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Research Article

Epidemiological Profile of Juvenile Idiopathic Arthritis in Batna-Algeria

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Abstract

Background and Purpose: Previous studies show a disparity in the prevalence of Juvenile idiopathic arthritis (JIA) subsets between different geographical areas or ethnic groups. There is paucity of data that describes JIA in Arabic and African populations. The purpose of this study is to describe the main epidemiological characteristics of JIA in Batna-Algeria-and to compare the findings with other JIA populations worldwide.

Methods: We conducted a multicenter retrospective descriptive study based on data collected on JIA patients diagnosed in Batna health centers (public and private sectors), over a seven-year period from January 2013 to December 2019. The studied variables are: gender, age at the initial symptoms, age at diagnosis, JIA subtype based on International League of Associations for Rheumatology (ILAR) criteria, symptoms at onset, disease duration at the latest follow up, uveitis presence, auto antibodies pattern and joint imaging results, JIA medications, JIA status at the time of enrollment and the latest follow-up.

Results: Sixty-nine cases of JIA were collected. The female to male ratio was 1.83. The median age at diagnosis was 9 years (range 1 - 16). Forty-six patients (72%) were diagnosed within the first year after disease onset. At the latest follow-up, the median disease duration onset was 1 year (range 1 - 8 years). There were 34 oligoarthritis (49.3%), 9 polyarthritis rheumatoid factor (RF) negative (13%), 8 polyarthritis (RF) positive (11.6%), 6 systemic arthritis (8.7%), 6 enthesitis-related arthritis (8.7%), 3 psoriatic arthritis (4.3%), and 3 undifferentiated arthritis (4.3%). Nine patients (18.7%) were anti-nuclear antibody (ANA) positive, and 21 patients (30.4%) had indeterminate ANA status. Sixty-three patients (91.3%) had benefited from a slit lamp examination, uveitis was found in 7.9% of cases. The used medications included non-steroidal anti-inflammatory drugs (NSAIDs) in 54 patients (79.4%), steroids in 37 (54.4%), intra articular steroid injections in 17 (24.6%), conventional disease-modifying anti-rheumatic drug (cDMARDs) in 51 (72.5%), and biologic agents in 11 patients (15.9%).

Conclusion: Oligoarthritis was the most common JIA subtype in our study with cases of uveitis at diagnosis. The RF positive polyarthritis frequency was higher than in literature. The use of cDMARDs was common whilst few patients received biologics.

Keywords: *Juvenile Idiopathic Arthritis; Epidemiological Features; Challenges; Algeria*

Abbreviations

JIA: Juvenile Idiopathic Arthritis; ILAR: International League of Associations for Rheumatology; RF: Rheumatoid Factor; ANA: Anti-Nuclear Antibody; NSAIDs: Non Steroidal Anti-Inflammatory Drugs; cDMARDs: Conventional Disease-Modifying Anti-Rheumatic Drug; sJIA: Systemic Arthritis; oJIA: Oligoarticular JIA; PsA: Psoriatic Arthritis; ERA: Enthesitis-Related Arthritis; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; Anti-CCP: Anti Cyclic Citrullinated Peptide; MAS: Macrophage Activation Syndrome; JAMLess: Juvenile Arthritis Management in Less Resourced Countries

Introduction

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood and often the cause of short- and medium-term mobility impairment [1]. JIA is not just one disease but an umbrella term that gathers all forms of chronic arthritis of unknown origin and with onset before 16 years [2]. The current classification of JIA has been established by the International League of Associations for Rheumatology (ILAR) and seven main categories of JIA were distinguished: systemic arthritis (sJIA), rheumatoid factor (RF)-positive polyarthritis, RF-negative polyarthritis, oligoarthritis (oJIA), psoriatic arthritis (PsA), enthesitis-related arthritis (ERA), and undifferentiated arthritis [3].

There is a worldwide discrepancy in the prevalence and subtypes distribution of JIA, because of the heterogeneity of used classifications, time, geographical zone, and methods [4]. However, the epidemiological studies remain the best tool to understand the disease and to improve its management.

To the best of our knowledge, there is only one epidemiological data published from an Algerian center, reporting 70 patients [5]. There is also overall a paucity of epidemiological data on JIA in Arabs and African regions that are thus underrepresented.

