Original Article

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Prevalence of Knee Osteoarthritis and its Associated Factors in Type 2 Diabetes Mellitus Patients: A Cross-sectional Study

Internal Medicine Section

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ABSTRACT

Introduction: Knee Osteoarthritis (OA) and Type 2 Diabetes Mellitus (T2DM) are both highly prevalent chronic conditions that lead to significant disability and economic burden on society. This study primarily focuses on the prevalence of knee OA in T2DM, individual risk factors, and their impact on knee OA in T2DM patients.

Aim: To estimate the prevalence of knee OA and to determine the factors associated with knee OA among patients with T2DM attending the diabetes clinic.

Materials and Methods: This cross-sectional study was conducted at the Department of General Medicine, Hind Institute of Medical Sciences, Barabanki, Uttar Pradesh, India among 200 T2DM patients (103 males and 97 females) according to the American Diabetes Association (ADA) guidelines. Demographic data and disease variables were recorded for all patients. Knee OA was assessed using clinicoradiological American College of Rheumatology (ACR) criteria for knee OA, with the right knee considered as the index knee. Radiographs were evaluated using the Kellgren Lawrence (KL) grading system for knee OA. Functional status for knee OA was assessed using the Western Ontario and McMaster Universities Arthritis Index (WOMAC). Statistical analysis was performed using Epi Info version 7.0 software.

Results: A total of 200 patients were included in the study, with 103 (51.5%) males and 97 (48.5%) females. The mean age was 53.93±9.94 years, and the mean BMI was 23.29±3.6 kg/m^2. The mean duration of T2DM was 49±52.22 months. The prevalence of knee OA in T2DM patients was 46.3%. Among the disease variables in patients with knee OA and without knee OA, the mean age was 54±10 years and 50±7.9 years, respectively. The mean BMI was 23.29±3.61 kg/m^2 and 22.69±3.04 kg/m^2, respectively. The mean duration of T2DM was 49±52 months and 30.1±33.33 months, respectively. The mean serum uric acid level was 5.9±1.5 mg/dL and 5.5±1.25 mg/dL, respectively. The mean serum cholesterol was 205.7±75.9 mg/dL and 170.9±51.1 mg/dL, respectively.

Conclusion: Knee OA is highly prevalent in patients with T2DM, highlighting the importance of investigating the presence of knee OA in each patient with T2DM. The association of knee OA with patient age and duration of T2DM indicates the need for early intervention, and the significant association with co-morbidities suggests the inclusive management of co-morbidities.

Keywords: Dyslipidaemia, Hyperglycaemia, Obesity, Uric acid

INTRODUCTION

Knee OA and T2DM are two highly prevalent chronic diseases in India, as there is an increase in the ageing population. The prevalence of knee OA in India is 28.7%, as reported by a community-based cross-sectional study conducted in selected geographical areas of India [1]. Knee OA is a leading cause of disability and economic burden not only in India but across the world [2]. The prevalence of T2DM in India is 9.3%, and it is increasing. India is considered the diabetes capital of the world [3]. T2DM also leads to significant disability and economic burden for the ageing population [4]. Both of these conditions often coexist in the ageing population and are likely to cause greater disability and economic burden [5]. Existing data suggests that patients with T2DM have an increased susceptibility to develop knee OA compared to those without T2DM (46% versus 27%) [6]. Even though knee OA and T2DM share common risk factors like obesity and advanced age, evidence suggests that the metabolic alterations in T2DM, such as chronic hyperglycaemia and insulin resistance, may serve as a link between the two diseases, leading to the production of proinflammatory cytokines [7]. Pathak B et al., reported the prevalence of knee OA to be 14.3% in 258 patients with T2DM [8]. Singh A et al., reported knee OA (14%) to be the most common rheumatological manifestation in 100 T2DM patients [9]. Mathew AJ et al., reported knee OA to be 21% in 300 patients with T2DM [10].

Thus, the present study was planned with the aim to estimate the prevalence of knee OA and determine the factors associated with knee OA among patients with T2DM attending the Diabetes clinic.

