

Radiographic osteoarthritis and serum cholesterol

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ABSTRACT

Objectives: To find out the relationship between radiographic osteoarthritis (OA) of the knee, generalized OA and serum cholesterol.

Methods: Over a period of 7 months from September 1998 through to March 1999, 246 patients attending 14 primary care clinics in Northern Riyadh, Kingdom of Saudi Arabia, for different non-musculoskeletal complaints were recruited in the study. Their knees, hands and wrists were radiographed. Their ages, sex, weight, height, body mass index (BMI), fasting serum cholesterol, triglycerides and uric acid were recorded.

Results: There were 113 females and 133 males with average ages 46 ± 14.2 and 51.54 ± 16.0 years. One hundred

and twenty-two (49.6%) cases of knee OA and 58 (23.6%) cases of generalized OA were found and analyzed for the association with serum cholesterol levels. Crude odds ratio (OR) for the relationship between knee OA and the third tertile of serum cholesterol was 2.33 (95% CI, 1.19-4.58) which on adjusting for age, sex, BMI, serum uric acid and triglycerides were 2.68 (95% CI, 2.00-3.64). For generalized OA, the crude odds ratio (OR) in relation to the third tertile of serum cholesterol was 1.65 (95% CI, 0.78-3.53), adjusted OR was 2.18 (95% CI, 1.55-3.15).

Conclusion: The results showed an association between high serum cholesterol level and both knee and generalized OA.

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Osteoarthritis (OA) is the most frequent form of arthritis worldwide with proportional increase with age.¹ Hypercholesterolemia is also very common worldwide.² Whether cholesterol levels influence the occurrence of osteoarthritis is a matter of debate? Epidemiologic studies have addressed this question.³⁻⁷ These studies came up with different conclusions regarding the association between osteoarthritis and cholesterol. Some found a modest association between elevated serum cholesterol level and OA.^{3,5,6} Others did not.^{4,7} Osteoarthritis and hypercholesterolemia are common in Kingdom of Saudi Arabia.⁸⁻¹¹ We set out to find whether a relationship exists between osteoarthritis and serum cholesterol in our population.

Methods. Over a period of 7 months extending from September 1998 through to March 1999, and as part of a study of rheumatic diseases in Riyadh, Kingdom of Saudi Arabia (KSA), radiographs of knees and hands (anteroposterior and lateral) were obtained for 249 patients, attending 14 Northern Riyadh primary care centers, for different non-musculoskeletal complaints. Out of these, 246 had serum cholesterol measured. The results of the radiographic finding for osteoarthritis were reported elsewhere.⁸ Those 246 consenting patients also had their age, sex, weight, height, fasting serum cholesterol, triglycerides, and uric acid recorded. The Kellgren-Lawrence grading system for osteoarthritis was

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used to evaluate the radiographs.¹² This system has the following grade (0: normal, 1: minute osteophytes of doubtful significance, 2: definite osteophytes, 3: moderate joints space narrowing, grade 4: greatly reduced joint space and subchondral bone sclerosis). Osteoarthritis was diagnosed if grade 2 or more were present. The comparison was made for osteoarthritis of the knee and generalized osteoarthritis defined here as the presence of hand and knee osteoarthritis. The reporting of x-rays were carried out with no knowledge of the results of serum cholesterol levels.

The serum cholesterol values were divided into tertiles, and the presence of osteoarthritis in patients in the higher second and third serum cholesterol tertiles were compared to those in the lowest first tertile. The odds ratio (OR) was used as the measure of association in this cross-sectional study and was calculated and then adjusted for BMI (weight in kg divided by squared height in meters), age, sex, serum triglyceride level, and uric acid using contingency tables and stratification analysis of Mantel-Haenszel summary odds ratio to adjust for confounding by these factors. Multiple regression method was used to see the effect of incremental rise in cholesterol level on risk of knee OA and generalized OA utilizing statistical package for social sciences, 9 computer package.

Results. Two hundred and forty-six patients had knees, hands x-rays and serum cholesterol available. There were 113 females and 133 males. Their average age was 49.1 ± 15.4 years (females 46.3 ± 14.2 years, males 51.54 ± 16.0 years). There were 122 (49.5%) cases of OA knees and 58 (23.6%) cases of generalized OA.

