Association between diabetes mellitus and knee osteoarthritis

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Objective The aim of the current work was to estimate the metabolic and hormonal parameters in osteoarthritic patients with and without diabetes mellitus.
Methods Sixty patients who visited to the National Diabetic Center/Al-Mustansirya University between 2016 and 2017 at the age of (45–65) years were employed in this study. Fasting serum glucose, glycated hemoglobin, lipid profile, alkaline phosphatase activity, serum luteinizing hormone, and follicle stimulating hormone were determined in this study.
Results A significant increase in fasting serum glucose, glycated hemoglobin, serum insulin, and homeostasis model assessment for insulin resistance was found in osteoarthritic with diabetes mellitus as compared to osteoarthritic without diabetes mellitus group, ($P \leq 0.05$). While there was a significant reduction in serum luteinizing hormone and follicle stimulating hormone in osteoarthritic with diabetes mellitus as compared to osteoarthritic without diabetes mellitus group, ($P \leq 0.05$). There was an elevation in serum total cholesterol, triacylglycerol, low-density lipoprotein cholesterol, alkaline phosphatase activity, and luteinizing hormone/follicle stimulating hormone ratio in osteoarthritic with diabetes mellitus as compared to osteoarthritic without diabetes mellitus group, but it was not significant.
Conclusions This study revealed high levels of serum glucose and lipids in osteoarthritic patients with low levels of LH and FSH in osteoarthritic with diabetes mellitus, which is indicative of irregular feedback mechanism in the hypothalamic-pituitary axis of these diabetic patients.
Keywords osteoarthritis, type 2 diabetes mellitus, metabolic syndrome

Introduction

Osteoarthritis (OA) is a progressive joint disease, predominance mainly in elderly, manifested by erosion of the articular cartilage, hypertrophy of bone at the margins as in osteophytes, subchondral sclerosis, and sequences of biological and morphological alterations of the joint capsule and synovial membrane.[1]

Symptomatic knee OA is vastly common in elderly people universally (10%–30%), particularly in rural regions, where occupational physical burden are elevate.[2] Actuality, knee OA is more responsible than several disease for frailty in the mid of people age equal to 50 or greater. Eventually, chronic OA including lower limb joints leads to decreased physical fitness with resultant raised risk of cardiometabolic comorbidity.[3] Unfortunately, OA can be connected with early or late infection, venous thromboemboli, neurovascular injury, septic and aseptic loosening, reflex sympathetic dystrophy, periprosthetic fractures, arthrofibrosis, wound complications, and even amputation.[4]

Current proposition has recommended a new categorization for phenotyping OA that involves ageing, metabolic syndrome (MetS) events also genetic-related OA. In MetS-related OA, the mechanical influence of obesity or overweight on joints may simply clarify knee OA. Though, in this phenotype, concerning the epidemiological involvement of obesity or overweight and hand OA, several systemic parameters may contribute in the pathogenic development; like, adipose tissue yields, may have a systemic influence at a distance on joints.[5] Beyond obesity-related OA, MetS and OA have been found to be connected in selected epidemiological studies, which suggest that the other constituents of MetS, such as dyslipidemia, diabetes mellitus (DM), or elevated blood pressure might collectively or separately contribute in the pathophysiology of OA.[6] Beside this line, hyperglycemia and DM seemed to be related to OA in some epidemiological data.[7] Furthermore, the relation between the two diseases might be maintained by the injurious function of glucose excess throughout the accumulation of advanced glycation end products (AGEs), oxidative stress, and promotion of systemic inflammation.[8] This state is well demonstrated by impulsive cartilage distraction in the rat model of streptozotocin-induced DM.[9] However, other researchers have questioned the relation between DM and OA.[10]

More than 90% of people with DM are stated to be connected with main endocrine disorders, in specific hypogonadism.[11]

The aspire of the current study was to estimate the metabolic and hormonal parameters in osteoarthritic patients with and without DM.

Materials and Methods

Sixty patients who visited to the National Diabetic Center/Al-Mustansirya University between 2016 and 2017 at the age of 45–65 years were employed in this study. Demographic information were composed from all individuals. Body mass index (BMI) was calculated as weight in kilograms divided by height in meter squared. This study excluded patients who had been taking a steroid medicine and or bisphosphonate, but it included 30 diabetic patients, and they had been taking a medication for diabetes.

