EXTENDED REPORTS

Prevalence of articular chondrocalcinosis in elderly subjects in a rural area of Catalonia

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Abstract

Objectives—To undertake an epidemiological survey of the prevalence of radiological chondrocalcinosis in the elderly population of Osona, a rural area of Catalonia, north east Spain.

Methods—Knee and wrist radiographs were performed on 261 subjects (141 women, 120 men) aged at least 60 years, who attended a series of 35 general practitioners for various medical problems.

Results-Twenty seven had subjects articular chondrocalcinosis, which represents a crude prevalence of 10%. Articular chondrocalcinosis was more often observed in women than in men (14 v 6%). Articular chondrocalcinosis increases in occurrence with age, rising from 7% in subjects aged 60-69 years to 43% in subjects older than 80 years. A similar occurrence of articular chondrocalcinosis was noted in the indigenous population, in which several cases of familial chondrocalcinosis have previously been reported, and in subjects born in other areas of Spain. All but one subject with articular chondrocalcinosis had chondrocalcinosis of the knee. The occurrence of rheumatic disorders did not differ significantly between subjects with articular chondrocalcinosis and those without.

Conclusions—Articular chondrocalcinosis is an age related disorder, which could partly explain the discrepancies in its prevalence reported in previous studies. In most subjects with articular chondrocalcinosis recruited from an unselected population the clinical manifestations are probably mild or even absent.

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Since its initial description by Zitnan and Sitaj in 1958,¹ articular chondrocalcinosis has been considered a common disorder. It is well known that articular chondrocalcinosis is an age related disorder and occurs most often in elderly subjects. Data on the prevalence of articular chondrocalcinosis among the elderly is controversial, however, and ranges from 6 to 34%,²⁻¹⁷ depending on the characteristics of the population studied and the methods, anatomical²⁻⁴ or radiological,⁵⁻¹⁷ used to evaluate the presence of calcium pyrophosphate dihydrate deposits. Few extensive studies on the prevalence of articular chondrocalcinosis have been carried out and most of these are based on patients in hospital or rheumatic patients not representative of the general population. In the only two previous studies performed in the general population prevalence rates of $15\%^{16}$ and $8.1\%^{17}$ were reported. Some controversy therefore arises about the prevalence of articular chondrocalcinosis, its distribution between the sexes, and about the relation between articular chondrocalcinosis and rheumatic disorders.

Osona is a rural area of Catalonia, north east Spain. The total population of this area in 1988 was 111 931, of whom 20 791 (8896 men, 11 895 women) were aged at least 60 years. Most of these subjects were from other Spanish regions.

A rheumatology unit attached to a general hospital was first established in 1987 and since then several cases of familial chondrocalcinosis in the indigenous population have been reported.¹⁸ ¹⁹ In 1989 we undertook a survey of the prevalence of articular chondrocalcinosis in 261 subjects aged more than 60 years and analysed the relation between articular chondrocalcinosis and age, sex, geographical origin, and rheumatic disorders. To our knowledge this is the most extensive European epidemiological survey on the prevalence of articular chondrocalcinosis in an unselected elderly population.

Subjects and methods

In May-July 1989, 37 primary care doctors from 15 different rural areas of Osona were invited to participate in the study. It was decided that 10 subjects, each attending a different public primary care centre, would be recruited randomly by their doctor over a period of one week. On each day the first two subjects seen aged at least 60 years, irrespective of their sex and reasons for referral, were recruited for inclusion in the study. Some of these subjects attended their primary care doctor for a general check up as part of a programme to prevent disease in the elderly. For others the reason for referral was a medical disorder, mainly respiratory disease or hypertension. Verbal and written information was given to each subject before their inclusion in the study. After consent, a questionnaire including age, sex, place of birth (in the Osona

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Table 1 Prevalence of articular chondrocalcinosis (ACC) in subjects aged 60 years and older by age and sex

