Carotid Intima-Media Thickness in 100 Iraqi Patients with Hand Osteoarthritis

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Summary:

Background: Hand osteoarthritis (HOA) is a common joint disorder leading to considerable pain and with substantial impact on hand function. Carotid intima-media thickness (CIMT) is a measurable index of the presence of atherosclerosis. Increased CIMT is associated with increased cardiovascular mortality and morbidity, so early diagnosis and management may improve quality of life.

Objective: To assess the relationship between carotid intima-media thickness (CIMT) and hand osteoarthritis (HOA), and to evaluate the predictors of this relationship.

Patients and Methods: One hundred Iraqi HOA patients and 100 healthy controls were included in this study. Full history was taken and complete clinical examination was done for all patients. Disease characteristics [age, sex, duration, body mass index (BMI), waist circumference, family history of HOA, smoking history, lipid lowering agent use] were also documented. Laboratory analysis included complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and lipid profile. Individuals in both groups were assessed for CIMT by B-mode ultrasonography. X-rays of both hands was taken for patients and was graded according Kellgrenand Lawrence scale.

Results: Fifty five (55%) Iraqi HOA patients have increased CIMT compared with 38 % of controls (p=0.02). There was no statistical significant association between increased CIMT and HOA radiographical grading (p=0.72). The lipid profile was the only predictor of increased CIMT in patients with HOA [p=0.02, OR (95% CI) = 3.24 (1.20-8.75)]

Conclusions: There is increased frequency of increased CIMT (55%) in Iraqi patients with HOA. Abnormal lipid profile is the only significant predictor of increased CIMT.

Key words: carotid intima- media thickness, osteoarthritis, hand osteoarthritis**.**

Fac Med Baghdad 2011; Vol. 53, No. 3
Received June, 2011
Accepted Aug.2011

Introduction:

Osteoarthritis is the mostcommon form of joint disease in humans (1). It is characterized clinically by pain and functional limitations, radiographically by osteophytes and joint space narrowing, and histopathologically by alteration in cartilage and subchondralboneintegrity (2).Hand osteoarthritis is a common joint disorder leading to considerable pain and with substantial impact on hand function (3). It occurs commonly, though not exclusively, in the context of generalized OA (4).Hand osteoarthritis subsets are nodal HOA, non-nodal HOA& erosive HOA(5). Carotid intima – media thickness **(**CIMT) is the distance between intimal-luminal interface and the medial- adventitial interface (6). It may be the most sensitive marker for the earliest stages of atherosclerosis and considered be a marker of generalized atherosclerosis(7).A number of studies have shown the association between OA and cardiovascular comorbidity (8), and even cardiovascular deaths (9).The aim of this study is to assess CIMT in Iraqi patients with nodal HOA.

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Patients and methods

Patients: A cross-sectional study was conducted on 100 patients with HOA who were randomly seen between November 2009 and June 2010 at the Rheumatology unit, Department of Medicine in Baghdad Teaching Hospital, compared to 100 healthy individuals served as a control group who were randomly selected during the period of study; matched for age and sex of patient's group. The clinical assessment was performed using a comprehensive protocol. Full history was taken from all individuals including: name, age, sex, occupation, clinical features, family history of HOA, use of lipid lowering agents, smoking history, and complete clinical examination was done for both groups. Hand osteoarthritis (HOA) was diagnosed according to American College of Rheumatology (ACR) criteria(10). Patients with HOA only were included in the study and diseases that cause atherosclerosis and increased carotid intima- media thickness (CIMT) were excluded from the study like: diabetes mellitus and hypertension.

Methods:

The atherosclerotic outcome parameters were based on CIMT and measured on ultrasound images, which were acquired with Nemio 30 (Toshiba, Tokyo, Japan). Standard B-mode images were performed with 7.5- MHz linear- type probe by a single trained sonographer. The common carotid intima-media thickness (CIMT) was acquired to a

predefined segment of each common carotid artery (CCA; right and left).Carotid intima-media thickness (CIMT) values ≥ 0.9 mm are regarded abnormal (11-13).X-rays of both hands was taken and HOA was graded according to Kellgren and Lawrence scale(14).Blood sample was obtained for measurement of serum cholesterol, triglycerides, low density lipoprotein, fasting blood sugar, erythrocyte sedimentation rate (ESR), C-reactive protein, packed cell volume (PCV), white blood cells count (WBC), kidney function tests (blood urea, serum creatinine) and liver function tests(total serum bilirubin, serum alkaline phosphatase, serum aminotransferase).Patients with elevated lipid profile are those with cholesterol > 190 mg/dl, triglycerides > 150 mg/dl, LDL > 115 mg/dl, and HDL < 40 mg/dl(15).Body mass index (BMI) and waist circumference were measured.A signed consent was taken from all individuals studied. Ethical approval was obtained from the Ethics Committee of Baghdad University, College of Medicine, Medical Department.

Statistical analysis: Statistical analysis was done using statistical package for social sciences-version 17 (SPSS v17) for windows. Association between different categorical variables was measured using Chi square test or Fisher's exact test where appropriate. Difference between continuous variables was measured using t-test. Multiple logistic regression analysis was done to find the predictors of increased CIMT in HOA patients. Findings with p value < 0.05 were considered significant.

