

# Clinical and laboratory findings of children with identified idiopathic arthritis, investigation on treatment and prognosis - seven years experience

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## Abstract

**Objective:** We aimed to compare the clinical and laboratory findings of patients with juvenile idiopathic arthritis (JIA), to determine the preferred drugs and their efficacy and to evaluate the factors affecting prognosis and development of deformity.

**Methods:** Retrospectively, 75 children with JIA were evaluated. Patients were divided into subgroups according to the International Association of Leagues for Rheumatology diagnostic criteria. The joints, systemic and extraarticular findings, laboratory findings, remission, deformity and relapse rates of JIA subgroups were compared.

**Results:** 75 patients who were diagnosed with JIA, 50.7% were female and 49.3% were male. The largest group of patients were polyarticular JIA patients. Systemic symptoms were detected in 63 patients and extraarticular findings in 45 patients. In the systemic JIA group; anemia, leukocytosis, thrombocytosis, elevated erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and ferritin were most frequently detected. Rheumatoid factor (RF) and immunoglobulin elevation were detected in the polyarticular group. Nonsteroidal anti-inflammatory drugs were started as initial treatment in 25 (33.3%) of the patients. Combined drug treatments were applied according to the clinical status of the illness, prognostic features and treatment at the centers. The most commonly used combination was NSAID, corticosteroids and methotrexate (MTX) treatment with a rate of 29.3%. The rate of remission was 85.2% while the deformity rate was 14.7% and the relapse rate was 40.4%.

**Conclusion:** JIA is one of the most common chronic diseases of the childhood that is at the risk of sequelae and is one of the most common rheumatic diseases. In our study, the characteristics of the patients' male/female, subgroups, deformities and relapse rates were determined according to their socioeconomic and racial characteristics and clinical, laboratory features, treatments and remissions were determined.

## Introduction

Juvenile idiopathic arthritis (JIA) is a chronic, systemic and inflammatory joint disease with a high risk of childhood sequelae, which is occurred by various signs and symptoms, varying in the initial shape and clinical course, most common in childhood. The disease can also manifest itself as a chronic disease with chronic joint involvement as well as various organs and systemic involvement [1]. Despite the well-defined clinical manifestations of the disease, no definite diagnostic laboratory test has been found yet. If the clinical picture is not fully established, differential diagnosis with early diagnosis and other colloid tissue diseases is difficult [2]. In the absence of definitive diagnostic criteria, many classification and diagnostic criteria have been proposed according to the number of joints involved, the patient's disease, rheumatoid factor (RF) seropositivity and associated clinical findings [1, 3]. It is now accepted that JIA is a chronic disease, as a clinically in heterogeneous arthritis, beginning before the age of 16 years according to the different symptoms that develop within the first 6 months, which are defined in a large period [4]. In this study, we aimed to determine the factors affecting the development of prognosis and deformity development according to ILAR (International Association of Leagues for Rheumatology) diagnostic criteria for children undergoing JIA diagnosis, comparison of clinical and laboratory findings, determination of preferred drugs and their efficacy, prognosis and development of deformities.

## Methods

75 children with JIA according to ILAR criteria were evaluated retrospectively at Dr. Sami Ulus Children's Hospital which is a tertiary referral research unit. Patients were assessed for their gender, age that they started and symptoms began, whether they had received treatment prior to admission to the hospital, family history of kinship, number and location of joints involved, systemic findings (fatigue, loss of appetite, weight loss, growth retardation) and extraarticular findings (fever, skin rash, hepatosplenomegaly, Lymphadenopathy, rheumatoid nodule, uveitis, pericarditis), follow-up status of the patients, preferred medications in the treatment and side effects were evaluated.

According to laboratory findings Leukocytosis and thrombocytosis were defined as hemoglobin levels below 2 standard deviations according to the age of the patient, anemic white blood cells and

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thrombocytes above the upper limit determined by gender and age group. The rate of erythrocyte sedimentation (ESR) > 20 mm / h, C reactive protein (CRP) is considered to be higher than 5 mg / L. Ferritin was studied with nephelometric methods and was accepted as normal between 7-140 ng / ml [5]. Rheumatoid factor (RF) was determined by latex agglutination method and nephelometric method. Bone mineral densitometry was assessed using long bone and all joint graphs and DEXA method. Immunoglobulin levels were determined by immunonephelometric method and found to be above the age and sex defined limits [5].

