

Long-Term Outcome of Juvenile Idiopathic Arthritis in Early Adulthood: Clinical Experience from a Saudi Tertiary Hospital

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Abstract

Objective: To report the long-term outcome including disease activity, damage and social status, quality of life at the last follow-up visit in a Saudi cohort of adults with juvenile idiopathic arthritis (JIA), and to determine the predictive factors.

Methods: In this retrospective study adults with JIA who had regular follow-up between June 1990 and June 2016 at King Faisal Specialist Hospital and Research Center (KFSH-RC), Riyadh were identified. The disease status, educational and employment status and long-term outcome measures comprised Juvenile Arthritis Multidimensional Assessment Report (JAMAR), Juvenile Arthritis Damage Index (JADI) were obtained at the last follow-up visit.

Results: Forty patients (27 female) were included; the mean age was 21.9±6 years and mean disease duration was 15±6 years. Of the 40 patients, 45% had polyarticular subtype and 42% had systemic JIA. At the last follow-up visit, five patients were in complete remission and 35 patients were on treatment, 30 patients were in clinical remission and 5 patients had active disease. The mean articular JADI was 9.4±9 and mean number of joints with damage was 4.8±4. Patients with longer disease duration and late treatment with biologic agents had more joint damage and poor functional status (P 0.04). Nine patients underwent joint replacement. The mean functional ability scale was 5.6±5 and health-related quality of life (HRQoL) was 6±4. Twenty-six patients completed high school. Seven patients had work and five got married, all had healthy children.

Conclusion: Most of our patients were polyarticular onset or systemic JIA with a quiescent disease and satisfactory patient-reported HRQoL. Patients with longer disease duration and lately treated with the biologic agent have shown more joint damage.

Keywords: Juvenile Idiopathic Arthritis; Adulthood; Outcome; Juvenile Arthritis Multidimensional Assessment Report

Introduction

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children. It affects approximately one in 1000 children [1]. JIA is a diagnosis of exclusion; it represents a phenotypically heterogeneous group. However, they have similar inflammatory articular changes [2,3]. It was commonly thought that JIA might subside in adulthood, but several reports have shown that 30-50% of children with JIA enter adulthood with ongoing active disease or experience sequelae from their disease [4-6].

Patients with JIA especially polyarticular and systemic subtypes might experience a chronic course with cyclic disease activity states [7]. Published data on the long-term outcome of adult patients with JIA revealed that most of the patients who did not have the appropriate treatment at the initial follow-up visits may end in significant joint destruction and deformities with functional impairment and disability as well as extra-articular morbidity, including chronic uveitis, growth retardation and serious complications namely macrophage activation syndrome [8,9]. Furthermore, this group of patients remains at potential risk of adverse events

of these medications namely corticosteroids. Though, there is currently no cure for JIA. Nevertheless, there have been major advances in the recent years in the understanding of the pathogenesis of JIA accompanied by the implementation of new therapeutic strategies, including the early introduction of biologic medications, which led to remarkable improvement in the outcome of JIA [10,11].

As growing numbers of patients with JIA survive into adulthood, reviewing and characterization of the outcome of adult patients with JIA reveal the prime comprehensive transition of care from pediatric to adult rheumatology service. Fortunately, a number of studies published over the last decade have examined the long-term health, functional and quality of life outcomes of adults with childhood-onset rheumatic diseases including JIA [8,12-16]. However, to the best of our knowledge, there are no available published data from the Middle East about the long-term burden of JIA on the adults. In this study, our aim was to assess the long-term outcome of a Saudi cohort of adult patients with JIA seen in a single tertiary hospital. The patients assessed at the last follow-up visit in respect to the disease damage including articular and extra-articular damage in addition to the social status and quality of life.

Methods

We have the privilege at our institution to follow a large cohort of children with JIA. As per the hospital policy, those who exceed 14 years of age usually transferred to the adult rheumatology care to provide ongoing and comprehensive clinical care. The study cohort comprised all adult patients with JIA who were followed regularly at the pediatric Rheumatology clinic and transferred to the adult Rheumatology clinic at our institution from June 1990 to June 2016 at King Faisal Specialist Hospital and Research Center (KFSH-RC), Riyadh. All included patients fulfilled the International League of Association for Rheumatology (ILAR) criteria for the classification of JIA and a minimal follow-up period of 1 year in adult rheumatology clinic [2].

Medical records of all patients were reviewed for demographic data, age of first disease manifestations, disease duration, and follow-up duration, family history of JIA, clinical and laboratory and imaging findings. The disease duration was calculated from the onset of symptoms related to JIA, while the duration of follow-up was calculated starting from the first visit to KFSH-RC.

As part of our usual health care and routine follow-up visits, patients were seen every 3-6 months unless there was a flare demanded for a closer follow-up visit, a complete physical examination in addition to appropriate laboratory and imaging evaluation completed at each follow-up visit.

At the last follow-up visit, patients interviewed and assessed for the current treatment, the disease activity using Juvenile Arthritis Disease Activity Score (JADAS), which represent states of clinically inactive disease and remission and the long-term outcome using Juvenile Arthritis Multidimensional Assessment Report (JAMAR), which included health-related quality of life (HRQoL) and Juvenile Arthritis Damage Index (JADI) [17-19]. Additionally, social status including marital status, age at marriage and number of children, educational and employment history gathered from patients.

