Prevalence of Pain Conditions in Type 2 Diabetes Mellitus patient: A Cross Sectional Study

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Abstract

Background: Type-2 Diabetes mellitus (T2DM) is a metabolic disease characterized by hyperglycemia and may causes long term organs dysfunctions like retinopathy, nephropathy, neuropathy, cardiovascular and autonomic dysfunction. Musculoskeletal and nervous system can also be affected by T2DM resulting pain, dysfunctions and disabilities. Objectives: This study is to find the prevalence of different pain conditions in patients with T2DM. **Material & Methods:** The study was conducted in public and private hospitals of four cities (Brahmanbaria, Dhaka, Gazipur and Faridpur) of Bangladesh from 1st April to 31st September, 2021. The patients of type II diabetes mellitus with both gender and age above 40 were included, and patients with other active systemic disease of bones and soft tissues were excluded. A self-structured questionnaire was developed. The questionnaire was distributed among 500 patients, out of whom 450 patients responded. The non-probability convenient sampling technique was used for data collection. The data was analyzed by SPSS and percentages were calculated to estimate the musculoskeletal complications in patients with T2DM. **Results:** The result showed high prevalence of pain conditions in T2DM patients. Older age groups of 61-65 (24%) years suffering from T2DM for more than 3 years having higher blood sugar level 17-19 mmol/L with positive family history of DM were affected mostly. The prevalence of musculoskeletal pain condition in T2DM was 71.11%, while the low back pain was (42.88%), frozen shoulder was 31.33%, diabetic neuropathy was (26.89%) were the most common musculoskeletal problems, followed by knee pain (17.33%). **Conclusions:** It is concluded that the prevalence of different pain conditions are high among patients of T2DM and low back pain, shoulder pain, peripheral neuropathy and knee pain are common. These are mostly manageable conservatively.

INTRODUCTION

Diabetes mellitus (DM) is a chronic, metabolic disease characterized by elevated levels of blood glucose. It is a major public health problem and a leading cause of death all over the world.[1] In 2019, the International Diabetes Federation found that 465 million (9.3%) people

worldwide had diabetes and the projected number may rise to 700 million (10.9%) by 2045.[2] DM patients have disturbances of carbohydrate, fat and protein metabolism due to defects in insulin secretion or action or both. Endoplasmic reticulum control cellular homeostasis which is impaired due to some environmental factors and causes pancreatic B cell destruction in type-1 diabetes mellitus (T1DM) and pancreatic B cell failure in type-2 diabetes mellitus (T2DM). Thus the pancreas cannot produce insulin which help to maintain the normoglycaemia in human body.[3]

According to American Diabetes Association classification system, there are four basic types of DM that is, "Type 1 DM", "Type 2 DM", "Gestational Diabetes Mellitus"(GDM) and "other specific types". Type 1 DM is an Insulin dependent DM due to genetic and environmental factors where autoimmune β-cell destruction occur, usually leading to absolute insulin deficiency. Type II DM is also known as noninsulin dependent diabetes mellitus and is a major cause of death and disability for various complications, occurring due to due to a progressive loss of adequate β-cell insulin secretion, frequently on the background of insulin resistance as a consequence of population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity.[4] It is evaluated that by 2030, adults suffering from T2DM may rise to 439 million and 548 million by 2045.[5] The average life expectancy of patients with type 2 diabetes mellitus (T2DM) decreases by approximately 10 years, 80% of patients with T2DM die from cardiovascular complications.[6]

According to International Diabetes Federation there are 7.1 million people with diabetes mellitus in Bangladesh in 2015.[4] In a meta-analysis by Akhtar S et al. showed the pooled prevalence of diabetes in the general population was 7.8%.[4] Diabetes is the sixth most leading cause of death in the Bangladesh. [7] Diabetes mellitus affect connective tissues in many ways and causes different alterations in articular and periarticular region.[8] Hyperglycemia alters the structural matrix and mechanical properties of tissues by hastening non-enzymatic glycosylation and abnormal collagen deposition in periarticular connective tissue resulting diffuse arthrofibrosis affecting the limbs, feet and spine as a whole.[9] Diabetes mellitus is associated with a variety of musculoskeletal disorders and complications, causing pain, disease or even disabilities which later rendering inability to exercise and ensuing further hyperglycemia. Common pain conditions in T2DM include shoulder adhesive capsulitis, diabetic polyneuropathy (DPN), low back pain, neck pain, knee osteoarthritis (OA)1, elbow pain, epicondylitis, carpal tunnel syndrome, Dequervain's tenosynovitis, leg and foot pain, amyotrophy etc.[10] This has a undesirable impact on the health care facility and the patient which include the use of hospitals, trouble of daily life and loss of productivity through functional constrains.[11]