MATERIALS AND METHODS

This study was a hospital-based cross-sectional study conducted in the Diabetic Clinic, Department of General Medicine, Hind Institute of Medical Sciences, Barabanki, Uttar Pradesh, India. The total duration of the study was from January 2022 to June 2022. The study was approved by the Institutional Ethical Committee (IEC), with ethical clearance number IHEC-HIMSB/MD/MS (20)/RD-13/09-21, and written informed consent was obtained from each patient.

Inclusion criteria: Patients above 40 years of age with Type 2 DM according to the ADA criteria attending the diabetic clinic.

ADA criteria, 2022 [11]:

- Fasting Plasma Glucose (FPG) level of 126 mg/dL or higher
- Or 2-hour plasma glucose level of 200 mg/dL or higher during a 75-g Oral Glucose Tolerance Test (OGTT)
- Or Random plasma glucose of 200 mg/dL or higher in a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis
- Or glycated haemoglobin (HbA1c) level of 6.5% or higher

Exclusion criteria: Patients were excluded from the study if they had a known inflammatory joint disease, a history of knee trauma, or any congenital deformity of the knee. The total number of patients included in the study was 200 (103 males and 97 females).

Sample size: A convenient sample of 200 patients was consecutively taken during the study period.

Cochran's formula for sample calculation was used:

$$n=\frac{Z^2*p*(1-p)}{E^2}$$

Where:

Zα=Critical value of Z-score at the level of significance (α=5%, Zα=1.96)

p=Prevalence or incidence or proportion

E=Margin of error

In this case:

p=49%=0.49 (prevalence of OA in type 2 DM) [6]

E=7%=0.07 (absolute margin of error)

$$n=\frac{(1.96^2*0.49*(1-0.49)}{(0.07)^2}$$

=195.9≈196-Rounded off to the nearest 10.

n=200

Socio-demographic data and clinical history of all participants were recorded, and all patients were physically examined for the presence of swelling, crepitus, and tenderness in the knee joints. Furthermore, a proforma was filled out for each individual patient, including Body Mass Index (BMI), smoking status, socio-economic status, and assessment of co-morbidities such as hypertension, coronary artery disease, dyslipidaemia, and hyperuricaemia. Assessment of patients with T2DM was done according to the ADA criteria, along with recording the duration, medications being taken, current disease status (controlled or uncontrolled as per ADA criteria), treatment compliance, and disease complications. All patients were then assessed for the presence or absence of knee pain. The duration of knee pain was recorded, and pain intensity was assessed using the visual analogue scale (VAS 0-10 cm/0-100 mm) [12].

Radiographic evaluations were performed using weight-bearing Anteroposterior (AP) radiographs of the right knee. The radiographs were evaluated by one of the authors using the KL grading scale. The radiographs were graded as follows: Grade-0 - no features of OA, Grade-1 - small osteophyte of doubtful importance, Grade-2 - definite osteophyte but unimpaired joint space, Grade-3 - definite osteophyte with moderate diminution of joint space, and Grade-4 - definite osteophyte with substantial joint space reduction and sclerosis of subchondral bone [13]. Diagnosis of OA was made using the clinicoradiological ACR criteria, which includes the presence of knee pain along with one of the three criteria: age over 50 years, stiffness lasting less than 30 minutes, and osteophytes on radiographs [14]. Therefore, only patients with KL Grade-2 or higher on radiographs were considered as patients with OA.

The functional status was assessed using the WOMAC index. The WOMAC index is a self-administered questionnaire that assesses three dimensions, namely pain, disability, and joint stiffness in knee and hip OA, using 24 questions. Out of the 24 questions, five are related to pain, two are related to stiffness, and 17 are related to physical function. The total score of WOMAC-OA ranges from 0 (no disability) to 96 (severest disability) [15]. The WOMAC-KGMC index is a modified version of WOMAC tailored to Indian conditions for evaluating patients. In the WOMAC-KGMC index, there are a total of 28 questions. Four questions are specifically related to Indian settings, such as facing difficulty in getting on/off a rickshaw, sitting in a squatting position to relieve oneself, sitting cross-legged, and offering Pooja or Namaaz. The patients were presented with a questionnaire of 28 questions, and the response was graded from No Association (NA) to very severe problem [16]. Subsequently, scoring was done with respect to pain WOMAC, stiffness WOMAC, function WOMAC, function KGMC, total WOMAC, and total KGMC.

