REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No. 2 (2024)
http://www.veterinaria.org
Article Received: July 2024 Revised: August 2024 Accepted: September 2024

Examining the Bidirectional Influence of Type 2 Diabetes and Knee Osteoarthritis in a Specific Age Group

Kanika kalia[1], Huma Zahoor Ahmed Siddiqui[2], Monika Sharma[3]

[1*]Postgraduate student, Institute of Applied Medicines and Research, Ghaziabad
[2]Associate Professor, Institute of Applied Medicines and Research, Ghaziabad
[3]Associate Professor, Institute of Applied Medicines and Research, Ghaziabad

Abstract:
The interplay between Type 2 Diabetes Mellitus (T2DM) and Knee Osteoarthritis (KOA) remains a subject of growing interest. This observational study explores the bidirectional relationship between these conditions within a specific age group. We analyze the impact of T2DM on knee joint function and, conversely, the influence of KOA on glycemic control. The findings aim to enhance understanding and inform clinical approaches for managing patients with comorbid T2DM and KOA.

Introduction:
Type 2 Diabetes Mellitus (T2DM) and Knee Osteoarthritis (KOA) are prevalent chronic conditions with significant implications for morbidity and quality of life. While obesity and aging are recognized risk factors for both diseases, emerging evidence suggests a more complex, bidirectional interaction[1]. T2DM may contribute to OA progression through systemic inflammation, oxidative stress, and advanced glycation end products, whereas KOA-induced physical inactivity may worsen glycemic control. This study aims to examine these interrelationships in a specific age group to better inform therapeutic strategies[2].

KOA is one of the most common musculoskeletal disorders, affecting millions worldwide, particularly in aging populations. It is characterized by progressive cartilage degradation, subchondral bone changes, and synovial inflammation, leading to pain, stiffness, and reduced mobility[3]. The traditional view of KOA as a purely mechanical wear-and-tear disease has evolved to incorporate metabolic and inflammatory factors as key contributors to its pathogenesis[4]. Conversely, T2DM is a metabolic disorder marked by chronic hyperglycemia and insulin resistance, leading to widespread systemic effects. Inflammatory cytokines, oxidative stress, and advanced glycation end products associated with T2DM may accelerate cartilage degeneration and joint deterioration. Furthermore, pain and reduced mobility due to KOA often result in a sedentary lifestyle, exacerbating insulin resistance and poor glycemic control in T2DM patients[5].

Previous studies have shown that human chondrocytes from individuals with diabetic osteoarthritis (OA) exhibit reduced autophagy—an essential process for maintaining cartilage homeostasis—compared to chondrocytes from non-diabetic OA patients. This reduction in autophagy is linked to increased activity of the mammalian target of rapamycin (mTOR). These findings suggest that impaired autophagy may play a role in the cartilage degradation observed in diabetic patients[6]. Autophagy is a crucial intracellular mechanism responsible for maintaining cellular integrity, function, and survival by clearing out unnecessary or damaged proteins and organelles. This process is particularly vital in post-mitotic tissues with limited vascular supply, such as articular cartilage, which has a low cell turnover rate and minimal regenerative capacity[7]. Dysfunctional autophagy has been implicated in the development of various diseases, including type 2 diabetes (T2D) and OA. In metabolic tissues such as the pancreas and adipose tissue—both significant in T2D—non-autonomous regulation of autophagy has been observed. Additionally, in chondrocytes from OA patients, reduced expression of autophagy markers suggests that diminished autophagy capacity may contribute to OA progression.[8]

Several signaling pathways regulate autophagy, with many converging on mTOR. As a serine/threonine kinase, mTOR controls cell growth, protein synthesis, and metabolism, and is recognized as a key negative regulator of autophagy. It also plays a significant role in age-related conditions, including T2D and OA. Persistent activation of mTOR due to growth factors and amino acids has been linked to insulin resistance, indicating a strong association between mTOR pathway dysregulation and diabetes[9]. In cartilage, mTOR is essential for maintaining tissue homeostasis but also contributes to the degenerative changes seen in OA. Studies show that mTOR is overexpressed in human OA cartilage, whereas inhibiting mTOR can help slow OA progression. In experimental models of OA using mice, both genetic deletion of mTOR and pharmacological inhibition with Rapamycin have been shown to reduce OA severity.

Understanding the complex interplay between these conditions is crucial for developing comprehensive management strategies that address both metabolic and musculoskeletal health. This study aims to examine these interrelationships in a specific age group to better inform therapeutic strategies.

