CONCISE REPORT

Regional differences in Finland in the prevalence of rheumatoid factor in the presence and absence of arthritis

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Objectives: To look for possible regional differences in the prevalence of rheumatoid factor (RF) in the presence and absence of arthritis.

Methods: The study covered a representative sample of the Finnish population aged 30 years or over, primarily comprising 8000 people, of whom 7217 participated in the field survey carried out in 1978–80. RF from serum samples from 7116 subjects was determined by the Waaler-Rose (sensitised sheep cell agglutination) test. Titres ≥ 32 were regarded as positive and titres ≥ 128 as strongly positive. Arthritis was diagnosed by a thorough clinical examination.

Results: In the absence of arthritis the prevalence of positive and strongly positive RF reactions was 2.1% and 1.0%, respectively. The lowest prevalence of strongly “false positive” RF occurred in south western Finland. After adjustment for age, sex, smoking, and coffee consumption the odds ratio of having a strongly “false positive” RF reaction in eastern Finland was 3.16 (95% confidence interval 1.29 to 7.72) and in northern Finland 2.94 (1.13 to 7.64) compared with south western Finland. The corresponding odds ratio of strongly RF positive arthritis in eastern Finland was 5.08 (1.41 to 18.27).

Conclusion: Regional differences are found in the prevalence of a strongly positive RF reaction in the Finnish population. The findings are in accordance with recent results from another study concerning regional differences in the incidence of rheumatoid arthritis in Finland.

Figure 1 Geographical areas of the Mini-Finland Health Survey and order of examinations. Prevalence rates (with 95% confidence intervals) of strongly “false positive” rheumatoid factor reactions (titres ≥ 128) in each social insurance region are given in the boxes. Numbers show the order in which the 40 study areas were examined.

Rheumatoid factors (RFs) are antibodies specific enough to be used as diagnostic and prognostic markers of rheumatoid arthritis (RA). They often appear many years before the onset of clinical RA.¹ Thus, factors associated with “false positive” RF reactions might be risk factors for RA. Smoking is associated with RF production in healthy subjects^{2,3} and also is a risk factor for RA, especially in men.⁴ A recent study from Finland suggested that daily coffee consumption was associated with an increased prevalence of “false positive” RF reactions and seemed to be a risk factor for RF positive RA.⁵ In England the prevalence of a “false positive” RF reaction was higher in polluted areas than less polluted areas.⁶ The prevalence of positive RF has been reported to be high in Pima Indians,⁷ related to the high incidence of RA among the Pima⁸ and declining in line with the temporal trends in RA.⁹

The prevalence of RA is 0.5–1% among adults in Europe, but it seems to be much lower in some Asian and African populations.⁴ In Finland the prevalence of RF positive RA in adults was reported to be 0.7%.¹⁰ The annual incidence has varied from 32 to 42 per 100 000 in different studies during

the past two decades,^{11,12} and was highest in eastern and lowest in western Finland.¹³

We now report on regional differences in the prevalence of “false positive” RF and RF positive arthritis in Finland.

MATERIAL AND METHODS

The Mini-Finland Health Survey was a comprehensive epidemiological project to evaluate the health of the Finnish adult population. In 1978–80 a representative population sample of 8000 Finns aged 30 years or over was invited to participate in a comprehensive health examination. There are five social insurance regions in Finland, and the sample of each region was also representative of that region (fig 1). The order in which the 40 study areas were examined was planned to

Abbreviations: RA, rheumatoid arthritis; RF, rheumatoid factor

Table 1 Adjusted* odds ratios and 95% confidence intervals (CIs) of "false positive" rheumatoid factor reactions in titres ≥ 32 and ≥ 128

Factor	No of subjects examined	Sensitised sheep cell agglutination test					
		Waller-Rose ≥ 32			Waller-Rose ≥ 128		
		No of cases	Odds ratio	95% CI	No of cases	Odds ratio	95% CI
Region							
Southwest	1650	29	1.00		7	1.00	
South	2320	59	1.49	0.95 to 2.35	25	2.55	1.09 to 5.94
West	1051	22	1.17	0.67 to 2.05	10	2.25	0.85 to 5.94
East	1156	24	1.17	0.68 to 2.02	16	3.22	1.32 to 7.88
North	770	14	0.99	0.52 to 1.90	11	3.00	1.15 to 7.80
Age							
30–44	2641	44	1.00		18	1.00	
45–54	1562	32	1.26	0.79 to 1.99	20	1.96	1.03 to 3.73
55–64	1285	25	1.23	0.75 to 2.02	12	1.60	0.76 to 3.36
65–75	1018	33	2.24	1.40 to 3.57	12	2.36	1.11 to 5.01
≥ 75	441	14	2.39	1.28 to 4.49	7	4.04	1.61 to 10.15
Sex							
Men	3216	72	1.00		37	1.00	
Women	3731	76	1.11	0.76 to 1.63	32	1.31	0.75 to 2.27
Smoking							
Never smoked	3852	67	1.00		21	1.00	
Quit	1444	37	1.61	1.02 to 2.56	18	2.67	1.31 to 5.47
Cigars, pipe or <20 cigarettes/day	1027	32	2.00	1.25 to 3.19	20	4.12	2.08 to 8.17
≥ 20 cigarettes/day	624	12	1.25	0.63 to 2.48	10	3.46	1.43 to 8.35
Coffee							
Per cup per day	6947	148	1.05	0.99 to 1.12	69	1.09	1.00 to 1.19

*All variables in the table were included in the logistic regression model.

minimise effects of seasonal variation on comparisons between the social insurance regions. Altogether 7217 (90%) subjects complied. The examinations were carried out by the mobile clinic of the Social Insurance Institution in two phases: a screening phase and a diagnostic (clinical) phase.

