Original article

Clinical features of rheumatic heart disease in children and adults in Western Ukraine

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Abstract

Background: Rheumatic heart disease (RHD) is still a big problem affecting children and adults in many countries all over the world. ***Objectives*:** The aim of our study was to determine the clinical course of RHD in children and adults of Western Ukraine, to ascertain the reasons for development and progression of the disease, and outline prospects for its prevention. ***Material and methods:*** The study included 32 children aged 11 to17 years and 35 adults aged 20 to 42 years with RHD. All patients underwent a standardized examination protocol, which consisted of detailed medical history, laboratory tests, ECG, Doppler echocardiography. ***Results:*** The mean age in the children group was 15.8±1.5 years and in adults group - 35.4±7.3 years. Rural areas residents were the majority in both children and adults groups, 71.9% and 77.1% respectively. Recurrent acute rheumatic fever (ARF) was observed in 35.0% of children and in 54.3% adults with history of ARF. Long-term secondary prevention of streptococcal infections was satisfactory in 40.0% of child cases and in 31.6% of adult cases. The lack of compliance and poor health awareness among patients and their parents were most common reasons for inadequate prophylaxis. Subclinical RHD was diagnosed in 37.5% of child cases and in 45.7% of adult cases. Isolated mitral regurgitation (MR) was common in child cases (43.8%) while mitral stenosis (MS) (isolated or combined) was the most common in adult cases (88.6%). Clinical signs of heart failure were absent in half of child cases, but were present in all adult cases at functional class II and III (42.3% and 57.7% respectively). Atrial fibrillation occurred in 34.3% of adult cases. ***Conclusion:*** MR is the predominant cardiac valvular lesion in children with RHD. Inadequate secondary prevention was identified as one of the main causes of development and progression of the disease, leading in adults to MS, combined valvular lesions, arrhythmic and infectious complications. Education of patients and their parents is very important for improving compliance with long-term prophylaxis. Special attention should be given to patients from rural areas and those with difficulties in adhering to antibiotic prevention regimes.

Keywords: rheumatic heart disease; children; adults.

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Background: Rheumatic heart disease (RHD) remains a significant issue affecting children and adults in many countries all over the world, especially in middle-income and low-income countries[1]. Rheumatic valvular damage is the result of acute rheumatic fever (ARF), in particular of rheumatic carditis[2]. Despite the reduction in the incidence of ARF in recent decades, the prevalence of RHD is high. Using echocardiography to detect RHD led to its increased diagnosis, especially of subclinical carditis (it exists to 10 times higher than that diagnosed by auscultating) [1-4].

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Valvular damage of rheumatic origin is the main cause of cardiovascular diseases and death from them during the first 35 years of life in developing countries[5-6]. In the world, the number of surgical interventions for rheumatic heart disease do not decrease and the rates of disability from RHD remain high [7-8].

It is very important to diagnose RHD early, so that preventive measures can be promptly adopted giving better outcomes [9]. Until the wide implementation of echocardiography in clinical practice, clinical exam, especially detection of cardiac murmur by auscultation, was the main method of RHD diagnosis[1,7]. Using echocardiography with Doppler has significantly improved diagnosis for RHD, in particular by identifying of subclinical carditis. Numerous papers focused on the diagnosis of subclinical carditis were published in the last decade [3-4, 10-12].

The problem of standardization of echocardiographic screening for RHD, determining the significance of subclinical carditis has emerged over time[9]. In 2012 World Heart Federation formulated and published criteria for echocardiographic diagnosis of RHD on the basis of the best available evidence[1]. In 2015 revision of the Jones criteria for the diagnosis of ARF in the era of Doppler echocardiography was produced by American Heart Association[13].

RHD course and progression also depends on the patient's age, genetic predisposition, country of residence, living conditions, the efficiency of secondary prevention, etc[7].

The aim of our study was to determine the clinical course of RHD in children and adults of Western Ukraine, to ascertain the reasons for development and progression of the disease, and outline prospects for its prevention.

Material and methods

The study included 32 children aged 11 to17 years and 35 adults aged 20 to 42 years with rheumatic heart disease. The study was conducted during the inpatient treatment of the children at Ternopil City Children's Hospital, Ternopil District Children's Hospital and adults at Ternopil University Hospital.

All patients underwent standardized examination protocol, which consisted of a detailed medical history recorded by the physician, general and special laboratory tests, ECG, echocardiography, Doppler echocardiography.

The patients were administered a survey. It included a questionnaire containing the following parameters: age, gender, living conditions (urban or rural residence), genetic history, recurrent rheumatic fever, the lack or irregularity of the secondary prevention. A separate block of questions addressed patient's adherence of secondary prevention of ARF. Questions about recurrent rheumatic fever and secondary prevention were given only to patients with history of ARF.