STATISTICAL ANALYSIS

Statistical analysis of the data was performed using Epi Info version 7.0 software. Continuous variables were expressed as mean and standard deviation, while categorical variables were expressed as percentages. To compare the characteristics between patients with knee OA and without knee OA, an independent sample t-test was used for continuous variables and the Chi-square test for frequencies. Correlations between independent variables and the WOMAC scores were analysed using Spearman's correlation test. The level of statistical significance was set at 0.05, and the confidence interval was 95%.

RESULTS

Out of 200 patients with T2DM, 103 (51.5%) were males, and 97 (48.5%) were females. The demographic and disease variables of the patients are shown in [Table/Fig-1]. The mean age of the patients was 53.93±9.94 years, and the mean BMI was 23.28±3.60 kg/m^2. A total of 87 (43.5%) patients belonged to the lower socio-economic class. Hypertension was seen in 85 (42.5%) patients.

Variable	Patients (n-200)
Age (years), mean±SD	53.93±9.94
Sex, n (%)	
Males	103 (51.5)
Females	97 (48.5)
BMI (kg/m^2), mean±SD	23.28±3.60
Socio-economic class, n (%)	
Upper	47 (23.5)
Middle	66 (33)
Lower	87 (43.5)
Smokers, n (%)	74 (37)
Associated co-morbid conditions, n (%)	
Hypothyroidism	43 (21.5)
Hypertension	85 (42.5)
Coronary artery disease	36 (18)
Dyslipidaemia	40 (20)
Hyperuricaemia	38 (19)
Duration of T2DM (months) Mean±SD	49±52.22

[Table/Fig-1]: Demographic and disease variables.
SD: Standard deviation; BMI: Body mass index; T2DM: Type 2 diabetes mellitus

Knee OA was present in 92 (46%) patients. Among them, 74 (80.4%) patients had Grade-2 knee OA, and 18 (19.6%) patients had Grade-3 knee OA according to the KL grading. An independent sample t-test was used to compare the demographic and disease variables in patients with knee OA and without knee OA. As shown in [Table/Fig-2], the mean age in patients with knee OA was 54±10 years, while it was 50±7.9 years in patients without knee OA. The mean duration of T2DM, mean cholesterol, and mean uric acid were found to be significant in patients with knee OA. Co-morbidities like hypertension and coronary artery disease were also found to be significant in patients with knee OA. There was no significant difference with respect to BMI, socio-economic class, smoking, and the status of T2DM control.

Variables	T2DM with Knee OA (n-92)	T2DM without Knee OA (n-108)	p-value
Age (years), mean±SD	54±10	50±7.9	0.0018*
Male (n-103)	55±9	51±8.4	0.0013*
Female (n-97)	53±10	49±7.2	0.0012*
BMI (kg/m^2), mean±SD	23.29±3.61	22.69±3.04	0.203*
Socio-economic class, n (%)			
Upper	19 (20.7)	28 (25.9)	0.304#
Middle	30 (32.6)	36 (33.3)	

