Juvenile idiopathic arthritis: a clinical audit

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Background
Juvenile idiopathic arthritis (JIA) is an autoimmune, inflammatory noninfective joint disease that includes different disease subtypes that are characterized by the onset of arthritis starting before the age of 16 years with symptoms lasting at least for 6 weeks.

Objective
The aim of this study was to evaluate the compliance of healthcare providers at the Pediatric Rheumatology Unit, Assiut University Children's Hospital, to the 2011 American College of Rheumatology recommendations for treatment of JIA.

Patients and methods
The study was conducted on 50 patients who were younger than 16 years and diagnosed as having JIA at the Pediatric Rheumatology Unit, Assiut University Children's Hospital, to assess compliance of the unit's healthcare providers to American College of Rheumatology recommendations for treatment of JIA.

Results
The patients were grouped according to age into two groups: from 1 to 7 and 8 to 16 years. Polyarticular JIA was the most common type among studied cases followed by systemic-onset JIA. All studied cases presented with arthritis at the time of diagnosis. Complete blood count and erythrocyte sedimentation rate were done for all studied cases at the time of diagnosis. Rheumatoid factor was done for 84%. The most common complications among the studied group were those related to treatment. NSAIDs and corticosteroids were the most common drugs used.

Conclusion
Treatment of JIA includes pharmacological and nonpharmacological interventions and surgical treatment. Pharmacological treatment includes NSAIDs, steroids, disease-modifying antirheumatic drugs, and biological agents. The degree of disease activity and the presence or absence of features of poor prognosis greatly affect onset of complications and treatment of JIA. Nonpharmacological interventions include psychosocial therapy, nutrition, physical and occupational therapy, lifestyle factors, and home remedies. Through this study, some defects were found. First, there was deficiency in data recording. Second, there was also deficiency in laboratory (mainly rheumatoid factor and antinuclear antibody/anti-double stranded DNA) and radiological workup. Moreover, nonpharmacological therapy and surgery were not considered. Lastly, there was deficiency in regular follow-up of safety drug monitoring.

Keywords:
assiut, audit, juvenile idiopathic arthritis

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Introduction

Juvenile idiopathic arthritis (JIA) is a disease of arthritis seen in childhood, which may be transient and self-limited or chronic. Arthritis or arthralgia associated with morning stiffness, swelling, and limitation of joints movement is the main finding of JIA. The disease course of JIA includes remission and exacerbation with chronic joint inflammation [1,2]. Laboratory and radiological workup is helpful in the diagnosis of JIA. Radiological workup includes computed tomography, MRI, and ultrasonography on affected joints for early detection of the disease or its complications [3]. Complications of JIA, including infections, macrophage activation syndrome (MAS), pericarditis, pulmonary hypertension, interstitial lung disease, and other forms of internal organ involvement, are commonly present and are associated with high mortality [4].

Osteoporosis, bone fractures, cataracts, avascular necrosis, and gastric ulcers are complications related to treatment [5]. Preventing or minimizing joint damage, preserving joint function, decreasing pain, and improving function are important goals to be considered during treatment of JIA. These goals are particularly important in JIA to decrease or minimize

joint deformity, which can occur early in disease course. The strategy in treatment of JIA is to produce remission and decrease frequency of relapse by using the smallest effective dose of drugs. Physical examinations as well as history taking and recording should regularly be done in patients with JIA. Effective pharmacological therapy helps in reducing the need for surgical intervention in JIA [6]. In patients who failed to response to medical therapy, surgery should be considered. Possible interventions include synovectomy, osteotomy, arthrodesis, and joint replacement [7]. Cemented hip replacements may reduce mechanical pain and improve functional ability for better quality of life.

The aim of this study was to evaluate the compliance of healthcare providers at the Pediatric Rheumatology Unit, Assiut University Children's Hospital, to the 2011 American College of Rheumatology (ACR) recommendations for treatment of JIA. The ACR issued recommendations for the treatment of JIA based on the following five treatment groups [8]:

(1) History of arthritis in four or fewer joints (oligoarticular JIA).
(2) History of arthritis in five or more joints (polyarticular JIA).
(3) Active sacroiliac arthritis.
(4) Systemic arthritis without active arthritis.
(5) Systemic arthritis with active arthritis.

Within each group, choice of therapy was guided by the degree of disease activity and the presence or absence of features indicating a poor prognosis.

Patients and methods

Setting and patients

A clinical audit with data recording using checklist aimed to evaluate treatment of JIA was conducted in the period September 2016 to September 2017 at the Pediatric Rheumatology Unit, Assiut University Children's Hospital, Assiut, Egypt. Patients included in this study were younger than 16 years attending the Pediatric Rheumatology Unit, Assiut University Children Hospital, and diagnosed as having JIA. This study was approved by the Ethical Committee of Faculty of Medicine, Assiut University.

