

Prevalence of Chondrocalcinosis in Patients above 50 Years and the Relationship with Osteoarthritis

Abstract

Background: Some studies showed a relation between chondrocalcinosis and osteoarthritis (OA). Hence, considering the importance of chondrocalcinosis diagnosis and necessity for its integration with OA, the current study aims at investigating prevalence of chondrocalcinosis in patients above 50 years admitted to Isfahan Al-Zahra Medical Center and its relationship with OA. **Materials and Methods:** In a cross-sectional study, 600 patients who referred to the radiology units of Al-Zahra Hospital for radiography of different joints were studied during 2013–2014. The patients images were studied for chondrocalcinosis and OA by a radiologist and also examined clinically and results of imaging by an expert rheumatologist. The prevalence of chondrocalcinosis and its relation with OA was determined by Statistical Package for Social Sciences software and using of Chi-square and *t*-test. **Results:** 23 patients under study had chondrocalcinosis (3.83%). patients with chondrocalcinosis had higher age average, and they were in age group of 70 years and older, but no significant difference was observed regarding the prevalence of the disease in both genders. Chondrocalcinosis prevalence in terms of body mass index showed significant differences ($P = 0.001$). All patients with chondrocalcinosis had a history of joint disease and prevalence of chondrocalcinosis in terms of joint disease history showed a significant difference ($P < 0.001$). **Conclusion:** Prevalence of chondrocalcinosis is relatively high in the Iranian population of 70 years and older. Hence, more investigation considering to the diagnosis of chondrocalcinosis among patients with OA is very important.

Keywords: Chondrocalcinosis, joint imaging, osteoarthritis

Introduction

Chondrocalcinosis is calcium pyrophosphate deposition disease resulting from the formation of calcium pyrophosphate crystal in articular cartilage. Their incidence increases with age so that it inflicts 30% of people over 80 years. Although, most patients show asymptomatic radiographic findings, known as chondrocalcinosis. The true prevalence of the disease has not been specified accurately.^[1] Meniscus of the knee, wrist triangular cartilage, and symphysispubis are the most commonly affected areas.^[2] Normally, only in 39% of the cases precipitation of crystals can be seen as chondrocalcinosis in radiographs.

Epidemiologically its incidence has been reported as about 0.009 in the population. The prevalence of idiopathic type is rare at the age under 40 years. At ages 60–75 years, it reaches to 10%, and at the age of 80 years to it reaches to 30% and more. In the family type, the disease can be observed in the

third decade of life.^[2] The most common area of the disease is a knee joint.^[2,3] In one study that done by Neame *et al.*, prevalence rate of knee chondrocalcinosis in UK community was 7%.^[4]

Although, the majority of the cases of calcium pyrophosphate deposition are idiopathic, almost 20% of cases are accompanied by underlying metabolic disorders such as primary hyperparathyroidism, hypomagnesemia, hypophosphatasia, hemochromatosis, chronic gout, and meniscectomy.^[3,5]

The secondary form of the calcium pyrophosphate deposition disease occurs at younger ages compared to idiopathic cases, and in hemochromatosis, it often affects special joints such as the second and third metacarpophalangeal joint.^[5]

Calcium pyrophosphate deposition in the joint may be completely asymptomatic or cause chronic inflammation of the joints, or

Hadi Karimzadeh,
Mehri Sirous¹,
Saeed Najafzadeh
Sadati,
Mahdiyyeh
Bashshash¹,
Peyman Mottaghi,
Behzad Ommani,
Mansoor Karimifar

From the Departments of
Rheumatology and ¹Radiology,
Isfahan University of Medical
Sciences, Isfahan, Iran

Address for correspondence:

Prof. Mehri Sirous,
Department of Radiology,
Isfahan University of Medical
Sciences, Al-Zahra Hospital,
Isfahan, Iran.
E-mail: sirous@med.mui.ac.ir

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it may be seen as a sudden inflammation of arthritis and similar to gout attack.^[6]

