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The Association between Type 2 Diabetes Mellitus and Knee Osteoarthritis in Patients in Baghdad Medical City

ABSTRACT

Objective: This study was conducted to investigate the prevalence of knee osteoarthritis in Iraqi patients with type 2 diabetes mellitus in comparison to non-diabetic controls.

Patient and methods: A case control study was conducted on 50 patients; known cases of type 2 diabetes mellitus, whose ages range between 40 - 70 years old were randomly enrolled in the study. Another group consists of 50 patients non diabetics, matched for age with the patients' group, and was kept as control. Only diabetic group was subjected to measurement of fasting blood sugar and HbA1c was done for patients' group to evaluate glycemic control. X-ray of the weight bearing bilateral knee joints were obtained from antero-posterior aspect. The Kellgren and Lawrence system was used to classify the severity of osteoarthritis using five grades. Quality of life and disease impact was assessed by using Western Ontario and McMaster Universities Osteoarthritis Index.

Results : The current study revealed that 25% of Iraqi diabetic type 2 patients had osteoarthritis and grade 1 of Kellgren Lawrence System was equal in both groups (34%) while grade 2 and 3 were higher in diabetic group (40%, 10%) respectively and (22%, 4%) in control group.

Conclusion

- Patients with type 2 diabetes mellitus had a higher prevalence of osteoarthritis

Compared with non-diabetic controls although statistically was not significant.

- Type 2 DM can be considered as a predictor for the development of OA

of the knee independent of age and other known risks for OA.

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Introduction:

Osteoarthritis (OA) is a chronic progressive degenerative joint disorder (1) with characteristics gradual loss of articular cartilage combined with subchondral bone thickening, bony overgrowth (osteophyte) at the joint margins along with mild nonspecific synovial inflammation (2) thus disrupting normal biomechanics of knee joint leading to persistent pain, shortly lasting stiffness, deformity and instability are seen in advanced cases (3-6).

OA is the most prevalent joint disease and leading cause of walking disability among elderly (7,8).Although the precise etiology remain unclear(9) the main risk factors are well known and include older age ,obesity ,female sex ,joint alignment and genetic predisposition(10) knee OA target the patellofemoral and medial tibiofemoral compartment(11).

Although the exact pathophysiology of joint degeneration still poorly understood , increase in mechanical stress and changes in biochemical factors within the affected joints are thought to be responsible for progression of the disease .It is a complex multifactorial process involving cartilage catabolism and anabolism as well as changes in the synovium, subchondral bone and tendons .Chondrocyte regulate cartilage metabolism (Homeostasis of extracellular matrix) is mainly done by enzymes secreted from chondrocyte .As a consequence of mechanical and biochemical events , imbalance between synthesis and degradation of articular cartilage matrix result in clinical OA .Advanced molecular studies emphasized that there is an ongoing inflammatory process in its pathophysiology(12-16).

Relation between DM and OA:

Several epidemiological studies have identified a strong association between T2DM and knee OA .As both diseases share over weight and obesity as strong common risk factors. One of the main underlying mechanisms

causing OA in T2DM patient thought to be the increased mechanical load on weight bearing joints especially the knee (17, 18).Impaired joint proprioception has been reported in OA and postulated to be a result of dysfunctional articular mechanoreceptors and reduced muscle spindle sensitivity in weak and atrophied muscles around the joints (19). Thus, impaired sensation in OA and diabetic neuropathy may conceal the perception of pain and further perpetuate joint damage by allowing constant harmful mechanical workloads.

T2DM has a pathogenic effect on OA through 2 major pathways: 1) Chronic hyperglycemia, which induces oxidative stress, overproduction of proinflammatory cytokines and AGEs in joint tissues; and 2) Insulin resistance, which could play a role locally but also through the systemic low-grade inflammatory state (20). Leptin, a major adipokine secreted mostly by adipose tissue, is able to promote chondrocyte apoptosis and also increase cytokine and MMP production by chondrocytes (21). An insulin-resistant state and obesity are also associated with elevated free fatty acids (FFAs), which may modulate OA progression (22).

