

EXTENDED REPORTS

Incidence of rheumatoid arthritis in Finland during 1980-1990

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Abstract

Objective—To obtain information on the incidence of rheumatoid arthritis and on its recent trends in Finland.

Methods—The study covered those subjects entitled to receive specially reimbursed medication for rheumatoid arthritis under the nationwide sickness insurance scheme in five out of 21 central hospital districts in Finland (population basis about one million adults) during three years: 1980, 1985, and 1990.

Results—The annual incidence of rheumatoid arthritis in 1980 and 1985, satisfying the American Rheumatism Association 1987 classification criteria, was 39/100 000 of the population \geq 16 years of age. The combined incidence of rheumatoid factor (RF) positive arthritis and RF negative polyarthritis was 46/100 000. A decline of approximately 40% occurred in the number of RF negative rheumatoid arthritis cases in 1990 compared with the earlier years. The declining trend was statistically significant ($P = 0.008$).

Conclusion—The decline in incidence of RF negative rheumatoid arthritis in Finland may reflect changes in the environment specifically affecting the risk of RF negative disease.

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The cause of rheumatoid arthritis is unknown. No place or ethnic group appears to be free of this disease, at least when population studies have been large enough to provide reliable estimates of its occurrence.¹ The prevalence of rheumatoid arthritis is about 0.5-1.0% of the adult population in most western countries. Figures as high as 3-6% have been reported among some North American Indian tribes. On the other hand, rheumatoid arthritis may be rare in rural populations in tropical areas.

For many purposes, incidence is a more useful measure of disease occurrence than prevalence. Problems occur, however, in conducting incidence studies of rheumatoid arthritis. In Caucasian populations the annual incidence of definite rheumatoid arthritis appears to lie at between 25 and 50 per 100 000 of the adult population,²⁻⁶ yet appreci-

ably lower figures have been reported from France.⁷ Only two of the above studies²⁻⁶ were truly population based. A much higher incidence of rheumatoid arthritis than in Caucasian populations has been noted in Pima Indians.⁸

Figures reflecting the incidence of chronic inflammatory rheumatic diseases are available in Finland from the nationwide register of the sickness insurance scheme. We report recent trends in the incidence of rheumatoid arthritis in Finland, using these data as a basis.

Methods

Since 1966, the Sickness Insurance Act has provided for the prescription of drugs free of charge for certain chronic diseases, including chronic inflammatory rheumatic diseases (since an amendment made in 1987, 90% of the costs have been reimbursed). During the study years glucocorticoids, non-steroidal anti-inflammatory drugs, and disease modifying antirheumatic drugs were reimbursed. The entitlement is usually for life, but can be for a fixed period. The national sickness insurance scheme covers the entire population of Finland. Eligibility requires a comprehensive medical certificate written by the attending physician and approved by an expert adviser on behalf of the sickness insurance scheme. All inflammatory rheumatic diseases are grouped under one code in the population register of the Social Insurance Institution. The main diagnostic subsets are rheumatoid arthritis, juvenile chronic arthritis, ankylosing spondylitis, chronic reactive arthritis, and psoriatic arthritis. Systemic rheumatic diseases are grouped under another code.

Finland is divided into 21 central hospital districts. The study embraced subjects entitled to specially reimbursed medication in 1980, 1985, and 1990 in five districts (Jyväskylä, Kotka, Kuopio, Lahti, and Tampere). The study area covered about one million adult inhabitants, that is, one quarter of the adult population in Finland.

Information on the patients was obtained from the drug reimbursement certificates, which proved to be sufficient in two thirds of the cases. Furthermore, sickness insurance offices maintain patient records for only three years after death. In most instances, however,

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Table 1 Incident cases of rheumatoid factor (RF)-positive and RF-negative rheumatoid arthritis (RA) in Finland during 1980, 1985, and 1990 (number of cases)

	1980		1985		1990		P value†
	Men	Women	Men	Women	Men	Women	
RF-positive RA*	108	194	103	199	97	192	0.483
RF-negative RA*	21	71	30	81	7	53	0.008
RF-positive arthritis	121	220	115	220	105	211	0.146
RF-negative polyarthritis	24	95	35	103	11	75	0.013
RF-negative oligoarthritis	4	18	12	26	10	30	0.040

* According to American Rheumatism Association 1987 classification criteria.

† Mantel-Haenszel test for linear trend (men and women combined in statistical analysis).

missing information could be obtained from hospital records. Altogether, hospital records were checked in one third of the cases. In 56 instances (2.4%) the information remained insufficient (see below). During the first years of sickness insurance, certificates were written for patients under treatment; however, a proportion of the patients gained entitlement many years afterwards. For present purposes, a case was regarded as an incident case if the onset of disease was after 1966 and no earlier entitlement to specially reimbursed medication had occurred for a fixed period.