Blood samples were obtained from all subjects following fasting after 8 h. Laboratory tests were done, which included fasting serum glucose (FSG), glycated hemoglobin (HbA1c),

lipid profile, and alkaline phosphatase (ALP) activity; They were measured using a chemical analyzer in the medical laboratories. Serum luteinizing hormone (LH) and follicle-stimulating hormone (FSH) were measured using enzyme-linked immuno sorbent assay (ELISA).

Statistical Analysis

The results were completed by computerized SPSS (Statistical Package of Social Science) program; *t*-test was used to estimate the differences between variant groups. *P* value ≤ 0.05 is measured to be significant.

Results

Anthropometric characteristics of the studied groups appear in Table 1. A significant increase in age, BMI, systolic blood pressure (SBP), and diastolic blood pressure (DBP) was found in OA group as compared to the controls, ($P \leq 0.05$).

Table 2 displays the metabolic and hormonal parameters in OA group and the controls. There was a significant raise in FSG, HbA1c, insulin, homeostasis model assessment for insulin resistance (HOMA-IR), TC, TAG, LH, and FSH in OA patients as compared to the controls, ($P \leq 0.05$). Also, there was an elevation in serum LDL-C, ALP activity, and LH/FSH ratio in OA patients but it was not significant.

Table 3 shows the metabolic and hormonal parameters in OA with and without DM. A significant raise in FSG, HbA1c, insulin, and HOMA-IR was detected in OA with DM as compared to OA without DM group, ($P \leq 0.05$). While there was a significant reduce in serum LH and FSH in OA with DM as compared to OA without DM group, ($P \leq 0.05$). There was an elevation in serum TC, TAG, LDL-C, ALP activity, and LH/FSH ratio in OA with DM group although it was not significant.

Discussion

Osteoarthritis and DM are frequent diseases that are predicted to augment in occurrence in the worldwide. Since of the subsequent increase in the concurrence of these two diseases and a number of indications proposing that DM might unfavourably influence articular tissues and worsen OA.[12]

A further limitation is the contact of confounding aspects, particularly age and obesity. Nevertheless, the present study counts patients older than 50 years.[13]

Osteoarthritis can be alienated in post-traumatic OA, metabolic, and age-related. Metabolic OA is larger than obesity-related OA since MetS and OA are epidemiologically connected.[14]

Table 1. **Anthropometric characteristics of osteoarthritis groups and the controls**

Parameter	Osteoarthritis	Control	*P* value
Number	60	30	-
Female/male	30/30	15/15	-
Age (years)	55.30 ± 10.17	45.0 ± 9.02	0.001
BMI (kg/m^2)	30.76 ± 9.32	26.04 ± 3.65	0.05
SBP (mmHg)	141.96 ± 1.90	125.14 ± 1.20	0.001
DBP (mmHg)	85.64 ± 1.28	75.0 ± 1.58	0.001

The biochemical outcomes of this study revealed a significant raise of FSG, HbA1c, and HOMA-IR in OA with DM in contrast to OA without DM and healthy group, also a significant elevation of FSG, HbA1c, and HOMA-IR in OA group as compared to the controls.

In diabetic patients, neuropathy may also influence OA progression. Hyperglycemia might promote joint inflammation and cartilage degradation.[15]

Further, type 2 DM is characterized by improved insulin resistance (IR) that might be implicated in osteophyte advance and subchondral bone sclerosis.[16] The current study shows a significant raise of TC and TAG in OA patients in contrast to the controls. Also, a reduce in serum ALP activity in OA patients with and without DM in contrast to the controls.

Metabolic changes like irregular glucose, lipids, and cholesterol might be one of the essential reasons of OA. In OA cartilage, increase of total fatty acids, arachidonic acid, and lipids were prominent with aggregating histological lesion severity.[17] Lipid peroxidation in chondrocytes or synoviocytes was associated with cartilage matrix protein oxidation and

Table 2. **Metabolic and hormonal parameters in osteoarthritis group and the controls**

