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The Association of Diabetes with Knee Pain Severity and Patterns in People with Knee Osteoarthritis

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ABESTRACT

Background: As one of the most common forms of joint disease, osteoarthritis (OA) causes progressive impairment in adults because of the deterioration of articular cartilage in the joints. Multiple variables, including comorbidities (such as diabetes mellitus, hypertension, obesity, and dyslipidemia), lifestyle choices, food, age, and genetics, might influence the occurrence, development, and severity of OA symptoms.

Objective: To assess knee pain severity & patterns in cases with OA & OA with diabetes mellitus.

Patients and Methods: This is cross-sectional research that was done in Benha University Hospitals on 100 cases, which were separated into two groups: Group one included fifty OA patients and group two consisted of fifty OA patients with diabetes mellitus (DM). Group two was divided into two subgroups: good control and poor control patients according to diabetes control. Knee pain was measured according to three subscales: WOMAC (The Western Ontario and McMaster Universities OA Index), KOOS (Knee Injury and OA Outcome Score) and VAS (visual analogue scale).

Results: There was a statistically significant variance amongst the examined groups concerning diabetes parameters (HbA1c, fasting glucose and two hours post prandial), Kellgren-Lawrence scale, correlation of diabetes duration with other parameters of pain in OA patients and correlation of HbA1c with other parameters of pain among OA patients with DM.

Conclusion: Our study concluded that WOMAC pain subscale was significantly increased with worsening of DM and KOOS pain subscale was significantly decreased with worsening of DM. This suggests the crucial need for management of DM to achieve better outcomes of OA.

Keywords: Diabetes, Knee pain severity, Knee osteoarthritis.

INTRODUCTION

In adults, OA causes the degradation of diarthrodial articular cartilage, which can lead to permanent impairment [(1)].

Comorbidities, lifestyle, diet, age, and genetics are only some of the variables that might impact the prevalence, development, and severity of OA symptoms [(2)]. Joint articular cartilage, subchondral bone, and synovium are all affected by OA, making it a multifaceted illness. Inflammation, both locally and systemically, at a low level, has been associated to OA [(3)].

There is evidence associating the presence of many comorbidities to more severe knee pain. Metabolic syndrome, which includes DM, high blood pressure, abnormal cholesterol levels, and obesity, has been associated to higher pain severity in people with OA of the knee [(4)].

As a chronic condition, diabetes is among the most prevalent. It now affects around 10% of the population. Insulin metabolic abnormalities are the root cause of hyperglycemia, the hallmark of DM. Oxidative stress, advanced glycated end products (AGEs), and low-grade inflammation are produced in response to prolonged hyperglycemia, both during and after meals, causing damage to blood vessels throughout the body, most noticeably in the kidneys, heart, eyes & nerves [(5)].

There is evidence that synovial angiogenesis promotes the local proliferation of inflammatory cells. There is increased synovial inflammation in diabetes in vivo models [(6)]. Increased pain perception was observed by individuals with poorly managed glycemia compared to those with well-controlled DM [(2)].

Different meta-analyses verified the epidemiological association among type two DM (T2DM) and OA, demonstrating the real presence of a higher hazard of developing OA in diabetic persons [(7)]. There is a lot of overlap between the comorbidities and hazard factors in the pathophysiology of OA and T2DM [(1)].

In terms of the health burden, they place on individuals and communities alike, OA and DM are major contributors [(8)]. This work aimed to assess knee pain severity and patterns in cases with OA and OA with DM.

PATIENTS AND METHODS

This cross-sectional study was done to evaluate pain severity & patterns in cases with OA and OA with DM in Department of Rheumatology, Rehabilitation and Physical medicine, Benha University Hospitals. The field work was carried out during the period from 1st of June to 31st of December 2022 (seven months) on OA patients who fulfilled inclusion criteria and agreed to participate in the study.

Inclusion criteria: Patients who had symptomatic knee OA: mechanical pain, swelling, reduction in the range of motion of the knee, which can make it difficult to get in and out of seats or automobiles, use the stairs, or walk, a crackling sound that can be heard whenever the knee is

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moved), radiographic signs of knee OA (according to Kellgren-Lawrence scale) and diabetic patient (according to fasting and 2 hours post prandial glucose test and HbA1c test) involved and subdivided into two groups:
Group one: Fifty cases with knee OA and **group two:** Fifty cases with knee OA and DM. The second group is classified into two subgroups according to diabetes control: Subgroup (1) with good diabetic control and subgroup (2) with poor diabetic control.

Pain was measured according to:
WOMAC [9]: Designed to estimate cases' levels of pain, stiffness & overall physical function who suffer from OA of the hip or knee.

