



Prevalence of chondrocalcinosis in a Mexican tertiary care institution of musculoskeletal disorders

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Abstract

Introduction/objectives The prevalence of chondrocalcinosis (CC) was reported as variable according to the geographic populations. However, there are no data regarding its prevalence in Mexico. Thus, we decided to investigate the Mexican prevalence of CC in a cohort of patients from a tertiary health care institution.

Methods A retrospective analysis of radiographs of knees and wrists from our institution was performed. Inclusion criteria included patients > 50 years old having radiographs of knees and wrists. Radiographic presence of CC was classified according to a dichotomous evaluation assayed by two rheumatologists experts on the area.

Results A total of 3.350 radiographs from 1.602 patients were evaluated. Forty-seven patients showed calcifications in at least one knee or wrist for an overall prevalence of 3%, of which 23.4% were men and 76.6% women. The knee was more commonly affected than the wrist (85.1% and 14.9% respectively). The prevalence according to gender was 2.9% in women, whereas, it was 3.2% in men. Only two patients (4.3%) showed a contemporaneous presence of CC in both hands and both knees. At knee level, the prevalence was 2.7%, whereas at the wrist, we reported a prevalence of 4.9%.

Conclusions The prevalence of CC for Mexican population had not been reported so far. This a starting point to break the silence and encourage the knowledge of how this disease is associated with possible risk factors in Mexican population.

Key Points

- The prevalence of chondrocalcinosis in Mexico was 3%.
- The prevalence of knee chondrocalcinosis increases according to the age in women's.
- The nixtamalized meals could be a protective factor for CC in Mexican population.

Keywords Chondrocalcinosis · Prevalence · Radiographs

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Introduction

Calcium pyrophosphate deposition disease (CPPD) is a chronic disorder characterized by intraarticular and/or periarticular deposition of crystals. The crystal deposits provoke inflammation in the joint, which can cause the joint cartilage to break down [1]. Chondrocalcinosis (CC) is the presence of calcifications in hyaline and/or fibrocartilage that usually is detected by radiography. Joints that display higher CC are the knees and wrists [2]. It is more frequent in women over 50 years; however, prevalence increases along with age (3.7% between 55 and 59 years old versus 17.5% in women over 80 years old) [3, 4].

CPPD diagnosis is usually based on clinical history, physical examination, and imaging findings [1, 5–8]. However, the definitive diagnosis is based on the direct observation of the CPP crystals under polarized light microscopy from synovial fluid samples or histological examination [1, 9].

The prevalence of CC increases along with age ranging from 3.7% in women between 55 to 59 years old versus 17.5% in women over 80 years [3, 4]. CC prevalence also varies between geographic populations, i.e., the Chinese population reported a 2.3% approximately [1], whereas UK 7% [4], USA 8.1% [10], and Spain 10% [11]. In spite of these pieces of information, there are no consolidated data regarding the frequency of CC in Latin America. In particular, no data on the frequency of CC in Mexican population are currently available. Taking into account of this gap, we conducted the present study with the aim to investigate the Mexican prevalence of CC in a cohort of patients from a tertiary health care institution.

Methods

Study population

We conducted a retrospective study by an analysis of radiographs of knees and wrists joints from patients who were attending outpatient/inpatient of the National Institute of Rehabilitation, Luis Guillermo Ibarra Ibarra (Mexico City, Mexico), from January 2016 to December 2016.

Inclusion criteria included patients > 50 years old having radiographs of both knees and/or wrist in anteroposterior and oblique views. For the knee, lateral view was also required. The radiographs were taken due to hand or knee pain as referred by the patients. Exclusion criteria included poor visualization and/or technically low quality of radiographs (to avoid misinterpretation), severe osteoarthritis (grade IV according to the Kellgren-Lawrence radiographic scale), acute fractures, presence of joint prosthesis or orthopedic hardware in adjacent anatomic areas, and history of burns or frostbite.

The study was conducted according to the Declaration of Helsinki and local regulations. The presented study was approved by the institutional ethics committee (INR-LGII_07/17).

