

CLINICAL FEATURES OF ACUTE RHEUMATIC FEVER IN CHILDREN AT THE PRESENT STAGE

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Abstract

Introduction. Despite significant progress in reducing the incidence, acute rheumatic fever (ARF) has been observed in all countries of the world over the past decades. Determining the features of the course of the disease is important for timely diagnosis, which requires a thorough analysis of clinical, laboratory and instrumental data.

Purpose of the work. Improving the diagnosis of children with acute rheumatic fever based on the analysis of anamnestic data and the clinical course of rheumatic fever in children in the Samarkand region.

Materials and methods. The prospective study involved children aged 5 to 18 years who were treated at the multidisciplinary clinic of the Samarkand State Medical University in 2022. Clinical and anamnestic features of ARF in children from the Samarkand region were revealed. ARF was diagnosed according to the Kissel-Jones criteria. It was studied: indicators of a clinical blood test, data of biochemical analyzes, bacteriological studies, C-reactive protein (CRP), rheumatoid factor (RF), ASLO, the level of cytokines in the blood; data analysis of instrumental research methods: ECG, Echo-KG, ultrasound of internal organs.

Results. Most of the 71 patients (67.6%) with ARF were hospitalized between October and March, with a peak hospitalization in February. Articular syndrome occurred in 60 (57.1%) children. Arthritis was noted in 29 (27.6%) children and arthralgia in 31 (29.5%). Polyarthritis was characterized by a migratory character. In 28 (26.7%) children, chorea was noted. Among 24 patients with chorea, 7 ARF were diagnosed as isolated chorea, and 17 children developed chorea in combination with other manifestations of ARF. Erythema annulare 3 (2.86%) children. Rheumatic nodules were not detected in our study. ECG changes in children with carditis: tachycardia was observed in 28 (26.7%) children, sinus arrhythmia - in 29 (27.6%), bradycardia - in 16 (15.2%) children. Prolongation of the PQ interval, which refers to the small criteria for ARF, was observed in 8 (7.6%) patients. Echocardiography revealed tachycardia, mitral regurgitation in 68 (65%) children, a combination of mitral and tricuspid regurgitation in 41 (39%) children, and aortic regurgitation in 1 child.

Conclusion. Our study shows the need for further research to improve the diagnosis and treatment of ARF. The significant rate of misdiagnosis in children with ARF upon admission to the hospital indicates that doctors need more research in our region and awareness of primary care physicians.

Keywords: acute rheumatic fever, criteria Kiselya -Jones, children, clinical and anamnestic features, cytokines.

Rheumatic fever (RF) develops in genetically predisposed children (from 5 to 15 years old) after suffering from streptococcal tonsillitis or pharyngitis associated with group A β -hemolytic streptococcus, during which the patient develops manifestations of the disease in the form of carditis, arthritis, chorea, subcutaneous nodules and erythema annulare.

The diagnosis of rheumatic fever is based on the Kessel-Jones criteria, developed in 1944, then revised twice by the American Heart Association (AHA) in 1992 and in 2015.

According to WHO, rheumatic heart disease remains one of the leading causes of disability and mortality in young people under 35 years of age due to cardiovascular diseases [1, 2].

The original Jones criteria proposed by Dr. T. Duckett Jones were modified four times, and the updated revised criteria were published in 1992 [15,16,17] According to this latest publication, the main manifestations are carditis, polyarthritis, chorea, erythema annulare, and nodules. Minor criteria include fever, arthralgia, and laboratory evidence of elevated erythrocyte sedimentation rate, C-reactive protein, and prolongation of the PQ interval on the ECG. For a diagnosis of acute rheumatic fever, two major or one major and two minor manifestations must be accompanied by supporting evidence of prior group A streptococcal infection in the form of a positive throat culture or an elevated or rising antistreptolysin titer. The updated guidelines also identified a subgroup of "exceptions to the Jones criteria" for patients with chorea, latent carditis, and a history of rheumatic fever or "rheumatic heart disease". The role of echocardiography in these modifications has not been determined, but may be important as clinical detection of soft murmurs may be difficult due to tachycardia. Doppler and color flow mapping are more sensitive in detecting minor abnormalities in valvular regurgitation. Several studies have confirmed that the incidence of carditis with valvular regurgitation is increased by the use of echocardiography in patients with acute rheumatic fever. Echocardiography is also of great help in mixed valvular lesions to determine the severity of each lesion. Other abnormalities seen on echocardiography in acute carditis include valve prolapse, focal nodular leaflet thickening, and pericardial effusion.