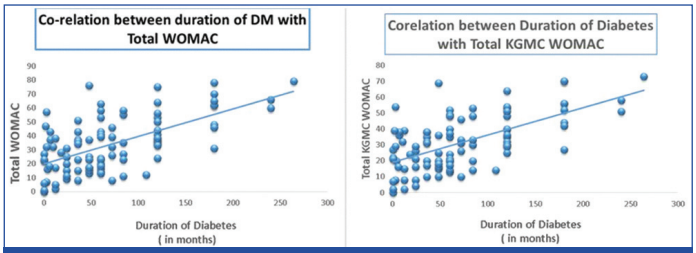
Lower	43 (46.7)	44 (40.7)	
Smoking, n (%)	33 (35.9)	41 (38.0)	0.471#
Associated co-morbid conditions, n (%)			
Hypothyroidism	23 (11.5)	20 (10)	0.733#
Hypertension	57 (28.5)	28 (14)	0.00001#
Coronary Artery Disease	27 (13.5)	9 (4.3)	0.0004#
Dyslipidaemia	28 (14)	12 (6)	0.0012#
Hyperuricaemia	27 (13.5)	11 (10.5)	0.0005#
Duration of T2DM (in months), mean±SD (mg/dL)	49±52	30.1±33.3	0.002*
Status of T2DM (controlled), n (%)	38 (19)	62 (31)	0.053#
Laboratory investigations			
Serum uric acid, mean±SD (mg/dL)	5.9±1.5	5.5±01.25	0.029*
Serum cholesterol, mean±SD (mg/dL)	205.7±75.9	170.9±51.1	0.0001*
Drugs, n (%)			
Oral hypoglycaemic agents	71 (48.6)	75 (51.4)	
Insulin	12 (92.3)	1 (7.7)	0.000025
Alternative/no medication	9 (22)	32 (78)	21.1752

[Table/Fig-2]: Comparison of demographic and disease variables in T2DM patients with and without knee OA.
*Independent sample t-test
#Chi-square test
SD: Standard deviation; BMI: Body mass index; OA: Osteoarthritis

The mean total WOMAC was 34±19.6, and the mean total WOMAC KGMC was 31.4±17.1. Using Spearman's correlation coefficient (rho), it was observed that there was a significant positive correlation between the duration of T2DM and all domains of WOMAC [Table/Fig-1,3]. Knee pain on VAS scales and the duration of pain were also compared to the duration of T2DM, revealing a significant positive correlation [Table/Fig-3]. The linear scatter diagram showed a positive correlation between the duration of T2DM and WOMAC, WOMAC KGMC by Spearman's correlation coefficient [Table/Fig-4].

Variable	n-92	Spearman's correlation coefficient (ρ)	p-value
VAS pain (0-100 mm) mean±SD	21+26.1	0.54	<0.0001
Duration of knee pain (months) mean±SD	11.1+20.4	0.37	<0.0001
Total WOMAC mean±SD	34±19.6	0.54	<0.0001
Total WOMAC KGMC mean±SD	31.4±17.1	0.54	<0.0001
Pain WOMAC mean±SD	9.9±5.4	0.55	<0.0001
Stiffness WOMAC mean±SD	3.1±2.12	0.41	<0.0001
Function WOMAC mean±SD	21±13.3	0.49	<0.0001
Function KGMC mean±SD	18.4±10.9	0.511	<0.0001

[Table/Fig-3]: Relationship between duration of T2DM with selected variables of knee OA.
WOMAC: Western Ontario and McMaster universities index; VAS: Visual analogue scale; SD: Standard deviation



[Table/Fig-4]: Linear scatter diagram showing positive correlation between the duration of T2DM and Western Ontario and McMaster Universities Index score (Conventional and KGMC): (a) Spearman correlation coefficient ρ-0.54 (p<0.001); b) ρ-0.54 (p<0.001).

DISCUSSION

The present hospital-based cross-sectional study was conducted to estimate the prevalence and risk factors of knee OA in T2DM patients attending the medicine Outpatient Department (OPD) in a tertiary care centre in Barabanki, Uttar Pradesh, India. The prevalence of knee OA in T2DM was found to be 46%, which was quite high compared to the prevalence of knee OA in the general population (28.7%) [1]. A similar hospital-based cross-sectional study on knee OA in T2DM patients conducted in India with 258 subjects found that the overall proportion of OA in diabetic subjects was 48.4%. The proportion of only hand OA was 25.2%, only knee OA was 14.3%, and both hand OA and knee OA were 8.9% [8].