Radiography

Radiographic presence of CC was classified according to dichotomous evaluation (presence/absence). Fibrocartilage calcifications were classified as positive when the image showed thick, shaggy, punctate, or linear radiodensity areas within the meniscus and/or triangular fibrocartilage, and in the hyaline cartilage as linear or punctate radiodensity areas that were parallel and separated from the subjacent subchondral bone [12]. All images were analyzed by using the DICOM Viewer System that allows radiography editing to improve the imaging interpretation accuracy. Radiographs images were selected, codified, and classified by an independent operator.

The authors before the beginning of the study determined the selection of the imaging editor system as the pathological findings.

Radiographs findings were analyzed blindly and interpreted by two different expert Rheumatologists on CC, one of them trained also in musculoskeletal radiology. Radiographs consensual interpretation was performed for discordant opinions. Consequently, both specialists determined the score.

Statistical analysis

Statistical analysis was obtained by using IBM SPSS 20 version. Statistical analysis of prevalence was carried out considering the unitary basis of CC value present for each patient, when the pathology is observed in at least one joint. Mean standard deviation (SD) and *n* (%) were used to describe continuous and categorical variables. The *t* test for independent samples was applied for parameters of age and sex with respect to CC presence or absence. The Pearson correlation coefficient was used to measure linear association between variables (age, sex, CC, laterality, and location). On the other hand, the prevalence of CC and 95% confidence interval (CI) was calculated at each joint region for knees and wrist, unilateral, bilateral, and isolated CC.

Results

A total of 3,350 radiographs (2,980 knees and 370 wrists) from 1,602 consecutive patients were evaluated. From those, 348 patients (21.5%) were men and 1,253 patients (78.2%) were women. Mean age of all subjects was 65.6 ± 10.1 years old, 95% CI (65.1–66.1).

A total of 47 patients showed calcification in at least one knee or wrist (Fig. 1), for an overall prevalence of 3.0%, of which 23.4% (11/47) were men and 76.6% (36/47) were women. The knee joint was more commonly affected than the wrist (85.1% and 14.9% respectively).

Taking into account separately the prevalence according to gender, we found 2.9% (36/1.253) of CC in women, whereas, it was present in 3.2% (11/348) of men.

Only two patients (4.3%) showed a contemporaneous presence of CC in both hands and both knees.

CC at knee level

A total of 2.982 radiographs of knees (2.324 of women and 658 of men) from 1.491 patients (1.162 women and 329 men) were assessed.

CC was present in at least one knee joint in 2.7% (40/1.491 patients) (11/40 (27.5%) men; 29/40 (72.5%) women). Female population displayed a frequency of 2.5% (29/1.162) for knee with CC while men showed a 3.3% (11/329) (Table 1) (Fig. 2).

The mean age of patients was significantly higher when CC was present versus those without CC (71.2 and 65.8 years respectively, $p = 0.001$). This tendency was confirmed in women ($p < 0.001$) but not in men ($p > 0.05$) (Table 1).

The presence of CC in both knees (bilateral) was slightly less frequent (47.5%) than when occurred in only one joint 52.5%. In women, age was significantly higher (77.3 years) when bilateral CC was present than when CC was present unilaterally (68.8 years), $p < 0.051$.

Bilateral CC increased in women along with age, thus women between 50 and 69 years old showed a 20% of CC presence, while women older than 70 years old showed a 68.4% of CC.

With respect to the men, bilateral CC was in decline along with age since patients < 70 years old displayed 42.9%

whereas patients > 70 years old showed 25.0% for the same condition. Table 1, Fig. 3.

Unilateral knee with CC among women was higher for the right knee (64.4%) than the left knee (35.7%). This finding was different in men, where the left knee was more affected (71.4%) than the right knee (28.6%). Table 1, Fig. 3.

Radiographic findings at wrist level

A total of 370 radiographs of the wrist from 185 patients were assessed, (women 159 (85.9%); men 26 (14.1%)).

Unilateral CC was present in a 4.9%, (9/185 patients) (1/9 (11.1%) men; 8/9 (89.0%) women). Among men, only one of 26 patients (63 years old) showed characteristic images of CPP crystals (3.8%) on the left wrist, while eight out of 159 women had CC presence (5.0%) (mean age of 64.3 ± 7.9 years) of which five had unilateral CC 62.5% (mean age 62.2 ± 6.2 years old) (4 (80%) on the right hand and 1 (20%) on left hand) three women presented bilateral CC (37.5%) the mean age 67.7 ± 10.6 years. Table 2.