Parameter	Osteoarthritis	Control	*P* value
FSG (mmol/l)	9.81 ± 2.22	4.25 ± 0.77	0.05
HbA1c (%)	9.15 ± 2.01	3.82 ± 0.56	0.05
Insulin (µmol/l)	20.43 ± 3.67	12.25 ± 1.72	0.01
HOMA-IR	8.91 ± 5.34	2.31 ± 1.33	0.01
TC (mmol/l)	8.0 ± 2.18	3.57 ± 0.31	0.05
TAG (mmol/l)	13.41 ± 1.02	5.27 ± 1.70	0.01
HDL-C (mmol/l)	1.20 ± 0.51	1.69 ± 1.20	0.09
LDL-C (mmol/l)	4.12 ± 3.19	0.83 ± 0.35	0.50
ALP (IU/l)	2.83 ± 1.73	1.32 ± 1.20	0.06
LH (µmol/l)	22.68 ± 9.55	12.69 ± 1.02	0.01
FSH (µmol/l)	32.52 ± 8.58	7.04 ± 4.50	0.001
LH/FSH ratio	0.70 ± 0.70	1.80 ± 0.92	0.07

Table 3. **Metabolic and hormonal parameters in osteoarthritis with and without DM**

Parameter	OA with DM ($n = 30$)	OA without DM ($n = 30$)	*P* value
FSG (mmol/l)	13.65 ± 3.28	5.97 ± 1.15	0.01
HbA1c (%)	12.93 ± 2.01	5.36 ± 0.49	0.01
Insulin (µmol/l)	24.36 ± 4.99	16.50 ± 2.45	0.001
HOMA-IR	13.44 ± 8.04	4.38 ± 2.63	0.01
TC (mmol/l)	9.50 ± 2.37	6.50 ± 1.98	0.50
TAG (mmol/l)	14.62 ± 1.34	12.20 ± 0.69	0.06
HDL-C (mmol/l)	1.05 ± 0.33	1.35 ± 0.69	0.07
LDL-C (mmol/l)	5.53 ± 4.42	2.71 ± 1.96	0.50
ALP (IU/l)	2.43 ± 1.50	3.23 ± 1.96	0.06
LH (µmol/l)	19.81 ± 6.20	25.55 ± 14.90	0.05
FSH (µmol/l)	26.52 ± 4.47	38.52 ± 2.68	0.001
LH/FSH ratio	1.11 ± 0.90	0.82 ± 0.49	0.08

degradation, sustaining the function of lipid metabolism in the pathogenesis of cartilage aging.[18] The genetic expressions of cholesterol efflux, which can reduce lipid deposits in the chondrocytes, were extensively lesser in osteoarthritic cartilage, proposing that impaired expression of cholesterol regulatory genes may be a serious role in OA.[19]

The present study shows a significant raise of LH and FSH in OA patients (with and without DM) in contrast to the controls. Also, a significant reduce in LH and FSH in diabetic patients as compared to non-diabetic, which is a covenant with the study of Onah et al.[20]

Obesity and IR, situations that are frequently related to type 2 DM, could be associated with dysfunction of hypothalamic–pituitary unit.[21]

Elevated levels of tumour necrosis factor alpha and interleukin-1β in obese subjects were initiated to lessen LH secretion in animal and *in vitro* studies.[22] It is probable that there is a defect at the hypothalamo-hypophyseal level in subjects with IR, which is linked to a faulty insulin receptor/insulin action. Certainly, in mice with a selective knockout of the insulin receptor in neurons, a selective fault of hypogondotrophic hypogonadism is experimentally detected.[23]

Hussein and Al-Qaisi presented a significant decrease in serum LH and FSH of diabetic patients for both gender as paralleled to healthy individuals.[24] In this situation, LH level should be significantly greater than what is obtained considering its influence in testosterone production. A study amongst diabetics showed that in hypogonadism cases, LH and FSH levels were greatly lesser than predictable. This postulates that there is a connection between insulin/glucose and LH/FSH levels in serum, although the mechanisms by which insulin, glucose, or both control these two hormones are uncertain.[25] Additional cause for these outcomes may be as a product of extraordinary oxidative stress generated in diabetic patients, which could influence the ordinary effective of the pituitary gland and hypothalamus.

Conclusions

This study revealed high levels of serum glucose and lipids in OA patients with low levels of LH and FSH in OA with DM, which is indicative of irregular feedback mechanism in the hypothalamic-pituitary axis of these diabetic patients.

Conflict of Interest

None.

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