Age (years)	Women			Men		
	All women	No with ACC	Percentage with ACC (95% CI)	All men	No with ACC	Percentage with ACC (95% CI)
6069	93	10	11 (4·4 to 16·7)	75	1	1 (1·2 to 3·8)
70–79	39	5	13 (2·3 to 23·3)	40	5	13 $(2 \cdot 2 \text{ to } 22 \cdot 7)$
80+	9	5	56 (22·5 to 87·5)	5	1	20 (15 to 55)

Table 2 Number and percentage of subjects with articular chondrocalcinosis with radiological evidence of calcification in joints

Joint	No (%) of subjects		
Knee meniscus	26 (96)		
Triang ligament	14 (52)		
Carpus	7 (26)		
Metacarpophalangeal	3 (11)		

region or in other Catalonian or Spanish areas), medical disorder that led to primary care referral (rheumatological or not), and previous rheumatic disorders (arthralgia, arthritis, or both) was administered by their family practice doctor. Most of these elderly subjects were pensioners and had previously worked as farmers, housewives, or in the textile industry. All were covered by the social security system.

Standard radiographs of both knees (anteroposterior view) and both hands (palmar view) were obtained for all participants. Radiographs were assessed independently by three rheumatologists (RS, DP, MAB) who had no knowledge of the questionnaire data. The presence of typical linear calcifications was recorded in the knee meniscus, wrist triangular ligament, carpus, and metacarpophalangeal joints. Chondrocalcinosis was classified as absent, questionable, or present. Interobserver agreement on each of the three categories was high, with an estimated κ value of 0.88 (RS-DP), 0.92 (RS-MAB) and 0.90 (DP-MAB) respectively. A definitive diagnosis of articular chondrocalcinosis was assumed if the presence of linear calcifications compatible with the disorder in at least one of the eight joint sites examined was confirmed by two observers. A second evaluation was performed when a patient was classified as having questionable disease by two or three observers and, if doubt persisted, definitive diagnosis was obtained by combined assessment.

STATISTICAL METHODS

Frequencies were compared using the χ^2 test with Yates's correction when necessary. Confidence intervals were determined for the

Table 3 Relation between rheumatic disorders and articular chondrocalcinosis (ACC)

	No (%) subjects with ACC	No (%) subjects without ACC	
Rheumatic symptoms as the reason for consultation	4 (15)	36 (14)	
No previous rheumatic disorders	5 (19)	56 (24)	
Arthralgia	18 (67)	157 (67)	
Arthritis plus arthralgia	4 (15)	16 (7)	
Arthritis alone	0 (0)	2 (1)	

No statistical differences were observed in the variables for either group.

prevalence estimates and odds ratios were calculated for age and sex variables. The female:male odds ratio was adjusted for age by the Mantel-Haenszel method. Age strata for this analysis were the age decades 60-69, 70-79 years, and 80+ years. The Mann Whitney test was used to compare differences between means; p<0.05 was chosen as the level of statistical significance.

Results

Thirty five of 37 family practice doctors agreed to take part in the survey. Each doctor recruited a mean of 7.7 subjects (range 2–10), resulting in a total sample of 269. Two were excluded for age younger than 60 years and six for technical reasons or poor quality of radiographs. The final number of subjects studied was 261 (141 women, 120 men), which represents 1.3% (1.4% of women and 1.2% of men) of the population of Osona aged 60 and over. The mean (SD) age of all subjects was 68 (5.8) years with a range of 60–88 years. The mean age of women was 68.1 (6.3) and the mean age of men was 67.9 (5.8) years.

PREVALENCE OF ARTICULAR CHONDROCALCINOSIS

In the first evaluation 23 subjects were considered to have definite chondrocalcinosis and in seven others this diagnosis was questionable. After the second evaluation and the subsequent consensus, definite articular chondrocalcinosis was diagnosed in four of these seven questionable cases. Thus the total number of subjects with articular chondrocalcinosis was 27, which represents a crude prevalence of articular chondrocalcinosis in those aged 60 years and over of 10% (95% confidence interval (CI) 6.6 to 14).