Discussion

Our results showed an overall CC prevalence of 3% in a population over 50-years old. To the best of our knowledge, this is the first epidemiological study aimed to determine the prevalence of this condition in a Mexican population.

The prevalence reported in our study is similar to that reported for a Chinese population (2.3%), [13] but significantly lower than the rate calculated from the American and European cohorts (7.0 to 18.0%) [4, 10, 14].

Some authors formulated different theories explaining the prevalence of CC found. Zhang et al. suggested that Chinese individuals in Beijing may lack a systemic predisposition to CC due to the calcium levels in tap water which is 15-fold

Fig. 1 Deposition of CPPD crystals: **a** involving meniscal cartilage and **b** radioulnar joint

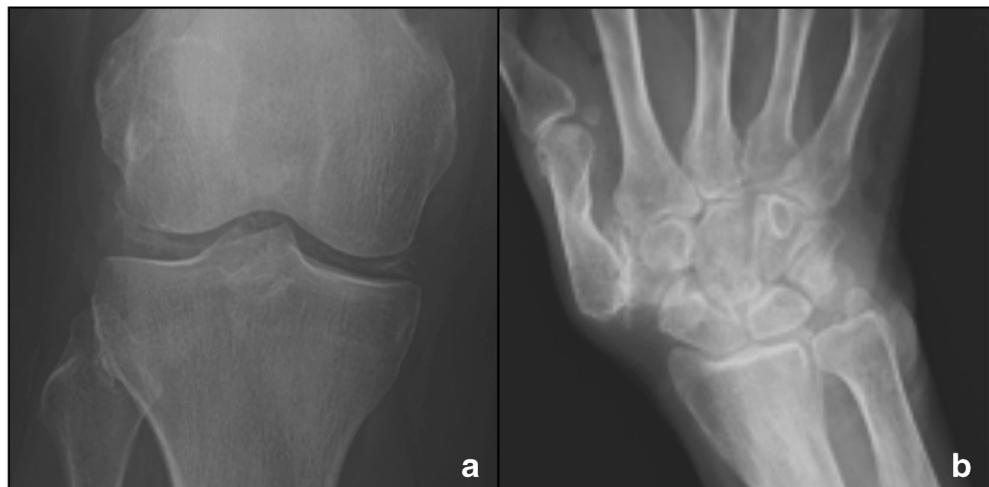
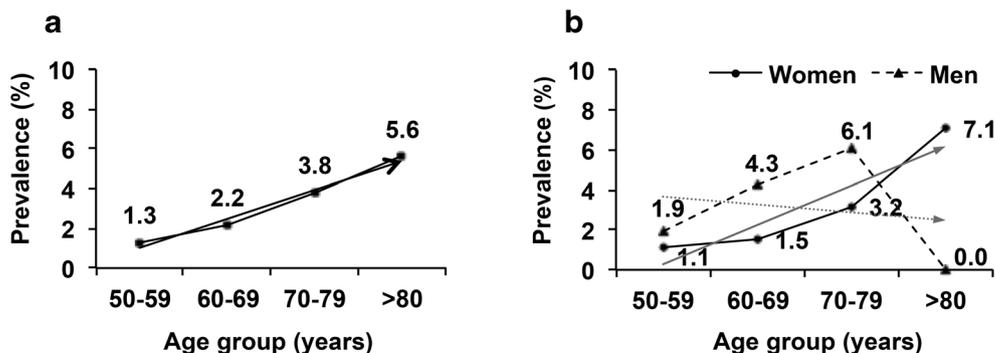