All the collected data were the result of routine medical procedure and extracted from the patient's file. All collected data were saved and the confidentiality of the patients was protected. Personal identifying data were not collected for this research project. Consent procedure in accordance with our institution guidance including obtaining informed consent from young individual people was obtained. Our institutional ethics committee and the research advisory council approved the study (RAC# 2161001).

The results expressed as the mean \pm standard deviation (SD) for continuous variables and percentages for categorical variables. Regression analysis carried out to examine the influence of the variables on the outcome measures. The P value of < 0.05 was considered significant. The variables compared using 2-sample t-tests, chi-square tests and Fisher's exact tests.

Results

At the time of this review, a total of 92 adult patients with JIA were in our database; 52 patients were excluded because they lost follow-up or transferred to other institutions. Patients who failed the successful transfer to the adult rheumatology care were either oligoarticular JIA patients with inactive arthritis, poor compliance patients with irregular follow up visits or patients preferred follow-up at the local hospitals. Forty adult patients (27 female) with JIA had a regular follow-up in the adult rheumatology clinic at KFSH-RC and were included. The mean age was 21.9 ± 6 years while the mean age at disease onset and mean disease duration were 6.4 ± 4 and 15 ± 6 years, respectively.

Polyarticular subtype and systemic arthritis were the most frequent subtypes. Fifteen (37.5%) patients had a family history of autoimmune diseases among their first-degree relatives; out of them 6 (15%) patients had a family history of JIA. Table 1 summarizes the demographic and clinical data. All patients were transferred to the adult rheumatology service at the age of 14 years; either they had active disease or they were in clinical remission but required maintenance treatment. All patients treated with non-steroidal anti-inflammatory drugs, corticosteroids and disease-modifying anti-rheumatic drugs (DMARDs) including biologic agents during their follow-up. Thirteen patients commenced biologic agents late during their disease course (mean disease duration prior biologic agent treatment was 8 ± 3 years); the biologic agents were not available as they need or they were referred to the pediatric rheumatology clinic at KFSH-RC late in their disease course.

40 patients (Female: Male)	27: 13
Age at the last visit, years (mean± SD)	21.9± 6
Age at disease onset, years (mean± SD)	6.4±4
Disease duration, years (mean± SD)	15±6
JIA subtypes:	
Polyarticular	18 (45%)
RF+ Poly	10
RF- Poly	8
Systemic arthritis	17 (42.5%)
Oligoarticular	3 (7.5%)
Psoriatic arthritis	1 (2.5%)
Enthesitis related arthritis	1 (2.5%)
Family history of autoimmune disease:	
JIA	6 (15%)
Hypothyroidism	3 (7.5%)
Vitiligo	3 (7.5%)
DM type I	2 (5%)
IBD	2 (5%)
SLE	1 (2.5%)
RA	1 (2.5%)
Ankylosing spondylitis	1 (2.5%)

JIA= Juvenile Idiopathic Arthritis, DM= Diabetes Mellitus, IBD= Inflammatory Bowel Disease, SLE=Systemic Lupus Erythematosus, RA= Rheumatoid Arthritis.

Table 1: Summarizes the demographic and clinical data.

At the last follow-up visit, five (12.5%) patients were in complete remission, two patients with persistent oligoarticular subtype, two patients with polyarticular subtype and one patient with systemic arthritis, none of them required maintenance treatment. In contrary, 35 patients were in need of treatment, 21 (60%) patients received methotrexate and 28 (70%) received biologic agents. Table 2 shows the treatment at the last follow-up visit.

Medications	Frequency	Percentage
NSAIDs	15	42.8%
Corticosteroids	6	15%
Methotrexate	21	60%
	13 parenteral	62%
	8 oral	38%
Salazopyrine	2	5.7%
Etanercept	2	5.7%
Infliximab	3	8.6%
Adalimumab	5	14%
Abatacept	2	5.7%
Tocilizumab	14	40%
Anakinra	1	2.8%
Rituximab	1	2.8%

Table 2: The treatment at the last follow-up visit

Thirty, (75%) patients were in clinical remission, 15 patients with polyarticular subtype, 12 patients with systemic arthritis, one patient each with a persistent oligoarticular subtype, psoriatic arthritis and enthesitis related arthritis, while five (12.5%) patients were found to have active articular disease, one patient had polyarticular subtype and four of them were systemic arthritis; none of them had active systemic manifestations or history of macrophage activation syndrome. The mean JADAS at the last follow-up visit was 2±2; wrist and proximal interphalangeal (PIP) joints were the most active joints. In contrast, the mean articular JADI was 9.4±9 with mean damage joints of 4.8±4; the damage was more prominent in wrist, knee and hip joints. Patients with longer disease duration (mean disease duration was 21±4 years) and late treatment with biologic agents had more joint damage and poor functional status (P 0.04). Furthermore, patients with a family history of JIA had more articular damage, but it was not statically significant (P= 0.06).