The collected data concerned the following: (a) patients' demographics (age, sex, and residence); (b) types of JIA (oligoarticular arthritis, polyarticular arthritis, systemic-onset, psoriatic arthritis, enthesitis-related arthritis, or undifferentiated arthritis); (c) clinical signs (arthritis, fever, skin rashes, organomegaly, and lymphadenopathy), (d) investigations that included complete blood count (CBC), erythrocyte sedimentation rate (ESR), rheumatoid factor (RF), antinuclear antibody (ANA), anti-double stranded DNA (anti-dsDNA), and radiography on affected joints; (e) complications (growth retardation; height <5th percentile for age and sex), joint deformity, MAS, and complications of treatment; and (f) treatment and its clinical response.

Patients with the following diseases were excluded: arthritis of connective tissue disease (systemic lupus erythematosus, juvenile dermatomyositis, or scleroderma), infected arthritis (bacterial, viral, fungal, or Lyme disease), reactive arthritis (post streptococcal, rheumatic, toxic synovitis, or Reiter's syndrome), traumatic arthritis, and hematological disorders (leukemia, sickle cell disease, or thalassemia).

Statistical analysis

The data were tested for normality using the Anderson–Darling test and for homogeneity variances before further statistical analysis. Categorical variables were described by frequencies [*n* (%)]. χ^2 and Fisher exact tests were used to compare between categorical variables. A two-tailed *P* value less than 0.05 was considered statistically significant. All analyses were performed with the IBM SPSS 20.0 software (IBM Corp., Armonk, New York).

Results

The study was conducted on 50 patients at Pediatric Rheumatology Unit of Assiut University Children's Hospital. The patients were grouped according to age into two groups: from 1 to 7 and 8 to 16 years. Overall, 44% of the studied cases were males and 56% were females. Most of the patients were from urban areas (60%) (Table 1). Polyarticular JIA was the most common type among studied cases followed by systemic-onset JIA (32%), then oligoarticular (24%), and lastly enthesitis-related arthritis (4%). No patients were classified as having psoriatic arthritis or undifferentiated arthritis (Table 2). All studied cases presented with arthritis at the time of diagnosis.

Table 1 The demographic characteristics of the patients with juvenile idiopathic arthritis (*n*=50)

Clinical response	Improved	Not improved	*P*
NSAIDs	10 (25)	30 (75)	<0.001
Corticosteroid	15 (37.5)	25 (62.5)	0.044
DMARDs (methotrexate)	19 (76)	6 (24)	0.001
TNF-α inhibitor (enabrel)	2 (100)	0 (0)	<0.001
Interleukin-6 inhibitor (actemra)	4 (66.6)	2 (33.3)	0.565

Data presented are frequency; *n* (%) and *P* value of χ^2-test.
DMARDs, Disease-modifying antirheumatic drugs; TNF, Tumor necrosis factor.

Overall, 50% of the studied cases presented with fever, 30% of the studied cases presented with skin rashes and lymphadenopathy, and 20% of the studied cases presented with organomegaly (Table 3).

CBC and ESR were assessed for all studied cases at the time of diagnosis. CBC was normal in 60% of our patients. Anemia presented in 18% among studied cases, leukocytosis in 12%, and thrombocytosis in 10%. Raised ESR was seen in 100% of studied cases (Table 4). RF was done for 84% patients, where 71.4% had positive results, whereas 28.6% had negative results (Table 5). Both ANA and anti-dsDNA were done for 80% of cases. Negative results for both were seen in 60% of cases, whereas positive results were seen in 40% of cases (Table 5). Abnormal radiographic findings were found in 64%. Osteopenia was the commonest finding among studied cases (62.5%), whereas narrowing of joint space and joint erosion were seen in 21.8 and 15.6%, respectively (Table 6). The most common complication among studied cases was those related to treatment followed by growth retardation (8%); joint deformity was present in two cases, whereas only one case developed MAS (Table 7).

NSAIDs and corticosteroids were the most common drugs used. NSAIDs and corticosteroids were given to 80% of cases, methotrexate was given to 50%, interleukin-6 inhibitor (Actemra, Roche, Basel, Switzerland) was given to six cases, TNF-α inhibitor (Enbrel, Wyeth, New York) was given to two cases, and interleukin-1 inhibitor (anakinra) was not given (Table 8).