PREVALENCE OF ARTICULAR

CHONDROCALCINOSIS RELATED TO SEX AND AGE In women the frequency of articular chondrocalcinosis was higher than in men: 14% (95% CI 8.5 to 19.9) v 6% (95% CI 1.6 to 10; p < 0.05). The odds ratio of articular chondrocalcinosis in women v men was 2.7 (95% CI 1.0 to 7.2) and the age adjusted odds ratio was 2.8 (95% CI 1.0 to 7.6). The overall crude prevalence increases from 7% in patients aged 60-69 years to 13% in subjects aged 70-79 and 43% in those aged 80 years and over. This increasing prevalence was noted in both sexes (table 1). Furthermore, the mean (SD) age of subjects with articular chondrocalcinosis was significantly higher than the mean (SD) age of subjects without articular chondrocalcinosis (72·7 (6·8) v 67·5 (5·7); p<0·0001).

LOCATION OF RADIOLOGICAL CALCIFICATIONS All but one subject with articular chondrocalcinosis had typical calcifications on the knee menisci (prevalence of knee chondrocalcinosis 96%). Table 2 gives the frequency of chondrocalcinosis in the other articular areas.

	Indigenous (n=155)	Non-indigenous (n=106)	
No of subjects with ACC	17	10	
Prevalence of ACC (%(95% CI))	11 (6·1 to 15·9)	9 (3.8 to 14·9)	
Mean (SD) age (years)	68.1 (6.3)	67.8 (5.7)	
Female to male ratio	1.3	1.1	

No statistical differences were observed in the different variables were compared.

RELATION BETWEEN THE PRESENCE OF ARTICULAR CHONDROCALCINOSIS AND THE REASON FOR MEDICAL CONSULTATION AND RHEUMATIC DISORDERS

Rheumatic disorders as the reason for medical consultation at the time of inclusion in the study were observed in a similar proportion in subjects with or without articular chondrocalcinosis. Most of the subjects had a previous history of rheumatic disorders, without statistical differences between subjects with or without chondrocalcinosis (table 3).

PREVALENCE OF ARTICULAR

CHONDROCALCINOSIS DEPENDING ON PLACE OF BIRTH

No significant differences in the occurrence of articular chondrocalcinosis between indigenous (born in Osona) and nonindigenous (born out of the Osona region) subjects were observed (11% v 9.4%). The two populations had a similar mean age and female:male ratios (table 4).

Discussion

Since the first epidemiological survey of the prevalence of knee chondrocalcinosis by Bocher *et al*⁵ in 1965, performed in a hospital based population, several prevalence surveys of articular chondrocalcinosis have been carried out with controversial results. The different characteristics of the population analysed, with special emphasis on the age group of the subjects and the radiological methods used to evaluate the presence of typical linear calcifications, may explain the discrepancies observed in the different surveys. Only two of these previous studies¹⁶ ¹⁷ have been performed in the general population. The first was a

Swedish study that analysed the prevalence of different rheumatic diseases at 79 years of age; chondrocalcinosis was found in 12 (15%) of the 81 subjects analysed.¹⁶ The largest epidemiological survey of the prevalence of articular chondrocalcinosis in the general population was carried out in the American population of Framingham.¹⁷ In this study, radiological knee chondrocalcinosis was found in 8% of subjects, a similar figure to our results