RHD was diagnosed by clinical and echocardiographic Doppler examination. Some cases of RHD had a history of ARF, diagnosed according to the Jones criteria. Subclinical rheumatic carditis was diagnosed in patients with heart defects without a clear history of ARF. All patients were evaluated using morphological features of RHD and criteria for pathological mitral and aortic regurgitation according to the World Heart Federation criteria for echocardiographic diagnosis of RHD (2012)[1]. Other causes of heart defects (congenital heart diseases, cardiomyopathy, infective endocarditis etc.) were excluded.

Heart failure severity was ranked according to the New York Heart Association (NYHA) Functional Classification.

The results were analyzed using standard procedures with Statistica StatSoft 6.0 software package. The distribution of variables was assessed by Chi-square test and the Fisher's exact test. Significance level of the tests was set at $\alpha = 0.05$.

Ethical approval: Ethical approval for the study was provided by the scientific ethics committee at I. Horbachevsky Ternopil State Medical University. The adult patients and parents of the children participating in this study signed their informed consent.

The study conformed to the principles outlined in the WMA Declaration of Helsinki.

Results. The mean age of children with RHD was 15.8±1.5 years and the majority of them, 24 (75%) were 16-17 yrs. The mean age of adult cases was 35.4±7.3 years (Table 1).

19 (59.4%) of child cases and 13 (37.1%) of adult cases were male, with respectively - 13 (40.6%) and 22 (62.9%) of them female.

Among the children, there were significantly more residents from rural areas than the residents from urban areas (23 (71.9%) versus 9 (28.1%) respectively, χ^2- 4.17, p=0.0411).

Among the adults, the residents from rural areas also were more than from urban areas, 27 (77.1%) versus 8 (22.9%) respectively, χ^2- 7.11, p=0.0077.

Table 1. Baseline characteristics of patients with rheumatic heart disease included in this study

Parameter	Child cases (n=32) n (% of cases)	Adult cases (n=35) n (% of cases)
Age (years) mean/range	15.8±1.5 / 11-17	35.4±7.3 / 20-42
Gender		
male	19 (59.4%)	13 (37.1%)
female	13 (40.6)	22 (62.9%)
Place of residence		
urban	9 (28.1%)	8 (22.9%)
rural	23 (71.9%)	27 (77.1%)
History of ARF		
yes	20 (62.5%)	19 (54.3%)
no (subclinical disease)	12 (37.5%)	16 (45.7%)

Twenty (62.5%) of children RHD cases had a history of ARF, which was diagnosed according to the revised Jones criteria. In these cases the duration of the disease after ARF ranged from 1 to 12 years, with the average duration being 5.80 ± 3.16 years. In most cases (12, 60.0%) RHD has developed during the first 5 years after undergoing ARF, and often during the first 3 years (9, 45.0%).

Recurrent ARF was seen in 7 (35.0%) children with history of ARF: in 4 cases rheumatic heart lesions have developed after the first episode of recurrent ARF, in 2 cases – after the second episode and in 1 cases – after the third episode. The rest of the patients reported frequent tonsillitis/pharyngitis, respiratory infection, but recurrent ARF had not been diagnosed.

A history of ARF was reported in 19 adults (54.3%). In these cases the duration of the disease after ARF ranged from 8 to 30 years.

Recurrent ARF was seen in 9 (47.4%) adults with history of ARF.

Antibiotics for secondary prevention were given for 15 (75.0%) children and for 14 (73.7%) adults with history of ARF. It includes prolonged forms of penicillin injections once monthly. However only in 8 (40.0%) child cases and in 6 (31.6%) adult cases the secondary prevention of streptococcal infections completely adheres to the WHO guidelines. Its irregularity and short duration of the antibiotic prevention were the most common. The lack of secondary prevention was only in 3 cases due to an allergy to penicillin drugs, in other cases the main reasons were the non-compliance and poor health awareness among patients and their parents.

Subclinical rheumatic carditis was diagnosed in 12 (37.5%) child cases and in 16 (45.7%) adult cases. Heart defects in these cases often were discovered incidentally after hospitalization for other diseases. In some child cases, the pathology of the heart was suspected during a medical examination before admission to the athletic team or during a scheduled medical examination.

Adult RHD patients without a history of ARF in most cases were admitted to the hospital with marked changes of the cardiovascular system and signs of heart failure. Patients were hospitalized for further examination after losing consciousness, with pronounced dyspnea, or arrhythmia. In 3 patients the heart defects were found during treatment for pneumonia or severe course of respiratory infection. In 2 cases the valvular heart disease was detected during pregnancy examination.

