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# CLINICAL ASPECTS OF HLA-B27 POSITIVE ENTHESITIS-RELATED ARTHRITIS IN CHILDHOOD

Veronika Zhelezova, Martin Boyadzhiev, Boryana Varbanova

*Department of Pediatrics, Faculty of Medicine, Medical University of Varna*

## ABSTRACT

**INTRODUCTION:** Enthesitis-related arthritis (ERA) is a form of juvenile idiopathic arthritis (JIA) according to the International League Against Rheumatism (ILAR) classification. Enthesitis-related arthritis accounts for 8.6 to 18.9% of all children with JIA. The first clinical sign of ERA is usually asymmetrical arthritis of large joints, especially of the lower extremities. Axial involvement is typically presented by unilateral or bilateral sacroiliitis. Enthesopathy is a unique feature of ERA.

**AIM:** The aim of this study is to determine the most common clinical characteristics in children with HLA-B27 positive ERA.

**MATERIALS AND METHODS:** We performed a retrospective analysis of 55 patients up to 16 years of age, diagnosed with HLA-B27 positive ERA. We used physical and laboratory tests as well as imaging techniques to assess various clinical aspects of ERA in every patient.

**RESULTS:** Demographic characteristics showed prevalence of male gender—44 boys vs. 11 girls (4:1 ratio). The mean age of onset was 13.3 years for boys and 9.9 years for girls. The most commonly affected joints were as follows: knees in 49% of the cases, ankles—in 43.6%, hip joints—in 36.3%, intertarsal/metatarsophalangeal joints—in 20%. Physical examination found enthesitis in 24 of the patients (43.6%). The most commonly affected entheses were: the site of attachment of the Achilles tendon in 66.6% of the cases, the site of attachment of the plantar fascia in 45.8%, the site of attachment of the patellar tendon in 12.5%. Plain X-ray of the sacroiliac joints detected sacroiliitis in 34 of the patients (61.8%). In over 90% of the cases, the sacroiliitis was bilateral.

**CONCLUSION:** HLA-B27 positive ERA is a rare pathology in childhood. This study confirms typical epidemiological and clinical characteristics of the disease among Bulgarian children.

**Keywords:** *arthritis, enthesitis, HLA-B27*

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### Address for correspondence:

Veronika Zhelezova  
Faculty of Medicine  
Medical University of Varna  
55 Marin Drinov St  
9002 Varna  
e-mail: [veronika\\_zhelezova@abv.bg](mailto:veronika_zhelezova@abv.bg)

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## INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the most common rheumatological disease in childhood. According to the International League Against Rheumatism (ILAR), juvenile idiopathic arthritis is classified into seven subtypes. One of the subtypes of JIA is enthesitis-related arthritis (ERA) (6). The International League Against Rheumatism defines ERA as arthritis along with enthesitis or the presence of

either arthritis or enthesitis along with any two of the following features: uveitis, onset in a male child  $\geq 6$  years of age, presence of human leucocyte antigen B27 (HLA-B27), presence of either inflammatory low back pain or clinically elicitable tenderness on palpating the sacroiliac joints, family history of an HLA-B27-associated disease. Enthesitis-related arthritis represents 8.6–18.9% of all cases of JIA.

Enthesitis-related arthritis refers to a certain group of arthritis, called spondyloarthritis. Spondyloarthritis as a term is first used by Wright and Moll and it unites certain subtypes of arthritis, having common characteristics. Most typical characteristics of spondyloarthritis are: late onset of clinical presentation (9–13 years); axial involvement; prevalence of male gender; strong correlation with the HLA-B27 antigen, negative result for antinuclear antibodies (ANA) and rheumatoid factor (RF); family history of HLA-B27-related diseases (1,4,7,8,12). The clinical presentation at the onset of juvenile ERA is usually presented by asymmetrical arthritis of large joints, especially of the lower extremities (knees, ankles, hip joints). Very common is the involvement of the foot joints—metatarsophalangeal and intertarsal joints. Axial involvement is usually presented by unilateral or bilateral sacroiliitis. Enthesopathy is a unique feature of this subtype of juvenile arthritis. It usually affects the entheses of the lower extremities—the site of attachment of Achilles tendon, plantar fascia, and patellar tendon (2,3,4,8).