Patients and Methods

A case control study conducted at outpatient clinics in Baghdad Teaching Hospital. A total of 50 (35 females) Iraqi patients who were known cases of T2DM diagnosed according to ADA criteria (23) with more than or equal to 6 months disease duration and age between (40-70) years. We recruited men and women aged above 40 years and below 70 non diabetic with symptomatic knee osteoarthritis as defined by American college, confirmed by radiograph for target knee joint and staged by Kellgren and Lawrence staging scale. The degree of glycemic control was evaluated by conducting an HbA1c test, the level above 6.5 was considered as uncontrolled diabetes based on the recommendations of ADA. Knee osteoarthritis assessment: the presence

of knee pain was defined by asking the participant if they had experienced knee pain for > 1 month of the past 3 months .Plain x-ray of the weight bearing bilateral knee joint were obtained from the anteroposterior aspects . The severity of osteoarthritis was assessed according to Kellgren Lawrence (KL) grading system .The Kellgren Lawrence uses four radiographic features: joint space narrowing, osteophyte, subchondral sclerosis and deformity (24). Quality of life and disease impact assessment was done by using Western Ontario and Mc Master Universities Osteoarthritis Index (WOMAC) (25).WOMAC is a self-administrated health status measure that assesses the dimensions of pain, stiffness and function. The WOMAC consist of 24 item divided into 3 subscales (26). Physical activity measurement: the leisure time – physical activity index (27) is a frequently used indicator of physical activity at the population.

Patients with the following features were excluded: Inflammatory and autoimmune disease (SLE and RA), malignancy, patients who underwent knee surgery,history of knee trauma, post infectious arthropathy,gout and Pseudo gout crystals,endocrine disorders (acromegaly, thyroid disease, cushing syndrome) and history of previous local injection.

Results

The current study involved 100 individuals divided into two groups of 50 individuals .Mean age of diabetic patients was 55.26±7.99 years, while mean age of control was 53.68±6.274 years. The mean BMI of diabetic patient was 30.67±4.1 and BMI of control was 33.75±5.7.Morbid obesity was reported in 18%, 50% in diabetic and control respectively. An eighty eight and 96% were married in both diabetic and control groups. A 50% and 60% had primary education in both groups, only 12% and 10% were post graduated and had college education. Sixteen percent and 24% were smokers in both groups respectively as shown in table1.

Table 1 Basic sociodemographic characteristics of diabetic patients versus control

	Patient		**Control**		**P –Value**
Age (years)	Number	Percentage	Number	Percentage	
40-49	10	20 %	15	30 %	
50-59	26	54 %	23	46 %	0.196
>60	14	26 %	12	24 %	
Mean±SD	55.26±7.99		53.68±6.274		
Gender					
male	15	30 %	10	20 %	1.000
Female	35	70 %	40	80 %	
Education					
illiterate	19	38 %	15	30 %	0.851
Primary	14	28 %	17	34 %	
Secondary	11	22 %	13	26 %	
College, post graduate	6	12 %	5	10 %	
Smoking					
Non-smoker	42	84 %	38	76 %	0.33
Smoker	8	16 %	12	24 %	
BMI Kg/m²					
Normal	3	6 %	3	6 %	
Overweight	20	40 %	12	24 %	0.54
Obese	18	36 %	10	20 %	
Morbid obesity	9	18 %	25	50 %	
Mean±SD	30.67±4.1		33.75±5.7		
Marital Status					
Single	1	2 %	1	2%	
Married	44	88 %	48	96 %	
Widow	3	6 %	1	2 %	
Divorced	2	4 %			
Occupation					
Unemployed	31	62 %	41	82 %	
Employed	14	28 %	7	14 %	0.76
Retired	5	10 %	2	4 %	

SD:standered deviation,
P-Value:probability value,
BMI:body mass index,
Kg:kilogram ,m:meter.

The diabetic patients were uncontrolled chronic patients, and the FBS reported among such patients were high as 200 mg/dl. Higher level of glucose was observed among IDDM and NIDDM patients (241, 199.8 mg/dl) respectively as shown in table 2.