Aim of the Study

The main aim of this study was to determine the demographic, clinical, and therapeutic features of JIA in Batna (Algeria). This report was also designed to point the future challenges to improve care in pediatric rheumatology in a middle-income country. The results were compared with reports from the literature and the international studies.

Methods

We conducted a multicenter retrospective descriptive study based on the data collected on JIA patients diagnosed in Batna health centers, over a seven-year period from January 2013 to December 2019. As public sector source, we referred to the department of pediatrics of the University Hospital Center (CHU Benflis Touhami Batna), and as private sector source, we referred to private adult rheumatologists based in Batna. Batna is the fifth most populous city in Algeria and known for its strategic geographical location at the junction of the east north and the vast south: the Algerian desert.

There are three specialized hospitals and one University Hospital Center in Batna. These tertiary care centers contribute to the health care coverage not only of the province of Batna, but of the entire south-eastern region of the country i.e. a population pool of nearly 4 million inhabitants.

Recorded data for each patient included public or private consultation, date of birth, gender, family history of inflammatory disease, age at the initial symptoms, age at diagnosis, JIA subtype based on ILAR criteria, symptoms at onset, number of involved joints, type of joint involvement, presence of uveitis, laboratory tests results at diagnosis including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), anti-nuclear antibody (ANA), rheumatoid factor (FR), Cyclic citrullinated peptide (CCP), joint imaging including conventional radiography and ultrasonography, JIA medications, JIA status at the time of enrollment (active, remission with medication or without medication), and JIA complications or sequels.

Data were collected through a questionnaire and were stored on a database. Clinical and demographic characteristics were summarized by mean and standard deviation for continuous variables and count and percent for categorical variables. Statistical analyses were performed using SPSS software, version 22.0.

The study was approved by local ethics committee of University Hospital Center of Batna.

Results

Over the 7-year study period, 69 cases of JIA were identified. 71% (n = 49) were from Batna and 29% (n = 20) came from the neighboring towns and the south Eastern region. Among the 69 patients, 82.6% (n = 57) were managed by an adult rheumatologist (private medical sector) and only 17.4% (n = 12) were managed by pediatricians (public medical sector).

Among patients, 64% (n = 44) were girls and 35.3% (n = 24) were boys with a female to male ratio of 1.83. Age at diagnosis ranged from 1 to 16 years, median age at diagnostic was 9 years. At the latest follow-up, the median disease duration onset was 1 year (range 1 - 8 years). 72% (n = 46) of these patients were diagnosed during the first year of the disease. The longest time from onset of symptoms to diagnosis was 6 years for a child with oligoarthritis who lived in a rural region in the extreme south of Algeria (travelling distance of 533 Km to the outpatient center).

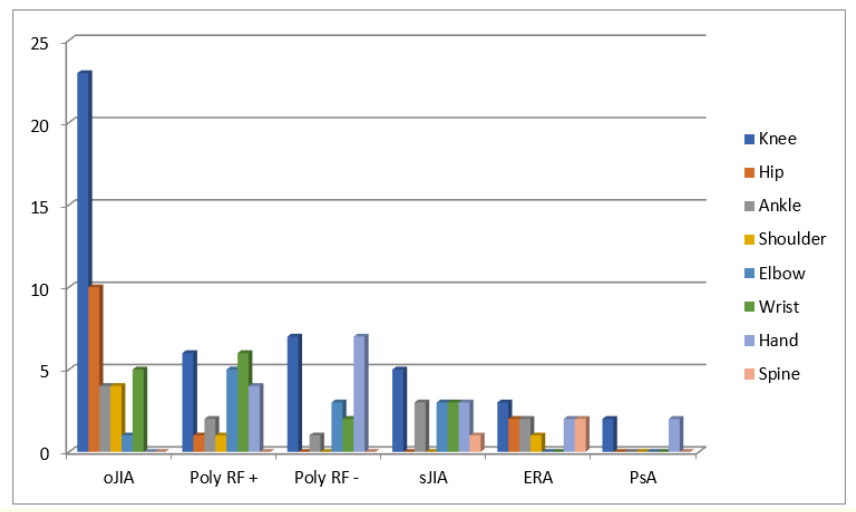
In our cohort, the most common JIA subtype was oligoarticular JIA (oJIA) in 49.3% of cases (n = 34), followed by RF-negative polyarthritis 13% (n = 9), RF-positive polyarthritis 11.6% (n = 8), systemic arthritis 8.7% (n = 6), and enthesitis related arthritis 8.7% (n = 6). While psoriatic arthritis was detected in 4.3% (n = 3) of cases, there were 3 patients (4.3%) who were classified as undifferentiated arthritis. The frequencies and the demographic characteristics of JIA subtypes are shown in table 1.