Table 1 Prevalence of knee CC in patients aged 50 years and older by age and sex

Sex	Patients		CC		Unilateral			Bilateral			Total				
	Total	%	Absent	Present	% of total	Right	%	Left	%	Total	%	n	% with CC		
Both sex	1491	100	1451	40	2.7	11	52.5	10	47.6	21	52.5	19	47.5	40	100
Mean age (years)	65.9 ± 10.1		65.8 ± 10.1	71.2 ± 11.1B		68.2 ± 12.9		68.4 ± 9.9C		68.3 ± 11.3		74.3 ± 10.2D		71.2	
Women	1162	77.9	1132	29	2.5	9	64.3	5	35.7	14	48.3	15	51.7	29	72.5
Mean age (years)	65.9 ± 10.2		65.8 ± 10.1	73.2 ± 11.8A		69.3 ± 14.1		67.8 ± 13.0C		68.8 ± 13.2		77.3 ± 8.8C		73.2	
Men	329	22.1	318	11	3.3	2	28.6	5	71.4	7	63.6	4	36.4	11	27.5
Mean age (years)	65.5 ± 9.9		65.5 ± 10.1	65.8 ± 6.9D		63 ± 0.0		69 ± 7.3D		67.3 ± 6.6		63.2 ± 7.5D		65.8	

The age in years is expressed as the mean age ± SD. T test for equality of means was applied for differences and a CI of 95% for the mean age of absent CC vs present CC, right CC vs left CC and unilateral CC vs bilateral CC. AP ≤ 0.0001, BP ≤ 0.001, CP ≤ 0.05, DP ≥ 0.05

Fig. 2 Prevalence of knee CC in **a** both gender, **b** women/men, 50 years or older



higher (67.6 mg/l) than those of other countries (4.5 m/l) [13]. As noted, metabolic and/or endocrine disorders, such as hyperparathyroidism, are associated with the occurrence of CC. [15, 16]. It has been demonstrated that free serum calcium concentration is the major determinant of the rate of parathyroid hormone (PTH) secretion [17] and even slight reductions in serum calcium levels will increase the function of parathyroid glands [18]. Accordingly, our hypothesis is that the Mexican prevalence of CC could be similar to the Chinese population due the maize nixtamalization process (that is the main food source of Mexican people), by which the corn is cooked in water and quicklime (calcium oxide), which increases the free calcium rate 30-fold higher than the original levels [19]. This type of food does not provide the amount daily of calcium required, but it could help to compensate some metabolic or endocrine imbalance of calcium that in other conditions could increase the functioning of the

parathyroid glands and calcium deposition in joints, especially of the knees.

Additionally, it is important to know that the study populations from European works were older than our cohort (mean age over 68 years), which can influence in the final prevalence due to the fact that CC is more prevalent at this age [10, 11, 14].

From further analysis of our results, we can consider the following aspects.

First, the age and sex as parameters influence CC. The analyzed population means age is younger than 70 years old and displayed a higher CC prevalence for the knee in men 3.2% with respect to women 1.3% but, for older populations (> 70 years old) the CC prevalence for men was lower than for women 3.7% vs 4.7% respectively. This is in line with previous studies reported different CC prevalence according to the sex [1, 4, 10, 11, 14, 20, 21].