Finding chondrocalcinosis in radiography raises diagnosis of calcium pyrophosphate arthropathy, but does not prove it.^[6] Aspiration of synovial fluid with showing intercellular crystal rhomboid and with positively birefringent is necessary to prove the diagnosis of pseudogout or chronic arthropathy calcium pyrophosphate.^[7] However, there may be small crystals and pieces that are difficult to detect, and they are harder to find compared to urate crystals.^[8,9]

Some studies have shown that calcium pyrophosphate deposits in the cartilage around the joints are observed in considerable numbers of patients above 50 years with osteoarthritis (OA). Thus, it is estimated there is relationship between OA and chondrocalcinosis.^[1,2]

In the study by Shafahi *et al.* 65 patients with knee OA, the prevalence of chondrocalcinosis was estimated 23.9% that all above 60 years old and they were in the stage 4 according to Kellgren-Lawrence scale.^[10] In a recent study in Kuwait, no case of chondrocalcinosis was observed in 69 patients with average age 53 years with OA of the hip and knee areas,^[11] while its prevalence was reported as 5% in a study in Spain on 57 patients with average age 50 years without OA.^[11] Felson *et al.* reported that relative risk for emerge of chondrocalcinosis in patients with OA is 1.52 times more than those without OA.^[12] Because the idiopathic form of chondrocalcinosis is rare under the age of 50 years. For this reason, the patient age above 50 years enrolled the study. Hence, because any study was done about community prevalence of chondrocalcinosis in Isfahan areas, relation between chondrocalcinosis and lifestyle, different prevalence to several area,^[4] different treatment method in osteoarthritis and chondrocalcinosis, and considering importance of chondrocalcinosis diagnosis and necessity for its integration with OA, current study aims at investigating prevalence of chondrocalcinosis in patients above 50 years admitted to Isfahan Al-Zahra Medical Center and its relationship with OA.

Materials and Methods

This study is a cross-sectional study which was conducted during 2013 and 2014 in Al-Zahra Medical Center. Research statistical population includes all consecutively patients above 50 years who experienced joint radiography for any reason in this center.

Inclusion criteria include as follows: Age 50 years and above, lack of trauma history in the joint area under study, lack of surgery on joints, and agreement of the patient for participation in the study. Lack of patient's ability or his companion for answering questions was considered as the exclusion criterion. Patients with a history of trauma to current joint are were excluded.

The sample size was specified using sample size estimation formula for prevalence studies considering confidence level

as 95% for chondrocalcinosis prevalence in patients above 50 years. It was considered as 0.5 due to lack of similar study. Given error level as 0.05, the sample size was specified as 384 patients. For more confidence, 400 patients were considered as initial sample size. But considering sampling method and sampling error as 1.5, the total sample size was estimated as 600.

In this study, 600 patients with inclusion criteria were selected who referred to the center for radiography of different joints, and their demographic information including age, sex, major complaint, risk of joint disease, family history of chondrocalcinosis and OA, records of underlying diseases such as diabetes, hyperparathyroidism, hypomagnesemia, and hemochromatosis and hypophosphatasia were investigated and recorded in the specific forms for this purpose.

Patients were examined clinically by an expert rheumatologist, and results of imaging were studied by one expert radiologist and rheumatologist and collected findings recorded in the questionnaire in a rheumatology clinic. Height and weight were also measured and recorded. Knee, wrist and shoulder joints were assessed. Each of three joints that the patients had complained was assessed. In this study, joint infection was separated from inflammation of joint, by synovial analysis, and culture.

Radiographic findings for OA were classified according to Kellgren-Lawrence scale grading. These criteria are:

- Grade 0 (none): There is no finding in favor of OA
- Grade I (doubtful): Presence of small and insignificant osteophytes
- Grade II (minimal): Definite osteophytes but unimpaired joint space
- Grade III (moderate): Moderate reduction in joint space
- Grade IV (severe): Clear reduction of the joint space with sclerosis of subchondral bone.

