Incidence of Pediatric Rheumatic Diseases in a Regional Population in Austria

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ABSTRACT. ***Objective.*** To establish a population based disease registry for pediatric rheumatology in a defined population of Austria; to describe the demographic and diagnostic classification of children referred to pediatric rheumatology clinics; and to estimate the incidence of pediatric rheumatic diseases in Eastern Austria.

Methods. For 2 years (1997–98) all pediatric rheumatology centers in the area contributed data on all new cases to a prospective multicenter patient registry. Diagnostic criteria defined the rheumatic disease cases, determined by a pediatric rheumatologist, and record linkage was carried out to avoid duplication of subjects.

Results. Rheumatic conditions were diagnosed in 107 subjects. Juvenile rheumatoid arthritis (JRA) was the most frequently encountered rheumatic condition (49.5%), followed by spondyloarthropathy (SpA, 33.6%) and systemic lupus erythematosus (SLE, 5.6%). The mean annual incidence of JRA, SpA, and SLE among children referred to pediatric rheumatology centers was 4.28, 2.9, and 0.48 per 100,000 children at risk, respectively.

Conclusion. Establishment of a population based disease registry led to collection of descriptive epidemiologic data on a defined regional cohort of children with rare disorders. Our registry will provide data on pediatric rheumatic diseases in a European population and will allow more accurate comparisons between populations for future research. Our data also indicate that more resources should be designated for the care of pediatric rheumatic diseases in view of the relatively high incidences of these diseases. (J Rheumatol 2001;28:2116–9)

Key Indexing Terms:
INCIDENCE DISEASE REGISTRY CHILDHOOD RHEUMATIC DISEASES

Epidemiological studies of pediatric rheumatic diseases are an important tool allowing identification of patients for studies of etiology and prognosis. Several reports describe the incidence and spectrum of arthritis in children[1-8], but only a few give incidence data on other pediatric rheumatic conditions. Rosenberg[9] presented prevalence data for 875 patients referred to a pediatric rheumatology clinic in Saskatoon, Canada. Pelkonen, *et al*[10] report a nationwide prospective study from Finland, but their data were restricted to systemic onset juvenile rheumatoid arthritis (JRA) and connective tissue diseases. Demographic data from a regional cohort in Massachusetts presented by Denardo, *et al*[11] comprised all pediatric rheumatic diseases assessed by a prospective multicenter patient registry. Malleson, *et al*[12] reported the nationwide disease registry for the Canadian Pediatric Rheumatology Association from 13 centers all over Canada. Symmons, *et al*[6] presented data from the British Pediatric Rheumatology Group National Disease Registry summarizing the contributions of 23 centers. For 2 centers with well defined catchment areas, the incidence of juvenile arthritis was estimated. Incidence data for juvenile dermatomyositis in the UK were reported by Symmons, *et al*[13]. A study by Kaipiainen and Savolainen[8] provided incidence data on pediatric rheumatic diseases for Finland using the national sickness insurance scheme.

In this prospective study we investigated all children with rheumatic diseases that were referred to 3 pediatric rheumatology centers covering a defined catchment population in Austria. We collected descriptive epidemiological data to establish a population based disease registry that would serve future research and provide incidence data for our catchment population.

MATERIALS AND METHODS

Study period. The study was performed prospectively from January 1, 1997, to December 31, 1998.

Population. The study area included 3 provinces in Eastern Austria: Vienna, Lower Austria, and Burgenland, which are a contiguous part of northeast Austria including the capital, Vienna. The area is well separated from other parts of Austria in the west and south. The mean population of children at risk up to 16 years of age was 618,311. The studied population constituted 38.8% of the population at risk in Austria. Demographic statistics were obtained

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from the Austrian Bureau of the Census, Vienna[14]. The subjects include all outpatients evaluated by 3 pediatric rheumatology centers, which constitute all pediatric rheumatology services in the area.

For 2 years beginning January 1997 all primary care physicians, pediatricians, and orthopedic surgeons from the 3 adjacent areas were asked to refer all patients up to 16 years of age who were living in these areas and who fulfilled one or more of the diagnostic criteria for pediatric rheumatic disease. All the physicians received 2 letters providing information about the project. All referral hospitals for children (including adult rheumatology, dermatology, and orthopedics clinics) were regularly contacted by phone and through professional meetings throughout the study period. All eligible patients within the 3 areas who had been referred by doctors other than the ones informed were also included in the study.

Diagnostic criteria. Standardized diagnostic criteria were used to ensure reliability of reporting among centers.

Data collection. The medical reports of all possible or probable cases of rheumatic disease were reviewed by a trained pediatric rheumatologist in each center (CH, HS, and GA) and entered into a standardized patient form by one of the authors (TD), who also searched for duplicate entries for the same patients. An incidence case was defined as a child up to age 16 years, living in the study area, experiencing onset of symptoms during the study period, and meeting the inclusion criteria for any of the diagnoses. The following variables were recorded using a standardized data sheet: name (initials), sex, date of birth, place of residence at time of onset, date and age at onset of disease, date of diagnosis, specialty of referring physician, family history, clinical symptoms (systemic symptoms and musculoskeletal symptoms) as assessed by a pediatric rheumatologist.