Concerning clinical response, 25% of patients improved on NSAIDs, whereas 30% showed no improvement. Moreover, 37.5% of cases showed clinical improvement on corticosteroids, and 62.5% showed no improvement. Methotrexate was effective in 76% of cases, Actemra was effective in 66.6%, whereas Enbrel was effective in 100% of cases (Table 9).

Table 2 Types of juvenile idiopathic arthritis according to International League of Associations for Rheumatology classification

Parameter	Done, 42 (84)			Not done
RF	Positive	Negative	*P*	8 (16)
	30 (71.4)	12 (28.6)	<0.001	
	Done, 40 (80)			
ANA and anti-dsDNA	Positive	Negative	*P*	10 (20)
	16 (40)	24 (60)	0.118	

Data shown are frequency; *n* (%) and *P* value of χ^2-test.

Table 3 Clinical signs of juvenile idiopathic arthritis in the study patients

Treatment	Given	Not given	*P*
NSAIDs	40 (80)	10 (20)	<0.001**
Corticosteroid			
Intra-articular	40 (80)	10 (20)	<0.001**
Systemic	3 (37)		
DMARDs (methotrexate)	25 (50)	25 (50)	1.000
TNF-α inhibitor (Enbrel)	2 (4)	48 (96)	<0.001**
Interleukin-1 inhibitor (anakinra)	0 (0)	50 (100)	<0.001**
Interleukin-6 inhibitor (Actemra)	6 (12)	44 (88)	<0.001**

***P* value is significant. Data shown are frequency; *n* (%) and *P* value of χ^2-test. DMARDs, Disease-modifying anti-rheumatic drugs; TNF, Tumor necrosis factor.

Discussion

JIA is not a single condition but rather a heterogeneous group of disorders characterized by arthritis of unknown etiology that manifests itself before the age of 16 years and persists for at least 6 weeks [9].

In this study, oligoarticular JIA was present in 24% among studied cases, which is in contrast to Danner *et al.* [10], who found that oligoarticular JIA was the most frequent subtype of JIA, accounting for up to 40% of cases. Symmons *et al.* [11] also found that polyarticular JIA was the second most frequent subtype of JIA accounting for up to 22% of cases, which is in contrast to the current work, in which polyarticular JIA represented the most common type accounting for 40% of cases. In our study, systemic-onset JIA was present in 32% of cases, whereas Prahalad [12] found systemic JIA was one of the least common JIA subtypes, accounting for ~10% of all JIA cases.

Anemia was found in 18% of our patients, which is similar to Tsai *et al.* [13], who stated that anemia occurring with JIA is characterized by decreased serum iron and total iron-binding capacity with fair

Table 4 Complete blood count and erythrocyte sedimentation rate findings of the studied patients with juvenile idiopathic arthritis

Sign	Present	Absent	*P*
Arthritis	50 (100)	0	<0.001
Fever	25 (50)	25 (50)	1.000
Skin rashes	15 (30)	35 (70)	<0.001
Organomegaly	10 (20)	40 (80)	<0.001
Lymphadenopathy	15 (30)	35 (70)	<0.001

Data shown are frequency; *n* (%) and *P* value of χ^2-test.

Table 5 Rheumatoid factor, antinuclear antibody, and anti-double stranded DNA in the studied patients

Done, 32 (64)			Not done, 18 (36)
Joint erosion	Osteopenia	Narrowing of joint space	
5 (15.6)	20 (62.5)	7 (21.8)	
P=0.002			

Data shown are frequency; *n* (%) and *P* value of χ^2-test.

Table 6 Radiographic findings on affected joints in the studied patients

State	Complete blood count	Erythrocyte sedimentation rate
Normal	30 (60)	0
Abnormal		
Anemia (Hb<11 mg/dl)	9 (18)	50 (100)
Leukocytosis (WBCs>12×10^3/μl)	6 (12)	
Thrombocytosis (Plt>500×10^3/μl)	5 (10)	
All	20 (40)	
P	0.072	<0.001

Data shown are frequency; *n* (%) and *P* value of χ^2-test.
Hb, Hemoglobin; Plt, Platelets; WBC, White blood cells.

Table 7 Complications of juvenile idiopathic arthritis in the studied patients

Complication	Present	Absent	*P*
Growth retardation (height<5th percentile for age and sex)	4 (8)	46 (92)	<0.001
Joint deformity	2 (4)	48 (96)	<0.001
Macrophage activation syndrome	1 (2)	49 (98)	<0.001
Complications of treatment	8 (16)	42 (84)	<0.001

Data shown are frequency; *n* (%) and *P* value of χ^2-test.