The criteria which used to identify chondrocalcinosis is the presence of typical calcification on radiographs: Heavy punctuate and linear calcification in fibrocartilage, articular (hyaline) cartilage and joint capsules.^[2]

In this study, The Western Ontario and McMaster University OA index (WOMAC) criterion was used for patients with OA of the knee to evaluate the clinical severity and living quality due to OA. This criterion is used for evaluating pain, stiffness, and physical performance in patients with OA of the knee or hip. WOMAC consists 24 items classifying into three sub-groups. It is also used for evaluating back pain, rheumatoid arthritis, juvenile rheumatoid arthritis, systemic lupus erythematosus and fibromyalgia. Duration of WOMAC evaluation is about 12 min, but may be also 5–6 min.

The WOMAC is used for patients of the knee OA or hip OA to evaluate the clinical severity and living quality due to OA. The score is zero (good function) to 96 (severe disability).^[2]

Research data were collected and entered into the computer, and they were analyzed in Statistical Package for Social Sciences software (SPSS. 22, manufactured in IBM, USA), using statistical tests including Student's *t*-test, Chi-square, one-way variance analysis and Pearson correlation test.

Results

In this study, 600 patients admitted to the radiology department of Al-Zahra Medical Center were investigated. The average age of patients under study was 62.43 ± 8.08 with range 50–90 years. 243 cases (40.5%) were male patients, and 357 cases (59.5%) were female patients. The reason for referral was trauma at any part of the body in 235 cases (39.3%) and the reason for referral was bone, and joint diseases such as chronic joint pain, stiffness, and swelling in 365 cases (60.7%). Also, 174 cases (29%) suffered from underlying disease including diabetes (46 cases), thyroid disorder (2 cases), hypertension (72 cases), heart disease (16 cases), and hyperlipidemia (38 cases).

Of 600 patients under study, 214 cases (35.7%) had joint diseases including OA in 138 patients (64.5%), swelling and inflammation in 68 patients (31.8%), and joint infection in 8 patients (3.7%). Also, above 8 patients suffered to infection in the previous time and were treated.

Eighty-six cases (40.2%) had no previous treatment, 92 cases (43%) were under treatment using nonsteroidal anti-inflammatory drugs, 10 cases (4.7%) were under physiotherapy, 24 cases (11.2%) were under treatment with nonsteroidal anti-inflammatory drugs and physiotherapy, and 2 cases (0.9%) were under treatment with platelet rich plasma. The average time for suffering from the joint disease in the patients under study was 3.2 ± 2.8 years with range 3 months for 15 years.

Four hundred and sixty-seven cases (77.8%) of graphs were related to unilateral knee, 51 cases (8.5%) were related to bilateral knee, 45 cases (7.5%) were related to wrist and 37 cases *6.2% (were related to the shoulder). In the investigation of 518 knee graphs in terms of OA, 280 cases were normal, 74 cases were Grade I, 29 cases were Grade II, 54 cases were Grade III, and 81 cases were Grade IV.

The mean score of WOMAC in patients with OA of the knee was 75.9 ± 9.8 with range 45–96. The mean score of WOMAC in patients with Grade 0 to IV of OA was 60 ± 16.2, 72.4 ± 6.8, 73.9 ± 6.6, 76.8 ± 9.3, and 81.2 ± 9.3. According to one-way variance analysis, there is a significant relationship between OA severity and WOMAC score (*P* < 0.001).

According to the studied graphs, 23 patients under study had chondrocalcinosis, 19 of whom (82.6%) had chondrocalcinosis of knee joint, 3 cases (13%) had

chondrocalcinosis of hand wrist and 1 case (4.3%) had shoulder joint chondrocalcinosis. Table 1 gives the distribution of demographic variables in terms of infliction or no infliction. According to this table, patients with chondrocalcinosis had higher age average, and they were in age group of 70 years and older, but no significant difference was observed regarding the prevalence of the disease in both genders. On the other hand, chondrocalcinosis prevalence in terms of body mass index (BMI) showed significant differences (*P* = 0.001), and patients with this disease had higher average BMI, and all 23 patients were fat or had overweight. Also, the prevalence of this disease showed a significant difference in terms of the reason for referral and underlying disease, and the disease was more common in patients with bone and joint disease and underlying disease.

