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Could Metabolic Risk Factors Affect the Severity of Knee Osteoarthritis in Type-2 Diabetes Mellitus Patients? A Cross-Sectional Study

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Abstract

Introduction: Osteoarthritis (OA) is a common joint disease with varying degrees of severity. Patients with type-2 diabetes mellitus (T2DM) demonstrate a higher prevalence of OA, and several mechanisms have been proposed to explain the severity of OA in DM. In this study, we aimed to explore the effect of metabolic risk factors on the severity of knee OA in T2DM patients. **Methods**: This cross-sectional study was conducted in 2018 and included 57 patients with T2DM. Data were collected in terms of demographic variables and metabolic tests. After obtaining a medical history and examination, anteroposterior (AP) and lateral radiographs of both knees were taken, and the severity of OA was classified using the Kellgren-Lawrence (KL) classification system and categorized into two groups. Group A demonstrated patients with mild OA equivalent to grade 1 or 2 KL and group B showed moderate to severe OA (grade 3 or 4 KL). **Results**: A total of 57 patients with T2DM enrolled in the study, of which 32 patients exhibited grade 1 or 2 KL (group A) and 25 with grade 3 or 4 KL (group B). The mean age and mean body mass index (BMI) were higher in group B compared to group A, and the differences were statistically significant (P-value = 0.01). As with the other metabolic tests, the mean serum hemoglobin A1C (HbA1c) level was not statistically significant (P-value = 0.34). **Conclusion**: The data revealed that metabolic factors play a minor role in the severity of OA in patients with DM and that these changes are primarily influenced by increasing BMI and age.

Keywords

Osteoarthritis Severity, Diabetes, Metabolic Factors

1. Introduction

Osteoarthritis (OA) is a common degenerative disease of the cartilage and bones, with a multifactorial etiology [1]. The knee is the most frequently affected joint by OA [2]. Numerous studies have been conducted to ascertain the modifiable and non-modifiable risk factors associated with knee OA, and evidence indicates that increasing age and weight are strongly associated with knee OA [3] [4] [5] [6].

OA and type-2 diabetes mellitus (T2DM) co-occur due to aging and obesity [7]. Additionally, various studies have established a role for T2DM in developing OA based on pathophysiologic mechanisms [8] [9] [10] [11]. The coexistence of T2DM and knee OA, according to previous research, also increases pain perception, regardless of the radiological severity of obesity [12] [13]. There is a correlation between symptomatic knee OA and metabolic factors [14], and some studies demonstrate that hyperglycemia contributes to joint destruction in knee OA [15] [16] [17]. However, one study suggests that impaired glucose significantly affects hand OA, but no correlation with knee OA [18].

Fasting plasma glucose (FPG) and hemoglobin A1c (HbA1c) are the two clinical tests used to determine the status of blood sugar, with HbA1c measuring the glucose level over the previous two to three months [19]. Murata *et al.* reported that patients with HbA1c ≥ 6.5 have a higher prevalence of knee OA [20]. In comparison, Nielen *et al.* demonstrated that patients with HbA1c > 9.5 have less severe OA, with approximately half of them requiring no surgery [21]. Furthermore, a systematic review revealed a negligible association between impaired glucose and the progression of knee OA [22].

The plain X-ray is still the gold standard for diagnosing OA. Kellgren-Lawrence (KL) is a grading system that is widely used in clinical and research settings [23]. While KL has some limitations, when combined with a comprehensive examination, it is suitable for detecting OA or determining its severity [24].

To date, various studies have attempted to explain the relationship between metabolic factors and the severity of knee OA, but the results remain inconsistent.

The present study aimed to investigate the effect of metabolic risk factors on the severity of knee OA in T2DM patients.

2. Methods

2.1. Study Participants

This cross-sectional study was conducted in 2018, and 57 subjects were enrolled with T2DM who met the American Diabetes Association's diagnosis criteria (ADA2022) [25] for T2DM. Participants had diabetes for a minimum of ten years. Data were collected from Endocrinology Research Center in Isfahan, Iran.

2.2. Inclusion and Exclusion Criteria

The participants were over the age of 50, had been under the supervision of the

research center for at least five years, and their metabolic tests had been completed. All cases had a history or positive physical examination of knee OA based on the American college of rheumatology (ACR) criteria [26]. Patients with type-1 DM, a history of inflammatory arthritis with elevated ESR/CRP, and who declined to participate in the study were excluded. The study protocol was approved by the ethical committee of Isfahan University of Medical Sciences, and all participants signed an informed consent form.

