Prevalence and short-term outcome of juvenile idiopathic arthritis: a population-based study in Estonia

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ABSTRACT

Objectives. *To study the point prevalence of juvenile idiopathic arthritis (JIA) in children in Estonia on December 31, 2000. To examine the short-term clinical outcome of the disease.*

Method. *Identification of patients diagnosed with JIA between 1995-2000. Prospective follow-up of new cases diagnosed between 1998–2000 for two years. Retrospective analysis of the medical records of patients diagnosed between 1995-1997. The study was population-based.*

Result. *One hundred and ninety-seven (197) patients fulfilled the study criteria. On December 31, 2000, the point prevalence of JIA was 83.7 (95% CI: 72.4; 95.8) per 100 000 children aged 0-15 years, 90.7 (95% CI: 74.1; 108.9) for girls and 77.1 (95% CI: 62.2; 93.5) for boys. Prevalence was the highest among 11-15 year-old girls (132; 95% CI: 100.7; 167.4) and the lowest in 0-3 year-old girls (9.6; 95% CI: 1.2; 26.7). For 44 patients (22.3%), the disease was inactive after 2 years since the onset of the disease. For 76 patients (38.6%). the disease was active or stable after 2 years.*

Conclusions. *This is the first population-based study on the prevalence and outcome of JIA in Estonia in which the new ILAR criteria have been used. A longer follow-up of JIA patients is needed to have a better overview of the course of the disease. Good cooperation between family doctors and specialists is crucial for diagnosing JIA as early as possible.*

Introduction

Juvenile idiopathic arthritis (JIA), previously also known as juvenile rheumatoid arthritis (JRA) and juvenile chronic arthritis (JCA), begins before the 16th birthday and is defined as sterile inflammation in at least one joint that is persistent for at least six weeks, and in which there is no defined diagnosis (1). The term "juvenile idiopathic arthritis, or JIA" was introduced by the Task Force of Pediatric Standing Committee of the International League of Associations for Rheumatology (ILAR) in 1995 (1); this classification was revised in 1997 (2) and in 2001 (3). JIA is, by nature, a heterogeneous disease with a chronic course which can cause disability already in early childhood. JIA has seven clinical subtypes. The course of the disease and outcome vary between different subtypes (4-6).

The incidence rate and the prevalence rate of JIA vary in different geographic areas and can be influenced by environmental and/or genetic factors (7, 8). The prevalence of juvenile arthritis ranges according to several authors from 7 to 401 per 100 000 children aged 0-15 years (9). The reasons for the variation in these wide limits are most likely connected to different classification criteria used, different study designs (hospital and community-based studies), and varied patient selection.

The aim of this study was to investigate the prevalence of JIA in Estonia on Dec 31, 2000 using the ILAR criteria (the 1997 revision) and to examine short-term clinical outcome of the disease.

Materials and methods

The study area

Estonia is the northernmost of the three Baltic States, with a population of 1.3 million. Fourteen of the 15 counties of Estonia participated, and only the eastern part of Virumaa was not included, due to a lack of feedback from the doctors of the region.

The study population

According to the Statistical Office of Estonia (www.stat.ee) the mean population at risk (children aged 0-15 years) in the year 2000 was 235,395 (120,676 boys and 114,719 girls).

The study period

The study period covered the years 1995-2000. Active patient and data collection was started on Jan 1, 1998 and carried out between 1998-2000.

Study design

Before starting the collection of the series, in late 1997, a meeting to confirm the study design and inclusion/exclusion criteria was held, with the presence of the administrations of the two tertiary hospitals – Tallinn Children's Hospital and Children's Clinic of

Tartu University Hospital – and of all pediatricians participating in the study. A couple of meetings were held with local pediatricians in charge of the 14 counties (one in each) and family doctors via teaching seminars, where the inclusion criteria and classification of JIA were introduced (10). Altogether 50 separate family doctors and family medicine centres (with more than one family doctor) were practising at the beginning of the study; they were all contacted by mail. There are only few orthopaedic surgeons and physical therapists consulting children in Estonia and they work in these two centres which participated in the study.

In addition to the above-mentioned doctors, county hospitals, county outpatient clinics and medical and health care centres (altogether 47) were informed by mail about the beginning of the study, and the criteria for JIA were added to the letters.