Results for investigation of the relationship between chondrocalcinosis and joint diseases are given in Table 2. According to the table, all patients with chondrocalcinosis had a history of joint disease and prevalence of chondrocalcinosis in terms of joint disease history showed a significant difference (*P* < 0.001). In terms of the type of disease, most cases of chondrocalcinosis (21 cases) were observed in patients with OA. Also, in patients with chondrocalcinosis, duration of having the joint disease

Table 1: Distribution of demographic characteristics of patients under study in terms of infliction by chondrocalcinosis

Variable	Chondrocalcinosis		<i>P</i>
	Yes	No	
Age (years)			
Mean	70.07±11.1	62.1±7.8	<0.001
50-59	4 (1.5)	264 (98.5)	<0.001
60-69	5 (2.3)	213 (97.7)	
≥70	14 (12.3)	213 (87.7)	
Sex			
Male	10 (4.1)	233 (95.9)	0.77
Female	13 (3.6)	344 (96.4)	
BMI			
Mean	29.98±2.26	26.68±4.69	0.001
Low weight	0 (0)	8 (100)	<0.001
Normal weight	0 (0)	236 (100)	
Over weight	14 (6.8)	192 (93.2)	
Obese	9 (6)	141 (94)	
The reason of referring			
Trauma	2 (0.9)	233 (99.1)	0.029
Pain and OA	21 (6.5)	344 (93.5)	
Background diseases*			
Yes	12 (6.9)	162 (93.1)	0.018
No	11 (2.6)	415 (97.4)	

*Underlying diseases include diabetes, hypertension, thyroid disorders, kidney and liver disease and hyperlipidemia. BMI: Body mass index, OA: Osteoarthritis

was significantly longer. Also, significant relationship was found between OA grade and chondrocalcinosis, and most cases of the disease was observed in patients with Grade II OA (9 cases), Grade III (5 cases), and Grade IV (4 cases), and no cases of chondrocalcinosis in patients with Grade 0 OA was observed. It should be noted a mean score of WOMAC in patients with and without chondrocalcinosis showed no significant difference.

Regression logistic test using backward conditional approach on data showed among variables under study, four variables of age, duration of disease, grade of OA and BMI had significant impact in prevalence rate of chondrocalcinosis, so that rate of chondrocalcinosis prevalence increases by 1.154 times by increasing every age of the patient. Also, by increasing every year of duration of disease, the prevalence rate is increased by 1.138 times and by an increase of every grade of OA, the prevalence rate is increased by 19.37 times. By the increase of every unit of BMI, it increases by 1.194 times. Results are given in Table 3.

Table 2: Frequency distribution of chondrocalcinosis in terms of joint and OA disease history

Variable	Chondrocalcinosis		P
	Yes	No	
Arthral diseases			
Yes	23 (9.8)	211 (90.2)	<0.001
No	0 (0)	366 (100)	
Kind of arthritis diseases			
Arthritis	2 (1.4)	136 (98.6)	<0.001
OA	21 (23.9)	67 (76.1)	
Septic arthritis	0 (0)	8 (100)	
Disease duration	5.13±3.85	2.99±2.57	<0.001
Osteoarthritis grade			
0	0 (0)	280 (100)	<0.001
I	1 (1.4)	73 (98.6)	
II	9 (31)	20 (69)	
III	5 (9.3)	49 (90.7)	
IV	4 (4.9)	77 (95.1)	
Mean score of WOMAC	78.58±9.58	75.67±9.82	0.22

Table 3: Results obtained from multivariate analysis on impact of variables on chondrocalcinosis prevalence