Shoulder pain is common in T2DM patients, mostly due to frozen shoulder, rotator cuff tendinopathy, tears, subacromial subdeltoid bursitis and glenohumeral and acromioclavicular joint arthritis involving joints, bursa, tendons and ligaments.[12] Ultimately, pain and reduced movement of shoulder leads to Frozen shoulder (Adhesive capsulitis).[13] It is also associated with patient age, duration and control of DM. In frozen

shoulder, both active and passive range of motion is limited. It is classified as (i) primary, in which etiology of restricted range of motion is not known and (ii) Secondary, in which etiology is known. Main causes of the frozen shoulder are (i) Intrinsic causes mean ROM is restricted due to any rotator cuff muscle. (ii) Extrinsic causes include any surgery of chest wall, cervical radiculopathy. (iii) Systemic causes include any systemic disease like DM. In frozen shoulder all ROM is restricted and painful but abduction, extension and external rotation movement is more affected, hampering daily works and sleep. With the time, many advance treatments are developed for the management of frozen shoulder. Frozen shoulder can be treated affectively with analgesics, short course low dose glucocorticoid therapy, physiotherapy and sometimes with pregabalin in most of the cases.[14] Suprascapular nerve block, intra-articular injections of steroid and progression to hydrodilatation, manipulation under anaesthesia or arthroscopic capsular release may be done when conservative and physiotherapy fails.[15]

Diabetic polyneuropathy is the most common neuropathy in the Western world. A large American study estimated that 47% of patients with diabetes have some peripheral neuropathy.[16] The prevalence depends on both the severity and duration of hyperglycemia. The patients suffer from burning, tingling, numbness of both hands and feet with typical "stocking-glove" sensory loss. On severe cases, weakness, muscles atrophy, less contractile property of muscle but increase antagonist muscle contraction and many neurological problems leading to foot ulcer can occur. It is

mostly caused by alpha motor neuron dysfunction and changes in muscle fibers. Muscles strength is reduced, planter and dorsiflexion power is reduced in DPN. Smoking, abnormal glucose control, females, long duration of DM, elevated lipids, blood pressure, increased height, and high exposure to other potentially neurotoxic agents such as ethanol, genetic factors and retinopathy are the risk factors of DPN.[17] Normal muscle mass and contractile property of muscle is eventually reduced.[18]

Low back pain prevalence in diabetic patients is increasing but the link with T2DM is still unclear. In one study, 60% of T2DM patients reported low back pain.[19] The pathophysiology behind low back pain may be due to raised glycosylated hemoglobin (HbA1c) causing cartilage inflammation, tissue remodeling, matrix destruction, stiffness and chondrocyte destruction are mediated by advanced glycation end products (AGEs). Other effects are neuropathy, reduced muscle strength and flexibility. There is also evidence of intervertebral disk degeneration by cellular death due to a chronic inflammation which eventually leads to loss of the matrix, incidence of disc prolapse and subsequently narrowing the spinal canal.[20,21,22]

Knee pain is caused by predominantly osteoarthritis (OA), tendinopathies, tear of tendon, ligaments or meniscus. T2DM increase the vulnerability by factors like obesity, reduces the joint space and load in knees which causes pain.[23] Moreover, high glucose levels may affect cell function and alter extracellular matrix components of the connective tissue producing damage of the joint.[24,25] Additionally peripheral neuropathy in DM patients increase

the risk of aggressive forms of OA.[26] Increased age and Females are more vulnerable to develop OA.[27]

The prevention of musculoskeletal problems due to diabetes requires preventive approach involving diabetic patients and multidisciplinary team. Optimum diabetic management, musculoskeletal care, life style education and exercise for the patients and their family, screening and risk assessment may have a critical role in prevention of diabetic related musculoskeletal problems.[28]

In Bangladesh these problems are even more severe. As a developing country, many T2DM patients are undiagnosed, inadequately treated due to lack of awareness and poverty, under compliance due to low literacy. Additionally, majority of population is laborer, repeated microtrauma and inadequate rest, medications and nutrition aggravates these conditions. This study aims to address these problems and frequency of pain conditions so that early prevention, adequate management can be done in a cost effective manner.

MATERIAL AND METHODS

This was cross sectional survey because the study is an attempt to investigate within six months' time frame. The study was conducted in hospitals of three major cities (Brahmanbaria, Dhaka and Faridpur) of Bangladesh. Duration of study-6 months. The duration of the study was from 1st April to 31st September 2021. Total 450 patients were included in the study. The Non probability convenient sampling technique was used to collect data.

Inclusion criteria were given below

- Type II DM patients
- Having age above than 40
- Both genders male and females

Exclusion criteria were given below:

- Type I DM patients
- Age below 40
- History of trauma
- Post traumatic pain
- Malignancy
- Autoimmune disease
- Other systemic disease
- Prior history of any rheumatological or neuromuscular condition

A self-structured pre-tested questioner was used to collect the data. It was a non-probability convenient sampling study to find out the prevalence of musculoskeletal pain conditions in T2DM. Questionnaires were distributed among 500 patients in whom 450 patients responded. 49.3% females and 50.7% males participated in the study. Patients having age above 40 years were included. Data was analyzed on SPSS-22 and percentages were calculated to estimate the prevalence of different pain conditions in patients with T2DM.