The Jones Criteria are guidelines to assist the clinician and should not replace clinical judgement, as their strict adherence may lead to misdiagnosis of this disease.

Acute rheumatic fever (ARF) has been a major public health problem in the past century and a leading cause of cardiovascular disease among children [15]. Adequate treatment of streptococcal throat infection, primary and secondary prevention of ARF have reduced its frequency in recent years [16].

Poor socioeconomic status, malnutrition, and overcrowding are the most common risk factors for ARF cases [16]. Improving hygiene and increasing the availability of medical care for children are additional factors contributing to a decrease in morbidity [4]. A long-term study also showed a decrease in the incidence of ARF in children from middle- and high-income families with access to qualified medical care [5]. However, ARF remains a serious problem among children in developing countries [6]. The highest documented rates in the world have been found among Maori and Pacific Islanders in New Zealand, Australian Aborigines, and Pacific Island peoples [6 , 7].

WHO experts argue that there is not enough reliable data on the incidence of ARF. There are great differences between countries, even between populations within the same country (The world health report 2001)

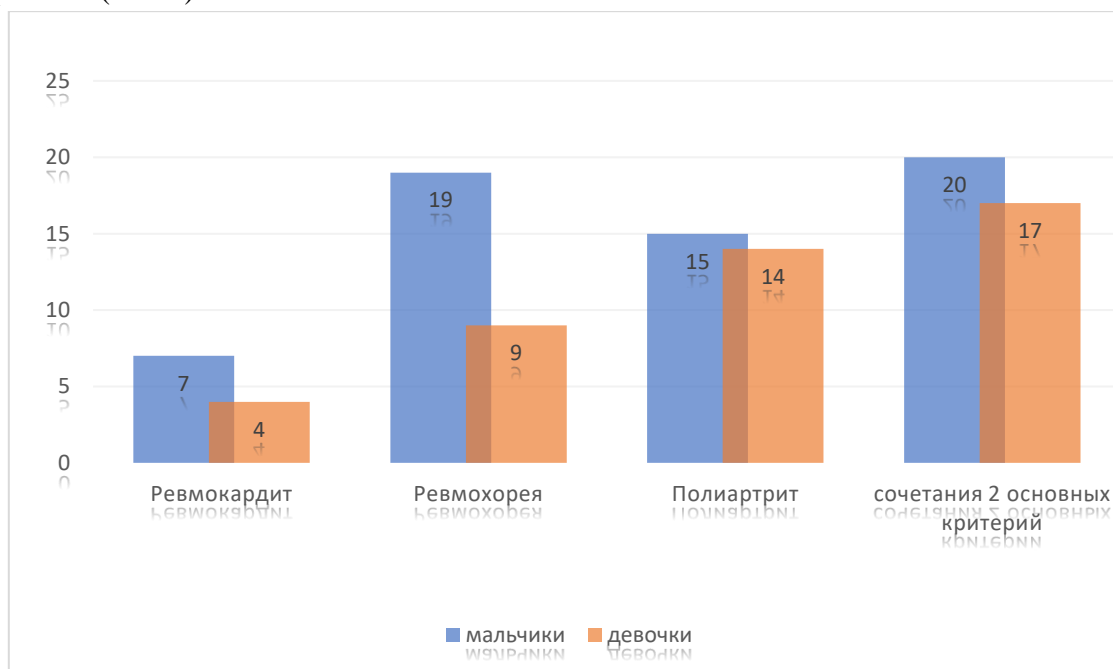
ARF may have different clinical manifestations in different countries depending on genetic predisposition, prevalence of rheumatogenic strains, socioeconomic conditions [8]. There are also differences in the prevalence of Jones criteria across continents [16], which can be explained by epitopamyrrheumatogenic streptococcal strains and genetics [8].

Studying the course and features of this disease is especially important for early diagnosis. The decrease in the incidence of ARF has led to low alertness of family doctors and pediatricians in relation to this disease.

The purpose of this study was to improve the diagnosis of children with acute rheumatic fever based on the analysis of anamnestic data and the clinical course of rheumatic fever in children in the Samarkand region.