Our patients were evaluated according to the presence or absence of poor prognostic criteria. Persistent RF positivity, radiological narrowing or erosion of joint space, polyarticular synovitis, non-steroidal treatment for one year and dramatic improvement in combination with methotrexate, intraarticular steroid or slow acting antirheumatic drugs, HLA-DR4 positivity in patients with polyarticular arthritis, the prognosis was considered to be a poor prognostic criterion because of the presence of polyarthritic JIA, systemic JIA with polyarticular involvement, deep anemia accompaniment, presence of hypergamaglobulinemia, and at least 2 cases of very high ESR [6]. Remission is accepted as our patient hadn't morning stiffness that did not last longer than 15 minutes, fatigue, absence of soft tissue swelling and joint sensitivity, absence of motion, pain and limitation of motion, and ESR of less than 30 mm/h were considered as 5 or more.

In addition to clinical findings in deformed joints, joint space narrowing, articular surface erosion, subcortical cysts, ankylosis and fusion formation were identified by radiographic findings.

### Statistical analysis

In the comparison of the ratios of the obtained data, "significance test of the difference between the percentages in the independent groups" was used. The "Fischer exact and chi-square test" was used to determine the significance of the difference between observed frequencies and expected frequencies. "Kruskal Wallis test" was used in the intergroup comparisons. SPSS (Statistical Package for Social Sciences) for Windows 15 was used for statistical analysis and  $p < 0.05$  was accepted meaningful.

### Results

In the 7-year period of this tertiary education and research hospital in the Department of Nephrology who were diagnosed with JIA, 38 (50.7%) were girls and of 37 (49.3%) were boys and the girl/boy ratio was found as 1.03. Age average of the majority of patients according to onset of symptoms was between 2 and 7 years (42.7%). When the cases were classified according to clinical findings in the first six months, the largest group consisted of 49 patients (65.3%) with polyarticular JIA, 48% of them were RF (-) and 17.3% were RF (+) patients. Thirteen patients (17.3%) with systemic onset JIA, 12 (16%) with oligoarticular JIA and 1 patient (1.3%) with associated JIA were detected. Age of onset of the disease were found as  $7.6 \pm 3.40$  in the polyarticular RF group,  $10 \pm 2.86$  in the RF (+) group,  $8.5 \pm 3.48$  in the oliartic group and  $4 \pm 4.15$  in the systemic group.

Mean time between onset of symptoms and admission to hospital were 16.5 months in polyarticular RF (-) group, 4 months in RF (+) group and 6 months in oligoarticular and systemic group. In 21 of our patients (28%) kinship was detected, 57.1% of them were first-degree relatives.

Arthritis was the most common finding and arthritis was present in all groups in the course of application. In all patients, limitation of

motion was detected in 58 patients (77.3%), temperature increase in 29 patients (38.7%), redness in 23 patients (30.7%) and stiffness in 35 patients (46.7%). The most frequently involved joint was found to be the knee joint with 88% frequency, the ankle, fingers, wrists and toes with decreasing frequency.

Extraarticular findings were detected in 45 (60%) patients. Fever was the most common finding in all patients in the systemic group, although 18 (36.7%) patients were found in the polyarticular group and no cases were found in the oligoarticular group patients. In the systemic JIA group, rheumatoid skin rash was detected in 6 (42.6%) patients and in lymphadenopathy in 4 (30.8%) patients. The rate of rheumatoid nodule in the polyarticular group was 4.1%. Uveitis was the most common in 3 (25%) patients in the oligoarticular group. Pericarditis 3 (4%) was detected in the patient. Hepatomegaly, splenomegaly and hepatosplenomegaly were detected in the most systemic group, 7 (53.8%), 4 (30.8%) and 4 (30.8%) patients, respectively.

When laboratory findings of the cases are evaluated anemia was found in 76.9%, leukocytosis in 38.5% and thrombocytosis in 76.9%. ESR and CRP were very high in all patients with systemic JIA. Ferritin was detected again in 70% of patients with the most frequent systemic JIA and 50% with polyarticular JIA. Immunoglobulin elevation was detected in the polyarticular and systemic JIA groups.

