapse of the anterior leaflet were detected by echocardiography, and pathological aortic insufficiency developed in one patient without prior relevant evidence. None of the patients developed valvular stenosis during follow-up. No patient needed replacement of the valve.

## DISCUSSION

RHD is a major health problem in developing countries and is one of the leading causes of acquired heart disease worldwide [6, 10]. Early recognition of the disease is important because it is known that secondary prophylaxis with penicillin prevents the progression of RHD. In recent years, with the frequent use of echocardiography diagnosis of subclinical cases and early detection of the disease has been made possible which emphasized the fact that the frequency of RHD is much more higher than previously thought [8, 11].

It is known that echocardiography is more sensitive than physical examination in detecting mild or asymptomatic CHD [7]. For this reason, WHF has developed echocardiographic screening programs specifically for use in endemic areas and recently published in 2012 consensus guidelines that allow the standardized definitions of RHD as 'definite' or 'borderline' in diagnostic echocardiography [9]. These guidelines include Doppler evaluation of mitral regurgitation and aortic regurgitation

along with morphological features that can be caused by RHD in mitral and aortic valves (Table 1).

The echocardiographic findings of asymptomatic and non-ARA cases, whose information could be accessed during the 6-year period in our study, were evaluated in accordance with the current criteria of WHF. According to our knowledge, our study carries importance in that it is the first study performed in our country that evaluated asymptomatic cases in the pediatric age group according to the current diagnostic criteria of WHF.

The most common isolated mitral valve involvement is rheumatic heart disease, but isolated aortic valve involvement can be seen in approximately 3–5% of the patients [12, 13]. In our study, mitral valve was also mostly affected in 75 subclinical cases with RHD (89.5%) consistent with the literature. Isolated aortic valve involvement alone was found in 2.7% of the cases.

Although there are no clear echocardiographic criteria for mitral valve prolapse (MVP) in adults as in childhood, MVP is associated with pathologic mitral valve insufficiency seen in RHD such as valve thickening, excessive movement at the leaflet tip, and restricted leaflet movement [14, 15]. Thus, it has been emphasized in children that irregular focal thickening of the mitral valve, especially the excessive mobility of the anterior leaflet in systole, and its prolapsus together with the eccentric insufficiency jet accompanying the restricted mobility of the posterior leaflet, should be evaluated in favour of rheumatic etiology [15].

In our study, valvular prolapse accompanied by pathologic mitral valve insufficiency was evaluated as rheumatic MVP and these cases were accepted as definite RCC cases. According to this, a total 26 (34.6%) patients were diagnosed with baseline echocardiography and 3 patients (4%) with rheumatic MVP were detected by follow-up echocardiography.

Although persistence of valvular insufficiencies in subclinical carditis is often reported in various studies, the natural course of this condition is not yet known [12, 16]. In the RHEUMATIC study, one of the largest case series, 6270 children aged 5–15 years were screened, and subclinical RHD was found during echocardiographic examinations, in 128 patients (especially girls in families with low socioeconomic status) and 4% of these patients disease progressed within 3–27 months [17].

Similarly, in a different study by Figureo et al., patients were followed up for 5 years, valvular findings remained the same in 60% of the patients with subclin-



ical [18]. In our study, valvular insufficiency remained the same in 78.7% of the cases, 2.7% the patients were completely healed and in only one patient valvular insufficiency worsened. Taking into consideration the existing studies, conduction of a study with large case series with long-term follow-up results is needed so as to be able knowledgeable about the natural course of the disease.

Though, the pediatric age group gains the most benefit from the secondary protection after early diagnosis of RHD, but typical valve pathologies may not be established due to their young age. For this reason, the definition of 'borderline RHD' has been introduced with current WHF diagnostic criteria, with the aim of increasing the diagnostic sensitivity especially in patients aged  $\leq 20$  years. Since our present study includes only pediatric cases, we advocate that regular follow-up at certain intervals in cases of borderline RHD in childhood, especially in endemic regions such as our country and emphasize the necessity of launching nationwide screening programs for the early detection of these cases.

Secondary prevention is absolutely necessary when diagnosing "subclinical definite RHD" using echocardiography. However, secondary prevention is recommended in patients with borderline RHD, in areas where the prevalence of RHD is too high with inadequate access to valve surgery [19]. In our study, secondary prophylaxis with penicillin was initiated in all cases with definite RHD and in patients diagnosed as borderline RHD due to the higher prevalence of RHD in our country, and recurrent episodes of ARA were not observed in any case during follow-up.

Limitations of our work include the lack of a screening study, limited number of patients and the inadequate length of the follow-up period.

As a result; RKH is a health problem that still retains seriousness in our country. The sensitivity of echocardiography in the detection of subclinical, mild or asymptomatic cases is well known. Detection and follow-up of subclinical cases with RHD thanks to the development of echocardiographic screening programs especially in an endemic region like our country are necessary to overcome this relevant lack of information. For this reason, although not a yet routine approach yet, it is important to launch nationwide echocardiographic screening programs.

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