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Growth patterns in early juvenile idiopathic arthritis: Results from the Childhood Arthritis Prospective Study (CAPS)

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ABSTRACT

Objectives: To investigate early vertical growth patterns and factors associated with poor growth in a modern inception cohort of UK children with juvenile idiopathic arthritis (JIA) using data from the Childhood Arthritis Prospective Study (CAPS).

Methods: A study period of 3 years was chosen. Children included in this analysis had a physician diagnosis of JIA and had height measurements available at both baseline and at 3-years of follow-up. Height is presented as *z*-scores calculated using World Health Organisation growth standards for age and gender. Growth over the 3-year period was assessed using change in *z*-score and height velocity. Univariable and multivariable linear regressions were used to identify factors associated with height *z*-score at baseline and change of height *z*-score at 3 years.

Results: 568 patients were included; 65% female, median baseline age 7.4 years [interquartile range (IQR) 3.6, 11.2], median symptom duration at presentation 5.5 months [IQR 3.1, 11.6]. Height *z*-score decreased significantly from baseline to 3 years ($p \leq 0.0001$); baseline median height *z*-score was −0.02 (IQR −0.71, 0.61), decreasing to −0.47 (IQR −1.12, 0.24) at 3 years. Growth restriction, defined as change of height *z*-score ≤−0.5, was observed in 39% of patients. At 3 years, higher baseline height *z*-score was the strongest predictor for a negative change in height *z*-score [−0.3 per unit of baseline height *z*-score (95% CI: −0.36, −0.24), $p < 0.0001$].

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Conclusions: Although overall height at 3 years after initial presentation to rheumatology is within the population norm, as a cohort, children with JIA experience a reduction of growth in height over the first 3 years of disease. Late presentation to paediatric rheumatology services is associated with lower height at presentation. However, patients with the lowest height *z* scores at presentation were also the most likely to see an improvement at 3 years. The impact of JIA on growth patterns is important to children and families and this study provides useful new data to support informed clinical care.

Key messages

- The study identified that growth restriction in JIA can occur early after disease onset.
- Growth restriction was observed in 39% of patients.
- Decrease in height *z*-score occurred across all JIA subtypes and was greatest in sJIA and PsJIA.

Introduction

Inflammatory arthritis is one of the most common chronic inflammatory illnesses in childhood. It has been estimated that approximately 1:10,000 children will develop an inflammatory arthritis each year [1] with the majority subsequently diagnosed with juvenile idiopathic arthritis (JIA).

Growth disturbance is an important complication of JIA, with significant implications for both physical and psychosocial health. Although initially reversible, long-standing growth impairment results in irreversible short stature and altered adult body composition. It is a significant concern for the families of young children with JIA and an additional challenge for older children and adolescents coping with the impact of chronic illness [2].

Understanding the prevalence of short stature in JIA has traditionally been challenging, with estimates ranging from 1% to 17% [3]. Previous studies have defined juvenile arthritis according to different classification criteria and have included different subtypes of disease [4–6], using retrospective or cross-sectional study designs with variable lengths of follow-up, even within the same study. This risks the introduction of selection bias towards those children with the most severe disease requiring long-term rheumatological follow-up.

In recent years, biologic therapies such as etanercept and tocilizumab have been associated with improvements in vertical growth [7]. As a consequence, studies predating the widespread use of methotrexate or biologics may no longer be relevant to current populations of children and young people with JIA. More recent studies suggest that growth impairment persists in around 10% patients [8], despite intensification of treatment regimens and the advent of biologic therapies [7,9–11].

The reasons for poor growth in JIA are multifactorial and may relate to the degree of systemic inflammation, corticosteroid use [12] or nutrition [13]; appetite may be impaired as a consequence of chronic inflammatory disease or as a side-effect of drugs with gastrointestinal toxicity such as methotrexate (MTX). Protein/energy malnutrition is thought to occur in children with JIA [14] and has been found to correlate with disease severity [15]. The extent of growth failure may vary with the ILAR subtype and is well described in children with polyarticular and systemic JIA [12,16,17]. In 2011, a review of 95 patients with oligoarticular JIA identified growth restriction in 36% patients [18]. Systemic corticosteroid use in JIA has been associated with a reduction in final adult height [12,19,20]. There is evidence that glucocorticoids interfere with the production or action of growth hormone and its mediators at different levels of the GH-insulin-like growth factor I axis [21].

The aim of this analysis was to investigate early growth patterns and factors associated with poor growth in a modern inception cohort of UK children and young people (CYP) with JIA over the first 3-years following diagnosis, using data from the Childhood Arthritis Prospective Study (CAPS).

Materials and methods

Study population

Children in this analysis were participants in CAPS, an ongoing inception cohort study launched in 2001 [22]. Children aged < 16 years presenting to one of 7 paediatric and adolescent rheumatology referral centres across UK with a new diagnosis of inflammatory arthritis lasting for at least 2 weeks in at least one joint, are eligible to participate. The study was approved by the UK Northwest Multicentre Research Ethics Committee.

Baseline data collection

Data are obtained through medical case note review, patient questionnaires and interview. Data collected include active and limited joint counts, 100-mm physician's global assessment (PGA) visual analogue scale (VAS), 100-mm pain VAS, and a 100-mm parent general evaluation (PGE) VAS, the child health assessment questionnaire (CHAQ). The physician assigns an International League Against Rheumatism (ILAR) subtype where appropriate. Additional demographic and health information data are provided by the families alongside completion of patient reported outcome questionnaires. Follow-up data are collected annually for the first 5 years following presentation and include all of the same information as collected at baseline. When children are discharged from paediatric rheumatology care, a study nurse will continue to collect follow-up data for a further 2 years.

Measurement of height

The height in centimetres and weight in kilograms of all children are measured routinely during hospital clinic appointments as per local hospital protocol and recorded in the hospital case notes. For the purpose of this study, height measurements from the first paediatric rheumatology visit constituted baseline. Study nurses were advised to record the measurements which most closely corresponded to the study follow-up intervals, along with the date of measurement. Body mass index (BMI) was calculated subsequently.

Analysis

A study period of 3 years was chosen to enable capture of definitive treatment data and early growth patterns. Children were included in this analysis if they had a diagnosis of JIA and had height measurements available at both baseline and at 3-years (± 3 months) of follow-up. Height and BMI are presented as *z*-scores, a standard score that indicates how many standard deviations an observation differs from the age and gender adjusted population median. Population data for the determination of *z*-scores were obtained from the World Health Organisation (WHO) website (http://www.who.int/childgrowth/en/) and the following calculation per child and height/BMI measurement was used: *[observed*