68 patients who underwent direct radiography were evaluated by a radiologist. 12 normal finding, 27 soft tissue swelling, 26 osteopenia and 15 osteoporosis were detected in patients. Bone mineral densitometry (BMD) was performed on 31 of our patients and osteoporosis was detected in 18/47 (38.3%) patients in the polyarticular group, 6/12 (50%) in the oligoarticular group and 7/11 (63.6%) in the systemic group. Of 31 patients with osteoporosis, 28 (90.3%) received steroid treatment.

Disease treatment was began as taking into consideration the subgroup characteristics of the disease, the severity of the joint and systemic findings of the patient, the duration of the illness, the medications used, the response provided by these medications and the presence of poor prognostic criteria. 25 patients (33.3%) took nonsteroidal anti-inflammatory drug (NSAID) alone, Naproxen and Tolmetin were the most commonly used. Sulfasalazine, methotrexate (Mtx) and steroid treatments were added to the treatment of 12 patients who could not receive NSAID treatment. Steroids, methotrexate and other slow-acting antirheumatic drugs were added to the patient's NSAIDs at the time of admission, limited mobility, multiple poor prognostic criteria, or treatment at the external centers. Cytotoxic agents were administered to 5 patients. 4 patients were systemic JIA, 1 patient was oligoarticular JIA group with uveitis.

Side effects were observed in 33 (44%) patients due to the drugs used. Cataract, glaucoma in 1 patient and cataract and glaucoma in 1 patient developed in 5 patients who took steroid treatment, osteoporosis was detected in 23 patients, and bisphosphonate, calcitonin, vitamin D and/ or calcium treatment were given to these patients.

Cushingoid appearance in steroid-induced 16 patients, increase the virilisation in 3 patients, acne in 2 patients, myopathy in 1 patient, muscle atrophy in 1 patient, triglyceride and cholesterol uptake in 1 patient, blood sugar and elevation in 1 patient and depression in 1 patient were detected. In these patients, diet and medication dose adjustments were made. Anemia in 4 patients receiving methotrexate, leucopenia in 2 patients, pancytopenia in 1 patient, and pancytopenia due to cyclosporin-A in 1 patient were discontinued. Elevation of the liver function tests of 2 patients treated with Mtx and 1 patient using

naproxen was detected and the treatment was interrupted for a while. Drug reduction has been reduced on the development of nausea in a patient receiving Mtx treatment. In patients with oligoarticular JIA who had begun cyclosporine-A due to uveitis, there was slight deterioration in kidney function tests and the patient was offered abundant hydration. In a patient who received Tolmetin, proteinuria developed, but it was determined that there was a pseudopregnant proteinuria.

64 (85.3%) of the patients regularly used their medication. 85.7% of patients with polyarticular JIA, 83.3% of patients with oligoarticular JIA, and 84.6% of patients with systemic onset JIA had regularly used their medication. Of the 75 patients, 61 (81.3%) had follow-up. The follow-up duration of the patients was at least 6 months, maximum 7 years, and average 1.5 years.

1 (1.6%) patient with systemic onset JIA amyloidosis died subsequently developed pancytopenia and sepsis after 2 years of follow-up.

Deformity developed in 9 (14.7%) of the patients and 8 (20.5%) in the polyarticular group and 1 (10%) in the systemic onset group. There was no development of deformity in the oligoarticular group and intracerebral JIA patient. The developing deformities were knee, wrist, flexion contracture of the fingers and ulnar deviation.

Twenty-one patients (40.4%) developed relapses among the 52 patients who were followed-up. There were 12 (37.5%) relapses in the polyarticular group, 2 (18.2%) in the oligoarticular group and 7 (87.5%) patients in the systemic onset group.

## Discussion

Juvenile idiopathic arthritis (JIA) is a childhood disorder characterized by chronic synovitis and various subgroups. Despite being a long-known disease, etiopathogenesis has not been explained completely. Various publications concerning JIA indicated that the initial findings, clinical course, and laboratory findings of the disease are very variable [7,8]. The epidemiological studies on JIA are based on the distribution of the disease and the subgroup characteristics varying in different ethnic groups and socioeconomic levels.

