Association between Knee Osteoarthritis and Type 2 Diabetes Mellitus

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ABSTRACT

Background: Osteoarthritis is the most common cause of musculoskeletal disability and it is one of the most common joint disorders in the elderly. Diabetes mellitus affects connective tissues in many ways and causes different alterations in periarticular and skeletal systems.

Aim: The aim of the present study was to evaluate the association of knee osteoarthritis and type 2 diabetes mellitus.

Patients and Methods: The present study adopted a case control design. It has been approved by the Regional Research Committee of Ninevah Directorate of Health, and the Scientific Research Committee of the College of Medicine, University of Mosul. It was performed during the period between 1st of November 2011 and 1st of June 2012 in Al-Waffaa Center for Diabetes and Endocrinology, and in the Rheumatology Outpatient Department attached to Ibn Sina Teaching Hospital. Participants included 65 known cases of type 2 diabetes mellitus, whose ages range between 40 - 50 years old, and were randomly chosen. Another group consisted of 65 patients non diabetics, matched for age with the patients group, and was kept as control group. Both studied groups were subjected to the measurement of fasting blood sugar and HbA1c was done for patients group to evaluate glycemic control. X-ray examination of both knees were performed for both groups taken in standing position (stress position), the findings were recorded according to the severity of osteoarthritis found in the examination.

Results: Data obtained from the present study revealed that there was a significant difference; regarding knee joint space narrowing grading i.e. occurrence of grade 1 knee joint space narrowing was higher in diabetic group than non diabetic one, while grade 2 and grade 3 knee joint space narrowing were noted to occur only in diabetic group. The present study revealed that diabetic group patients have high numbers of osteophytes in grades 1, 2, 3 and 4. This study also exposed that diabetic group patients have high numbers of subchondral sclerosis than non-diabetic one.

Conclusions: There may be a possible association between diabetes mellitus type 2 and development of osteoarthritis of the knee joint.

Key Words: type 2 diabetes mellitus, osteoarthritis, knee joint

INTRODUCTION

Diabetes mellitus (DM) affects connective tissues in many ways and causes different alterations in periarticular and skeletal systems (¹).
Several musculoskeletal disorders have been described in diabetic patients who can be divided into three categories: disorders which represent intrinsic complications of diabetes, such as limited joint mobility or diabetic cheiroarthropathy, stiff hand syndrome, and diabetic muscular infarction.

Arthritis is among the leading causes of disability, and osteoarthritis (OA) is the most common type of arthritis \(^\text{(2)}\). The population burden from arthritis is considerable with an estimated 48 million people in the US, 8 million in the United Kingdom and 108 million across Europe suffering from some form of this condition \(^\text{(3-6)}\).

Knee OA is a slowly developing chronic disease that has a multifactorial origin. A variety of etiologic risk factors and path physiologic processes contribute to the progressive nature of the disease and serve as targets of behavioral and pharmacologic interventions. Although several factors including obesity, acute joint injury and occupational factors are important in its pathogenesis \(^\text{(7-9)}\), a modest but significant genetic effect for knee radiographic osteoarthritis (ROA) has been reported in most studies \(^\text{(10-11)}\).

Disability in knee OA is influenced by many factors including pain, increasing age, decreasing educational status, obesity, female gender, co-morbidity, and quadriceps muscle weakness. The role of psychosocial factors, notably depression and anxiety, is less clear \(^\text{(12)}\).

Long term complications of diabetes include retinopathy, renal failure, peripheral neuropathy with risk of foot ulcers, amputation, and Charcot joints. Furthermore, autonomic neuropathy causing gastrointestinal, genitourinary, cardiovascular symptoms and sexual dysfunction. Patients with diabetes have an increased incidence of cardiovascular, peripheral vascular and cerebrovascular disease \(^\text{(13)}\).

The aim of the present study was to evaluate the association of knee OA in type 2 diabetic patients.

**PATIENTS AND METHODS**

The present study had approval from Regional Research Committee of Nineveh Directorate of Health. It was performed during the period between November, 2011 and June, 2012 in Al-waffaa Center for Diabetis Researches and Management, and in the Rheumatology outpatients clinic in Ibn Sina Teaching Hospital.

**Study design**

The present study adopted a case control design.