Step	Variables	B	SE	P	OR	95% CI for Exp(B)	
						Lower	Upper
Step 6	Age	0.143	0.034	0.000	1.154	1.079	1.234
	Duration	0.327	0.101	0.001	1.386	1.138	1.688
	BMI	0.177	0.071	0.013	1.194	1.038	1.373
	OA	2.964	1.213	0.015	19.37	1.797	208.766

SE: Standard error, OR: Odds ratio, CI: Confidence interval, BMI: Body mass index, OA: Osteoarthritis

Discussion

Current work was conducted aiming at determining frequency distribution of chondrocalcinosis in patients above 50 years admitted to Al-Zahra Medical Center during 2013 and 2014. In this study, 600 graphs related to patients above 50 years admitted to Isfahan Al-Zahra Medical Center were studied, and it was found 41.3% of patients had OA, and 3.8% had chondrocalcinosis. On the other hand, findings showed patients with chondrocalcinosis have higher average age, BMI, OA grade and disease duration compared to patients without disease. In addition, other factors such as the type of joint disease, grade of OA, the reason for referral and having the joint disease also probably are involved in the prevalence of the diseases.

Previous studies showed that in old women, mild chronic polyarthritis may be accompanied by calcium pyrophosphate deposition (chronic arthropathy).^[1] For unknown reasons, chronic pyrophosphate arthropathy tend to catch knee, wrist, shoulder, elbow, hip, ankle, small joints of the hand and joints between the tarsus which are the atypical locations for primary OA,^[1] as observed in our study some cases of chondrocalcinosis was reported in wrist (3 cases) and shoulder joint (1 case).

Previous studies showed almost 20% of chondrocalcinosis cases are accompanied by underlying metabolic disorders such as primary hyperparathyroidism, hypomagnesemia, hypophosphatasia, hemochromatosis, chronic gout, and meniscectomy.^[3] Undoubtedly, this accompaniment results from role of calcium, magnesium, iron and alkaline phosphatase in pathways mediated with chondrocyte metabolism of adenosine triphosphate (magnesium, alkaline phosphatase) and the formation of crystals (calcium, iron).^[5] Although our study showed no case of above disorders, other underlying influential factors including diabetes, hypertension, and hyperlipidemia had a higher prevalence in the patients. Previous studies indicated prevalence of chondrocalcinosis is along with prevalence of different risk factors such as nutritional status, lifestyle, genetic factors, use of diuretics and underlying diseases such as hypertension, diabetes, cardiovascular disease, chronic kidney disease and metabolic syndrome,^[2] which have high prevalence in our society.

Regarding the prevalence of the disease, some studies showed that calcium deposits in the cartilage around the joints are observed in considerable numbers of patients above 50 years with OA. Thus, it is estimated there is a relationship between OA and this disease.^[13] Such relationship was obtained also in this research. In the study by Shafahi *et al.* 65 patients with knee OA were estimated all above 60 years, and they were in the stage 4 according to Kellgren-Lawrence scale.^[10] 23.9% of them suffered from chondrocalcinosis all above 60 years, which suggests increased prevalence of chondrocalcinosis by increasing age and severity of OA. In this study, overweight and

fatness was observed in 87.7% of patients with OA, which is similar to findings by the current study.^[13] Of course, considering sample size in this study, it seems prevalence of chondrocalcinosis in the population under study has over-estimation. In the study by Malaviya *et al.* in Kuwait, no case of chondrocalcinosis was observed in 69 patients with average age 53 years with OA of the hip and knee areas,^[11] while its prevalence was reported as 5% in a study in Spain on 57 patients with average age 50 years without OA.^[12] Findings of the latter study are closer to findings in the current study. Felson *et al.* reported that relative risk for emerge of chondrocalcinosis in patients with OA is 1.52 times more than those without OA;^[12] this rate was higher in the current study.

Conclusion

The results of this study showed that Prevalence of chondrocalcinosis is relatively high in the Iranian population of 70 years and older. Hence, more investigation considering to the diagnosis of chondrocalcinosis among patients with OA is very important

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Conflicts of interest

There are no conflicts of interest.

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