Baseline characteristics of patients with RHD with or without history of ARF are shown in table 2. There was no significant difference between the cases with history of ARF and without it.

Table 2. Baseline characteristics of patients with rheumatic heart disease with or without history of ARF

Parameter	Child cases (n=32) n (% of cases)		Adult cases (n=35) n (% of cases)	
	RHD with history of ARF (n=20)	RHD without history of ARF (n=12)	RHD with history of ARF (n=19)	RHD without history of ARF (n=16)
Age (years) mean/range	15.7±1.4/11-17	15.9±1.6/12-17	33.9±8.1/20-42	37.2±6.0/25-42
Gender				
male	14 (70.0%)	5 (41.7%)	8 (42.1%)	5 (31.3%)
female	6 (30.0%)	7 (58.3%)	11 (57.9%)	11 (68.7%)
Place of residence				
urban	7 (35%)	2 (16.7%)	9 (47.4%)	4 (25.0%)
rural	13 (65%)	10 (83.3%)	10 (52.6%)	12 (75.0%)

Classification characteristic of rheumatic heart disease cases based on the type of valvular lesions and functional classes of heart failure are presented in table 3.

Mitral valve lesions were observed most often, in 31 (96.9%) of the child cases and in 32 (91.4%) of the adult cases. Isolated mitral regurgitation (MR) was more frequently detected in children (14 (43.8%) versus 1 (2.9%); χ^2-10.34, p=0.0013). Combination of MR with aortic regurgitation (AR) without valvular stenosis was higher in children as well (11(34.4%) versus 0; χ^2-10.42, p=0.0012).

Mitral stenosis (MS) (isolated or combined) occurred more often in adults, 31 (88.6%) than in children, 5 (15.6%), χ^2-11.67, p=0.0006; similarly, aortic stenosis (AS) frequently occurred in adults (9 (25.7%) versus 1 (3.1%) respectively; χ^2-5.07, p=0.0244).

Tricuspid regurgitation (TR) occurred in 8 (22.9%) of the adult cases and in all cases was combined with mitral and/or aortic valvular lesions.

Table 3. Classification characteristics of rheumatic heart disease cases in this study

Parameter	children (n=32)		adults (n=35)	
	n	%	n	%
Type of lesion				
Mitral regurgitation (MR)	14	43,8	1	2.9
Mitral stenosis (MS)	-	-	4	11.4
MR, MS	3	9,4	8	22.9
MR, MS, Tricuspid regurgitation (TR)	-	-	2	5.7
Aortic regurgitation (AR)	1	3,1	-	-
AR, AS	-	-	3	8.6
MR, AR	11	34,4	-	-
MR, MS, AR	2	6,2	11	31.4
MR, MS, AS, TR	-	-	2	5.7
MR, MS, AR, AS, TR	-	-	4	11.4
AR, AS, MR	1	3,1	-	-
Heart failure:				
Absent	16	50.0	-	-
Functional class (FC): I II III IV	 10 5 1 -	 31,3 15.6 3.1 -	 - 15 20 -	 - 42.3 57.7 -

Clinical signs of heart failure (HF) presented in 16 (50.0 %) of children and in all adults. Functional class (FC) I was determined more often in children cases (10 (31.3%); χ^2-9.58, p=0.002), while in all adult cases FC II and FC III was determined.

There were no significant differences between type of lesion and classes of heart failure in child and adult RHD cases with or without history of ARF.

RHD complications diagnosed in this study were atrial fibrillation (AF), which occurred in 12 (34.3%) of adult cases, frequently episodic and paroxysmal and in 4 cases – persistent; infective endocarditis (IE), which was diagnosed in 2 adult cases and in 1 child case; exudative pericarditis which occurred in 2 adult cases.

Discussion:

This study did not detect sex differences in children and adult cases with RHD, consistent with some literature[6]. However, in many countries ARF and RHD are more common in females [14-15], as they are more sensitive to streptococcus A[16]. Marijon E. et al.[14] did not reveal female predominance using only WHO criteria for diagnosis, however using combined criteria (morphological signs and Doppler criteria) they found the increased incidence of RHD in females. In our study females make larger proportion among adult cases, especially in cases with subclinical RHD, although the difference was not significant, evidently, because of the small number of cases.

We found that RHD more frequently developed in patients living in rural areas (both children and adults) rather than in urban, which is in agreement with the findings of some studies[10, 17], while others reported prevalence in patients residing in urban settings[18]. Prevalence of RHD among rural residents may be associated with inferior social conditions compared to urban areas. Children residing in rural areas more often experience cold conditions, have less access to quality healthcare due to the greater distance to the nearest health center and low awareness about the importance of preventive measures.