The doctors were asked to send all the new patients with JIA (and those they suspected of having JIA) to the two children's hospitals. In addition, the doctors were asked to report on all patients meeting the JIA criteria and diagnosed since Jan 1, 1995 in their region.

The active collection of patients and data started on Jan 1, 1998 and consisted of two parts which were carried out in a parallel fashion. The first was a prospective population-based study, during the years 1998-2000, in which the mean annual incidence rate of JIA was determined (10); and the second was a retrospective analysis of the medical records of patients diagnosed between 1995-1997. The short-term clinical outcome was determined following the incidence group prospectively. The follow-up of the early JIA series was accomplished using the data from patients' records.

All the doctors were reminded about ongoing study twice by mail. The primary care system was, at the same time, rapidly developing and the number of family doctors practising in the counties increased significantly during the study period. At the end of the study, already 412 family doctors and family medicine centres were contacted. The received information was compared with the data of the two hospitals.

The patients

We included two populations of patients in the study: a) children under the age of 16 years (born on Dec. 31, 1984 and afterwards), living in the study area, fullfilling the ILAR criteria of JIA (the revised version of 1997) and having an onset of arthritis between 1995-1997, the early JIA series, and b) children with onset of arthritis during 1998-2000 and diagnosed during the incidence study (10), the incidence series. On Dec. 31, 2000, of the above-mentioned two groups of patients, we included in this study only those in whom JIA was: (1) active, *i.e.*, the number of active joints increasing irrespective of drug therapy; (2) stable, *i.e.*, a stable number of joints but requiring drug therapy, or; (3) inactive, *i.e.*, no evidence of active arthritis and/or active extraarticular features and without drug therapy for less than 2 years on the date given above. To estimate the disease activity we used the definitions suggested by the EULAR Standing Committee on Paediatric Rheumatology in Moscow, 1983, (11). Patients diagnosed during the study period but in remission – *i.e.*, those with no signs of active synovitis and/or active extraarticular features, blood inflammatory markers within normal limits and at least two years without drugs were excluded.

One of the authors (CP) visited the second centre – Tallinn Children's Hospital – regularly, and all cases in which there was doubt in the diagnosis or classification were discussed with the team (CP, KU, HL, ST). The final determination of the subgroups was determined by CP, taking into account all the inclusion and exclusion criteria of the ILAR classification, the revision of 1997.

Statistical analysis

The statistical analysis was performed using the statistical package SAS Version 8.02. Continuous variables are presented as mean values (95% CI), while qualitative variables are presented as absolute and relative frequencies. The prevalence rate for children under 16 years of age per 100,000 was calculated using the data given by the Estonian Statistical Office. Kolmogorov-Smirnov criterion was used for the assessment of normality. Comparisons between groups were performed using the nonparametric test – the Wilcoxon-Mann-Whitney test. Ninety-five percent confidence intervals (CI) for the prevalence rate were calculated based on the Poisson distribution.

The study was approved by the Ethics Committee of Tartu University. All the parents or the patients were asked to give informed consent for participation in the study.

Results

Prevalence

On Dec 31, 2000, there were, 197 children (93 boys and 104 girls) aged 0-15 years and living in the 14 counties of Estonia in whom JIA, diagnosed in 1995-2000, was active, stable or inactive. Thirty (30) patients were diagnosed between 1995-1997 and 167 patients between 1998-2000.

The point prevalence for children under 16 years of age was 83.7 (95% CI: 72.4; 95.8) per 100,000, for boys it was 77.1 (95% CI: 62.2; 93.5) and for girls 90.7 (95% CI: 74.1;108.9) (Table I). Prevalence was the highest among 11-

Table I. Prevalence rates according to sex and age groups (Dec 31, 2000).

Age groups (yr)	Number of cases	All cases (95% CI)	Girls (95% CI)	Boys (95% CI)
0 - 3	7	16.3 (6.6;30.4)	9.6 (1.2;26.7)	22.6 (7.3;46.2)
4 - 6	27	76.4 (50.4;107.8)	92.6 (52.9;143.2)	60.9 (30.4;101.9)
7 - 10	53	82.8 (62;106.5)	80.3 (52;114.7)	85.2 (56.6;119.5)
11 - 15	107	115 (94.2;137.7)	132 (100.7;167.4)	98.7 (72.6;128.9)
0 - 15	194*	83.7 (72.4;95.8)	90.7 (74.1;108.9)	77.1 (62.2;93.5)

*in 3 patients the exact birth date was not found in records.