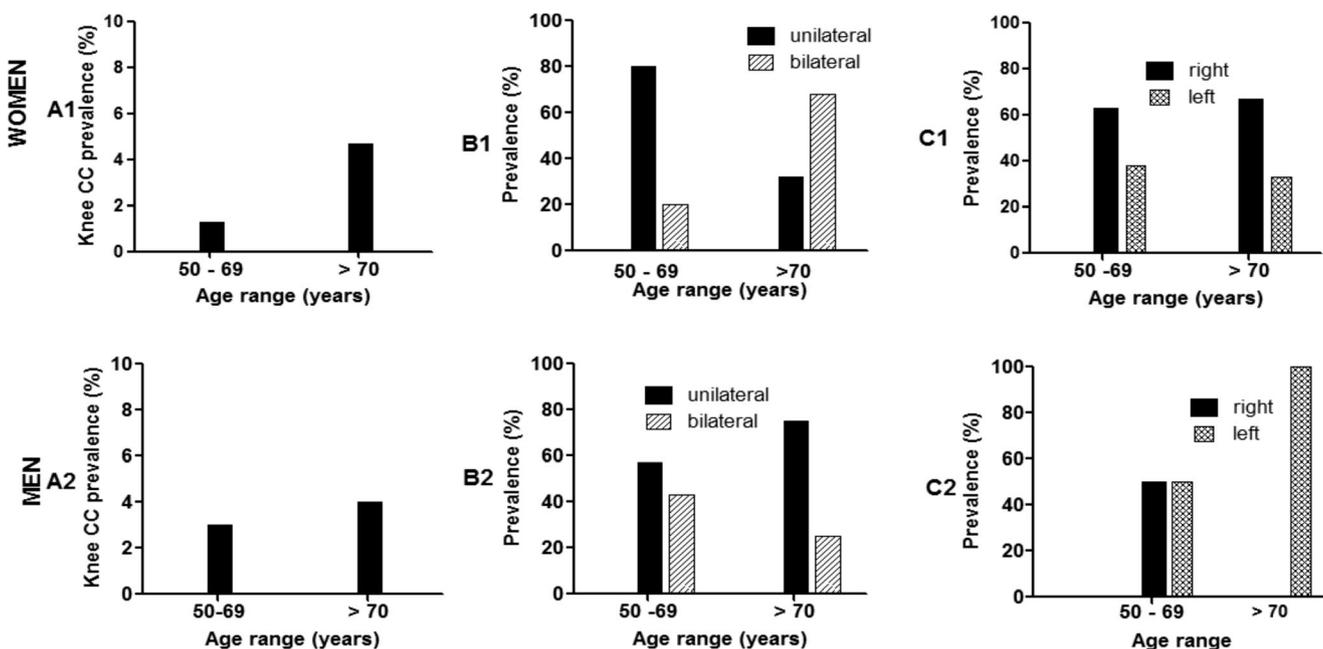


Fig. 3 Knee CC, sex, and age range: prevalence of CC in at least one knee (A1, A2), only one (unilateral) or both knees (bilateral) involvement (B1, B2), limb involvement (right or left) (C1, C2). Note how CC in

women increases substantially around the 7th decade of life (A1) and bilateral involvement becomes more frequent (B1). Note that in the woman when CC presented unilaterally, the right knee was more affected (C1)

Table 2 Prevalence of wrist CC in patients aged 50 years and older by age and sex

Sex	Patients		CC			Unilateral				Bilateral		Total			
	Total	%	Absent	Present	% of total	Right	%	Left	%	Total	%	n	%	n	% with CC
Both sex	185	100	176	9	4.9	4	66.7	2	33.3	6	52.5	3	33.3	9	100
Mean age (years)	62.2		62.1	64.1A		64.3		58.5A		62.3		67.7D		64.1	
Women	159	85.9	151	8	5.0	4	80.0	1	20.0	5	62.5	3	37.5	8	88.9
Mean age (years)	62.0		61.9	64.3A		64.3		54.0A		62.2		67.7D		64.3	
Men	16	14.1	25	1	3.8	0		1	100	1	100	0		1	11.1
Mean age (years)	63.4		63.4	63.0A				63.0		63.0				63.0	

The age in years is expressed as the mean age \pm SD. *T* test for equality of means was applied for differences and a CI of 95% for the mean age of absent CC vs present CC, right CC vs left CC and unilateral CC vs bilateral CC. AP \geq 0.05

Our results for patients < 50 years old compared with those observed by Neame et al., slightly higher in men than women (8.2% vs 6.1%) for a UK population (mean age 63.7 years) [4], but different from that reported by Felson et al., were CC was most frequent in women than men (9.0% vs 6.9%) for American population [10], Sanmartín et al., (14% vs 6%) [11], and Ramonda et al., (12.8% vs 7.0%) for European populations [14]. Our study points out that for a population > 70 years the prevalence of CC was greater for women than for men, coinciding with the reported by Felson et al., Sanmartín et al., and Ramonda et al., but distinct from the results reported by Neame et al. We showed that the prevalence of CC knees plays a different role between genders in relation to age; the prevalence seems higher in men's < 65 years, whereas, it resulted higher in women's > 65 years.

There are different hypothesis that may explain the variability of prevalence according to the age and sex. Ushiyama et al. demonstrated that there were in vivo estrogen receptors in human articular chondrocytes of cartilage specimen that may influence in conserving the integrity of cartilage [22]. On the other hand, studies have reported that overdosage of intra-articular estradiol has adverse effects on the articular cartilage of rabbit [23, 24]. Taken together, our hypothesis states that change in the prevalence of knees with CC in male/female ratio is due to aging and could be determined by a hormonal post-menopausal effect in the balance of calcium in the joint tissue, accelerating its deposition in the joint cartilage, although this assumption is not clearly established and further investigation will be needed [10]. On the other hand, in our results, we observed that the trend of the prevalence of CC in the 50–79 age range is upward; however, in 28 patients with age > 80 years, no CC was found, which affect the slope of the trend of CC for population of men > 50 years analyzed here. We consider it desirable to perform the CC study in a larger population that allows observing in more detail the behavior in people older than 80 years.