of 10%. Table 5 summarises the various studies of the prevalence of radiological chondrocalcinosis carried out so far, the prevalence rate of articular chondrocalcinosis ranging from 6.1% to 34%.⁵⁻¹⁷ It is important to note that of these studies most used small samples^{7 8 11 13-16} and these were recruited from patients in hospital,^{5 8 10-12 14} patients in homes for the elderly,^{6 7 13} or clinics for rheumatic diseases⁹¹² which were probably not representative of the general population. Although our study was not performed in the general population and the effect of a selection bias cannot be ruled out, we believe that our population sample was representative of the elderly population in the Osona region as a whole for three reasons. First, subjects were randomly chosen from outpatients attending primary care facilities (common in the elderly) irrespective of the reason for consultation. Secondly, male to female ratios and the distribution by age groups are similar in this population to the whole elderly population registered in 1988 in the Osona region. Thirdly, subjects with articular chondrocalcinosis consult primary care doctors for rheumatic disorders in a similar percentage to subjects without articular chondrocalcinosis, suggesting that the overall crude prevalence of articular chondrocalcinosis was not influenced by the fact that subjects with rheumatic symptoms were more likely to participate in the study.

The articular chondrocalcinosis prevalence of 10% in our elderly population is lower than other epidemiological surveys in which a much higher occurrence was reported. The results reported in this study agree with those of other workers⁶ ¹⁴ ¹⁷ in that articular chondrocalcinosis is an age related disorder and its occurrence increases dramatically with age.

Table 5 Prevalence of radiological articular chondrocalcinosis (ACC) in elderly subjects as reported in previous surveys

Reference	No of subjects (population type)*	Female to male ratio	Age (mean) (years)	Radiographs studies	Total prevalence (%)	Percentage with ACC	
						Women	Men
Bocher <i>et al</i> (1965) ⁵	455 (hosp)	1.9	>59 (80)	Knee	7	8	6
Cabanel et al (1970)6	360 (ger)	1.2	>60 `	Knee	6	6	6
Ellman and Levin (1975) ⁷	58 (ger)	6.3	>70 (82.6)	Knee, wrist, pelvis	28	32	_
Delauche et al (1977) ⁸	62 (hosp)	2.6	>80 (85.1)	Knee, wrist, pelvis	32	28	41
Leonard et al (1977) ⁹	272 (rheum)	2.8	>50	Knee, wrist	16	19	7
Rodriguez Valverde et al (1978) ¹⁰	183 (hosp)	0.8	>60 (73.1)	Knee, wrist, pelvis	17	20	15
Memin et al (1978) ¹¹	108 (hosp)	All women	>80 (88.4)	Knee	23	23	
Ellman <i>et al</i> $(1981)^{12}$	574 (hosp)	2.2	>50 (65)	Knee	10	8	12
Megard et al (1983) ¹³	120 (ger)	4.5	>68 (83.2)	Knee	13	_	
Wilkins <i>et al</i> $(1983)^{14}$	100 (hosp)	2.2	>65 (79.4)	Knee, wrist, pelvis	34	39	23
Gordon et al (1984) ¹⁵	127 (rheum)	1.4	>55 (70.4)	Knee, wrist, pelvis	16	24	4
Bergström et al (1986)16	81 (gener)	1.4	All 79	Knee, wrist	15	23	6
Felson et al (1989)17	1402 (gener)	1.4	>63 (73)	Knee	8	9	7
Sanmartí et al (1993)	261 (prim)	1.2	>60 (68)	Knee, wrist	10	14	6

*hosp=hospitalised; ger=homes for the elderly; rheum=rheumatic population; gener=general population; prim=primary care attention.

This is of critical importance in any study carried out on the prevalence of articular chondrocalcinosis and may explain most of the discrepancies between the different surveys. Studies that reported a much higher frequency of articular chondrocalcinosis were performed in subjects with a significantly higher mean age than in our population.^{7 8 11 13 15} This phenomenon emerges in the second report of Ellman et $al_{,12}^{12}$ in which a prevalence of 9.6% was noted in a large population sample with a mean age of 65 years, a figure which is similar to that observed in our population with a mean age of 68. Moreover, in the Framingham study,¹⁷ with an average age of 73, the prevalence of articular chondrocalcinosis was also similar (8%).