JIA Subtype	Frequency N (%)	Gender (male/female) N/N (%/%)	Age at diagnosis (years)
Oligoarthritis (oJIA)	34 (49.3)	14/20 (41.2/58.8)	8 [3-16]
RF-positive polyarthritis (Poly RF+)	8 (11.6)	3/5 (37.5/62.6)	8 [3-15]
RF-negative polyarthritis (Poly RF-)	9 (13)	2/6 (25/75)	9 [1-13]
Systemic arthritis (sJIA)	6 (8.7)	1/5 (16.7/83.3)	4.5 [1-11]
Enthesitis related arthritis (ERA)	6 (8.7)	4/2 (66.7/33.3)	12 [6-16]
Psoriatic arthritis (PsA)	3 (4.3)	0/3 (0/100)	11 [10-12]

Table 1: *Subtype frequencies and demographic characteristics of the patients.*
Age at diagnosis values are expressed as medians and ranges as they show non normal distribution overall.

The most common symptoms at JIA onset were joint pain (60 patients, 90.9%), joint swelling (53 patients, 80.3%), and limping (41 patients, 62.1%). Less frequent symptoms were extra-articular features including fever (17.4%, 12), evanescent rash (8.7%, 6), hepatosplenomegaly (1.4%, 1) and serositis (4.3%, 3).

The most affected joints at diagnosis were the knees (54 patients, 83.1%), small joints of hands and feet (20 patients, 33.1%), wrists (18 patients, 27.7%), hips (15 patients, 23.1%), ankles (13 patients, 20%) and elbow joints (12 patients, 18.5%). The less frequently affected joins were the shoulders (7 patients, 0.8%) and spine (3 patients, 4.6%). The pattern of joint involvement in each subtype is shown in graph 1.



Graph 1: *Joint involvement at diagnosis according to the juvenile idiopathic arthritis (JIA) subtypes.*
oJIA: Oligoarticular JIA; Poly RF+: Polyarthritis Rheumatoid Factor Positive; Poly RF-: Polyarthritis Rheumatoid Factor Negative; sJIA: Systemic JIA; ERA: Enthesitis Related Arthritis; psA: Psoriatic JIA; JIA: Juvenile Idiopathic Arthritis.

Sixty-three patients (91%) had at least one slit lamp examination. Uveitis was found in 5 patients (7.9%), 4 boys and 1 girl. Three of these patients presented oligoarthritis and two presented polyarthritis. All these patients had negative ANA on one single test.

X-rays were performed in 87% (60) of cases and were normal in 66.7% (46). Musculoskeletal ultrasound was done in 81.2% (56) and was pathological in 72.5% (50) of cases.

A total of 24 patients (34.8%) had an elevated erythrocyte sedimentation rate (ESR); 24 patients (34.8%) had elevated C-reactive protein (CRP). The highest inflammatory markers at disease onset were observed in patients with systemic onset JIA, the mean recorded ESR value was 100 mm/h. Rheumatoid factor (RF) was found in 13% (9 patients) of cases and the Cyclic citrullinated peptide (CCP) in 2.9% (2 patients).

Forty-eight patients (69.5%) had ANA tests done at least once. Only 9 patients (18.7%), 7 girls and 2 boys were ANA positive (4 polyarthritis, 2 oligoarthritis, 2 ERA, and 1 sJIA). Seventeen patients with oligoarthritis (44.1%) had undetermined ANA status. Table 2 summarizes the different biological characteristics of juvenile idiopathic arthritis (JIA) subtypes.