Second, we observed that age modifies also the CC distribution (unilateral or bilateral). In our analysis of Mexican

population > 50 years age (mean age 65.8 years), women that presented both knees with CC were older (mean age 77.3 years) than those affected unilaterally (mean age 68.8 years) ($p = 0.051$). From the total of cases that presented knees with CC, there were a 47.7% of bilateral cases, slightly less than unilateral cases that are opposite to the data reported by Felson (1989) where 73.7% of the cases (mean age 73 yrs) [10] displayed bilateral CC. Similar results were presented by Ramonda (2009) wherein a cohort taken from an Italian population showed a 71.7% of bilateral CC [14].

Thus, the observation was that the possibility to develop bilateral CC increases from a 20% among women younger than 70 years old to a 68.4% among older women, that resembles the data reported for Italian [14] and American population [10]. Interestingly, there was a 42.9% of prevalence of bilateral CC in men younger than 70 years old and 25% in older men. Our result could be affected by the difference in the number of men > 70 years (133 patients) compared with those < 70 years (235 patients) included in the study, where the number of individuals and prevalence of involvement CC bilateral of the knee were around twice as high

We are inclined to think that in women the CC within the knee does not develop in both knees simultaneously at early stages of the pathology, rather developing along aging and that the presence of OA, and menopausal stages may accelerates the progression to bilateral CC.

Contrary, hand CC was less often 14.9% than knee CC in our cohort in > 50 years (mean age 65.7 ± 10 years). These data is similar to other reports [24, 25]. Abhishek et al., in a study for English population (mean age 66.6 years old) found that wrists are the second most common site for CC development after the knees [24]. Zhang et al. reported that prevalence of knees and wrists CC in elderly Chinese subjects in Beijing were much lower, but in the wrists, CC was very rare [13]. When crystalline pathology in the wrist was present, it was more frequent in women 5.0% than in men 3.8%. This was not different from what is reported for the American and Chinese population [13]. As we suggested above, sex hormones and

post trauma among other factors could be responsible for the imbalance of calcium around ligaments and synovial tissue in the hand resulting in the deposit of crystals, explaining the preponderance of pathology and its increase with aging in the postmenopausal stage of the woman [20, 26, 27].

We are aware that our study has limitations. Firstly, the results are expression of a single tertiary center of musculo-skeletal disorders, which did not permit to have an extended panorama of the real prevalence of the region. Second, only a retrospective lecture of the radiographs was performed without a physical examination or contact with the patients, which have limited the possibility to analyze correlations with clinical data or to detect elements for risk of CC.

In conclusion, prevalence of CC for Mexican population had not been reported so far. This a starting point to break the silence and encourage the knowledge of how this disease is associated with possible risk factors in Mexican population.

Here, there would be no studies aimed at determining whether the intake of water high in calcium and foods high in calcium-like corn that has been nixtamalized throughout life, they have been a protective factor against CC in the Mexican population.

Underdiagnosis of CC in Mexican population may lead to a lack of knowledge of the prevalence of the disease, non-diagnosis of the CC, lack of treatment, progressive joint damage due to lack of treatment, and impairment of the patient's quality of life.

Authors' contributions PDLG-M and MG participated in designing the study, acquiring and interpreting the data, drafting of the manuscript, and giving final approval of the version of the paper to be published. CL, KC, and MF-H were involved in the selection of radiographs to be interpreted. Made substantial contributions to the manuscript preparation and were involved in revising the manuscript for important intellectual content. AA-L and GR-DLG were involved in the statistical analysis. CP and MG were involved in the lecture of radiographs. CB and DC-C participated in the review conception and gave substantial input to the data evaluation and manuscript preparation.

All authors read and approved the final version of the manuscript.

Compliance with ethical standards

Disclosures None.

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