Table 2 Clinical characteristics of DM patient

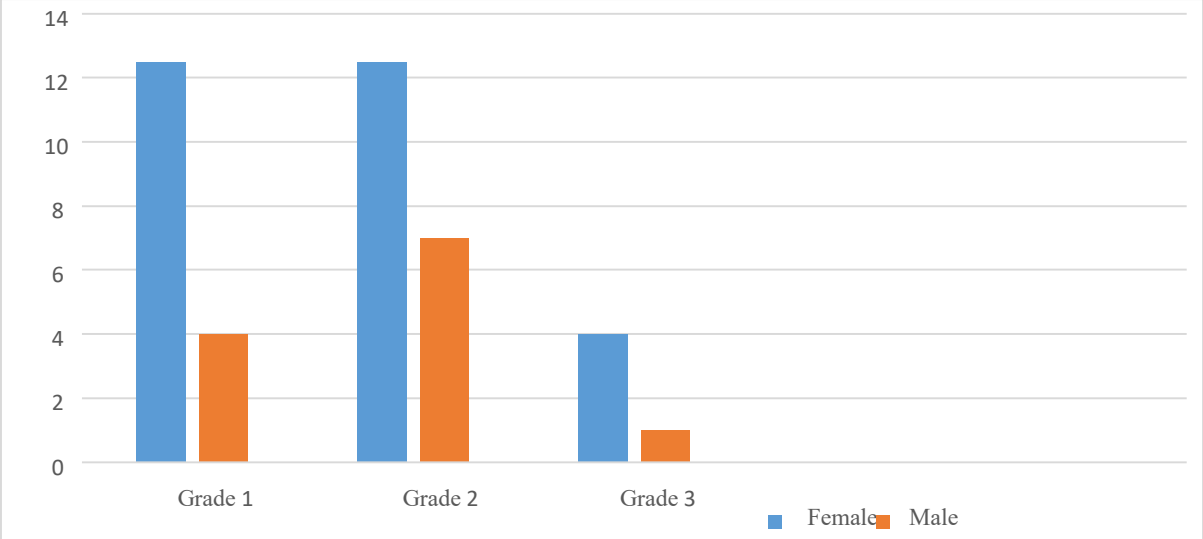
	Frequency	**Percentage**
Duration of DM		
< 1 Years	5	10 %
1 – 10 Years	31	62 %
> 10 Years	14	28 %
Family history		
No family hx	16	32 %
+V Family hx	34	68 %
Complications		
Absence of hypertension	25	50 %
Presence of hypertension	25	50 %
Type of Treatment		
No Tr.	2	4 %
Oral Tr.	38	76 %
Insulin	7	14 %
Mixed	3	6 %
HbA1bc		
$<_{6.5}$	1	2 %
$>_{6.5}$	49	98%
FBS < 126	2	4 %
>126	20	96 %

Grade 1 joint space narrowing was equal in both groups (34%) While grade 2 and 3 had 50%, 26% Kellegren-Lawrence scale respectively as shown in table 3.

Table 3 X-ray grading according to Kellgren Lawrence scale

X-ray	**Patient**		**control**		**P-value**
	Number	Percentage	Number	Percentage	0.94
Normal	8	16 %	19	38 %	
Grade 1	17	34 %	17	34 %	
Grade 2	20	40 %	11	22 %	
Grade 3	5	10%	2	4%	
Grade 4	0		1	2 %	

Figure 1 Bar chart demonstrate higher prevalence of all grades of Kellgren Lawrence grading in female group.



Discussion

The overall prevalence of OA in diabetic patients in the current study was 25% in comparison to Italian study 17% this may be due to different factors such as ethnic/racial factors, obesity is another complex and multifactorial disorder explained by overloading of weight bearing knee joints (94% were

overweight and obese in current study) and educational level (88% were illiterate and with primary education) (28). Per contra, there is increased susceptibility to develop arthritis in those with T2DM, which is supported by observations of higher prevalence of arthritis in those with T2DM (52%) compared to those without it (27%) (29).Both groups were matched concerning the number and their ages as confirmed statistically by the absence of significant differences between the studied groups. This matching of individual group's number, and age may exclude any effect of these parameters on the results of the study.