Results:

One hundred patients with HOA, 83 females and 17 males, their mean age (58.86 ± 7.54) years, and 100 healthy control group, 80 females, and 20 males, their mean age was (57.05 ± 6.78) years were included in this study. The age and sex of patients and control are shown in Table 1 (p-value = 0.08 and 0.59) respectively, shows that no statistical difference between patients and controls.

The carotid intima-media thickness (CIMT) was increased in 55 patients (55%), and normal in 45 (45%), while it was increased in 38 healthy individuals of control group (38%), and normal in 62 controls (62%) and (p-value = 0.02) which was statistically significant, as shown in Table 2.

In Table 3, only lipid profile is a significant predictor for increased CIMT in patients with HOA. Age, duration of HOA, waist circumference, smoking history, and C-reactive may increase CIMT, but statistically not significant. Sex, family history of HOA, and body mass index (BMI) are not predictors for increased CIMT.

Table 1: Demographic characteristics of 100 patients and 100 controls n.s, not significant; n., number; %, percentile.

Variables	Patients = 100	Controls = 100	p-value
Age(years) Mean ± SD	58.86 ± 7.54	57.05 ± 6.78	0.08$^{n.s}$
Sex Male n. (%) Female n. (%)	 17 (45.9) 83 (50.9)	 20 (54.1) 80 (49.1)	 0.59 $^{n.s}$

Table 2: Distribution of CIMT in 100 patients and 100 controls.

Group	CIMT Increased n. (%) Normal n. (%)	p-value
Patients =100 **Controls = 100**	55 (55) 45 (45) 38 (38)62 (62)	0.02*

***p-value is significant; n., number; %, percentile; CIMT, Carotid intima-media thickness.**

Table 3: Multiple logistic regression analysis of predictors for increased CIMT in 100 patients with HOA.

Variables	OR (95% CI)	p-value
Age (year)	1.05 (0.98-1.12)	0.15
Sex	0.99 (0.27-3.67)	0.99
Duration (year)	1.26 (0.91-1.75)	0.16
Waist circumference (cm.)	1.04(0.97-1.11)	0.29
Lipid profile	3.24(1.20-8.75)	0.02*
Smoking history	1.47(0.40-5.44)	0.70
Family history of HOA	0.77(0.23-2.53)	0.66
CRP	1.32 (0.28-6.15)	0.73
ESR (mm/hr.)	0.98 (0.94-1.02)	0.27
HOA grade	1.34 (0.27-6.63)	0.72
BMI (Kg/m^2)	0.92 (0.78-1.08)	0.30

*** P-value is significant; OR, odd ratio; CI, confidence interval. All listed variables above were entered at the same equation.**

Discussion:

In the present study, we found a significant association between CIMT and HOA. Possible explanation is that: the vascular pathology is an integral part of osteoarthritis process, possibly contributing to the initiation or progression of HOA, in which a suggestive pathway that OA leads to a state of hypercoagulation and hyperfibrinolysis, and subsequently to circulatory disturbances in the subchondral bone contributing to the perpetuation of cartilage destruction and the pathophysiological process of OA(16).Also, in view of strong genetic inheritance of HOA, genetic factors can contribute to this relationship(17, 18). The KLOTHO gene, which codes for an anti-aging protein have recently been implicated both as a susceptibility factor for HOA in women (19), and as a candidate gene for atherosclerosis (20). Up to the best of our knowledge, this is the first cross-sectional study investigating CIMT in Iraqi patients with HOA. In this study, we observed an increased frequency of increased CIMT in patients with HOA compared controls, this finding agreed with previous studies done by Jonsson*etal*(11)and Peter *et al*(21). In our

study, increased CIMT is not significantly associated with HOA radiographic grading, which contrasted with the Jonsson*et al* (11); that showed linear and significant association, this may be due to larger study population in that study and racial differences. This study showed that only dyslipidemia is a significant predictor for increased CIMT in patients with HOA that agreed with previous study by Signorelli *et al*(22). In the present study: we found that age, duration of HOA, waist circumference, smoking history, and HOA grade may increase CIMT but statistically not significant. In this study, we found no significant association between CRP and increased CIMT that agreed with Jonsson*et al* (11). Also: sex, family history of HOA, ESR, and BMI were not predictors of increased CIMT. Inflammatory diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are associated with accelerated atherosclerosis and increased cardiovascular morbidity and mortality, in previous study by Salmon and Roman (23) found that the presence of carotid atherosclerosis was associated with disease duration in both RA and SLE, which contrasted with our study. This might be explained by smaller studied sample in our study and in OA: synovial inflammation is mild, chronic, and nonspecific (1). In patients with primary antiphospholipid syndrome, Medina *et al* (6) observed increased prevalence of increased CIMT that was not associated with smoking and BMI; which agreed with our study. The suggestion that OA is associated, or is part of, the metabolic syndrome may be of clinical relevance and an important finding as it demonstrates another potential etiology in the development of more effective treatments to inhibit the progression of OA. We associated an indirect sign of the metabolic syndrome, the CIMT, with HOA. The main limitations of our findings are the small size of the studied sample, and being a cross sectional study has limited the conclusions regarding cause and effect relationship between HOA and vascular pathology. We recommend proper attention to the diagnosis and management of atherosclerosis in HOA patients to prevent cardiovascular morbidity and mortality and to improve their quality of life.An association between HOA and metabolic syndrome should be considered in a study in the future.

Conclusions:

There is increased frequency of increased CIMT (55%) in Iraqi patients with HOA.Abnormal lipid profile is the only significant predictor of increased CIMT.

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