In this study, we evaluated the epidemiological, clinical, laboratory findings, treatment and prognostic features of patients who were diagnosed with JIA in our hospital. When all types of the disease are considered, the ratio of Girls / Boys is 2/1, and oligoarticular type is 3 times more than girls. There is no gender difference in the systemic onset type (G / B: 1/1) [6]. In a study that performed about JIA in our country, male patient dominance was found [9]. Of the 75 patients included in our study, 38 (50.7%) were girl and 37 (49.3%) were boy and the ratio of girl to boy was 1.03. Contrary to classical information, the ratio of Girls / Boys was equal to each other. It can be inferred that boys may have been brought to reference centers more frequently than girls since boys are much more in our society. According to previous studies, the ratio of girls / boys in our study is equal to that of girls and it can be explained by the increase in socio-cultural level and bringing them to advanced health institutions. In our study, there were more girls in the systematic and polyarticular JIA group while the boys in the oligoarticular JIA group were found much more.

Although the disease may occur at any age in childhood, age distribution according to sex and subgroups is reported differently by various researchers. The symptoms are observed most frequently under 5 years, especially between 1 and 3 years and increase slightly again towards puberty. This distribution is more pronounced in girls and in

oligoarticular cases [3]. In males, the peak is around 2 and 9 years [10]. In systemic onset JIA, the age onset of the disease is less obvious [6]. In our study, it was determined that 42.7% of the patients were between 2 and 7 years of age. These results are consistent with other studies (17,23). In our study, the second age group that the male patients most frequently concentrated on was found to be the 8-11 age groups. In girls, the age of onset of the disease was found to be approximately equal between 2-7 and 8-11 years of age. These results were consistent with the literature [6,10].

Of the 75 patients included in our study, 65.3% had polyarticular JIA patients whereas 16% had oligoarticular JIA patients, 17.3% had systemic onset JIA patients, and 1.3% was associated with intensity JIA patients.

The RF (-) polyarticular group accounts for 48% and the RF (+) group accounts for 17.3%. Kasapçopar Ö. and his colleagues did a study on the subgroups of JIA, (35.6%), RF (-) polyarticular group, 15.6% RF (+) group, 17.3% persistent oligoarticular group, 15.6% prolonged oligoarticular group and 15.6% systemic onset group [11]. The ratios in this study are consistent with the results of our study. However, the high proportion of polyarticular JIA patients in our study may be attributed to the fact that the patient's age between admission to the hospital and the onset of symptoms was long and may have been included in the polyarticular subgroup of patients with prolonged oligoarticular JIA. In the literature, it has been reported that 30-60% of JIA produces oligoarticular, 20-40% polyarticular, 5-20% systemic onset type and 1-11% incidence-related arthritis [4]. In their series, Schaller and Wedgwood detected 37% of polyarticular and oligoarticular types and 26% of systemic type [12]. In the studies it is found that polyarthritis subtype is common in Costa Rica, India, New Zealand, and South Africa, although oligoarticular subtype is more prevalent in Western European countries [13,14]. In North America and Europe, oligoarticular JIA was the most common, followed by polyarticular JIA and least frequently seen is systemic JIA [15,16]. The appearance in Asia is quite different. The oligoarticular group is less common. In Fujikawa and Okuni's study of 570 JIA children in Japan, 54% of patients with systemic onset JIA, 25% with polyarticular JIA and 21% with oligoarticular JIA were found [17]. In an Indian study, 14% and 24% of patients with systemic onset JIA, 52% and 46% polyarticular JIA, 35% and 30% oligoarticular JIA were detected [18]. Compared with the results in these studies, the difference in the rates of subgroups of the disease in our study may be due to our racial and genetic characteristics. The butcher and his colleagues support our work in this direction on the findings of his work.

The age groups frequently seen in subgroups of the disease vary. Early and late onset types of polyarticular JIA have been reported while oligoarticular JIA begins at an early age. It has been reported that an early-onset type occurs before the age of 8, and a late-type type occurs after the age of 8. Late-onset polyarticular JIA is usually seen with RF (+). In systemic onset JIA, the age at onset of the disease is less obvious [16]. In our study, the average age of onset of illness;  $7.9 \pm 3.40$  in the polyarticular RF (-) group,  $10 \pm 2.86$  in the polyarticular RF (+) group,  $8.5 \pm 3.48$  in the oligoarticular group and  $4 \pm 4.15$  in the systemic group. In a study of 67 JIA ILAR classifications in France, in the systemic onset group age of onset the symptoms were detected as 4.2 in the oligoarticular group and 6.7 in the RF (-) polyarticular group [19]. They reported that the systemic type started at an early age, whereas oligoarticular and polyarticular types appeared at a later age. These results are consistent with our study.

