Seminars in Arthritis and Rheumatism ▮ (2016) ▮▮▮–▮▮▮

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

Population-based study of outcomes of patients with juvenile idiopathic arthritis (JIA) compared to non-JIA subjects

Megan L. Krause, MD[a,*], Jorge A. Zamora-Legoff, MD[a], Cynthia S. Crowson, MS[b], Theresa Wampler Muskardin, MD[a], Thomas Mason, MD[a], Eric L. Matteson, MD, MPH[a,c]

[a] Division of Rheumatology, Mayo Clinic College of Medicine, 200 First St SW, Rochester, MN 55905
[b] Division of Biomedical Statistics and Informatics, Department of Health Sciences Research, Mayo Clinic College of Medicine, Rochester, MN
[c] Division of Epidemiology, Department of Health Sciences Research, Mayo Clinic College of Medicine, Rochester, MN

ARTICLE INFO

Keywords:
Juvenile idiopathic arthritis
Healthcare utilization
Depression

ABSTRACT

Objective: Evaluate healthcare utilization and occurrence of comorbidities in a population-based cohort of patients of juvenile idiopathic arthritis (JIA) with an age- and sex-matched comparator group.
Methods: Prevalent cases of JIA in 1994–2013 were identified in Olmsted County, Minnesota, along with age- and sex-matched non-JIA comparators. Surgeries, hospitalizations, pregnancies, and comorbidities were identified by medical record review. Poisson methods were used to generate rate ratios (RR) with 95% confidence intervals (CI) to compare outcomes between JIA and non-JIA cohorts separately during childhood (age $<$ 18 years) and adulthood (age $\geq$ 18 years).
Results: A total of 89 JIA and 89 non-JIA comparators were identified [64% female; mean (SD) age 8.6 (5.1) years at JIA incidence/index date and mean follow-up in childhood 6.3 (4.4) years for JIA; similar for comparators]. Among them, 38 pairs had follow-up into adulthood with mean follow-up of 8.0 (5.5) years for JIA. Children with JIA were more likely to have joint surgery (RR = 3.93, 95% CI: 1.18–24.94), non-joint surgery (RR = 1.90, 95% CI: 1.05–3.67), and hospitalizations (RR = 2.25, 95% CI: 1.04–5.53) than non-JIA comparators. As adults only joint surgeries remained significantly different (RR = 8.5, 95% CI: 2.27–120.1). Depression during childhood was more common in JIA (RR = 2.49, 95% CI: 1.01–6.13). There were no differences in educational achievement, employment status, or pregnancy outcomes between the 2 groups.
Conclusions: In a population-based cohort, inpatient healthcare utilization is higher for patients with JIA including surgery and hospitalization during childhood but not extending into adulthood. Understanding long-term comorbidities and healthcare needs for patients with JIA is necessary to provide comprehensive care.

Juvenile idiopathic arthritis (JIA) causes wide ranging manifestations extending beyond inflammatory arthritis [1]. Classification criteria have evolved over time with the most recent being the ILAR criteria with different long-term outcomes associated with different subtypes [2,3]. While defined by symptoms starting before the 16th birthday, JIA is not isolated to symptoms in childhood. In long-term study patients evaluated 30 years after their diagnosis of JIA, over a third had evidence of active disease and an additional 7% were taking ongoing medication to maintain remission [4]. Even in the absence of active disease, patients suffer the complications of damage [5].

Understanding disease activity and its associated damage in isolation will not describe the full impact of JIA on a single individual in the long term. Comorbidities above and beyond JIA impact fatigue, pain, functional capability, and quality of life measures [6]. This underscores the requirement of long-term follow-up to understand the impact of JIA as a chronic illness.

This study sought to compare inpatient healthcare utilization and comorbidities among patients with JIA and age- and sex-matched non-JIA comparators in a geographically defined population. Outcomes were assessed during childhood and adulthood to capture the long-term impact of the disease.

Methods

Patient cohort

All prevalent cases of JIA were identified in Olmsted County, Minnesota, between January 1, 1994 and December 31, 2013 utilizing the Rochester Epidemiology Project with its associated access to full medical records for all medical care received in the

* Corresponding author.
E-mail address: krause.megan@mayo.edu (M.L. Krause).

http://dx.doi.org/10.1016/j.semarthrit.2016.07.003
0049-0172/

county including all inpatient and outpatient medical care, telephone communications, medication prescriptions, hospitalizations, and surgeries/procedures [7]. In 2010, the total population in Olmsted County was 144,248 persons. Over the time of follow-up, there were 1–2 pediatric rheumatologists at a single time in the county.

These individuals were identified first by diagnosis code and then confirmed by medical record review to meet ILAR criteria for JIA [2]. Additional information regarding the search is available in an earlier publication [8]. The index date for each subject was the date they first fulfilled ILAR criteria for JIA and lived in Olmsted County. If their diagnosis occurred when they were not living in Olmsted County, then the index date was when they first moved to Olmsted County. Non-JIA comparator subjects were age- and sex-matched, and selected at random from the same population of Olmsted County, Minnesota. Index date for comparators was the same as the index date of the corresponding JIA case. All subjects were followed retrospectively through their complete medical records (inpatient and outpatient) until death, migration from Olmsted County or December 31, 2014. There was no minimum follow-up time required for inclusion.