Materials and research methods . We examined 105 patients diagnosed with ARF, aged 5 to 18 years, who are being examined and treated in the pediatric department of the multidisciplinary clinic of the Samara State Medical University in Samarkand in 2022. ARF was diagnosed according to the Kissel-Jones criteria. Of the laboratory methods of diagnostics, the following were studied: indicators of a clinical blood test, biochemical analysis data, bacteriological studies, C-reactive protein (CRP), rheumatoid factor (RF), ASLO, the level of cytokines in the blood; data analysis of instrumental research methods: ECG, Echo-KG, ultrasound of internal organs.

Results and discussion. Among 105 patients with rheumatic fever: 58 children with the 1st attack and 47 with a recurrent attack of the disease. Boys (58.1%) prevailed among patients with LC, and the largest number of patients was in the age group of 5-12 years (77.1%). The median age at the time of admission was 9 years. As a result of observation, the following main clinical manifestations of ARF were diagnosed: Rheumatic chorea - in 26.7% of patients (n= 28), rheumatic heart disease - in 10.4% of patients (n=11), polyarthritis - in 68.6% of patients (n= 72).



1-drawing. Frequency of detection of large ARF criteria

An increased incidence of ARF (72%) was observed in children from urban and low-income families. Crowded living conditions continue to be a predisposing factor, contributing to the spread of respiratory infections. In addition, lack of vigilance and poverty among the population lead to a delay in access to health services . (Al- Eissaetal ., 1993; EssopandNkomo , 2005; Carapetis , 2007). Therefore, to optimize the primary prevention of ARF, it is necessary to educate the population in general and children in particular, using all available resources. Most of the 71 patients (67.6%) with ARF were admitted to hospital between October and March, with a peak in February, and (32.4%) were admitted from April to September.



2-drawing. Distribution of ARF patients by months of the year (n).

Most children with ARF sought medical help late, were referred for hospitalization with other diagnoses, and were treated by other specialists for a long time. Difficulty in diagnosis occurred especially in children with minor chorea, who were treated by a neurologist for a long time for neurosis or neuritis of the facial nerve. Anamnestic data confirmed the transferred nasopharyngeal infection in all patients.

Also, the anamnestic data revealed that not all children received standard treatment, in particular, bicillin prophylaxis was carried out at low doses, and some children did not undergo echocardiography at the primary level.

Patients who were diagnosed with carditis (n = 11) complained of pain in the region of the heart upon admission, more often the pain was of a stabbing nature. There were no other complaints from the cardiovascular system. In all children, a systolic murmur was heard at the apex and the Botkin- Erb point , there was a weakening of the heart sounds, especially the first one, and an accent of the second tone over the pulmonary artery.

ECG changes were observed in all children with carditis. Tachycardia was observed in 28 (26.7%) children, sinus arrhythmia - in 29 (27.6%), bradycardia - in 16 (15.2%) children. Prolongation of the PQ interval, which refers to the small criteria for ARF, was observed in 8 (7.6%) patients. Violation of metabolic processes of varying severity was observed in 9 (8.6%) children. Echocardiography in all patients with carditis revealed tachycardia, mitral regurgitation in 68 (65%) children, a combination of mitral and tricuspid regurgitation in 41 (39%) and aortic regurgitation in 1 child . In 15 (14.3%) children, arrhythmias of the type of tachycardia were detected.

Articular syndrome occurred in 60 (57.1%) children. Arthritis was noted in 29 (27.6%) children and arthralgia in 31 (29.5%). Most often, large and medium joints were involved in the pathological process: knee (38.8%), ankle (20.2%), elbow (5.6%). Polyarthritis was characterized by a migratory character.

In 28 (26.7%) children, minor chorea was noted, which was manifested by hyperkinesia in the form of facial muscle twitching, blinking of the eyes, a change in the child's handwriting, irritability, emotional lability, and muscle hypotension. Among 24 patients with chorea, 7 ARF were diagnosed as isolated chorea, and in 17 children, chorea developed in combination with other manifestations of rheumatism. Annular erythema. In 3 (2.86%) children, mothers noticed hyperemic spots, which disappeared within 2 to 5 days.

Rheumatic nodules were not detected in our study. The most frequent main criteria for Jones ARF in Samarkand are polyarthritis (84.7%). Chorea was much more common than carditis.