JIA Subtype	ESR↗ N (%)	CRP+ N (%)	ANA+ N (%)
Oligoarthritis	7 (20.6)	8 (23.5)	2 (5.9)
RF-positive polyarthritis	5 (62.5)	2 (25)	3 (37.5)
RF-negative polyarthritis	3 (33.3)	3 (33.3)	1 (11.1)
Systemic arthritis	6 (100)	6 (100)	1 (16.7)
Enthesitis related arthritis	1 (16.7)	2 (33.3)	2 (33.3)
Psoriatic arthritis	0 (00)	0 (00)	0 (00)

Table 2: *Biological characteristics of juvenile idiopathic arthritis (JIA) subtypes.*

Treatment modalities used for these patients included non-steroidal anti-inflammatory drugs (NSAIDs) in 54 (79.4%) patients, steroids (prednisolone) in 37 (54.4%), conventional disease-modifying anti-rheumatic drug (c DMARDs)in 51 (72.5%), biologic agents in 11 (15.9%), and intraarticular injections in 17 (24.6%) patients. Treatment modalities details for each JIA subtype can be seen in table 3.

JIA Subtype	NSAIDs N (%)	Steroids N (%)	c DMARDs N (%)	Intra articular steroids N (%)	Biologics N (%)
Oligoarthritis	31 (91.2)	12 (35.3)	24 (70.6)	12 (35.3)	0 (00)
RF-positive polyarthritis	5 (62.5)	6 (75)	8 (100)	0 (00)	4 (50)
RF-negative polyarthritis	7 (77.8)	8 (88.9)	8 (88.9)	0 (00)	3 (33.3)
Systemic arthritis	3 (50)	5 (83.8)	4 (66.7)	0 (00)	2 (33.3)
Enthesitis related arthritis	5 (83.3)	3 (50)	3 (50)	0 (00)	0 (00)
Psoriatic arthritis	2 (66.7)	1 (33.3)	2 (33.3)	0 (00)	0 (00)

Table 3: *Treatment modalities of juvenile idiopathic arthritis (JIA) subtypes.*

The most used conventional disease-modifying anti-rheumatic drug was methotrexate 42 (63.7%). It was associated with other c DMARDs in 2 cases. Sulfasalazine was used in 8 cases, leflunomide in 1 case, and hydroxychloroquine in 1 case.

Biologics were used in 11 cases (15.9%). RF-positive polyarthritis 4 (50%), RF-negative polyarthritis 3 (33.3), systemic arthritis 2 (33.3) were the groups that most needed a biologic. Used biologics included rituximab (n = 2), tocilizumab (n = 1), anakinra (n = 1), etanercept (n = 1), infliximab (n = 1). The median duration between the first biological agent and the diseases onset was 2 years (range 1 - 8 years).

At the time of enrollment, 31 patients (44.9%) were in remission, including 20 patients (29%) on treatment; twelve patients (17.4%) had active disease. Early renal amyloidosis was observed in one case and resulted in death after two years of evolution. This patient, a five-year-old girl, had no history of familial Mediterranean fever and no genetic test has been performed. Macrophage activation syndrome (MAS) complicated 2 cases of systemic arthritis. One patient had a growth delay and two patients had functional impairment.

Discussion

Our study is the first epidemiological study conducted on JIA in Batna. In addition, it included both private and public sector, pediatricians and adult rheumatologists, hence reducing the risk of bias in recruiting patients.

In our country, Pediatric Rheumatology as a subspecialty has not yet gained ground. Adult rheumatologists and pediatricians are still the doctors who take care of children with rheumatic and musculoskeletal diseases. In our study, most patients (82.6%) consult private adult rheumatologist. Only 17.4% consult pediatrician in a hospital. The latter patients present a complex clinical picture with extra-articular manifestations associated with joint manifestations. Indeed, children with isolated joint problem are usually seen by adult rheumatologist more than general pediatrician.

Different studies have shown a remarkable disparity in the frequency of JIA subtypes in different geographical areas or ethnic groups. Although some recruitment biases were often suspected, it appears that in Western countries the most common subset of JIA is oligoarthritis, while this form seems to be rare in Costa Rica, India, New Zealand, and South Africa in which polyarthritis predominates [1]. In Asia, the greater subtype prevalence is of the systemic arthritis and enthesitis related arthritis (ERA) [6]. In our cohort, the subtype frequency is like the western countries except that RF-positive polyarthritis was more prevalent, whereas it is the least common subtype

in the literature [1]. In the US, this form has been found to be more common among African American children than in non-Hispanic white children [7]. An Algerian study also found that the polyarthritis RF positive frequency is higher but the polyarthritis subtype is more frequent than oligoarthritis [5]. Table 4 shows the frequency of subtypes in different national and international studies compared to our study.