In JIA, the most common finding of the disease is joint pain and swelling in the joints. Restraint of mobility may be accompanied by pain or tenderness, increased temperature locally and redness. Arthritis was initially present in all of our patients. Polyarticular JIA is characterized by involvement of five or more joints. This type of arthritis tends to be symmetrical and can involve any joint in the body. In the hands, small joints, especially proximal interphalangeal joints, metacarpophalangeal joints and wrists are characteristic. It is similarly affected by small joints. Large joint involvement; knee, elbow, ankle joints are often. In oligoarticular JIA, large joints are involved, and knee, elbow, hand and ankle joints are the most frequently affected as synovial structures. Joint involvement in systemic JIA is similar to other subgroups [4,10,20]. In our study, knee and ankle joint involvement was most frequently seen in parallel with this information. In all JIA groups, knee involvement is seen as 88% followed by ankle 80%, hand fingers 61.3% and wrist 52% frequently.

The frequency of joint involvement in the polyarticular group 91.8% of the knees; the most common, 85.7% of the ankles, 73.4% of the fingers and 55.1% of the wrists were found. It is observed that in the oligoarticular group, 83.3% knee joint and 41.7% ankle involvement. These two joints were the most commonly involved joints in the oligoarticular group. In all patients with systemic onset JIA, ankle involvement was detected in 92.3% of the cases, wrists and toes in 76.9%, and knee and fingers in 76.9% of cases. There is no proportion about involvement joints in the literature; these findings are consistent with classical information about joint regions in JIA [1,3,10,13].

In the literature, it has been reported that hand and toe finger involvement is more frequent in polyarticular and there isn't given proportion. Systemic onset JIA large and small joints usually involve as polyarticular. In our patients, hand fingers were affected by 61.3% and toes were affected by 48%. Polyarticular JIA showed that hand fingers were affected by 73.5% and toes were affected by 48.9%. According to a study done, this rate was found to be higher [10].

The involvement of the hands and toes was higher in patients with systemic onset JIA. In our study, 92.3% of toes and 76.9% of fingers were held in this subgroup. Systemic onset JIA may have transient arthritis findings during periods of increased fever in almost all children. With fever, these findings disappear and the patient's clinic is dramatically improved. The presence of hand and toe involvement in such cases may be due to the evaluation of arthritis as a temporary joint finding in the acute phase of systemic disease that lasts for 6 weeks.

In JIA, fever can be observed in about one third of patients. One of the most common findings in the systemic group is intermittent fever that rise up to 39.5 °C, 1-2 times a day.

Fever may also be detected in the polyarticular group, but is less common in the oligoarticular group. Fever in the polyarticular group was reported as 30% and in the systemic group as 100% [13]. In our study, fever was observed in all of the patients with systemic onset JIA, while in the polyarticular group it was 36.7%. Patients in the oligoarticular group had no fever. These findings were consistent with the literature.

Rheumatoid rash is one of the classic findings of systemic JIA. Patients may have a solitary pink, pale, usually white, macular debris that can appear anywhere on the body, with fever elevation. It is less common in polyarticular and oligoarticular groups. A rheumatoid rash was detected in 16% of our cases. The rate of systemic onset JIA was 42.6%, polyarticular JIA was 10.2%, oligoarticular JIA was 8.3%. In literature this rate is 95%, 2%, 0% respectively [21]. In a study

conducted, rheumatoid rash was detected in 18.2% of all JIA subgroups [9]. The low rate of rheumatoid rash in systemic onset JIA can be attributed to the fact that our patients and families do not notice or worry about spillage.

In literature, the incidence of rheumatoid nodules is between 5-10% [3,13]. Nodules are usually reported in the polyarticular group. In our study, rheumatoid nodule was not seen in the systemic onset and oligoarticular group, but 4.1% in the polyarticular group. These ratios are compatible with the literature.