2.3. Data Extraction

The knee X-ray was taken from both sides, including the anteroposterior (AP) and lateral views in the upright position, and was categorized using the KL classification system [23]. Patients were divided into groups A and B. The former indicates grades 1 and 2 (possible or minimal OA), and the latter shows grades 3 and 4 (moderate or severe OA). The mean values of metabolic tests such as HbA1c, LDL, HDL, triglyceride, FBS, and BMI were obtained from health records at the time of diagnosis. However, kidney function tests were not recorded in this study.

2.4. Statistical Analysis

SPSS-26 software was used to analyze the collected data. The means and percentages were analyzed using an independent sample t-test. Additionally, the chi-squared test was employed to demonstrate an association between different groups, followed by logistic regression. A P-value ≤ 0.05 was deemed statistically significant.

3. Results

This cross-sectional study included 57 patients with T2DM. The mean age of patients in groups A and B was 59.15 ± 5.29 years and 63.52 ± 7.66 years, respectively, with a statistically significant difference (P-value = 0.01). The mean duration of disease was 13.81 ± 3.64 months in group A and 15.72 ± 5.74 months in group B. Group A comprised 32 (56.1%) subjects, 13 males and 19 females, while group B consisted of 25 (43.9%) subjects, 10 males and 15 females.

The metabolic factors were compared between the OA groups. The results indicated that the mean BMI in group A was 27.73 ± 5.6, while in group B, it was 31.30 ± 4.23, implying a statistically significant difference (P-value = 0.01). The mean HbA1c levels in groups A and B were 7.26 ± 0.34 and 7.56 ± 0.54, respectively, which was not statistically significant (P-value = 0.34). Furthermore, FBS and BS values were not statistically remarkable between the two groups (P-value = 0.69 and P-value = 0.11). Among lipid profiles, HDL was 47 ± 9.14 in group A and 45.53 ± 11.74 in group B, LDL was 98.63 ± 16.10 in group A and 96.32 ± 13.30 in group B, TG was 155.64 ± 54.67 in group A and 168.20 ± 54.95 in group B, and CL was 176.35 ± 22.132 in group A and 175.16 ± 18.99 in group B. As illustrated in **Table 1**, changes among the two groups were not statistically significant.

Table 1. Demographics and metabolic factors differences between two groups.

Variables	OA				P-Value
	Group A (KL 1, 2) N = 32		Group B (KL 3, 4) N = 25		
	Mean	SD	Mean	SD	
Age	59.15	5.29	63.52	7.66	0.01
Disease Duration	13.81	3.64	15.72	5.74	0.13
Mean of HbA1c	7.26	1	7.56	1.38	0.35
Mean of HDL	47	9.14	45.53	11.74	0.59
Mean of LDL	98.63	16.10	96.32	13.30	0.56
Mean of TG	155.64	54.67	168.20	54.95	0.39
Mean of CL	176.35	22.32	175.16	18.99	0.83
Mean of FBS	150.35	30.54	153.55	31	0.69
Mean of BS	205.45	42.84	224.13	43.48	0.11
Mean of BMI	27.73	5.6	31.30	4.23	0.01

Abbreviations: Hemoglobin A1C (HbA1C), High-density lipoprotein (HDL), Low-density lipoprotein (LDL), Triglyceride (TG), Cholesterol (CL), Fasting blood sugar (FBS), Blood sugar (BS), Body Mass Index (BMI).

The sample population was divided into four groups based on their mean HbA1c and BMI values: 1) a group with a high BMI (greater than mean) and a high HbA1c (greater than mean); 2) a group with a low BMI (less than mean) and a low HbA1c (less than mean); 3) a group with a high BMI (greater than mean) and a low HbA1c (less than mean); (more than mean). HbA1c and BMI cut-off values were 7.39 and 29.30, respectively. Subjects with both high BMI and low HbA1c were excluded. Table 2 shows a comparison of the remaining subjects. The severity of OA was significantly greater in a group with a high BMI and a low HbA1c than in a group with a high HbA1c and a low BMI (P-value = 0.01).