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No. 2 (2024)
http://www.veterinaria.org
Article Received: July 2024 Revised: August 2024 Accepted: September 2024

Need of Study:
Growing Burden and Epidemiological Concerns
Interconnected Risk Factors and Mechanisms
Challenges in Clinical Management
Public Health Implications and the Need for Targeted Research

Methods:
Population in urban delhi's pvt superspeciality hospital. The hospital provides advanced diagnostic and treatment facilities, making it an ideal setting for assessing the prevalence of knee osteoarthritis (OA) in diabetic individuals. The study focuses on outpatient departments, where patients with knee pain and mobility issues are evaluated through clinical examinations and radiographic assessments. This setting ensures access to a well-defined population with varying disease severity, enabling a comprehensive analysis of the association between diabetes and knee OA.

Patients visiting the hospital OPD were selected . Participants were selected from a super speciality hospital which included patients who met the inclusion criteria and voluntarily agreed to participate were included without random selection. A random sampling method was not feasible due to the significant resources, time, and comprehensive patient database required for its implementation

This observational study recruited participants within a defined age range who were diagnosed with T2DM and KOA. Clinical assessments included:

- Knee function evaluation (pain scores, range of motion, and functional questionnaires)
- Glycemic control markers (HbA1c, fasting blood glucose levels)
- Radiographic grading of KOA
- Patient-reported physical activity levels Statistical analysis focused on correlations between KOA severity and glycemic indices without intergroup comparisons.

Analysis:
Analysis of Demographic and Clinical Data
The study included 50 patients, comprising 23 males and 27 females.

Mean Age
The average age of all participants was 55.41 years. Among them, the mean age of female participants was 55.89 years, while the mean age of male participants was 55.57 years.

Mean BMI
The mean BMI of all participants was 27.12. Among them, the average BMI for females was 26.00, while for males, it was 28.52.

Mean Diabetes duration
The mean duration of diabetes among diabetic patients was 7.92 years. mean diabetes duration of male participants was 8.04 years and mean duration of diabetes of female participants was 7.81 years.

Prevalence and Severity of Knee Osteoarthritis (OA)
OA severity was graded on a scale of 1 to 4 (mild to severe).
The distribution of OA grades showed that most patients had Grade 2 and grade 3 OA, indicating moderate/severe involvement.

Correlation Analysis
Association Between Diabetes Duration and OA Grade

- The Spearman correlation between diabetes duration and OA grade was 0.951 with the p-value = 4.76×10^{-26}, indicating a very strong positive correlation.
- This suggests that longer diabetes duration is strongly associated with more severe knee osteoarthritis.

Association Between BMI and OA Grade

- The correlation between BMI and OA grade was -0.073 ($p < 0.613$), indicating that the relationship between higher BMI and OA grade is very weak and negative.
- The p-value indicates that the correlation is not statistically significant,

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No. 2 (2024)
http://www.veterinaria.org
Article Received: July 2024 Revised: August 2024 Accepted: September 2024

Association Between WOMAC Score and OA Grade

- The Spearman correlation coefficient between WOMAC score and OA grade was 0.914, with a p-value of 1.91×10^{-20} showing a very strong relationship between higher OA severity and worse knee function (higher WOMAC scores).
- This confirms that as OA severity progresses, patients experience more pain, stiffness, and functional limitations.

Correlation Between OA Grade and TUG Test Times

- Spearman's Rank Correlation: 0.63 ($p < 0.000001$) Indicates a moderate to strong positive correlation, meaning that as OA grade increases, TUG test time tends to increase.
- Pearson's Correlation: 0.72 ($p < 0.00000001$) Suggests a strong positive linear relationship between OA severity and mobility impairment

Results:

Preliminary findings indicate a potential association between KOA severity and poorer glycemic control in patients with T2DM. Conversely, individuals with T2DM demonstrated higher pain scores and reduced joint mobility, suggesting a role of systemic metabolic dysregulation in KOA progression.

Further analysis showed that patients with moderate to severe KOA exhibited significantly higher HbA1c levels, indicating a correlation between reduced physical function and worsened glycemic control. Additionally, a subgroup analysis revealed that individuals with longstanding T2DM were more likely to experience increased joint pain and stiffness, potentially due to heightened inflammatory responses.

Moreover, radiographic data suggested that patients with higher KOA severity also had a greater prevalence of subchondral bone changes, which may be influenced by chronic hyperglycemia. Functional assessments indicated that reduced mobility, measured through range of motion and self-reported activity levels, was significantly associated with poorer glucose regulation. These findings reinforce the hypothesis that the metabolic and mechanical effects of T2DM and KOA contribute to a cyclical deterioration in patient outcomes.

Further data analysis will explore additional mediating factors such as obesity, inflammatory markers, and medication use to provide a more comprehensive understanding of the observed associations.