**Study participants**

Sixty five patients, with type 2 DM (according to American diabetes association criteria) registered in Al-waffaa Center, whose ages ranged between 40–50 years were randomly enrolled in this study. Patients with history of trauma, local and systemic inflammatory condition, previous local injection, blood diseases, gout and pseudo gout crystals and neoplastic conditions were excluded from participation in the present study.

Considering controls, 65 non-diabetics persons, matched for age and sex with the patients group, were enrolled.

**Data collection**

The main source of data was obtained directly from all the participants by the investigators. A questionnaire form was designed to record subject’s particulars. It includes name, age, duration of disease for diabetic, and biochemical profiles.
Methods

After an overnight fasting both study groups, were subjected to the following biochemical and radiological assessment:

- Biochemical profile parameters
- Fasting blood sugar (FBS) was done for the control group to exclude DM, while in patients group FBS and HbA1c were done to evaluate glycemic control, such parameters were examined at the laboratory of Ibn Sina Teaching Hospital.
- Both groups were subjected to X-ray examination of both knees in standing position, and the findings were recorded according to the severity of radiological findings.

Statistical Analysis

Standard statistical methods were used to determine the mean and standard deviation. Unpaired t-test was used to compare the results of various parameters among the studied groups. Z-test for two proportion was used if indicated, p-value =<0.05 was considered significant.

RESULTS

Table 1 shows age, FBS and HbA1c of all studied groups. There was no significant difference between age groups, and FBS of the control subjects is within normal range. Higher value were reported among diabetics, (p= 0.001).

Table 1: Mean age, fasting blood sugar and HbA1c reported in the present study

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control group N=65</th>
<th>Diabetic group N=65</th>
<th>p-value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>44.5±3.42</td>
<td>45.4±3.13</td>
<td>0.214</td>
</tr>
<tr>
<td>FBS (mmol/l)</td>
<td>5.61±0.77</td>
<td>10.0±4.18</td>
<td>0.001</td>
</tr>
<tr>
<td>HbA1c</td>
<td>---</td>
<td>8.3±1.70</td>
<td>---</td>
</tr>
</tbody>
</table>

*Unpaired t-test was used.

Table 2 demonstrates the results of grading of right and left knee joint space narrowing (JSN) in both groups. Grade 0 was more prominent in the control group. The fraction of Grade 1 JSP narrowing was higher in diabetic group. while grade 2 and grade 3 JSN was only observed in diabetic group.

Table 2: X-Ray findings (JSN) of the right & left knee joints of both studied groups

<table>
<thead>
<tr>
<th>Grades of JSN</th>
<th>Right Knee</th>
<th>p-value*</th>
<th>Left Knee</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diabetics</td>
<td>Controls</td>
<td></td>
<td>Diabetics</td>
</tr>
<tr>
<td>Grade 0</td>
<td>10</td>
<td>38</td>
<td>58.5%</td>
<td>10.8%</td>
</tr>
<tr>
<td>Grade 1</td>
<td>39</td>
<td>60.0%</td>
<td>27</td>
<td>42.5%</td>
</tr>
<tr>
<td>Grade 2</td>
<td>13</td>
<td>20.0%</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Grade 3</td>
<td>3</td>
<td>4.6%</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

*Z-test for two proportions was used.
Table 3 depicts the presence of the osteophytes of right and left knee joints in both groups. Diabetic group patients have high numbers of osteophytes in grades 1, 2, 3 and 4.

Table (3): X-Ray findings (osteophytes) of the right & left knee joints of both studied groups

<table>
<thead>
<tr>
<th>Grades of osteophytes</th>
<th>Right Knee</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diabetics</td>
<td>Control</td>
</tr>
<tr>
<td>Grade 0</td>
<td>40</td>
<td>54</td>
</tr>
<tr>
<td>Grade 1</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td>Grade 2</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grades of osteophytes</th>
<th>Left Knee</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diabetics</td>
<td>Controls</td>
</tr>
<tr>
<td>Grade 0</td>
<td>38</td>
<td>57</td>
</tr>
<tr>
<td>Grade 1</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Grade 2</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

*p-Z-test for two proportions was used.

Table 4 elicits the presence of the subchondral sclerosis of knee joints in both groups. Diabetic group patients have high numbers of subchondral sclerosis.