Nine patients, (five systemic arthritis and four polyarticular subtype), underwent surgical intervention, four patients had hip replacement and two patients had knee replacement. Two patients underwent joint fusion (proximal interphalangeal joints, cervical vertebral C1-C2) and one patient had chin augmentation. Furthermore, the mean JADI for extra-articular damage was 2±2. Eighteen patients had significant growth retardation and 10 patients had severe osteoporosis with evidence of compression vertebral fractures. Table 3 summarizes the articular and extra-articular damage. The mean functional ability scale was 5.6±5 and HRQoL

was 6 ± 4 . Patients with systemic arthritis, particularly those with long disease duration had poor HRQoL and more functional limitations. However, the difference is statistically insignificant.

JADI (mean \pm SD)	9 \pm 9
Articular JADI (mean \pm SD)	9.4 \pm 9
Number of damage joints (mean \pm SD)	4.8 \pm 4
Hip joint replacement	4
Knee joint replacement	2
PIP joint fusion	1
Cervical vertebral fusion	1
Extra-articular JADI (mean \pm SD)	2 \pm 2
Growth retardation	45%
Delayed puberty	7.5%
Osteoporosis/ vertebral collapse	25%
Abnormal vertebral curve	20%
Avascular necrosis	10%
Leg-length discrepancy	25%
Uveitis	7.5%
Striae	17%
HRQoL (mean \pm SD)	6 \pm 4
Functional ability (mean \pm SD)	5.6 \pm 5

JADI= Juvenile Arthritis Damage Index, PIP= Proximal Interphalangeal, HRQoL= Health Related Quality of Life

Table 3: Summarizes the articular and extra-articular damage

Twenty-six, (65%) patients completed the high school, 11 of them joined a college with good educational achievement. Seven patients had work and five patients (three female) got married and had children, the average age at marriage was 23 years old and all children were healthy.

Discussion

JIA is a heterogeneous chronic disorder with variable clinical courses ranging from complete remission to persistent active disease with potential risk of long-term morbidity and probably physical disability resulting from the cumulative articular and extra-articular damage [8,20].

We studied the outcome of 40 adult patients with JIA with mean disease duration of 15 ± 6 years. Most of our patients had either polyarticular subtype or systemic arthritis with a chronic course and intermittent disease activity, our finding is consistent with the observation from the previous published data [5,6].

Thirty-five of our patients were in need of treatment, 30 of them were in clinical remission. However, despite the intensive treatment, five patients had active synovitis involving mainly the wrist and PIP joints. Comparison with other published cohorts, our patients had more frequent active disease required medication (87.5%), while 41% of the adult European patients with JIA required medication after 30 years of follow up; this may reflect the cultural and genetic differences [21]. It is worth mentioning that our data showed high frequency of familial aggregation of JIA, which reinforced the concept of genetic differences. We previously published the differences between familial JIA and sporadic JIA patients; familial patients had early disease onset, higher number of actively inflamed joints and worse functional capacity. Furthermore, genetic testing identified a homoallelic missense mutation in LACC1 [22,23].

Delayed diagnosis and longer disease duration and probably late initiation of biologic treatment have a predictive value in the development of the cumulative articular damage and poor functional outcome in adult patients with JIA [9,13,15]. Furthermore, the extended periods of exposure to corticosteroids probably have significant consequences. In contrast, the new therapeutic approach, especially with the availability of new medications showed remarkable improvement of the short-term survival and prognosis [24,25].

Twenty-six of our patients had significant destructive arthritis and limited functional capacity; most of them had long disease duration. In fact, half of them could not get the biologic treatment at the appropriate time because of unavailability at their initial visits. The rate of arthroplasty was high, six patients required joint replacement. Also, patients from multiplex families with JIA might be at high risk of cumulative articular damage.

Data on educational and employment performance in adults with JIA are limited, adult patients with JIA might encounter obstacles in education and work compared with those of age-matched individuals for different reasons including independence [26-28]. Two-thirds of patients had a satisfactory educational achievement. However, only seven patients had a permanent job. Nevertheless, we believe that further studies are needed to assess the quality of life of adults with JIA. The rate of unsuccessful transfer of our patients

to the adult rheumatology care (56.5%) was comparable to previous published data. The majority of patients with unsuccessful transfer had poor compliance 23. Certainly, presence of a transitional care program expedites unsuccessful transfer to the adult service. Unfortunately, we don't have such program yet.

Overall, to the best of our knowledge, this is the first study from the Middle East highlights the rate of unsuccessful transition management and the burden and long-term outcome of adult patients with JIA. Our study has several limitations, including one visit assessment of small number of participants and the lack of validation articular and extra-articular JIA damage in adulthood. This study may not accurately reflect the overall outcome of adults with JIA in Saudi Arabia, as it is a single tertiary hospital experience and represent a referral bias with severe cases. Furthermore, this study did not comprise all JIA patients entered adulthood seen in our clinics. Indeed, some of them lost follow-up either due to remission or transfer to other institutions. Nevertheless, we hope that such work will encourage the physicians to identify the obstacles and risk factors of poor outcomes for further improvement of therapeutic strategies for adults with JIA.

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