KOOS [10]: Patient's perceptions of their own knee's health, symptoms, and functioning, as measured by their own self-reporting of the result. **VAS [11]**: That was utilized for recording the evolution of a patient's pain or to contrast the levels of pain experienced by individuals who have comparable diseases.

Exclusion criteria: Patients who had knee joint replacement, patients who had local knee injection (steroid, hyaluronic acid, plasma, platelet-rich plasma, methotrexate & growth factors in the last 6 months) and Patients with traumatic knee injury.

Operational design:
At the time of admission, the following information had been gathered from every case:
Initial assessment: Complete full history taking (Personal history involving name, age, marital status, address**,** complaint**,** present history, past history of chronic disease, DM and hypertension...) and family history of any disease.
Clinical assessment: General examination involving Vital signs (blood pressure, heart rate, temperature, respiratory rate, signs of pallor, jaundice & cyanosis, and lymph node enlargement). Local examination of knee [Inspection, active mobilization, passive mobilization, isometric muscle testing, neurovascular examination, meniscal testing, medial instability, lateral instability and tests for knee effusion (Patellar tap test and bulge, wipe, or stroke test and fluid displacement test)]. Investigations including radiological assessment (plain x-ray anterior posterior view & lateral view on knee joint on weight bearing position). Laboratory assessment (fasting blood glucose, two hrs post prandial blood glucose and HbA1c).

Knee function and pain assessment in cases with knee OA: WOMAC, KOOS and VAS.

Ethical approval: The present research was approved by Medical Ethics Committee of Faculty of Medicine, Benha University, Egypt. It is consistent with the declaration of Helsinki principles. Written consents were taken from all cases before starting the research. The study no. was MS 21-4-2022.

Statistical Analysis

The SPSS software, version 18, was utilized to conduct the analysis of the data (SPSS Inc., Chicago: Inc.). The qualitative results were explained utilizing numerical and percentage terms. For non-normally distributed data, quantitative values were presented utilizing the median (minimum and maximum), while for regularly distributed data, the mean was used. Following determining that the data are normally distributed, the Kolmogorov-Smirnov test was used and the standard deviation was calculated. The level of significance (≤ 0.05) was used to evaluate the findings that were obtained. When comparing qualitative data among groups, Chi-Square, the Fischer exact test, and the Monte Carlo tests were utilized as applicable. When comparing 2 independent groups with data that is regularly distributed, the Student t test was utilized.

RESULTS

Regarding demographic distribution of the studied groups, there was no significant variance among the two examined groups concerning age, sex & BMI. There was a significant variance among the two diabetic groups concerning DM duration (Table 1).

Table (1): Demographic distribution of the two examined groups

Variable		**OA patients** (n=50)	**OA with DM** (n=50)	**t / χ^2**	**P**
Age (years) Mean ± SD		57.42 ± 9.37	59.71 ± 10.54	1.148	0.256
Sex	Male	16 (32%)	18 (36%)	.178	.673
	Female	34 (68%)	32 (64%)		
BMI (kg/m^2) Mean ± SD		26.53 ± 3.64	27.14 ± 3.45	0.860	0.394
DM Duration (years) Mean ± SD		--	8.27 ± 5.41		

BMI :Body Mass Index, DM: Diabetes mellitus. No significant variance among the two examined groups concerning age, sex & BMI. *: Significant variance among the two diabetic groups concerning DM duration

As regards knee pain of the two studied groups, there was no significant variance among the two examined groups concerning knee pain (Table 2).

Table (2): Knee pain of the two examined groups

Variable	OA patients (n=50)	OA with DM (n=50)	χ^2	P
Unilateral knee pain	29 (58%)	23 (46%)	1.442	0.2298
Bilateral knee pain	21 (42%)	27 (54%)		

No significant variance among the two studied groups concerning knee pain laterality

There was an extremely significant distinction among the two groups in FBS, 2h-PP, and HbA1c being were higher in OA with DM group (Table 3).

Table (3): Diabetes parameters of the two studied groups.

Variable	OA patients (n=50)	OA with DM (n=50)	T	P
FBS (mg/dL) Mean ± SD	76.3 ± 11.2	109.1 ± 4.17	**19.407**	**<0.001**
2h-PP (mg/dL) Mean ± SD	124.8 ± 11.67	166.48 ± 18.02	**13.728**	**<0.001**
HbA1c (%) Mean ± SD	5.32 ± 0.358	7.13 ± 0.726	**15.811**	**<0.001**

FBS: Fasting Blood Sugar, 2h-PP: 2 hours Post Prandial, HbA1c: Hemoglobin A1c. *: significant variance among the groups concerning FBS, 2h-PP, and HbA1c.