### AIM

The aim of this study is to determine the most common clinical characteristics of HLA-B27 positive ERA in Bulgarian children and to compare them with the typical clinical features of that form of arthritis worldwide.

### MATERIALS AND METHODS

We performed a retrospective analysis of 55 patients up to 16 years of age. Inclusion criteria for participation in the study were: children with diagnosed ERA and positive result for the HLA-B27 antigen. Exclusion criteria were: age above 17 years and children diagnosed with psoriasis. Data was collected for every single patient, including demographic and epidemiological data, family history for HLA-B27-related diseases as well as information about the clinical

presentation at the onset of the disease and during its course.

All included patients underwent a thorough physical examination with focus on the affected joints and entheses.

Laboratory tests included—complete blood count, differential blood count, C-reactive protein, erythrocyte sedimentation rate, rheumatoid factor, antinuclear antibodies, and plain X-ray of the sacroiliac joints.

### RESULTS

The demographic characteristics showed prevalence of the male gender: 44 boys vs. 11 girls (4:1). The mean age of onset was 13.3 years for boys and 9.9 years for girls (Fig. 1). Twenty-three of the patients (41.8%) had a family history of HLA-B27-related disease. The most commonly affected joints were as follows: knees in 27 of the patients (49%), ankles in 24 of the patients (43.6%), hip joints in 20 of the patients (36.3%), intertarsal/metatarsophalangeal joints in 11 of the patients (20%) (Fig. 2).

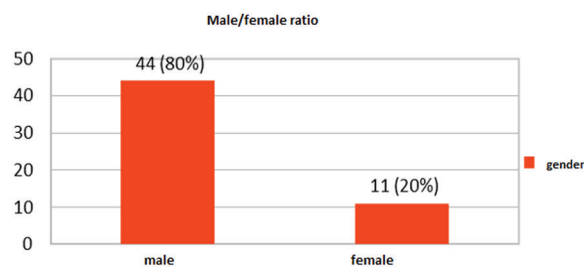


Fig. 1. Male/female ratio

Physical examination found enthesitis in 24 of the patients (43.6%). The most commonly affected entheses were: the site of attachment of the Achilles tendon in 16 of the patients (66.6% of the cases), the site of attachment of the plantar fascia in 11 of the patients (45.8%), the site of attachment of the patellar tendon in 3 of the patients (12.5%) (Fig. 3). Plain X-ray of the sacroiliac joints detected sacroiliitis in 34 of the patients (61.8%). In over 90% of the cases the sacroiliitis was bilateral.

### DISCUSSION

Juvenile idiopathic arthritis is a rare disease in childhood. There is a difference in the frequency of