In the present study, the male and female patients with knee OA had a mean age of 55±9 and 53±10, respectively, which contrasts the findings of the study where OA was found to be more prevalent in females [8]. The same study also stated that the prevalence of knee OA increased with age and duration of T2DM, and no significance was found with respect to socio-economic status and smoking, which were similar to the present study. Hypertension and BMI were also found to be significantly associated with both hand and knee OA in that study [8]. However, the present study did not find a significant association with BMI (mean BMI in patients with knee OA was 23.29±3.61 and without knee OA was 22.69±3.04).

A study conducted by Chowdhury T et al., suggested that the duration of DM and the chronic hyperglycaemic state induced oxidative stress and deposition of advanced glycation end products in the joints, which worsened OA [17]. However, in the present study, the status of blood sugar control was not found to be a significant factor for knee OA.

There was a significant association of knee OA with co-morbidities like hypertension, dyslipidaemia, and hyperuricaemia. Previous data does suggest that metabolic syndrome is a risk factor for severe knee OA [18]. There was a positive correlation between the duration of T2DM and the functional status of knee OA patients. Evidence suggests that patients with long-term T2DM have more quadriceps muscle atrophy along with peripheral neuropathy, which makes them prone to having a poor functional status [19]. Kaymaz S and Aykan SA studied the association of T2DM with the functionality of knee OA and found that T2DM has a negative effect on the functional capacity in knee OA [20].

In the present study, there was significance found regarding oral hypoglycaemic agents, with 71 (48.6%) patients with knee OA and 75 (51.4%) without knee OA, similar to a longitudinal analysis which suggested that medication-treated diabetes had no effect on knee OA incidence but was independently associated with decreased progression of knee OA [21]. The present study also compared patients with and without knee OA who were on insulin therapy. There was a significant difference with 12 (92.3%) patients with knee OA on insulin and 1 (7.7%) patient without knee OA on insulin, but this could not be considered since the sample size in the group without knee OA was very small. A cross-sectional study published in 2015 was carried out to investigate whether the radiographic changes observed in knee OA in T2DM patients on insulin therapy differed from those not on insulin therapy. It was found that patients with T2DM who were on insulin therapy had fewer radiographic osteophytes compared to those not on insulin [22]. A significant correlation was also seen with respect to patients taking alternative medications or no medications at all.

There was a significant correlation between the duration of T2DM and knee pain on the VAS scale. Furthermore, the duration of T2DM had a significant correlation with the total WOMAC score and total WOMAC KGMC score. The total WOMAC score was also found to have a significant correlation with the duration of T2DM in a cross-sectional study carried out in Turkey [20].

Thus, patients with T2DM have a high prevalence of knee OA, which can lead to significant functional limitation, a greater economic burden, and worse outcomes. Therefore, addressing knee OA in patients with T2DM becomes of paramount importance.

Limitation(s)

This study was a cross-sectional study, so a longitudinal study with a larger sample size would serve the purpose better, and the current study could be considered as a pilot study.

CONCLUSION(S)

The prevalence of knee OA in patients with T2DM was high (46%), so all patients with T2DM should also be screened for knee OA, similar to screening for other associated co-morbidities. The duration of T2DM was significantly higher in patients with knee OA, so early screening for knee OA is warranted. Furthermore, patients with knee OA had a significant association with age, so timely intervention should be done to slow the progression of knee OA in patients with T2DM. In laboratory investigations, the serum cholesterol and uric acid levels were significantly higher in patients with T2DM, so appropriate management of dyslipidaemia and hyperuricaemia may be incorporated into the management of knee OA in patients with T2DM. Since hypertension and coronary artery disease were also significant in patients with T2DM and knee OA, good control of blood pressure and routine screening for coronary artery disease may be recommended.

The key message would be early detection and intervention for knee OA in T2DM patients in order to counter the social and economic burden of these highly prevalent conditions, as well as the disability limitations they impose.

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