JIA Subtype	Batna (N: 69)	Algiers [5] (N: 70)	Morocco [8] (N: 80)	France [9] (N: 155)	England [10] (N: 507)	Canada [11] (N: 366)	Turkey [12] (N: 265)	India [13] (N: 520)	South Africa [14] (N: 78)
oJIA	49.3	37.5	42.5	35	45.9	40.7	32.9	13.1	26.8
PolyJIA	24.6	41.4	31.5	17	15.7	23.9	17.3	13.3	40.9
Poly RF+	11.6	20	-	2	2.3	3.7	3.8	-	14
Poly RF-	13	21.4	-	15	13.4	20.2	13.5	-	26.9
sJIA	8.7	10	26	17	5.3	7.3	13.2	23.8	7.69
ERA	8.7	11.4	-	7	6.3	10.1	32.9	47.5	23
psJIA	4.3	1.4	-	4	6.9	6.5	1.9	0.4	1.28
IndJIA	4.3	-	-	20	-	11.5	1.9	1.9	-

Table 4: *Frequencies of juvenile idiopathic arthritis subtypes in selected populations. Data represent percentages in each study.*

JIA: Juvenile Idiopathic Arthritis; oJIA: Oligoarticular JIA; PolyJIA: Polyarticular JIA; Poly RF+: Polyarthritis Rheumatoid Factor Positive; Poly RF-: Polyarthritis Rheumatoid Factor Negative; sJIA: Systemic JIA; ERA: Enthesitis Related Arthritis; psJIA: Psoriatic JIA; IndJIA: Undifferentiated JIA.

We observed a female predominance in our cohort as is classically described in western populations from Europe, and North America [6]. This female predominance was also present in all subtypes except ERA, which concords with literature.

Median age at diagnosis in our cohort is close to what was found in Morocco (7.53 years) and South Africa (8 years) [8,14]. Patients in Southern Europe had a markedly younger age at disease onset than that of those living in other geographical areas [6]. This observation might be partly explained by the greater prevalence of oligoarthritis, which typically occurs at an early age [1]. In our study, oligoarthritis is the most common subtype but the median age at diagnosis is 8 years for this category, and 67.7% of these patients are over 5 years old.

JIA-associated uveitis was uncommon in our series, however few patients had regular and repeated slit lamp assessment as recommended in many countries; thus, this complication might be underestimated. Uveitis geographical variations in the incidence of uveitis in JIA have been reported around the world [15]. Ocular involvement was recorded most in Northern and Southern Europe and less frequently in Latin America, Africa and Middle East, and Southeast Asia [6].

Contrasting with the wide use of NSAIDs, steroid injections, systemic glucocorticoids or cDMARDs, few of our patients received biologics in comparison with JIA patients from Europe or North America. Systemic glucocorticoids are widely prescribed in southeast Asia and Africa and Middle East and less often in North America and western Europe [6]. The costly biologic is less frequently used in low-income countries than in wealthier ones [6]. This is in part due to the reduced accessibility to these medications in lower-income settings, implying that many children with chronic arthritis might not benefit from the latest progress in disease management [15]. Recent recommendations about JIA management in less resourced countries (JAMLess) are developed in order to appropriate the care and treatment for children with JIA in these countries [16].

In Algeria, as a middle-income country, the greatest concerns with children with JIA are to deliver comprehensive multidisciplinary care and regular follow up, to access to diagnostic facilities and therapies despite the remote location, and to avoid the misdiagnosis or delayed diagnostic. Creating reference centers, promoting Pediatric Rheumatology training and enhancing regional and international network become a necessity to achieve these aims.

Limitation of the Study

This study has some limitations. First the number of patients was limited to draw conclusion regarding the relative frequency of the different subtypes. Second, as it is common for a retrospective study, some data are incomplete especially for the laboratory results data. However, to the best of our knowledge, this is one of the first population studies evaluating the clinical profile of JIA in Algeria and it provides a starting point in understanding the epidemiology of the disease in this country.

Conclusion

The determination of the epidemiologic profile of JIA is crucial for identifying JIA's specific aspects in our country. Prospective multicenter studies are necessary. Improving health management of children with JIA requires promoting pediatric rheumatology and creating referenced centers.

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Disclosures

The authors declare they have no competing interests.

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