RESULTS

During the 2 years of study, 231 patients were evaluated by the 3 participating centers. The numbers were 128 (55.4%), 56 (24.2%), and 47 (20.3%) patients, seen by the Department of Pediatrics (the only tertiary care center), the Gottfried von Preyersches Kinderspital, and the Donauspital, respectively. The distribution of rheumatic and nonrheumatic diseases was similar between the centers. Residence of the subjects reflected the population proportions of the 3 provinces: The majority (58.8%) resided in the province of Vienna (an area identical with the city of Vienna); 82 (35.5%) were from Lower Austria and 13 (5.6%) from Burgenland. All patients were Caucasian.

Rheumatic diseases. Rheumatic diseases were diagnosed in 107 children (46.3% of subjects; Table 1). JRA was the most frequently encountered (n = 53, 49.5%), followed by juvenile spondyloarthropathy (SpA) (n = 36, 33.6%), systemic lupus erythematosus (SLE) (n = 6, 5.6%), and vasculitides (n = 2, 1.9%). Mixed connective tissue disease (MCTD) was diagnosed in one patient. The majority of children with JRA had pauciarticular disease (n = 33, 62.2% of JRA), with a mean (SD) age of onset of 7.6 ± 4.8 years and an almost equal male to female ratio. Polyarticular rheumatoid factor (RF) negative disease was the next most frequent JRA subtype (n = 15, 28.3% of JRA): mean age of onset was 6.8 ± 3.7 years, and females outnumbered males 4:1. Systemic onset disease was diagnosed in 5 children (9.4% of JRA), with a mean age of onset of 7.2 ± 5.4 years and an almost equal male to female ratio. The majority of children with SpA had reactive arthritis (n = 25, 70% of SpA); the mean age of onset was 9.9 ± 4.5 years in this group and the male to female ratio was almost equal. Enthesopathy syndrome (SEA syndrome) was the next most frequent subtype (n = 7, 19% of SpA): mean age of onset was 12.9 ± 2.6 years, and males outnumbered females 6:1. Juvenile psoriatic arthritis was diagnosed in 4 children (11% of SpA); the mean age of onset for this group was 8.9 ± 2.9 years with an equal male to female ratio. Reiter's syndrome was diagnosed in one boy, at age 12.

Incidence of childhood rheumatic diseases presenting to pediatric rheumatology centers. The incidence of childhood rheumatic diseases presenting to pediatric rheumatology cen-

Table 1. Rheumatic diseases diagnosed in children referred to pediatric rheumatology centers (1997–98).

Diagnosis	N (%)	Male	Female	Age at Onset, yrs (SD)	Reference
JRA, total	53 (49.5)	20	33	7.38 (4.5)	Brewer[16]
Polyarticular, RF negative	15 (14.0)	3	12	6.82 (3.7)	
Pauciarticular	33 (30.8)	14	19	7.66 (4.8)	
Systemic	5 (4.6)	3	2	7.24 (5.4)	
SpA, total	36 (33.6)	21	15	10.34 (3.6)	
Enthesopathy syndrome	7 (6.5)	6	1	12.9 (2.6)	Rosenberg[18]
Reactive arthritis	25 (23.3)	13	12	9.97 (3.7)	Keat[17], Willkens[23]
Psoriatic arthritis	4 (3.7)	2	2	8.97 (2.9)	Southwood[20]
SLE	6 (5.6)	1	5	12.41 (1.4)	Tan[22]
MCTD	1 (0.9)	0	1	16	Sharp[19] and Bohan[15]
Vasculitis*	2 (1.9)	1	1	8.66 (4.2)	Kawasaki[24] and Allen[25]
Other rheumatic diseases**	9 (8.4)	4	5	9.35 (4.5)	Stollerman[21]
Total	107 (100)	51	61	9.82 (2.8)	

* Vasculitis (N): Kawasaki disease (1), Henoch-Schönlein purpura (1). ** Other rheumatic diseases (N): sarcoidosis (1), Sjögren's (1), acute rheumatic fever (3), Raynaud's phenomenon (2), livedo reticularis (1), familial Mediterranean fever (1). JRA: juvenile rheumatoid arthritis, SLE: systemic lupus erythematosus, MCTD: mixed connective tissue disease, SpA: spondyloarthropathy.

Table 2. Incidence rates (per 100,000/year) of pediatric rheumatic diseases in Eastern Austria 1997–98, compared with incidence rates of recent population based studies.