It is possible that geographical differences may have an effect on the prevalence of articular chondrocalcinosis and contribute to the discrepancies in the various surveys. In the Osona region, as in other Spanish areas,²⁰⁻²² several cases of familial chondrocalcinosis in the indigenous population have been described.¹⁸ ¹⁹ Although the prevalence of articular chondrocalcinosis could be influenced in part by this phenomenon, the prevalence of articular chondrocalcinosis in native subjects was similar to that observed in non-indigenous subjects, suggesting that the results of our study are probably representative of the real prevalence of articular chondrocalcinosis in elderly Spanish subjects. Furthermore, when our prevalence results were extrapolated to the Spanish population aged over 60 years, according to their age structure,²³ a standardised prevalence of 12% (95% CI 8·1 to 15·9) was calculated. Another Spanish study was carried out on patients in hospital,¹⁰ in an area in which familial chondrocalcinosis had also been reported²⁰; the prevalence of articular chondrocalcinosis was higher than in our survey, probably reflecting a different kind of population (in hospital vambulatory) and a higher mean subject age. We conclude that a result of around 10% is a good approximation to the real prevalence of articular chondrocalcinosis in the overall elderly population aged 60 years and over.

In our study articular chondrocalcinosis was more common in women. This gender predominance has been reported by most workers^{5 9 10 14 16 17} but not all.^{3 6 8 12} In this survey, the prevalence of articular chondrocalcinosis increases with age in both sexes, but in different proportions, resulting in a similar prevalence of articular chondrocalcinosis at 70-79 years. Felson et al,¹⁷ analysing the prevalence in both sexes in each five year age group, also reported a higher frequency in women in each group, but a similar prevalence of articular chondrocalcinosis in men and women aged over 80 years was noted. We do not have a satisfactory explanation for this phenomenon, but as age increases the differences in the occurrence of articular chondrocalcinosis between the sexes may decrease, reflecting a more important role of age than sex in the predisposition to articular chondrocalcinosis. Although we noted a

further increase in the prevalence of articular chondrocalcinosis in women in the group of subjects aged 80 years and over, this prevalence estimates must be interpreted with caution because the number of subjects in this age group was small.

As expected in the elderly, most of the subjects showed previous articular symptoms. It is of interest that these rheumatic disorders were recorded in the same percentage in subjects with or without chondrocalcinosis. This finding may reflect the fact that the clinical manifestations of articular chondrocalcinosis in elderly subjects recruited from the general population are less evident than in a clinical setting. Although no attempt was made to obtain a clinical assessment of joint disease and its severity in our subjects, the data should be interpreted cautiously. Other workers have reported a greater frequency of clinical joint disease in patients with articular chondrocalcinosis than in those without.7 8 12 14 17

clinical²⁴ described in and As epidemiological studies,7 14 almost all patients with articular chondrocalcinosis showed evidence of chondrocalcinosis in the knees. Only one subject in our sample with articular chondrocalcinosis did not have meniscal calcification. This emphasises the fact that anteroposterior view knee radiographs are sufficient to diagnose articular chondrocalcinosis in epidemiological surveys, as has been pointed out by several workers.

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- 1 Zitnan D, Sitaj S. Chondrocalcinosis articularis. Ann Rheum

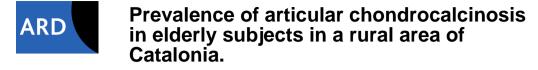
- Zitnan D, Sitaj S. Chondrocalcinosis articularis. Ann Rheum Dis 1963; 42: 243-53.
 McCarty D J, Hogan J M, Gatter R A, Grossman M. Studies on pathological calcifications in human cartilage. *J Bone Joint Surg [Am]* 1966; 48: 309-25.
 Mitrovic D R, Stankovic A, Iriarte-Borda O, et al. The prevalence of chondrocalcinosis in the human knee joint. An autopsy survey. *J Rheumatol* 1988; 15: 633-41.
 Sokoloff L, Varma A A. Chondrocalcinosis in surgically resected joints. Arthritis Rheum 1988; 31: 750-6.
 Bocher J. Mankin H J, Berk P N, et al. Prevalence of calcified meniscal cartilage in elderly persons. N Engl J Med 1965; 272: 1093-7.
 Cabanel G, Phelip X, Gras J P, et al. Frequence des calcifications meniscals et leur signification pathologique.