Recurrent ARF which was seen in our study in 35.0% children and 47.4% adults with history of ARF, was similar to other observations[6]. However, some studies[15] reported only about 9.6% of recurrent rheumatic fever among RHD cases. RHD is commonly caused by recurring valvulitis, which is one of the major clinical manifestations of recurrent ARF [2], and the risk significantly increases after the first recurrent episode of rheumatic fever.

According to our study, only in 40.0% of the child cases and in 31.6% of adult cases the secondary prevention of streptococcal infections was satisfactory. Other studies report 42.18% cases receiving regular benzathine penicillin prophylaxis[9], while irregular and discontinued antibiotics was

given in 70% of the patients[6], that are compatible to our research. The main reason for the lacking secondary prevention was the poor adherence to long-term prevention. Unsatisfactory compliance with the prophylaxis is reported in other studies[6, 12, 19, 20]. Low patient adherence to the therapy may be associated with the parents and patients unawareness of the problem, thus it is very important to focus more on education of doctors and parents. New Zealand guideline empfasize education of affected families and children affected as one of the key methods for improved adherence to prophylaxis [21].

MR was the most common cardiac valvular lesion in children, which is also supported by some of the reports[19, 22-23]. Other studies, however, reported that combined MS with MR[6, 15], or MS alone[24] is the most frequent valvular lesion in RHD cases. In our study MS (isolated or combined) occurred more often in adult cases than in children and MS combined with MR and AR was the most common cardiac valvular lesion in adults.

MS (isolated or combined) occurred in 88.6% of adult cases in our study. In other studies this rate was lower, from 47.3% [15] to 77.1% [6]. A low rate of MS among RHD cases in Ethiopia study[15] can be explained by a younger age of the patients (mean age 23 +/- 8 years) at the time of the survey. In this study we observed MS only in 15.7% of the child cases.

The rate of development MS depends on the geographical area[7]. In high-income countries it is commonly an indolent and slowly progressing disease with a long latency period (20-40 years) without clinical signs [25], but in developing countries valvular lesions progress much more rapidly due to more frequent recurrent ARF, genetic factors and socio-economic conditions [26].

This study confirms prevalence of MR in the young RHD patients. The progression of the disease is caused by unsatisfactory secondary prevention and other factors, leading to MS and combined valvular lesions.

Some authors attribute development of valvular disorders in RHD patients to genetic predispositions[27-28].

TR was found in 22.9% of adult cases and in all cases it was combined with other cardiac lesions. Frequency of TR in this study was in agreement with previous findings [29]. However, other studies were reported lower incidence, 5.7% [6], as well as higher incidence, 48.2% [23] of TR among RHD cases. TR is commonly secondary to right ventricular dilatation, rather than to primary rheumatic involvement [7] and confirms late stages of mitral stenosis complicated by the development of pulmonary hypertension, and by the failure of the right side of the heart.

Half of the RHD cases in children in this study did not have signs of congestive heart failure. Other authors also report relatively low rate of HF after RHD diagnosis with only 27% patients developing HF within 5 years [30]. However, some studies report that about 64% of children with RHD had FC IV and underwent cardiac valvular surgery before 16 years of age [2].

In all adults with RHD in this study have developed congestive HF. These cases were II and III FC according to the NYHA Functional Classification, which indicates progression of heart failure in adults. Other authors report 17%, 25%, 26% and 32% of FC I, II, III and IV, respectively in patients with mean age of 23 +/- 8 years[15]. Literature data indicates that congestive HF is the most common cause of mortality in RHD cases [19].

In this study AF was found in 34.3% adult cases with RHD which is a higher incidence than previously reported 22.8% of the cases and which likewise was the most common arrhythmia[15]. Development of AF in patients with mitral stenosis is most common complication, because of left atrial dilatation, and because of the inflammatory and fibrotic changes caused by the rheumatic process[7].

With age, there is not only the progression of heart failure, but also increase in the frequency of complications, often resulting in death.

Conclusions

MR is the predominant cardiac valvular lesion in children with RHD. Inadequate secondary prevention was identified as one of the main causes of development and progression of the disease, leading in adults to MS, combined valvular lesions, arrhythmic and infectious complications. A large number of cases with subclinical carditis require a careful approach to the diagnosis of all suspected cases. Education of patients and their parents is very important for improving compliance with long-term prophylaxis. Special attention should be given to patients from rural areas and those with difficulties in adhering to antibiotic prevention regimes.

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Study design: Oksana Boyarchuk, Tetyana Hariyan
Data gathering: Tetyana Hariyan, Tetyana Kovalchuk
Writing and submitting manuscript: Oksana Boyarchuk, Tetyana Hariyan ,
Editing and approval of final draft: Oksana Boyarchuk, Tetyana Kovalchuk

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