Table 8 Treatment of juvenile idiopathic arthritis in the studied cases

Types	*n* (%)
Oligoarticular JIA (≤4)	12 (24)
Polyarticular JIA (≥5)	20 (40)
Systemic-onset JIA	16 (32)
Psoriatic arthritis	0
Enthesitis-related arthritis	2 (4)
Undifferentiated arthritis	0
P	0.003

Data shown are frequency; *n* (%). DMARDs, Disease-modifying antirheumatic drugs; JIA, Juvenile idiopathic arthritis.

Table 9 Clinical response to given treatment in the studied cases

Items	*n* (%)	*P*
Age (1-7/8-16) (years)	23 (46)/27 (54)	0.549
Sex (male/female)	22 (44)/28 (56)	0.317
Residence (rural/urban)	20 (40)/30 (60)	0.072

Data shown are frequency; *n* (%) and *P* value of χ^2-test.

hemosiderin store owing to chronicity of disease, meanwhile other types of anemia can be present such as iron-deficiency anemia.

This result, the percentages of patients with elevated levels of ESR were 100%. This result is similar to that of Shin *et al.* [14], who found that ESR is a useful inflammatory marker that is indicative of disease activity in JIA, especially systemic-onset JIA, which typically has an elevated ESR often more than 100 mm/h.

Ruperto *et al.* [15] found that NSAIDs were the main line of treatment and have been most commonly used for decades. This is similar to our study in which NSAIDs were given to 40 (80%) patients as initial treatment. Systemic corticosteroid therapy was given to 37 patients (most of them were diagnosed as polyarticular JIA and systemic-onset JIA not responding to NSAIDs), and intra-articular steroid injections were given to three patients (diagnosed as oligoarticular JIA). This is similar to Kasapçopur *et al.* [16], who confirmed that systemic corticosteroid therapy should be used mainly for patients with systemic-onset JIA whose disease was not controlled or resistant to NSAIDs. According to Ravelli and Martini [17], methotrexate has become the most important agent of therapy for persistent or resistant arthritis and active arthritis because of its high efficacy and less toxicity. This point is similar to this study where methotrexate was given to 25 patients. Most of those patients were diagnosed as having systemic-onset JIA. Cases showed clinical improvement (resolution of arthritis and less exacerbation). In this study, etanercept was given to two cases diagnosed as having enthesitis-related arthritis (did not respond to other lines of therapy) [18]. Actemra monotherapy was superior to methotrexate monotherapy in JIA with a rapid improvement in symptoms and a favorable safety profile, as stated by Jones *et al.* [19]. To some degree, this is similar to our study in which Actemra was given to four cases that were resistant to all given treatment. Anakinra was used in treatment of unresponsive patients with systemic onset and polyarticular JIA [20]. Anakinra was not given to our patients because it is expensive and unavailable in our hospital. Through this study, some deficiencies were found. First, data recording was deficient. Second, there were also deficiencies in laboratory (mainly RF, ANA, and anti-dsDNA) and radiological workup, which were required for evaluation of degree of disease activity and poor prognostic factors. In addition, nonpharmacological therapy and surgery were not considered as lines of treatment. Lastly, regular follow-up of safety drug monitoring was deficient. Follow-up of safety drug monitoring included complete blood cell count, liver enzymes, and serum creatinine.

Conclusion

A clinical audit with data recording using checklist was done aimed to evaluate the compliance of healthcare providers at the Pediatric Rheumatology Unit, Assiut University Children's Hospital to the 2011 ACR recommendations for treatment of JIA. Patients included in this study were younger than 16 years attending the Pediatric Rheumatology Unit, Assiut University Children Hospital, and diagnosed as having JIA. ILAR classification was commonly used for classification of JIA. Laboratory and radiological workup (which were deficient) was important for

evaluation of degree of disease activity and poor prognostic factors. Pharmacological treatment given included NSAIDs, steroids, disease-modifying antirheumatic drugs, and biological agents, which were recommended by ACR. NSAIDs and corticosteroids were the most common drugs used. Regular medication safety monitoring is very important for early detection of complications of treatment.

Recommendations

(1) History taking and data recording are important in patients' assessment and follow-up.
(2) Disease activity can be determined by number of affected joints, ESR or CRP, physician global assessment of disease activity, and patient/parent global assessment of overall well-being.
(3) Disease activity and the features suggesting poor prognosis are important factors in the management of JIA.
(4) Poor prognostic features depend on site of affected joints (hip, ankle, wrist, and spine), inflammatory markers, and radiographic findings of affected joints.
(5) Nonpharmacological and surgical interventions should be considered.
(6) Safety drug monitoring should be done regularly.

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Conflicts of interest

There are no conflicts of interest.

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