- Cabanel G, Phelip X, Gras J P, et al. Frequence des calcifications meniscals et leur signification pathologique. *Rhumatologie* 1970; 7: 255-62.
 Ellman M H, Levin D. Chondrocalcinosis in elderly persons. *Arthritis Rheum* 1975; 18: 43-7.
 Delauche M C, Stehle E, Cassou B, et al. Frequence de la chondrocalcinose radiologique aprés 80 ans. Un étude prospective. *Rev Rhum Mal Osteoartic* 1977; 44: 555-7.
- conard A, Solnica J, Cauvin M, et al. La chondrocalcinose: 9 L Leonard A, Solnica J, Cauvin M, et al. La chondrocalcinose: étude de sa frequence radiologique et de ses rapports avec l'arthrose. Etude du taux de la parathormone. Rev Rhum Mal Osteoartic 1977; 44: 559-64.
 Rodriguez Valverde V, Sanz Ortiz, Saiz Garcia F, Gonzalez Tutor A. Condrocalcinosis en individuos a partir de los 60 años. Revista Espanola de Reumatologia 1978; 5: 29-32.
 Memin Y, Monville Cl, Ryckewaert A. La chondrocalcinose articulaire après 80 ans. Rev Rhum Mal Osteoartic 1978; 45: 77-82
- 45: 77-82.

- 12 Ellman M H, Brown M L, Levin B. Prevalence of knee
- Ellman M H, Brown M L, Levin B. Prevalence of knee chondrocalcinosis in hospital and clinical patients aged 50 or older. J Am Geriatr Soc 1981; 29: 189-92.
 Mégard M, André Fouet E. La chondrocalcinose chez les personnes agées. Rhumatologie 1983; 35: 249-52.
 Wilkins E, Dieppe P, Maddison P, Evison G. Osteoarthritis and articular chondrocalcinosis in the elderly. Ann Rheum Dis 1983; 42: 280-4.
 Gordon T P, Smith M, Ebert B, et al. Articular chondrocalcinosis in a hospital population: an Australian

- Gordon T P, Smith M, Ebert B, et al. Articular chondrocalcinosis in a hospital population: an Australian experience. Aust N Z J Med 1984; 4: 655-9.
 Bergsröm G, Bjelle A, Sorensen L, Sundh V, Svangor A. Prevalence of rheumatoid arthritis, osteoarthritis, chondrocalcinosis and gouty arthritis at age 79. J Rheumatol 1986; 13: 527-34.
 Felson D T, Andersson J J, Naimark A, Kannel W, Meenan R F. The prevalence of chondrocalcinosis in the elderly and its association with knee osteoarthritis: the Framingham study. J Rheumatol 1989; 16: 1241-5.
 Sanmarti R, Pañella D, Brancós M A, Anglada A. Condrocalcinosis articular hereditaria en la comarca de

- Fernandez Dapica M P, Gómez Reino J J. Familial chondrocalcinosis in the Spanish population. *J Rheumatol*
- 1986; **13:** 631-3. 22 Balsa A, Martin-Mola E, Gonzales T, Cruz A, Ojeda S, Baisa A, Martin-Moha E, Gonzales T, Cruz A, Ojeda S, Gijón-Baños J. Familial articular chondrocalcinosis in Spain. Ann Rheum Dis 1990; 49: 531-5.
 Padrón municipal de habitiantes: 1 de Abril de 1986. Resultados nacionales. Madrid: Instituto Nacional de Estadística,
- 1989
- McCarty D J. Calcium pyrophosphate dihydrate crystal deposition disease 1975. Arthritis Rheum 1976; 19(suppl): 275–85.



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