With the invitation to attend the health examination, the subjects received a questionnaire to elicit information on previous diseases, admissions to hospital, operations, and drugs used. A specific interview covering the musculoskeletal system included questions on pain and disorders, and their effects. To screen for musculoskeletal impairment, a standardised joint function test was performed by specially trained nurses. Subjects with a history of disease or symptoms or findings suggestive of musculoskeletal diseases were asked to participate in the diagnostic (clinical) phase, on average three and a half months after the screening examination. Clinical examinations were carried out by specially trained doctors according to a standardised written protocol, which included an evaluation of musculoskeletal symptoms and previous medical examinations, and an investigation of all health records and radiographs that the subjects had been asked to bring. Arthritis was diagnosed on the basis of the medical history, symptoms, physical examination, hand radiographs, and RF testing. The methods and diagnostic criteria used for studying arthritides have been described in detail elsewhere.¹⁰

The sensitised sheep cell agglutination test was performed for 7116 people on microtitre plates as described elsewhere.^{2–6,10} Titres ≥ 32 were regarded as positive and titres ≥ 128 as strongly positive. Owing to the order in which the 40 study areas were examined (fig 1), the accuracy of RF determination hardly varied between the social insurance regions.

The prevalences of RF positive RA and "false positive" RF reactions (excluding subjects with clinical arthritis) were computed for five social insurance regions: south western, southern, western, eastern, and northern Finland. The logistic regression model was used to estimate the strength of associations between the region and the prevalences of RF

reactions and RA. Sex, age, smoking, and coffee consumption were also entered into the models. These factors are determinants of RF^{2–4,6} that might vary according to region and therefore confound the analysis.

RESULTS

The prevalences of "false positive" and strongly "false positive" RF reactions were 2.1% and 1.0%, respectively. No significant difference in the prevalence of "false positive" RF reactions was noted between the regions when using the titre of 32 as the cut off point, whereas differences between south western Finland and other areas emerged when using the high titre of 128 for this purpose (fig 1). After adjustment for age, sex, smoking, and coffee consumption, the odds ratio of having a strongly "false positive" RF reaction in eastern Finland was 3.16 (95% confidence interval 1.29 to 7.72) and in northern Finland 2.94 (1.13 to 7.64) compared with south western Finland (table 1). No significant differences were found between urban and rural areas (data not shown).

Of the 40 RF positive cases with arthritis in the 7116 people for whom the Waller-Rose titre was determined, 29 were strongly RF positive, a prevalence of 0.4%. After adjustment for age, sex, smoking, and coffee consumption, the odds ratios of strongly RF positive arthritis cases in southern, western, eastern, and northern Finland were 2.06 (95% confidence interval, 0.55 to 7.67), 1.55 (0.31 to 7.70), 5.08 (1.41 to 18.27), and 2.24 (0.45 to 11.19), respectively, compared with south western Finland. No significant difference was found using the titre of 32 as the cut off point for RF positive arthritis.

DISCUSSION

This study showed significant regional differences in the prevalence of strongly "false positive" RF reaction in Finland for the years 1978–80. The findings paralleled those on the prevalence of strongly RF positive arthritis, representing half of the patients with chronic polyarthritis who had either an RF titre ≥ 32 or changes characteristic of RA in their hand radiographs.¹⁰ In this regard it is of interest to note that we previously found regional differences in the incidence of RA in

Finland in 1995, which could not be explained by genetic factors.¹³ The highest incidence was in eastern Finland near the Russian border and the lowest was in western Finland on the coast of the Gulf of Bothnia. Northern and south western Finland were not included in that study. A correlation between the prevalence of "false positive" RF reactions and RF positive RA is biologically plausible, because RF frequently precedes clinical RA.¹ In one study series the incidence of RA was even predicted by the RF (sensitised sheep cell agglutination) titre in a "dose dependent" fashion.¹⁴

The importance of RF titre has also been suggested in studies focused on determinants of "false positive" RF reactions. The higher the RF titre, the more closely it is associated with smoking history² and coffee consumption.⁶ In line with those findings, geography showed a significant association with high titre but not low titre RF.

Cells which can produce RF exist in most normal people. Several different stimuli have been shown to support, or suggested as supporting, RF production.¹ If appropriately stimulated under in vitro conditions, similar amounts of RF are synthesised by the B cells of normal subjects and patients with RA. Thus, the basic failure in RA may be an inability to down regulate autoantibody production or inappropriate "help" from T lymphocytes.

Our observation on the correlation between the prevalences of "false positive" RF reactions and RF positive arthritis needs confirmation from other temperate areas. On the other hand, the prevalence of RA in many tropical areas is probably low, whereas the prevalence of "false positive" RF reactions may be fairly high, possibly related to chronic infections. Thus, our observation would not be valid globally. Whether it is consistent over time remains to be seen in the Health 2000 survey.¹⁵

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