Table (4): X-Ray findings (subchondral sclerosis) of the knee joints of both studied groups

<table>
<thead>
<tr>
<th>Subchondral sclerosis</th>
<th>Diabetics</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Present</td>
<td>7</td>
<td>10.8</td>
<td>2</td>
</tr>
<tr>
<td>Absent</td>
<td>58</td>
<td>89.2</td>
<td>63</td>
</tr>
</tbody>
</table>

DISCUSSION

Several studies have reported an association of early OA and diabetes. Both large and small joint OA have been reported to be increased in type 2 diabetes. However, OA of the weight-bearing joints in type 2 diabetic patients may be related to their obesity and not to the diabetes itself. It is not yet known whether diabetes is a risk factor for OA independent of obesity (14).

The current study involved 130 individuals divided into two groups of 65 individuals. The study was designed to investigate the prevalence of knee osteoarthritis in patients with type 2 diabetes mellitus in comparison with non-diabetic patients. Sixty five patients type 2 diabetics, regularly followed up at the Al-Waffa Center for Diabetes management and research in Mosul, were included in the study. The mean age of patients was 45.4±3.13 years and the mean duration of DM was 10.1 years. Sixty five
apparently healthy, non-diabetic subjects their mean age 44.5±3.42 years were enrolled as control group.

The 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 groups’ number and age may exclude any effect of these parameters on the results of the study.

The diabetic patients in the present study were uncontrolled chronic patients, and the FBS reported among such patients were high as compared with the controls 10.0±4.18; 5.61±0.77mmol respectively.

Higher levels of FBS in patients with diabetes are thought that they have poor glycemic control, and will lead to cellular damage and are ultimately responsible for the complications of diabetes, including nephropathy, retinopathy, neuropathy and macro and microvascular damage. Data obtained in the present study which demonstrated high uncontrolled level of FBS was in agreement with the data reported in the majority of the previous studies. Higher levels of glucose were identified among insulin dependent and none insulin dependent patients (13.4, 11.1 mmol/l, respectively) compared to control group (4.8 mmol/l), measured FBS in 2 types of diabetic patients, newly diagnosed type 2 patients and patients on oral hypoglycemic agents. Both types of diabetic patients showed higher FBS (198 mg/dl for newly diagnosed and 185 mg/dl for the oral hypoglycemic group) compared to control group (90 mg/dl).

High FBS was also reported by Salman who demonstrated FBS of 205.47 mg/dl for the diabetic patients and 96.95 mg/dl for controls. In other studies which evaluated glycemic state of the diabetic patients by measuring FBS and HbA1C. Both parameters were identified higher than those identified in the control group.

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.

Diabetes is widely known to induce metabolic derangement leading to oxidant-antioxidant imbalance. The increase in oxidative stress may probably be related to the abnormal metabolic milieu such as hyperglycemia, dyslipidemia, and elevated free fatty acids, which commonly occur in patients who have diabetes and less than perfect glycemic control.

Hyper-glycaemia may lead to an increased generation of free radicals via multiple mechanisms such as glucose autoxidation, non-enzymatic glycation, the polyol pathway and reduced antioxidant defense system.

The pathophysiology of these disorders in diabetic patients is not obvious. It could be associated with connective tissue disorders, such as the formation of abnormally glycosylated end products or the impaired degradation of byproducts, it could be indirectly related to the vasculopathy and neuropathy commonly complicating the primary disease.

In a study done by Gorman and Krook, the prevalence of osteoarthritis in type 2 diabetic patients was found to be significantly higher than the estimated prevalence in the general population.

In a large study on osteoarthritis including 1026 patients, the mean fasting glucose concentration was higher in subjects with osteoarthritis than in subjects without OA. Diabetes was observed to be accompanied by an increased production of free radicals and/or impaired antioxidant defense capabilities, indicating a central contribution for reactive oxygen species in the onset, progression and pathological consequences of disease. The second is a symmetric, mainly sensory polyneuropathy often accompanied by autonomic neuropathy. This latter diabetic neuropathy could be one of the suggested alterations of the peripheral nervous system seen in patients with OA leading to muscle weaknesses and joint laxity. This speculates that such
peripheral nerve impairment induced by diabetes could be an added risk factor for OA in patients with diabetes.

The present study concluded that there is a significant difference, regarding knee joint space narrowing grading: grade 1 JSN was higher in diabetic group than non diabetic one, while grade 2 and grade 3 JSN were noted to occur only in diabetic group. 

This may be attributed to the fact that OA of the weight-bearing joints in the affected type 2 diabetic patients may be related to complications of long standing uncontrolled diabetes such as peripheral neuropathy and related muscle weakness.

REFERENCES