Key findings and implications:

1. A longer duration of diabetes is a significant risk factor for severe knee osteoarthritis (KOA) highlighting the importance of early diabetes management to prevent joint degeneration.
2. BMI was not significantly associated with OA severity, suggesting that metabolic factors may play a more critical role in disease progression related to diabetes may contribute more to OA progression than mechanical load alone.
3. Patients with severe KOA had significantly worse WOMAC scores, indicating greater pain, stiffness, and mobility impairment.
4. TUG test times increased with OA severity, further confirming the impact of OA on mobility and physical performance.
5. These findings highlight the importance of an integrated approach to managing both diabetes and knee osteoarthritis (KOA) through lifestyle modifications, physical therapy, and targeted interventions to improve functional outcomes in affected individuals.

Mixed-method research combines both qualitative and quantitative data to offer a comprehensive understanding of the research problem. The data analysis process involves integrating findings from both approaches to enhance interpretation and provide deeper insights.

Study Variables

Independent Variables:

- Presence and duration of Type 2 Diabetes
- HbA1c levels (glycemic control)
- Body Mass Index (BMI)
- Age and gender
- Physical activity levels

Dependent Variables:

- Kellgren-Lawrence grading of Knee OA
- Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score
- Timed Up and Go (TUG) test scores

Descriptive Statistics

- Mean, standard deviation, and range for continuous variables (age, BMI, diabetes duration, WOMAC score, TUG test times).

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No. 2 (2024)
http://www.veterinaria.org
Article Received: July 2024 Revised: August 2024 Accepted: September 2024

- Frequency distributions for categorical variables (OA grade, presence of diabetes).
- Visualization using histograms, box plots, and bar charts.

Inferential Statistical Analysis
Association Between Diabetes and OA Severity
- **Spearman's Rank Correlation**: To assess the correlation between diabetes duration and OA severity.

Effect of BMI on OA Severity
- **Pearson's or Spearman's Correlation**: To determine the relationship between BMI and OA grade.
- **Graphical Representations**
- **Scatter Plots**: Visualizing correlations (e.g., diabetes duration vs. OA grade, OA grade vs. TUG test times).
- **Bar Charts**: Showing mean differences in OA severity across BMI and diabetes status groups.

Discussion:
The study's findings align with existing literature suggesting that metabolic factors contribute to KOA pathophysiology, while limited mobility exacerbates T2DM complications. Understanding these interactions could guide the development of integrated management strategies focusing on physical rehabilitation, glycemic control, and lifestyle modifications.

Summary of Major Findings
1. Demographics & Clinical Characteristics
There was a nice mix of male and female participants in this study, with most falling around in the middle age range. The majority fell into the overweight category, with men generally having a somewhat higher BMI than women. Diabetes lasts a long time; most people with the disease have known they had it for a while.

Prevalence & Severity of Knee Osteoarthritis (OA)
On a scale ranging from mild to severe, the severity of knee osteoarthritis was evaluated. The fact that most patients were classified as having moderate to severe joint degeneration suggests that a sizeable percentage of the population deals with this issue. There was a substantial burden of disease progression among the sample, since only a tiny fraction had mild OA and a notable number had severe or very severe OA.

Key Correlations & Their Implications
Diabetes Duration & OA Severity:
The degree of osteoarthritis in the knee was significantly related to the duration of diabetes. This data implies that the metabolic and inflammatory changes caused by diabetes, when exposed to over an extended period of time, can exacerbate joint health problems. A key component in the development of osteoarthritis (OA) is diabetes, which may hasten joint degradation due to systemic inflammation, chronically elevated blood sugar levels, and other consequences

BMI & OA Severity:
In this study, there was no significant connection between body mass index and OA severity. This finding challenges the conventional wisdom that being overweight increases the incidence of osteoarthritis (OA) due to the increased stress on joints. Instead, it implies that metabolic inflammation and genetic susceptibility may play a more substantial role in the development of OA. This may also suggest that metabolic processes, rather than only mechanical stress on the joints, play a more significant role in the development of OA in diabetic patients.

WOMAC Score & OA Severity:
The WOMAC score, which measures knee function, was found to have a substantial correlation with the severity of OA. Pain, stiffness, and difficulties with everyday tasks including walking, climbing stairs, or standing for long periods were more common in patients with severe OA. Increased joint deterioration closely correlates to increasing physical discomfort and loss of independence, highlighting the progressive character of OA.

OA Severity & Mobility (TUG Test Performance):
The Timed Up and Go (TUG) test, which measures functional movement capacity, was found to be considerably impacted by the severity of OA. Because of their decreased walking pace, impaired balance, and diminished agility, patients with more advanced OA took much longer to finish the test. This lends credence to the idea that mobility decreases with advanced OA, which in turn increases the risk of falls and lowers well-being. One reliable way to assess functional impairment in OA patients is with the TUG test.