Overall 2350 subjects were entitled to specially reimbursed medication for chronic inflammatory rheumatic diseases during the three study years. In 56 instances (40 from 1980, 13 from 1985, and three from 1990) the available information regarding the diagnosis remained insufficient. In 1579 cases the diagnosis in the reimbursement certificate was rheumatoid arthritis and in 52 cases a related disease such as chronic polyarthritis. Of the 1579 cases, 144 were not classified as incident cases, either because the disease had started before 1966 or there had earlier been entitlement for a fixed period. The date of entitlement represents a well defined moment usually in the early course of the disease. Yet in 30% of rheumatoid arthritis cases (33% in 1980, 31% in 1985, and 24% in 1990) the period from onset of symptoms to the entitlement was more than two years.

Two methods were used for the classification of patients diagnosed as rheumatoid arthritis in the reimbursement certificate: first, a patient was considered to have rheumatoid arthritis if he or she met at least four of the American Rheumatism Association (ARA) 1987

classification criteria,⁹ and second, the classification by Kaarela and Sarna¹⁰ was used, in which patients are divided into three groups: rheumatoid factor (RF) positive arthritis, RF negative polyarthritis, and RF negative oligoarthritis. Arthritis was considered to be polyarthritis if \geq three joint areas were involved.

Information on the age distribution of the central hospital districts included in the study was obtained from the Finn Region database maintained by Statistics Finland at VTKK Group Ltd (formerly, the State computer centre) through the courtesy of Raimo Tuomainen, M Adm Sc.

STATISTICAL ANALYSIS

Statistical analysis was made using the SPSS/PC+ program (SPSS Inc, Chicago, Illinois, USA). The significance of the relation between the incident cases and the time period was tested by Mantel-Haenszel test for linear trend.¹¹ Incidence rates were age adjusted by the direct method¹¹ using the 1990 Finnish population as a reference.

Results

Overall, 1487 incident cases were considered to have rheumatoid arthritis or a related disease on the reimbursement certificate. Of these, 1156 satisfied the ARA 1987 classification criteria for rheumatoid arthritis. A total of 992 subjects had RF positive arthritis, 343 had RF negative polyarthritis, and 100 had RF negative oligoarthritis. The remaining 52 subjects, according to the available information, had an equivocal disease, for example, RF positive polyarthralgia or painful arthrosis with morning stiffness.

The findings reflecting the incidence of rheumatoid arthritis in 1980, 1985, and 1990 are given in detail in tables 1 and 2. The following points emerge. Rheumatoid arthritis occurred about twice as often in females as in males. From the clinical point of view, RF positive arthritis and RF negative polyarthritis may satisfy the concept of rheumatoid arthritis. The incidence of rheumatoid arthritis as defined by this means was about 15% higher than that defined by satisfying the ARA classification criteria. The annual incidence of rheumatoid arthritis in 1980 and 1985 satisfying the ARA 1987 classification criteria was 39/100 000 of the adult population \geq 16 years of age.

A small decline occurred in the number of rheumatoid arthritis cases in 1990 compared with the earlier years; however, when RF negative cases were considered separately the decline was significant (RF negative rheumatoid arthritis, $P = 0.008$; RF negative polyarthritis, $P = 0.013$). The decline was more marked in males than in females. All the five study areas behaved in a similar fashion.

Discussion

The annual incidence of arthritis diagnosed in the reimbursement certificates as rheumatoid arthritis was 46/100 000 of the adult population, corresponding to 1820 cases per

Table 2 Number of incident cases and annual incidence rates (per 100 000) of RF-positive and RF-negative rheumatoid arthritis (RA) defined by the 1987 ARA classification criteria and the same figures for RF-positive arthritis and RF-negative polyarthritis in Finland in 1980, 1985, and 1990

Year	1980	1985	1990
RF-positive RA	302	302	289
Incidence (95% CI)*	29.4 (26.1-32.5)	28.6 (25.5-31.7)	27.1 (24.0-30.2)
Adjusted† (95% CI)	30.9 (27.4-34.4)	28.7 (25.5-32.0)	26.5 (23.4-29.5)
RF-negative RA	92	111	60
Incidence (95% CI)	9.0 (7.2-10.8)	10.5 (8.5-12.5)	5.6 (4.2-7.0)
Adjusted† (95% CI)	9.3 (7.4-11.2)	10.4 (8.5-12.4)	5.5 (4.1-6.9)
RF-positive arthritis	341	335	316
Incidence (95% CI)	33.2 (29.7-36.7)	31.7 (28.4-35.0)	29.6 (26.3-32.9)
Adjusted† (95% CI)	34.9 (31.2-38.7)	31.9 (28.5-35.4)	28.9 (25.7-32.1)
RF-negative polyarthritis	119	138	86
Incidence (95% CI)	11.6 (9.4-13.8)	13.1 (10.9-15.3)	8.1 (6.3-9.9)
Adjusted† (95% CI)	12.1 (9.9-14.3)	13.0 (10.8-15.2)	7.9 (6.2-9.5)

* CI, confidence interval.