4. Discussion

The current findings revealed that subjects with moderate to severe OA (Group B) have a significantly higher BMI and age than those with mild OA (Group A). HbA1c, blood sugar (BS), fasting blood sugar (FBS), and triglyceride (TG) levels were also higher in the group with more severe osteoarthritis. However, the differences were not significant may be due to the small sample size. The number of OA cases with more severe radiologic involvement (Group B) was greater than that of mild OA subjects with a high BMI and a low HbA1c (Group A). By contrast, the number of patients with mild OA was higher than those with moderate-to-severe OA in the group with high HbA1c and low BMI. In other words, the only variables that had a significant effect on the severity of OA were BMI and age, while the remaining variables had no effect. According to the current

Table 2. Four groups based on their mean value of HbA1c and BMI.

Variable	Group A(KL 1, 2) N = 32	Group B(KL 3, 4) N = 25	Total	P-Value
BMI > 29.30 HbA1c > 7.39	2 18.2%	9 81.8%	11	0.01
BMI < 29.30 HbA1c < 7.39	14 82.4%	3 17.6%	17	
BMI > 29.30 HbA1c < 7.39	4 30.8%	9 69.2%	13	
BMI < 29.30 HbA1c > 7.39	12 75%	4 25%	16	

findings, the severity of OA increased in diabetes patients with a high BMI, which is a known risk factor for both T2DM and OA. Conversely, elevated HbA1c levels have little effect on the severity of knee OA.

Our results were in line with a study by Shin *et al.*, which concluded that the association between metabolic factors such as BMI, FBS, TG, HDL, and the severity of knee OA is due to extreme weight instead of the direct effect of metabolic factors. Furthermore, mechanical stress induced by greater weight plays a crucial role in the severity of OA [27]. Yasuda *et al.* demonstrated no correlation between the severity of radiographic findings and each metabolic marker separately or all together in patients with knee OA [14]. Eymard *et al.* observed a link between T2DM and radiographic changes in men with knee OA due to activation of the inflammatory responses following hyperglycemia, which caused joint destruction. On the other hand, other metabolic factors such as obesity, dyslipidemia, and hypertension were not associated with radiologic progression. As a result, they emphasized diabetes's independent role in osteoarthritis severity [28]. Another study run by Schett *et al.* obtained a similar result that DM alone is a powerful predictor of knee OA [29].

By contrast, certain studies have established a link between metabolic components and the severity of OA. Jungmann *et al.* discovered that metabolic risk factors increased cartilage degradation. They used a knee MRI to detect the changes. However, they examined the effects of multiple risk factors rather than assessing each separately [30]. Another study by Xie *et al.* demonstrated a positive correlation between metabolic syndrome and radiographic changes, including the formation of osteophytes. However, they were unrelated to the narrowing of the joint space [31]. Similar to the previous study, recent studies assessed the cumulative effect of various metabolic factors and found a direct association with knee OA severity [32] [33]. Ashmeik *et al.* stated that elevated glycemic markers are associated with more severe meniscal involvement; however, no correlation was observed between FG, HbA1C, total cholesterol, or LDL and the severity of knee cartilage construction [34]. Although in the previous study, a knee MRI was used to detect meniscal changes, which has higher accuracy and sensitivity in

diagnosing meniscal lesions than plain radiographs [35].

Numerous studies indicate that the prevalence of T2DM is higher in obese individuals [36] [37] [38] [39] and that patients with T2DM are also overweight compared to the general population [40] [41] [42] [43]. Furthermore, there is a vicious cycle between being overweight/obese and having a more severe form of OA, which means that people with more severe OA engage in less physical activity due to pain and discomfort, leading to weight gain. On the other hand, obesity increases mechanical forces across weight-bearing joints. Serum biomarkers are associated with the severity of knee OA, particularly in individuals with a BMI greater than >30, and adropin is a peptide hormone that decreases in a high BMI [44]. Moreover, sensory-motor polyneuropathy is a common complication of T2DM, resulting in muscle weakness, particularly in the quadriceps. Thus, knee joints are subjected to increased pressure, leading to more joint destruction [45] [46].

Some limitations apply to our study. The study's cross-sectional nature and the small sample size may influence the interpretation of the results.

5. Conclusion

Overall, the present study indicates no positive correlation between metabolic tests and the severity of radiologic grading. However, severity is more influenced by greater age and BMI.

Authors' Contributions

M.R designed the work. S.R, M.R, and N.K collected the data. All authors interpreted data. S.R and M.R wrote the main manuscript. M.R, M.S, A.S prepared tables. All authors reviewed the manuscript.

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Not applicable.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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