Chronic uveitis especially affects girls with oligoarticular JIA. This rate is 20% in the oligoarticular group, 5% in the polyarticular group and 1% in the systemic onset group [3,4,13]. Chronic uveitis rate was detected in 3 patients (25%) with oligoarticular JIA and 2 patients (4.1%) with polyarticular JIA. These rates were consistent with the literature [22]. Chronic uveitis was detected in 1 patient with systemic onset JIA.

Pericarditis is frequent in systemic onset JIA. It is usually asymptomatic, and some children may have dyspnea or precordial pain. The literature reports 35-73% in the systemic onset group, 5% in the polyarticular group and 0% in the oligoarticular group and 3-9% in all JIA patients [3,13,23]. Lietman and colleagues found a pericarditis ratio of 7%, but in postmortem studies this ratio increased to 45% (24). In our cases, pericarditis was detected in 1 patient with systemic onset JIA (7.7%), 2 patients with polyarticular JIA (4%), but oligoarticular was not detected in JIA patients. All of our JIA patients were detected at 4%. These rates in our study were found to be consistent with the literature.

Generalized lymphadenopathy (LAP), polyarticular is reported as 5% in patients with JIA and 70% in patients with systemic onset JIA. The most commonly involved parts are the anterior cervical, axillary and inguinal lymph nodes [13]. 4 of the patients in the generalized LAP systemic group (30.8%) and 3 of the patients in the polyarticular group (6.1%) were detected. 9.3% of all JIA findings had generalized LAP.

Hepatosplenomegaly most commonly occurs in the systemic onset group, which may occur within a few years after the onset of the disease [5]. In the literature, 85% of systemic onset JIA, 10% of polyarticular JIA, and 0% of oligoarticular JIA are reported [13]. In our cases hepatosplenomegaly was detected in 4 (30.8%) patients in the systemic onset group and 3 (6.1%) in the polyarticular group, but not in the oligoarticular group. The low ratio of generalized LAP and hepatosplenomegaly in systemic onset patients may be depend on the earlier treatment of these patients.

Anemia in JIA is a common finding especially in systemic patients, but is common in all forms of JIA. It is usually due to chronic disease and serum iron, iron binding capacity decreases. Serum ferritin levels may increase due to disease activity. Gastrointestinal blood loss due to NSAID intake or iron deficiency anemia may also be observed due to underlying absorption and underlying inflammatory disease and malfunction in use. 41.4% of our oligoarticular JIA patients had mild iron deficiency anemia, 71.4% of mild-to-moderate anemia in our polyarticular JIA patients, and 76.9% of moderate to severe anemia in our systemic JIA patients. It is thought that serum ferritin levels were found to be 53.6% higher in our observable patients. Ferritin levels are seen due to disease activity. These findings are consistent with classical information [3,10].

Leukocytosis is seen frequently in systemic onset JIA. Leukocytosis rate in systemic JIA is reported as 80% in the literature. Leukocytosis

was detected in 10 of our 75 patients (13.3%). Systemic JIA was the most common with 38.5%. The reason for this low rate can be attributed to the fact that 53.3% of our patients had been treated at the centers before applying to our hospital.

Thrombocytosis is usually seen in patients with systemic onset and in the polyarticular group [13]. Thrombocytosis was detected in 72% of our patients. It was found to be 76.9% in patients with systemic onset JIA, 73.4% in patients with polyarticular JIA, and 58.3% in patients with oligoarticular JIA, consistent with classical information [5].

Erythrocyte sedimentation rate (ESR) is useful following active disease and treatment. CRP is used in the same way. However, CRP is less affected than anemia and other factors [5]. ESR elevation in 94.7% of our patients and CRP increase in 93.2% of our patients were detected.

These findings are consistent with the literature [13].

In JIA patients, RF (+) is reported in 5-25% (9). In our cases, RF was examined with latex fixation technique. RF positivity was detected as 17.3%. In the polyarticular group 26.5% were detected, but no RF positivity was detected in the oligoarticular and systemic onset groups. Our results were consistent with the literature [1,3,13].

In studies conducted, Ig levels were found to be high in 6-37% of patients [25,26]. It has been reported that Ig increase is observed especially in the systemic and polyarticular group.