Demographic data including date of birth, sex, and race/ethnicity were obtained. Patient reported employment status, highest education status achieved, and tobacco use was also recorded for those individuals who had follow-up beyond the age of 18 years. Healthcare utilization, specifically joint surgeries, other surgeries (excluding joint surgeries), and hospitalizations (hospitalizations that occurred specifically for surgery were not included) that occurred after index date were recorded. Comorbidities including malignancy, diabetes mellitus type 1, celiac disease, and autoimmune hepatitis were identified based on clinician diagnosis irrespective of index date. Information regarding clinician diagnosed depression was also obtained in addition to hospitalizations specifically for depression. Pregnancy information was abstracted including information regarding live births, spontaneous abortions, and elective abortions.

This study was approved by the Mayo Clinic and Olmsted Medical Center Institutional Review Boards.

Statistical analysis

Characteristics of patients with JIA and non-JIA comparators were described using numbers with corresponding percentages for categorical variables and mean with standard deviation (SD) for continuous variables. Differences between patients with JIA and non-JIA comparators were tested using chi-square tests for categorical variables and rank-sum tests for continuous variables. Analysis was performed separately for outcomes in childhood, as defined prior to age 18 years, and in adulthood for pairs of patients with JIA and non-JIA comparators in which both individuals had follow-up past the age of 18. If only a single individual of the pair had follow-up into adulthood then they were excluded from the adult analysis.

Hazard ratios (HR) with 95% confidence intervals (CI) were obtained from Cox models adjusted for age, sex, and calendar year of index date to evaluate depression. Rate ratios (RR) with 95% CI were calculated using Poisson methods to compare rates of outcomes that could be more than once in the same patient, such as joint surgeries, non-joint surgeries, hospitalizations, hospitalizations for depression, and pregnancies. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) and R 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Demographics

Eighty-nine patients were identified with JIA as well as 89 corresponding non-JIA comparators. The mean age (SD) at index date was 8.6 (5.1) years for those with JIA and 8.9 (5.0) years for those without JIA (Table 1). Among the JIA, 82 (92%) were included at incidence and the remaining 7 prevalent cases had median disease duration at index date of 1.3 (range: 0.2–4.0) years, and all were seen by a pediatric rheumatologist at least once. JIA subtypes included 53 (60%) oligoarthritis of which 43 were persistent, 8 were extended, and 2 did not have follow-up for the past 6 months to further classify. Four (4%) had rheumatoid factor positive polyarthritis and 11 (12%) had rheumatoid factor negative polyarthritis. Three (3%) patients had psoriatic arthritis. An additional 3 (3%) had enthesitis-related arthritis. Two (2%) had systemic arthritis. Twelve (13%) were undifferentiated. A single patient had their diagnosis outside of the institution and there was insufficient data to categorize. In each group, there were 57 (64%) females. The follow-up time in the pediatric setting (<18 years old) was similar for both groups, mean 6.3 (4.4) years in patients with JIA compared to 6.5 (4.3) in patients without JIA with few patients (12 JIA and 7 non-JIA) migrating from Olmsted County prior to age 18 years. There were no differences in race/ethnicity between both groups ($p = 0.30$) with the majority of patients reporting Caucasian [75 (84%) in patients with JIA and 77 (87%) without JIA]. In those with JIA, additional self-reported race/ethnicity included 4 (4%) black, 3 (3%) Asian, 2 (2%) Hispanic, 1 (1%) other, and 4 (4%) unknown.

Thirty-eight pairs (43%) had follow-up over the course of this study into adulthood (≥ 18 years old) (Table 2). Length of follow-up during adulthood was similar in patients with JIA mean (SD) of 8.0 (5.5) years and 8.9 (5.7) years for those without JIA. No deaths occurred over the course of follow-up.

Table 1
Demographics of a population-based cohort of patients with juvenile inflammatory arthritis (JIA) and non-JIA comparator subjects during childhood

	JIA ($N = 89$)	non-JIA ($N = 89$)	p Value
Age at index date in years, mean ($\pm$ SD)	8.6 ($\pm$ 5.1)	8.9 ($\pm$ 5.0)	0.56
Female sex	57 (64%)	57 (64%)	1.00
Length of follow-up to age 18 in years, mean ($\pm$ SD)	6.3 ($\pm$ 4.4)	6.5 ($\pm$ 4.3)	0.66
Race/ethnicity			0.30
Caucasian	75 (84%)	77 (87%)	
Hispanic	2 (2%)	2 (2%)	
Black	4 (4%)	0 (0%)	
Asian	3 (3%)	6 (7%)	
Other	1 (1%)	0 (0%)	
Unknown	4 (4%)	4 (4%)	

Values in table are n (%) unless otherwise specified.