Table II. Subtypes of JIA at onset, proportion of girls, proportional distribution of subtypes, mean age at the onset of the disease.

Subtype	Number of cases (girls)	Percentage of all cases	Mean age at the onset of the disease, years (95% CI)
Oligoarthritis	111 (56)	56.3	8.2 (7.4;8.9)
Persistent	88 (40)	44.7	7.9 (7.1;8.8)
Extended	23 (16)	11.7	9.1 (7.3;10.9)
Polyarthritis RF neg	39 (25)	19.5	9.7 (8.7;10.8)
Polyarthritis RF pos	9 (8)	4.5	10.2 (7.3;13.0)
Systemic arthritis	8 (2)	4	4.7 (2.0;7.3)
Enthesitis related arthritis	11 (2)	5.5	11.1 (10.0;12.2)
Psoriatic arthritis	5 (2)	2.5	9.7 (3.3;16.0)
Other arthritis	13 (8)	6.5	8.5 (6.2;10.8)
All JIA	196/197*	100	8.7 (8.2;9.3)

*In 1 patient with polyarthritis the exact classification was not possible, as the RF analysis was not performed.

Table III. Two-years outcome of JIA.

Onset subtype	No. of patients	Patients with inactive disease**	Active or stable cases at 2 yrs	Same pattern of joint involvement at 2 yrs	Changes in course during 2 yrs	Patients for whom there are no data at 2 yrs
Oligo	111	22	37	37	23 - extended oligo	52
Persistent oligo	88	17	25	25		46
Extended oligo	23	5	12	12		6
Seropos poly	9		8	5	3 - oligo	1
Seroneg poly	39	14	15	8	7 - oligo	10
Systemic	8	4	3	1	2 - oligo	1
Enthesitis related	11	1	5	5		5
Psoriatic	5	1	3	3		1
Other	13	2	5	4	1 - oligo	6
All JIA	196*	44	76	63	36	76

*In 1 patient with polyarthritis the exact classification was not possible, as the RF analysis was not performed.
**"Inactive" includes patients in whom the disease is inactive and who have been off drugs for less than 2 years as well some patients who are still on drug therapy.

15 year-old girls, 132 and the lowest in 0-3 year-old girls, 9.6.

Of the 412 final reminding letters sent, 165 (40%) were answered by primary care practitioners. Nineteen additional patients were seen only by family doctors; they were not referred to the centres and therefore were not included in the study.

The mean age at the onset of JIA symptoms was 8.7 years (95% CI: 8.2; 9.3) (Table II); 9.1 years (95% CI: 8.3; 9.8) for girls and 8.3 years (95% CI: 7.5; 9.1) for boys. It was the lowest in the systemic subtype – 4.7 years – and the highest in the enthesitis related arthritis subtype – 11.1 years. The mean interval between the onset of the disease and the time the diagnosis was made was 7 months; it was the longest in extended oligoarthritis and psoriatic arthritis, 1 year for both, and the shortest for systemic arthritis, 1 month. The mean duration of JIA in the group was 2.3 years (95% CI: 2.0; 2.6).

Oligoarthritis was the most frequent subtype (111 cases (56.3%) (Table II). Thirty-two (28.8%) of those had monoarthritis. Oligoarthritis was followed by seronegative polyarthritis – 39 cases (19.5%). Systemic subtype was more frequent in boys (6 cases compared to 2 cases in girls). Polyarthritis (both seronegative and seropositive) was more often found in girls (33 cases compared to 16 cases in boys).

Clinical outcome at two years

The course of the disease was followed up for two years after the diagnosis was made (Table III). Data are available of 120/197 patients. Fourty-four of the patients (22.3%) had inactive disease at this point. For 76 patients (38.6%) the disease was active or stable after 2 years. There are 49/197 patients (24.9%, 35 with oligoarthritis) for whom the follow-up extended only to 6 months since the diagnosis, but their subtype could be determined. For 76 patients (38.6%), among them 46 with persistent oligoarthritis and 10 with seronegative polyarthritis, there are no data at 2 years as they were no longer seen by doctors. In 63 patients (32%, 25 of them with persistent oligoarthritis), the disease subtype remained the same during the follow-up period. During the follow-up, 23 of the 111 patients with oligoarthritis (20.7%) changed subtype to extended oligoarthritis.