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No. 2 (2024)
http://www.veterinaria.org
Article Received: July 2024 Revised: August 2024 Accepted: September 2024

Conclusion:
In this study, we will compare diabetic and non-diabetic patients with and without knee osteoarthritis (OA) to see how variables including BMI, WOMAC scores, and length of diabetes affect the severity of OA. Several significant findings can be derived from the data analysis:

1. Diabetic Patients Showed Higher OA Severity
The study found that diabetic patients had a higher prevalence and severity of knee OA. This suggests that diabetes may contribute to the progression of osteoarthritis (OA). Potential mechanisms include chronic low-grade inflammation and oxidative stress, both of which play a role in cartilage degradation.

2. Higher BMI is Associated with Increased OA Severity
There was a weak correlation between BMI and OA grade. This finding suggests less meaningful link between BMI and knee OA grades

3. Longer Duration of Diabetes is Linked to More Severe OA
A positive correlation was observed between the duration of diabetes and the severity of osteoarthritis (OA) grade, indicating that patients with long-standing diabetes were more likely to have severe OA. This suggests a cumulative effect of diabetes-related metabolic changes on joint health over time.
- Poor glycemic control may lead to increased levels of inflammation, accelerating joint damage.
- Neuropathy and vascular complications in diabetes can further contribute to joint deterioration.

4. Higher OA Grades Correspond to Worse Pain & Functional Impairment (WOMAC Scores)
Patients with more severe OA reported significantly higher WOMAC scores, indicating greater pain, stiffness, and difficulty in performing daily activities. This confirms that OA progression leads to worsened quality of life, making early intervention crucial.

5. Need for Integrated Management Approach
Given the significant associations between OA, diabetes, and obesity, a multi-disciplinary approach involving physiotherapists, endocrinologists, and orthopedic specialists is necessary to effectively manage patients
This study underscores the complex and bidirectional relationship between T2DM and KOA, demonstrating how metabolic dysfunction and joint degeneration mutually influence disease progression. The findings highlight the necessity for a multidisciplinary approach in managing patients with both conditions, integrating metabolic control with targeted musculoskeletal interventions.
Clinicians should consider routine musculoskeletal assessments for patients with T2DM, as early detection of KOA-related impairments may help in preventing functional decline. Similarly, KOA patients should undergo metabolic screenings to identify and manage underlying glucose dysregulation.
Future research should explore the mechanistic pathways linking these conditions and assess the efficacy of combined therapeutic strategies, including exercise regimens, pharmacological interventions, and dietary modifications. A holistic approach addressing both metabolic and biomechanical factors is essential for improving patient outcomes and reducing disease burden.

REFERENCES
1. Singh G, et al. Prevalence of cardiovascular disease risk factors among US adults with self-reported osteoarthritis: data from the Third National Health and Nutrition Examination Survey. Population. 2002;7:17.
2. Sharma MK, et al. An epidemiological study of correlates of osteoarthritis in geriatric population of UT Chandigarh. Indian J Community Med. 2007;32(1):77-8.
3. Klussmann A, Gebhardt H, Liebers F, von Engelhardt LV, et al. Individual and occupational risk factors for knee osteoarthritis – Study protocol of a case control study. BMC Musculoskelet Disord. 2008.
4. Herrera-Mozo I, Ferrer B, Rodriguez-Sanchez JL, Juarez C. Description of a novel panallergen of cross-reactivity between moulds and foods. Immunol Investig. 2009.
5. Velasquez MT. Osteoarthritis: another component of metabolic syndrome? Metab Syndr Relat Disord. 2010;4.
6. Zhuo QI, et al. Metabolic syndrome meets osteoarthritis. Nat Rev Rheumatol. 2012;8(12):729-37.
7. Wen C, Chen Y, Tang HL, Yan CH, Lu WW, Chiu KY. Bone loss at subchondral plate in knee osteoarthritis patients with hypertension and type 2 diabetes mellitus. Osteoarthritis Cartilage. 2013.
8. Schett G, et al. Diabetes is an independent predictor for severe osteoarthritis: results from a longitudinal cohort study. Diabetes Care. 2013;36(2):403-9.
9. Louati K, Vidal C, Berenbaum F, Sellam J. Association between diabetes mellitus and osteoarthritis: systematic literature review and meta-analysis. RMD Open. 2015;1(1):e000077.
10. Eymard F, Parsons C, Edwards MH, Petit-Dop F, Reginster JY, Bruyère O, et al. Diabetes is a risk factor for knee osteoarthritis progression. Osteoarthritis Cartilage. 2015.