	Pelkonen, Finland 1994[10]	Denardo, USA 1994[11]	Malleson, Canada 1995[12]	Symmons, UK 1996[13]	Kaipiainen, Finland 1996[8]	Present Study 1997–98
Population at risk (millions)	1.02	0.134	4.2	0.153	0.270	0.618
Disease						
JRA, total		4.0	3.14	10	14.1	4.28
Systemic onset JRA	0.47		0.49		0.9	0.40
SpA		2.0	1.44*		0.1	2.9
SLE	0.37	0.4	0.36		0.9	0.48
MCTD	0.10		0.06			0.08

* Juvenile psoriatic arthritis not included.

ters in Eastern Austria was calculated for the 2 year period 1997–98 (Table 2). The mean number of children up to 16 years of age in this period was 618,311 (1997: 615,531, 1998: 621,091 children at risk). Rheumatic diseases were diagnosed in an average of 53.5 children each year, creating an overall mean annual incidence rate of 8.6/100,000 children at risk. The mean annual incidences (5%, 95% CI) of JRA, juvenile SpA, and SLE were 4.2 (3.71, 4.8), 2.9 (2.58, 3.33), and 0.4 (0.27, 0.65) per 100,000, respectively.

DISCUSSION

Population based epidemiological studies of pediatric rheumatic diseases are important for identifiying possible etiological factors. The geographic variation of disease pattern could give insight to enviromental factors, and ethnic differences could elucidate genetic susceptibility. Our study summarizes the results of a population based disease registry established for all pediatric rheumatic diseases in a defined central European population, allowing comparisons with data from registries in the US and Europe[6,11,12] (Table 2).

The overall annual incidence of pediatric rheumatic disease in this study was 8.6 cases/100,000 children at risk. Previous studies of the incidence of rheumatic diseases in childhood vary widely. Data are difficult to compare due to differences in diagnostic criteria and study designs. Incidence figures on JRA, the most frequently studied disease, range from 1.3 to 19.6 per 100,000[1-12]. The incidences published by Denardo, *et al*[11] from Massachusetts, USA (4.0 per 100,000) and Malleson, *et al*[12] from Saskatchewan, Canada (3.14 per 100,000) are close to ours (4.28 per 100,000), probably indicating similarities of genetic and environmental background among the populations. However, the low incidence of JRA in our study might also reflect referral bias. Due to the design of the study those patients with benign disease might not all have been referred: e.g., in the pauciarticular JRA group slightly different results for sex ratio and age at onset probably reflect nonreferral of patients. The proportion of systemic onset JRA was low in our study (4.6% of all rheumatic diseases, 9.4% of JRA), but was in agreement with reports from Finland and Sweden[1,10]. The small proportion of systemic onset JRA is also reflected by low incidence (0.4 per 100,000) in our study, which corresponds with the studies from Finland[10] and Canada[12].

There have been only a few studies on the incidence of juvenile SpA as a group (comprising juvenile psoriatic arthritis). The incidence figures for SpA presented by the Canadian registry are difficult to compare, as they vary widely among the provinces (from 0.46 to 2.72 per 100,000) and do not include juvenile psoriatic arthritis. However, when the incidence rates for individual provinces such as British Columbia (SpA 2.71 per 100,000 and juvenile psoriatic arthritis 0.35 per 100,000) are taken into account, the data are very similar to the incidence figures in our study (2.9 per 100,000) and the study from Massachusetts[11].

Rheumatic diseases that are almost always treated during inpatient care, such as Kawasaki disease or other systemic vasculitides, are undoubtedly underreported in our study. Incidence figures for connective tissue diseases, on the other hand, are likely to be accurate, as those diseases are almost always referred to pediatric rheumatology clinics for followup. The incidence figures in our study for SLE (0.48 per 100,000) and MCTD (0.08 per 100,000) correspond with previous reports (Table 2). The incidence figures presented by Kaipianen and Savolainen[8] and Bowyer, *et al*[7] showed incidence rates for JRA (total) that were much higher (14.1 per 100,000 and 10 per 100,000) than our results: the design of the Finish study — retrieving patients using the nationwide sickness insurance scheme — probably reflects considerable selection bias. Differences in incidence rates between the UK registry[7] and our study indicate variation in types of rheumatic illnesses in different ethnic populations.

Our study is in accord with reports[11,12] that noted high rates of children with nonrheumatic conditions referred to pediatric rheumatology centers. The majority of children do not have rheumatic disease, but other conditions that need to be identified. The implications of these findings have been stressed by Malleson, *et al*, who emphasized the necessity for pediatric rheumatologists to be well trained diagnosticians[12].

As pointed out by Andersson Gäre in a recent editorial in the *Journal of Rheumatology*[26], registries not related to a pop-

ulation base are frequently complicated by bias in selection of cases, differences in methods of data collection, and the absence of uniform criteria for identification of homogenous disease entities. The registry we report here fulfills most of the criteria necessary for providing useful descriptive epidemiological data: the catchment population was defined using census data, explicit diagnostic criteria were used for rheumatic diseases, and disease categories were harmonized in order to be comparable with other studies. The lack of case ascertainment in our study certainly reduces the representation of patients with diseases usually requiring inpatient care, e.g., the systemic vasculitides. Nevertheless, our registry seems to be accurate for chronic arthritides, juvenile spondyloarthropathies, and connective tissue diseases such as SLE and MCTD, as in our experience those diseases are extremely rarely treated by other centers in the area. Our registry will therefore provide a valuable tool for future research in the assessment of therapeutic inverventions, selection of representative patient cohorts, and evaluation of outcome measures.

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