JIA is a systemic disease that causes osteoporosis [27]. Radiological examinations are used to evaluate the pathologies related to the disease, to evaluate the complications related to the disease and treatments used. In Brazil, a 50-60% reduction in bone density in the lumbar vertebra and femur neck was found [3]. Osteoporosis was detected in 18 (38.3%) patients with polyarticular JIA, 6 (50%) patients with oligoarticular group and 7 (63.6%) patients with systemic onset group who were not studying bone grafts and bone mineral densitometry studies. Totally in 31 patients (43.7%) osteoporosis was detected. These ratios are compatible with the literature. 90.3% of our patients diagnosed with osteoporosis were receiving steroid treatment. It is detected that steroids increase the frequency of osteoporosis according to our hospital and abroad studies [28,29].

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the basis of treatment in a large majority of patients in JIA. It is used in initial treatment in many children. NSAID therapy was initiated only in 25 of our patients (33.3%). Slow effective antirheumatic and immunosuppressive drugs were added to NSAIDs in 50 (66.7%) patients with poor prognostic criteria and various treatments at the external center. The most preferred NSAIDs are Naproxen and Tolmetin. Tolmetin in 5 patients (20%) and Naproxen therapy were given only in 20 patients (80%). Tolmetin treatment only was given to Naproxen in 11 (55%) of 20 patients who started Naproxen and Tolmetin treatment in 2 (40%) of 5 patients who started Tolmetin. However, 7 of these patients did not come to the controls.

There was no need to add slow-acting antirheumatic and immunosuppressive therapy to the treatment of 6 patients who only received NSAIDs in the follow-up patients. NSAIDs were in the oligoarticular and polyarticular groups of our patients. Only 5 of our NSAID-treated patients received remission. In 1 patient, treatment change was not considered because he did not use the drug regularly. In the literature Tolmetin activity is reported in 50-80%. Tolmetine was found in 25% and 86% of the other two studies [30,31]. The response to Naproxen varies from 24% to 89% [32]. In our study, the efficacy ratios of NSAID drugs were found to be consistent with the literature.

Early intervention of slow acting antirheumatic and immunosuppressive drugs in addition to NSAIDs is recommended in patients with prolonged active joint involvement or poor prognostic criteria. In this way, the active inflammatory process is stopped as soon as possible and the patients enter the remission rapidly [33].

Although steroids have limited use in JIA, they are recommended for use in life-threatening conditions or severe joint involvement [33]. It was learned that 39 (52%) patients with poor prognostic factors and steroid treatment in the external centers were given steroids in the initial treatment. According to clinical and laboratory findings, we have added steroid treatment for our following 10 patients. (pulse methylprednisolone or oral prednisolone) as well as treatments that they took.

If it is failed response to NSAID therapy it is recommended for treatment of methotrexate as a second option [34,35].

In the study performed by Giannini and his colleagues, the effectiveness of the method was investigated. In this study, one of the groups was added to the treatment of patients with 5 mg / m<sup>2</sup> / week methotrexate and 10 mg / m<sup>2</sup> / week as the second drug. These two groups were compared with the placebo group without taking 2nd drug treatment. Methotrexate was given to 38 of our follow-up patients (62.3%). Mtx was used at a dosage of 7.5-10 mg / m<sup>2</sup> / week. This dose is consistent with classical information [36].

Remission was seen in 33 (86.8%) of our Mtx-treated patients. Remission was observed in 6 (85.7%) of 7 systemic onset patients using Mtx 22 (84.6%) of 26 patients in the polyarticular group and 5 in the oligoarticular group (100%).

The remission rate was found low because patients in the polyarticular group receiving Mtx therapy did not use their medications regularly and the remission rate with Mtx treatment was found to be quite high in systemic onset patients. Mtx therapy should be recommended in patients with poor prognostic factors, such as polyarthritis and systemic onset who are not responding to NSAIDs in the presence of these findings.

Sulfasalazine was given to 16 (26.2%) of our follow-up cases. 8 of these patients were treated with NSAID, 8 with NSAID and steroid treatment with sulfasalazine treatment. Remission was detected in 6 (75%) patients receiving NSAID + sulfasalazine treatment. Remission was observed in each 1 patient with oligoarticular systemic onset amongst 4 of 6 patients 66.7% in polyarticular group. In a study conducted by Van Rossum and his friends, one group of patients in the oligoarticular and polyarticular group was treated with sulfasalazine and the other group with placebo. Sulfasalazine 50 mg / kg / day was used. The activity was detected as 44% which was found meaningful compared to the placebo group [37].