† Age adjusted to Finnish adult population in 1990.

year. In another study from Finland, a total of 1666 subjects entitled to specially reimbursed medication for rheumatoid arthritis died in 1989.¹² The number of new cases was thus about the same as the number of rheumatoid arthritis cases among those who had died (42/100 000).

A small error occurred in the incidence rates since relevant information was lacking in about 2% of the cases known to have entitlement because of chronic inflammatory rheumatic diseases; most of these cases were from the year 1980. The period from the onset of symptoms to the entitlement was slightly shorter in 1990 than in the earlier study years. Without this reduction in the onset to registration time the incidence rates for the year 1990 would have been slightly lower than those observed.

A proportion of patients diagnosed as having rheumatoid arthritis on the reimbursement certificate do not have this disease according to commonly accepted criteria. The incidence of rheumatoid arthritis in 1980 and 1985 satisfying the ARA 1987 classification criteria was 39/100 000 of the adult population. This figure, however, underestimates the true incidence to some degree, in that not all patients with rheumatoid arthritis are entitled to specially reimbursed medication. In recent years, the great majority of patients have ultimately gained this eligibility¹³ but a considerable delay can occur, particularly in patients with insidious onset. The ARA 1987 classification criteria were also defined on the basis of cases with long lasting disease, and the criteria do not allow for inclusion of a proportion of cases with recent onset.¹⁴ Patient records were also not keyed to the ARA criteria; in particular, information concerning morning stiffness was frequently lacking. On the other hand, RF status was known in all cases.

In addition to use of the ARA 1987 criteria, we divided the cases considered to have rheumatoid arthritis into three groups: those with RF positive arthritis, RF negative polyarthritis, and RF negative oligoarthritis. In an earlier community based follow up study of recent onset arthritis from Finland, the great majority of RF positive arthritis patients developed erosive disease, whereas virtually all patients with RF negative oligoarthritis attained remission.¹⁰ The outcome of RF negative polyarthritis was bimodal: a majority of patients had a favourable outcome and a minority did not do well. The combined incidence of RF positive arthritis and RF negative polyarthritis was 46/100 000 of the adult population in 1980 and 1985, that is, about 15% higher than the incidence of cases satisfying the ARA 1987 classification criteria.

In an earlier study from Finland in which the patient series was collected during 1974–1975, the incidence of definite rheumatoid arthritis according to the ARA 1958 criteria was found to be 42/100 000 of the adult population,² a figure which is in agreement with the present observations. Recent figures reported from the United States^{4,5} and from England⁶ have been of the same order of magnitude or slightly lower than ours.

A decline occurred in the incidence of rheumatoid arthritis during 1985–1990 which predominantly reflected the presence of RF negative disease, particularly in males. Patients with clinical features of rheumatoid arthritis but who have negative RF tests present a problem.¹⁵ The question arises as to what remains after the long list of diagnostic alternatives. Does any core exist that may represent genuine rheumatoid joint disease without the presence of RF? A collaborative Finnish-Russian study of patients from Heinola (Finland) and Moscow provided evidence that RF negative rheumatoid arthritis, as seen in the above two centres, differed in clinical and immunogenetic characteristics.¹⁶

One possibility for the declining trend in RF negative rheumatoid arthritis is a change in test techniques. RF testing is performed in Finland in many different laboratories. In 1980 and 1985 the tests used almost exclusively were the latex test and the sensitised sheep cell agglutination test. In 1990 the immunoturbidimetric method was used in one third of the cases. It can be argued that by using more sensitive test techniques a proportion of seemingly RF negative cases will actually be RF positive. Immunoturbidimetry probably offers better reproducibility than other tests used in Finland, but according to our experience it is not more sensitive. Another possibility is a change in the classification of RF negative polyarthritis. Indeed, there was some increase in the incidence of psoriatic arthritis (unpublished). However, only a few patients with psoriatic arthritis satisfied the ARA 1987 classification criteria.

Thus the declining trend in RF negative rheumatoid arthritis probably is a true phenomenon. One underlying mechanism might be related to selenium. For geochemical reasons Finland is a low selenium area. The serum levels were especially low in years when the intake depended solely on domestic grain.¹⁷ In 1984 it was decided to add selenium to multimineral fertilisers to increase the selenium intake of the population. As a result the mean serum selenium levels of healthy adults increased markedly.¹⁸ We have earlier presented preliminary evidence that low serum selenium levels may predict the development of rheumatoid arthritis.¹⁹ In a subsequent larger series this finding was confirmed but the association was confined to RF negative disease (to be published).

Because a declining trend was noted only for RF negative rheumatoid arthritis, the present data offer additional support for the view that classification of the rheumatoid arthritis type of polyarthritis into RF positive and RF negative cases is biologically meaningful.^{20,21}

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