We discovered that the Kellgren-Lawrence scale for OA cases and OA with DM patients was significantly higher in OA with DM. Using the Kellgren-Lawrence scale, we found that OA patients, those with good control of their disease, and those with poor management of their disease all differed significantly being was greater in the poor control group (Table 4).

Table (4): Kellgren-Lawrence scale of the two studied groups.

Variable	OA patients (n=50)	OA with DM (n=50)	χ^2	P
Grade 1	2 (4%)	20 (40%)	**19**	**<0.001**
Grade 2	5 (10%)	12 (24%)	3.47	.062
Grade 3	38 (76%)	16 (32%)	**20**	**<0.001**
Grade 4	5 (10%)	2 (4%)	1.38	.240

*: significant difference between the groups regarding Kellgren-Lawrence scale.

There was a positive significant association among diabetes duration with VAS, KOOS, and WOMAC. (Table 5).

Table (5): Correlation of diabetes duration with other parameters among OA patients with DM.

	Diabetes duration	
	R	**P**
VAS	**.432**	**<0.001**
KOOS	**.487**	**<0.001**
WOMAC	**0.561**	**<0.001**

WOMAC (The Western Ontario and McMaster Universities OA Index), KOOS(The Knee Injury and OA Outcome Score)and VAS (The visual analog scale).*: significant correlation between diabetes duration with VAS, KOOS, and WOMAC.

This table showed correlation of HbA1c with other parameters among OA patients with DM. There was a negative significant correlation between HbA1c with VAS and KOOS. There was a positive significant correlation between HbA1c with WOMAC Table (6).

Table (6): Correlation of HbA1c with other parameters among OA patients with DM

	HbA1c	
	R	**P**
VAS	**-0.394**	**<0.001**
KOOS	**-0.367**	**<0.001**
WOMAC	**0.412**	**<0.001**

HbA1c: hemoglobin A1c, VAS: Visual Analogue Scale, KOOS: The Knee Injury and OA Outcome Score, WOMAC: The Western Ontario and McMaster Universities OA Index.*: significant correlation between diabetes duration with VAS, KOOS, and WOMAC.

Table (7) showed correlation of WOMAC with other parameters among OA patients with DM. there was a positive significant correlation between WOMAC with DM duration, HbA1c, VAS, KOOS, and K-L scale.

Table (7): Correlation of WOMAC with other parameters among OA patients with DM.

	WOMAC	
	R	**P**
Age	.100	.489
BMI	.101	.484
DM duration	**.561**	**<0.001**
HbA1c	**.412**	**<0.001**
FBS	.202	.159
VAS	**.655**	**<0.001**
KOOS	**.372**	**.009**
K-L scale	**.287**	**.034**

BMI: Body Mass Index, DM: Diabetes Mellitus, FBS: Fasting Blood Sugar, VAS: Visual Analogue Scale, KOOS: The Knee Injury and OA Outcome Score, WOMAC: The Western Ontario and McMaster Universities OA Index, K-L: Kellgren-Lawrence scale, *: significant correlation between WOMAC with DM duration, HbA1c, VAS, KOOS, and K-L scale.

DISCUSSION

One of the most frequent degenerative disorders of the articular cartilage, OA that is characterized by hypertrophic alterations in the bone. Genetics, feminine sex, trauma history, advanced age, and obesity are other risk factors [(12)]. Joint discomfort is a typical sign of OA. We call this increase in discomfort with exercise the "gelling phenomenon," and it typically occurs after a period of rest. Morning stiffness from OA may last up to 30 minutes, however rheumatoid arthritis might induce stiffness that lasts 45 minutes or more. The patient may experience joint locking or instability. Loss of function occurs as a result of these symptoms, with cases reducing their activities of daily living due to pain and stiffness [(13)].

Regarding demographic data of the studied groups, there was no significant variance concerning age, sex & BMI. There was a significant variance among the two diabetic groups concerning DM duration. Our study is consistent with **Rehling *et al.*** [(14)] who aimed to examine whether if people with diabetes are more likely to experience musculoskeletal discomfort, OA, osteoporosis, and rheumatoid arthritis.

The study stated that age (years) was 59.71 ± 10.54 in diabetes group and was 57.42 ± 9.37 in no diabetes group. Men were 32% and women were 68% in no diabetes group. However, men were 36% and women were 64% in diabetes group. This is in agreement with our study **Rahman *et al.*** [(15)] who reported that the average age of OA cases was 61, and 60.5% of the cases were females. The mean follow-up time was 12 years, and the diabetes incidence rate (95% CI) was 11.2%.