Seven of the 8 patients (87.5%) who received NSAID + sulfasalazine + steroid treatment had remission. No remission was observed in 1 patient in the systemic baseline group with poor prognostic factors and cyclosporine treatment was added to the patient's treatment.

Slow-acting antirheumatic medications such as Hydroxychloroquine, D-penicillamine, gold salts and other new treatment approaches have not been used in our patients.

The prognosis of the disease varies depending on the clinical course of the disease, its complications, and the selected treatment response. Juvenile idiopathic arthritis is the major cause of morbidity, chronic arthritis in the polyarticular and systemic onset group, and iridocyclitis

in the oligoarticular group [3]. The prognosis is different in each patient. Despite the fact that it is a chronic illness and not a definite specific treatment, it is benign and usually there is no life threatening even in severe systemic involvement. Although the prognosis for RF (+) polyarticular type and systemic onset type is poor in terms of joint function, the general prognosis of the disease is good and 75-80% of patients enter remission [1]. When we evaluated the remission rates of our patients, 82% of the patients in the polyarticular group and 80% of the systemic-onset patients were admitted to remission while all patients in the oligoarticular group entered the remission. In our follow-up cases, the remission rate was 85.2%. This ratio was found to be consistent with the literature [10].

Systemic onset and RF (+) cases in JIA are at risk with regard to joint destruction. Severe arthritis in the systemic onset JIA is 30-50%, in the RF (-) polyarticular group is 10-15%, in the RF (+) polyarticular group is 50%, and when severe functional limitation is reported as 25% in all JIA patients [4,10,38]. In our present cases, the deformity rate was found as 14.7%. 20.5% in the polyarticular group and 10% in the systemic onset group, whereas no deformity developed in any of the patients in the oligoarticular group. A low detection of our rate of deformity can be attributed to our racial and genetic characteristics.

The frequency of recurrence and active arthritis recurrence in JIA is quite high. If there is poor prognosis criteria for treatment and if there is rapid progression of arthritis, it is suggested to reverse the treatment pyramid, start the Mtx and other second-line drugs immediately.

Relapses can occur after remitting in JIA patients. Relapse has been reported in 50% of patients with systemic onset JIA [38]. The relapse rate was 40.4% in our patients. The most frequent relapse was seen in 87.5% of systemic onset JIA, in 37.5% of polyarticular group and in 18.2% of oligoarticular group. Relapse rates may be due to racial and genetic differences and treatment compliance.

Macrophage activation syndrome (MAS), which is rarely seen in 5-8% of systemic onset JIA, is a life-threatening complication [39]. MAS developed in 1 of our systemic onset JIA patients (7.8%). This ratio was found to be consistent with the literature.

Juvenile idiopathic arthritis is rarely fatal. Mortality rate was reported as 0,1% [20]. In systemic onset disease, 4% of children die from amyloidosis and infection. The most common cause of death in patients with renal disease was amyloidosis [38,40].

In our cases, one patient died from pancytopenia and sepsis from the systemic onset JIA group. Our patient was on steroid treatment and amyloidosis was detected. The mortality rate in all patients was found as 1.3%.

Amyloidosis was detected in 3 of our patients (4%). The rate of amyloidosis in the literature is reported between 1-10% [38,41]. This rate was found to be compatible with our study.

In juvenile idiopathic arthritis which is a chronic disease, compliance with follow-up and treatment of patients is very important. JIA is a disease that is difficult to diagnose and treat, and should be followed for life. Despite high rates of recurrence, patients with delayed diagnosis and started to treatment late occur at high rates of deformity and their standard of living declines. Apart from drug treatment, patients should be provided with physical and occupational therapy and psychosocial support treatments. JIA treatment is a team work that includes children, family, pediatric rheumatologist, physical therapist, physiotherapist, psychologist, ophthalmologist, dentist, orthopedist,

nurse, occupational therapist, nutritionist and social workers. All team members must work in conjunction with each other.

## Conclusion

As we have shown in our study, the treatment of nonsteroidal anti-inflammatory drugs and steroids used in the early period of the disease was an effective treatment. Especially the addition of methotrexate and disease-slowing antirheumatic drugs could stop the progress of the disease and can prevent permanent joint damage and uveitis.

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