The mean age of the patients was 55.26± 7.994 year ranging from 40-70 years our patient were younger than those reported by Italian study which was with mean age 61 years (28), the duration of the diabetes disease was 10.1 years (30). In both studies female patients were more likely to have knee OA than males (70 % in current study).The observed higher association in female patients might be attributed to various factors, including anatomical differences as well as genetic, hormonal issues, kinematic, and kinetic characteristics (31, 32). It was known that both T2DM and OA is more prevalent in people above 55 years (33, 34), which was reflected by the co-occurrence in the current study. However, the high prevalence at the age group of 40-50 suggests that young adult are also susceptible. Notably, the higher association between DM and OA in non-obese patient in this study is contrary to previous reports showing obesity as a possible confounder (35, 36). Interestingly, BMI was not significantly different among KOA and non-KOA groups; however, we do not underestimate the influence of overweight and obesity as risk factors for development and progression of KOA. As stated before by Nieves-Plaza et al, T2D shares some common characteristics to OA such as its chronic evolution and association with age, overweight, and obesity; for this reason, an increase in mechanical load on knee is the underlying mechanism causing

damage to articular cartilage in weight-bearing joints(37). However, some studies suggested T2D as an independent risk factor with a metabolic role for developing KOA. At this respect, a possible explanation to our findings is that some shared environmental factors may influence the development of KOA, T2D, and obesity (38). Therefore, an association between KOA and BMI may be the result of an interaction between other determinants such as gender, genetic, and hormonal (39).We conclude that our study may suggest a potential association between T2D and primary KOA, which may be independent of age, BMI, gender.

The diabetic patients in current study were uncontrolled chronic patients, and the FBS reported among such patients were high as 200. Higher level of glucose was observed among IDDM and NIDDM patients (241,199.9mg/dl, respectively).The elevated FBS in the diabetic patients demonstrated in the present study may add some light on the fact that the majority of prolonged duration of diabetic with uncontrolled FBS may contribute to the appearance of diabetic complications. The existence of a significant positive Correlation between FBS and osteoarthritis (JSN and osteophyte) in both knee joints of diabetic group is an indicator of the probable effect of diabetes in the occurrence of osteoarthritis. In a large study on osteoarthritis including 1026 patients, the mean fasting glucose concentration was higher in subjects with osteoarthritis (OA) than in subjects without OA (40).The researcher concluded that T2DM predicted development of severe OA independent of age and BMI and this was applied in the current study as FBS ranging between 198-288 mg/dl associated with higher incidence of grade2 and grade3 osteoarthritis. (41, 42). Although the link between OA and T2D has been questioned, some studies have demonstrated that chronic hyperglycemia may induce damage in articular cartilage through several pathways (43, 44). Also, some studies

have reported that T2D is associated to progression and severity of OA, as an independent risk factor or as a component of Mets) 45, 46). In addition, some studies have also analyzed the association between OA and T2D, including some comorbidities and markers of glycemic control such as HbA1c and duration of diabetes (46).Another interesting finding is the high proportion of patients with knee osteoarthritis who had hypertension, these results are in accordance with results of a large survey showing that 40% of patients with osteoarthritis have hypertension as compared to general population. We observed more severe subchondral plate and articular cartilage damages in knee OA patients with type 2 diabetes and hypertension as compared to the subjects without these comorbidities. These findings further strengthen the concept of a strong metabolic component in the pathogenesis of OA. It has been theorized that hypertension might affect OA via narrowing of blood vessels and subchondral ischemia, which would initiate cartilage degradation (47, 48). Although several studies demonstrated higher prevalence of OA in individuals with hypertension (7072).In current study grade 1 JSN was equal in both groups (34%) while grade 2 and 3 were high in diabetic group (40%, 10%) respectively and (22%, 4%) in control group.

Grade 1 JSN was higher in diabetic group, while grade 2 and grade 3 JSN was only observed in diabetic group. (49). The differences between 2 studies may be attributed to higher number of Patients involved in the later study and the age limited between 40-50 years.

Conclusion

- Patients with type 2 diabetes mellitus had a higher prevalence of osteoarthritis compared with non-diabetic controls although statistically was not significant.
- Type 2 DM can be considered as a predictor for the development of OA of the knee independent of age and other known risks for OA.

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