As regards knee pain, there was no significant variance among the two examined groups concerning knee pain. This is consistent with **Alenazi *et al.*** [(16)] who investigated the relationship of diabetes with knee pain severity and distribution in people with knee OA utilizing data from the OA initiative and found similar results to ours.

There was an extremely significant distinction among the two groups in FBS, 2h-PP, and HbA1c.; all of these are measures of diabetes. Our findings corroborate with those of **Eitner *et al.*** [(17)] who had determined whether or not DM amplifies sensations of pain in human knees with OA. They found a significant variance in HbA1c levels among diabetes and non-diabetic subjects ($p < 0.001$). **Rogers-Soeder *et al.*** [(18)] assessed the relationships between DM and indicators of aberrant glucose metabolism with incidence radiographic knee OA, while also taking into account the participants' body mass index (BMI). There was a statistically significant distinction in fasting blood glucose levels among individuals with no history of diabetes at study entry and those with a history of diabetes at study entry ($p < 0.001$).

We discovered that the Kellgren-Lawrence scale for OA cases and OA with DM patients was significantly higher in the OA with DM. Also, greater in the poor control group compared to the good control group. While, **Chanchek *et al.*** [(19)] used MRI-based T2 relaxation time measurements to examine the relationship between the existence and severity of DM and articular cartilage composition, they found no correlation between DM and structural knee abnormalities, which runs counter to our findings. There was no significant change in Kellgren-Lawrence score ($p>0.05$) among diabetic and non-diabetic OA cases, according to the study. Previous research has demonstrated that once advanced cartilage loss happens, as demonstrated in individuals with a greater KL score, T2 values may be limited for the assessment of cartilage degradation, so this could explain why there was disagreement in the research. This could be because of the exclusion of subjects with moderate to advanced knee OA (Kellgren-Lawrence [KL] score ≥ 3) or missing KL score (n=1104).

Our findings revealed that there was a positive significant association among diabetes duration with VAS, KOOS, and WOMAC. There was a negative significant association among HbA1c with VAS and KOOS. There was a positive significant relationship among HbA1c with WOMAC. There was a positive significant relationship among WOMAC with DM duration, HbA1c, VAS, KOOS, and K-L scale.

Age and obesity, two frequent risk factors for both OA and T2DM, are particularly detrimental to functional capacity. Alterations in endocrine function, loss of skeletal muscle function (a reduced lean mass and muscle strength), and poor balance are just a few of the aging-related physiologic changes that lead to declines in functional ability and overall health, along with changes in lifestyle, for example reduced physical activity and nutritional deficiencies. Weight-bearing joint discomfort and an increased sense of pain throughout physical exercise have both been linked to obesity in a number of studies. It has been established that the degree of disabilities in obese people is closely correlated with the amount of pain they experience, which is likely mediated by elevated systemic inflammation. As a result, functional limitations are exacerbated and mobility is reduced due to obesity-related issues such as elevated pain, muscular weakness, and joint misalignment [(20)].

Even though diabetes and hyperglycemia have complicated effects on joints, **King *et al.*** [(5)] have provided a detailed explanation of those effects on bone, synovium, articular cartilage, tendons, and ligaments. Insulin insufficiency in type 1 diabetes (T1DM) reduces osteoblastic bone production and inhibits bone mass gain throughout growing up: moreover, age may directly and indirectly modify matrix characteristics. In contrast, type

2 diabetes is characterized by a constellation of variables that together inhibit osteocyte activity, change bone turnover, and degrade collagen characteristics. Increased amounts of adipokines, inflammatory cytokines and prostaglandins in DM tissues may contribute to the significant synovitis observed in OA. Inflammation in DM and OA may also be caused by signaling through toll-like receptors and other innate immune pathways [(21)]. Matrix catabolism is stimulated and reactive oxygen species generation is elevated in a hyperglycemic setting. The importance of normal glucose transport within cells in these conditions, and how its disruption, as in DM, can lead to excessive oxidative stress and tissue damage and hasten the progression of OA, was discussed at length in two studies by **Rosa *et al.*** [(22)]. Impaired function of ATP-sensitive K+ channels, which relate GLUT channels to intracellular ATP/ADP levels and membrane potential, may contribute to the detrimental consequences of excessive glucose. Consequently, OA worsens with increasing DM duration.

CONCLUSION

Our study concluded that WOMAC Pain subscale was significantly increased with worsening of DM and KOOS pain was significantly decreased with worsening of DM. This suggests the crucial need for management of DM to achieve better outcomes of OA.

DECLARATIONS

- **Consent for publication:** All writers consented to submission.
- **Availability of data and material:** Available
- **Competing interests:** None
- **Funding:** No fund
- **Conflicts of interest:** Conflict-free.

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