Table 1 showed the corresponding number of knee and generalized osteoarthritis for each cholesterol tertile value. This table showed an increase in the number of

cases of OA with rising cholesterol level particularly in the third tertile group and especially so in females. **Table 2** showed the crude and adjusted odds ratio (OR) for osteoarthritis of knee and generalized OA for the higher 2 tertile group compared to the lowest first tertile of serum cholesterol levels. From the tables, the crude OR for osteoarthritis knee is found to be significant only when comparing third tertile to the first tertile of cholesterol, 2.33 (95% CI, 1.19-4.58), $P=0.008$. When adjusted for age, sex, uric acid, BMI and triglycerides, the association persists at 2.68 (95% CI, 2.00-3.64) $P < 0.000001$. For generalized OA, the crude odds ratio for the second and third serum cholesterol tertiles were 0.93 (95% CI, 0.41-2.09) and 1.65 (95% CI, 0.78-3.53) which on adjustment for age, sex, BMI, triglyceride level, and uric acid increased to 1.59 (95% CI, 1.11-2.31) and 2.18 (95% CI, 1.55-3.15). The weakest association was between cholesterol 2nd tertile and knee OA (crude OR 1.05, adjusted OR 1.56). The adjusted OR for incremental rise in cholesterol level in association with knee OA is 1.23 (95% CI, 0.98-1.47).

Discussion. This study shows an association between high serum cholesterol and both knee and generalized OA. The association was stronger for knee OA. In addition, the results show an association between incremental rise in serum cholesterol and knee OA although its significance is less than that seen between high cholesterol level and knee OA. Previous studies on the subject showed differing results.^{3-7,13} Some of these studies showed an association between cholesterol level and knee OA.^{3,5,6,13} Others did not report such an association.^{4,7} Sturmer et al¹³ reported an association between high cholesterol levels and both knee and generalized OA. This is similar to the findings of the present study. However, their cases were patients

Table 1 - Cases of osteoarthritis (knee and generalized) and serum cholesterol.

Serum cholesterol (mmol/L) tertiles	Knee OA		Generalized OA	
	Present n (%)	Absent n (%)	Present n (%)	Absent n (%)
All				
First tertile (<4.73)	35 (43)	47 (57)	18 (22)	64 (78)
2nd tertile (4.73-5.71)	36 (44)	46 (56)	17 (21)	65 (79)
3rd tertile (>5.71)	52 (63)	30 (37)	26 (31)	56 (69)
Females				
First tertile (<4.76)	18 (47)	20 (53)	8 (21)	30 (79)
2nd tertile (4.76-5.79)	16 (42)	22 (58)	3 (8)	35 (92)
3rd tertile (>5.79)	25 (67)	12 (32)	11 (30)	26 (70)
Males				
First tertile (<4.72)	17 (39)	27 (61)	10 (23)	34 (77)
2nd tertile (4.72-5.65)	22 (49)	23 (51)	12 (27)	33 (73)
3rd tertile (>5.65)	24 (55)	20 (45)	15 (34)	29 (66)
OA - osteoarthritis				

Table 2 - The relationship between cholesterol (tertiles) and knee and generalized OA expressed as odds ratio, 95% CI.

Serum cholesterol (mmol/L) tertiles	Knee OA		Generalized OA	
	Crude OR	Adjusted OR*	Crude OR	Adjusted OR*
First (<4.73)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
2nd (4.73-5.71)	1.05 (0.54-2.04) P=0.87	1.56 (1.57-2.10) P=0.0024**	0.93 (0.41-2.09) P=0.84	1.59 (1.11-2.31) P=0.01**
3rd (>5.71)	2.33.(1.19-4.58) P=0.008**	2.68 (2.00-3.64) P<0.00001**	1.65 (0.78-3.58) P=0.159	2.18 (1.55-3.15) P<0.00001**

* Adjusted for age, sex, BMI, uric acid, serum triglycerides, ** Significant, OA - osteoarthritis
OR - odds ratio, CI - confidence interval

undergoing surgical joint replacement for OA and were not controlled for the situation of non-OA joints and cholesterol. The results of the current study may have been influenced by us not controlling for diabetes, medications, hypertension, smoking and, exercise levels. Obesity and age are the possible confounders in the association between cholesterol level and OA; however, this was taken into account in the study. How this association between OA and cholesterol originates is a matter of debate. Theoretically, osteoarthritis would lead to less physical activity and consequently, obesity and higher serum cholesterol levels. On the other hand, hypercholesterolemia may be working through systemic mechanisms to cause osteoarthritis. The association between hypercholesterolemia and OA of the hands as part of generalized OA would favor such a mechanism. The existing studies on patients with different forms of hyperlipidemia are cross-sectional and report on finding of articular disease in these conditions at the time of study.¹⁴⁻¹⁶ Most of these articular manifestations of hyperlipidemia in general, are tendinous and inflammatory in type. Whether some subclinical process in the joints of patients with high cholesterol, crystals or otherwise would lead to a repeated insult causing osteoarthritis is unknown. Although this study is cross-sectional and may be not as good as longitudinal studies in exploring disease associations, it nevertheless may be a pointer towards that possible link.

In conclusion, the results showed an association between high serum cholesterol level, knee and generalized OA.

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