Use of drugs on the prevalence date

On December 31, 2000, when the prevalence was calculated, the state could be determined for 158 patients. The mean duration of follow-up was 1.7 years. There were 37 (18.8%) patients for whom there are documented data stating that the disease had become inactive. Eighty seven patients (44.2%) were taking disease modifying antirheum-atic drugs; among them there were 20 for whom the disease was active and 54 for whom the disease was stable. Fifteen patients (7.6%) were taking other drugs, mainly non-steroid antiinflammatory drugs. Among those 39 for whom there is no information, 24 (61.5%) had oligoarthritis; this group includes children in whom the disease was with great probability inactive on Dec 31, 2000 and who were already without drugs, but for less than 2 years.

Discussion

This is the first population-based study on the prevalence of juvenile idiopath-

ic arthritis in Estonia in which the new ILAR criteria have been used.

According to our earlier findings, the incidence rate of JIA per 100 000 children aged 0–15 years in 14 counties of Estonia was 21.7 between 1998-2000; 22.9 for girls and 19.3 for boys (10). The point prevalence on Dec. 31, 2000 for the children under 16 years of age diagnosed with JIA as of Jan. 1, 1995 in the same area was 83.7 per 100,000.

In the published studies the prevalence rate varies extremely – ranging from 7 to 401 per 100,000 (9, 11-21). In the study by Andresson Gäre and Fasth, the rate was 86.3 for all the cases and 64.1 for the cases with recent or active disease (11). Peterson *et al*. has included all the cases diagnosed with JRA and calculated the prevalence rates for 1980 and 1990, those being 94 and 86 per 100,000 respectively (8). In our study, we have not included patients for whom the disease was in remission by Dec. 31, 2000 and those diagnosed before 1995; due to that selection effect our figure can be somewhat lower than in other community-based studies. Apart from methodological differences, the variable incidence and prevalence rates may also reflect geographic differences, as *e.g*. the high rates in Finland and Northern Norway, found by Kunnamo and Moe and Rygg and confirmed later on by Berntson *et al*. (11, 22-24).

Since active data collection was started in 1998, there is a discrepancy between the numbers of patients in 1995-1997 compared to that of 1998-2000. The reason for this could be the fact that active data collection was started in 1998 in a prospective fashion. Also, patients from the 1995-1997 series over 16 years of age on the prevalence date were not included.

In Estonia it is common to see a native pediatric rheumatologist rather than to seek medical care in neighbouring countries; due to this fact we assume that practically all new JIA cases are captured by Estonian clinics. In addition to those primary care practitioners who answered the letters, there were many of them who did not answer but just referred the patients directly to the two hospitals. All the cases were discussed with the study team to ensure that they were real JIA cases and to avoid the risk of overestimation by local doctors. The follow-up was performed by specialists in pediatric rheumatology.

In our study, the prevalence rate was lowest in girls, aged 0-3 years. Oligoarthritis with mild activity is usually frequent in this age group. These cases may remain undiagnosed by family doctors with little experience in JIA. The same has been reported also by Kiessling *et al*. (14). Tendency of prevalence to rise with increasing age could be explained by the short duration of the (active) disease among small girls with oligoarthritis (Table II); the latter was also the main subgroup among these patients who did not see the doctor any more after the two years.

We could estimate the short term prognosis in two thirds of our patients. Two years after the onset the disease was still active or stable in 76 patients (63.3%). We assume that with great probability, the disease had become inactive for those 49 patients (24.9%) for whom we have no data after the first six months following the diagnosis. At present, we cannot say what proportion of the patients will actually reach remission. The follow-up of two years is much too short for this and for comparing our results with other studies on outcome. All we know is that 21 per cent of the oligoarthritis patients changed subgroup to extended oligoarthritis.

On the prevalence day, when the disease had lasted on average for 2.3 years, there were 102 patients (51.8%) taking nonsteroidal or longacting antirheumatic drugs, which means that in many of them the disease was still active or stable.

The prevalence rate in our study is well in accord with those of several other series although the different criteria make comparison difficult. At least 22% of the patients were inactive after two years. A longer follow-up of JIA patients studied using the ILAR 1997 criteria, is needed in order to have a better overview of the course of the disease, to know the proportion of patients reaching remission and the actual prognosis of the patients.

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