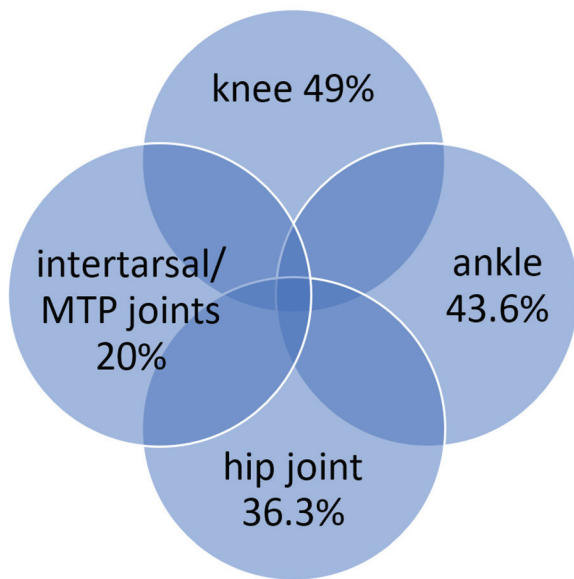


Fig. 2. Most commonly affected joints

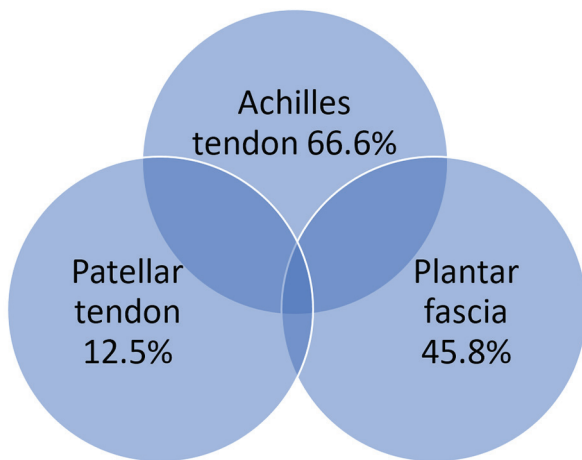


Fig. 3. Most commonly affected entheses

the disease worldwide. It depends primarily on ethnicity, immunological predisposition, and environmental factors. Various studies show quite big difference in the prevalence of JIA: from 10/100 000 in France up to 400/100 000 in Australia. A survey conducted by Saurenmann et al. estimated the prevalence of each subtype of JIA in different race groups. The results from the survey showed that ERA is most commonly found in Asians (8,10). In the USA and Canada, the prevalence of ERA is higher than in other countries: between 1.44 and 2.10/100 000 (3).

At the disease onset, in the majority of cases, peripheral joints are predominantly affected. Axial involvement, usually presented by low back pain, is

usually found at a later stage. Evolution to ankylosis is reported in one third of cases after several years of disease (1,5). The diagnosis of enthesitis, which is defined as chronic inflammatory pain or tenderness at the site of principal tendon insertion: plantar fascia insertion at the metatarsal heads and calcaneum, Achilles tendon insertion at the calcaneum, quadriceps insertion at the patella and proximal tibia, pelvis (anterior superior iliac spine, iliac crest), and greater trochanter, is of crucial importance (4).

The results from this study correspond to the previously reported clinical characteristics of ERA, such as:

- ◆ onset of clinical presentation later in childhood: 13.3 years for boys and 9.9 years for girls;
- ◆ prevalence of male gender—4:1;
- ◆ involvement primarily of large joints of the lower extremities: knees, ankles, hip joints, and also intertarsal/metatarsophalangeal joints;
- ◆ common involvement of entheses of the lower extremities: the site of attachment of the Achilles tendon, the site of attachment of the plantar fascia, the site of attachment of the patellar tendon;
- ◆ significant association with HLA-B27-related diseases in the family;
- ◆ high prevalence of clinically and radiographically established sacroiliitis—in 61.8% of the patients; some patients had history of inflammatory low back pain or tenderness in the sacroiliac joints on physical examination, but have no structural changes in the sacroiliac joints on X-ray. The imaging technique of choice for early detection of sacroiliitis is MRI which has a high sensitivity for the structural changes in the sacroiliac joints (5,9,11).

This study targets a group of patients with HLA-B27 positive ERA, which represents juvenile Bechterew's disease. According to the literature, this group represent 44– 88% of all patients with ERA. So far, no significant difference in the clinical presentation between HLA-B27 positive and HLA-B27 negative patients with ERA has been noted in the literature. However, it has been demonstrated that patients with a positive HLA-B27 antigen have a greater chance for axial involvement, higher clinical activity, and lower rate of remission (4). In our study there

was a family history for HLA-B27-related diseases in 41.8% of the patients, which proved the importance of heredity as a diagnostic factor. It is possible for the rate of the hereditary predisposition to be higher, but not being registered due to the insufficient knowledge of family history in some families.

The recognition and confirmation of crucial diagnostic features of HLA-B27 positive ERA is of significant importance for early diagnosis of this form of JIA. Being part of the so-called rare diseases, ERA is usually underestimated in the differential diagnosis of joint pain. This could lead to a delay in the diagnosis and treatment, as well as worsening in the prognosis and outcome.

### CONCLUSION

HLA-B27 positive ERA is a relatively rare pathology in childhood. This study confirms typical epidemiological and clinical characteristics of the disease among the Bulgarian population. The recognition of main clinical aspects of HLA-B27-associated ERA is of crucial significance for early diagnosis and treatment.

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