Small diagnostic criteria. Among the minor criteria for acute rheumatic fever, fever and arthralgia were most frequently observed. Arthralgia in the absence of arthritis was observed in 36 children (34.3%); it involved large joints, including knees, elbows, and wrists. All patients showed signs of intoxication syndrome in the form of general weakness, lethargy, loss of appetite, headache, pallor of the skin, and a decrease in academic performance in schoolchildren.

Group A, β -hemolytic streptococcus was isolated from throat cultures in 36 children (34.3%); This low result was likely due to previous antibiotic treatment, as many children were referred to our hospital by primary care physicians. So the ASLO titer remained the only tool available to confirm a previous streptococcal infection. An increase in the ASLO level as a marker of streptococcal infection was observed in 87 (82.5%) patients. In the general blood test, leukocytosis was observed in 23 (16.4%) sick children. A shift of the leukocyte formula to the left was more often noted. ESR acceleration was registered in 49 (35.0%) patients within the normal range in 5 children (4.76%) who had chorea . On the part of acute phase indicators of inflammation: an increase in the level of CRP was observed in 71 (50.7%) sick children.

1-table. Small manifestations of ARF in children.

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Manifestation	Number of cases	% of total
High ESR (>20 mm/ h)	49	89.5
Heat	56	53.3
Arthralgia	36	34.3

We also studied pro-inflammatory cytokines (TNF-a, IL-6, IL-10) in the blood serum of patients with LC (Table 2). As can be seen from Table 2, despite the cytokine levels, they were significantly increased.

2-table. Parameters of pro- and anti-inflammatory cytokines in patients with recurrent LC ($M \pm m$)

2-table. Indicators of pro- and anti-inflammatory cytokines in patients with recurrent RF ($M \pm m$)

No.	Indicators	Control (n= 3 0)	ORL (n= 40)	R
1	IL-2 (pkg /ml)	10.80 \pm 2.70	19 \pm 2.71*	< 0.05
2	IL-6 (pkg /ml)	11.50 \pm 3.80	18.5 \pm 1.37*	< 0.05
3	TNF-a (pkg / ml)	21 \pm 6.80	62.1 \pm 3.20*	< 0.01

Note: * P is a significant difference between the indicators of the control and the compared group

comorbidities were identified in children : anemia of I and II degrees, helminthic invasion, enuresis, primary pyelonephritis, calcium-penic syndrome and dental caries. Adequate treatment of previous streptococcal infection was carried out in 25 children (53.2%), mainly in children with tonsillitis and scarlet fever. Probably, manifestations of pharyngitis were interpreted as manifestations of viral etiology and antibiotic therapy was not prescribed.

A positive family history of ARF was determined in 12 patients (14.1%). When ARF was diagnosed, patients received antibiotic therapy for streptococcal infection. Penicillin was administered intramuscularly to 67 children (64%). Oral macrolides (erythromycin, clarithromycin, azithromycin) were used in 15 children (14.2%). In other cases, other antibiotics were used due to misdiagnosis upon admission to the hospital. The duration of antimicrobial therapy was 10 days.

Non-steroidal anti-inflammatory drugs were used in 96 patients with ARF (91.8%). Many were treated with diclofenac sodium (67.5%), rarely used acetylsalicylic acid (16.3%). In other cases, other non-steroidal anti-inflammatory drugs (ibuprofen, indomethacin) were prescribed. Steroids were administered to 26 patients (24.8%). Patients with chorea were prescribed anticonvulsants (phenobarbital). Of the side effects of aspirin, abdominal syndrome with abdominal pain was observed in 15 children (14.3%). No side effects have been reported with other medications.

Conclusions

The manifestation of rheumatic heart disease clinical and laboratory is not pronounced. Difficulties in diagnosis and late hospitalization of choreic children in whom symptoms of latent carditis were only instrumentally determined indicate low alertness of primary care physicians. Only a comprehensive analysis of clinical data allows timely diagnosis and appropriate therapy. Echocardiography studies have shown that at present, more changes occur in the tricuspid valve in the form of regurgitation and compaction of the tricuspid valves, although in previous years, as is known, the mitral valve was most often affected. Recently, the increase in the proportion of children with chorea is also different. Some children, hyperkinesia is difficult to treat. The anamnestic data of children with ARF complicated by chorea revealed the abuse of children with gadgets, infection with helminthic infestations. Our study shows the need for further research to improve the diagnosis and treatment of ARF. The significant misdiagnosis rate in children with ARF upon hospital admission indicates that additional awareness is needed for primary care physicians.

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