RESULTS

Hyperglycemia caused by diabetes mellitus alters the structural matrix and mechanical properties of tissues by hastening non-enzymatic glycosylation and abnormal collagen deposition in periarticular connective tissue resulting diffuse arthrofibrosis affecting the limbs, feet and spine as a whole [9]. The prevalence of musculoskeletal pain condition in

T2DM was 71.11% don't feel, while the low back pain (42.88%), frozen shoulder was 31.33%, diabetic neuropathy was (26.89%) were the most common musculoskeletal problems, followed by and knee pain (17.33%). These complications have high associations with increasing mean age and prolong duration of T2DM. The most involved age group was 61 to 65 (24%). The most commonly used way of treatment was medications and physical therapy, whereas few received intervention. It was proved in study that different musculoskeletal pain are quite common in T2DM in Bangladesh.

Table 1: Demonstrate and distribution of the baseline.

Variable	n=450	%
Age Distribution		
41-45	54	12.0
46-50	67	14.88
51-55	82	18.22
56-60	95	21.11
61-65	108	24.0
66-70	31	6.88
71-75	9	2.0
76-80	4	0.88
Mean±SD	62.0±8.5	
Min-Max	41-80	
Weight		
Mean±SD	57.6±6.5	
Min-Max	45-87	
Gender		
Male	234	52.0
Female	216	48.0
BMI		
Underweight (<18.5)	40	8.88
Normal (18.5 to 24.9)	227	50.44
Overweight (25 to 29.9)	160	35.55
Obese (≥30)	23	5.11
Mean±SD	28.4±5.3	
Duration of T2DM		
Mean±SD	5.0±2.0	
Pain area of the body		
Low Back Pain	193	42.88
Frozen Shoulder	141	31.33
DN	121	26.89
Knee	78	17.33
What type of Treatment		
Analgesics	350	77.77

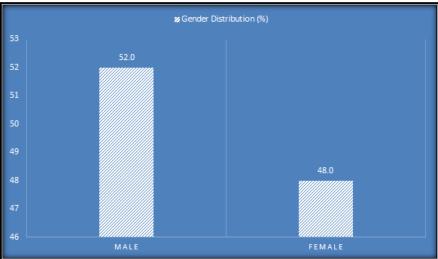| TCA/SNRI	112	24.88
Anti convulsants	55	12.22
Supplements	322	71.55
Physical therapy	72	16.0
Occupational therapy	0	0.0
Steroid injections	47	10.44
Other injections	1	0.22

Figure 1: Gender Distribution
The above graph shows that 52.0% Females and 48.0% Males participated in the study.
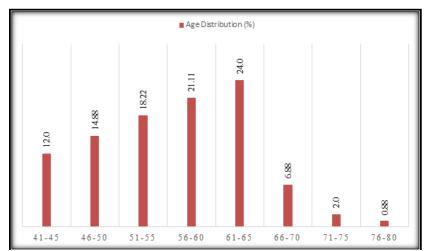

Figure 2: Age Distribution
The above graph shows that the percentage of the patients with the age group of 41-45 years are 12.0%, 46-50 years are 14.88%, 51-55 years are 18.22%, 56-60 years are 21.11%, 61-65 years are 24%, 66-70 years are 6.88%, 71-75 years are 2% and 76-80 years are 0.88%.
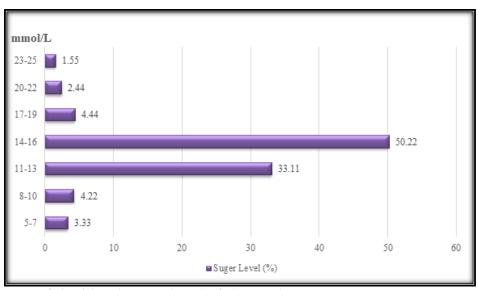
Figure 3: Distribution of the blood sugar level of the study

The graph shows that the percentage of patients having blood sugar level group of 5-7mmol/L are 3.33%, 8-10 mmol/L are 4.22%, 11-13 mmol/L are 33.11%, 14-16 mmol/L are 50.22%, 17-19 mmol/L are 4.44%, 20-22 mmol/L are 2.44%, 23-25 mmol/L are 1.55% and sugar level group of 26-28 are 0.6%.
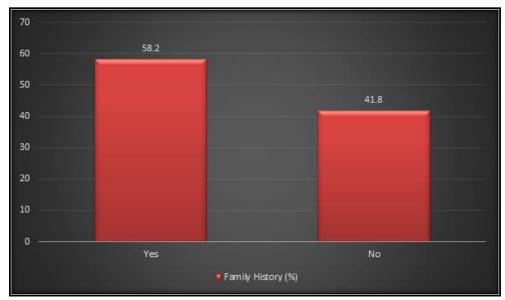

Figure 4: Family history of Diabetes
The graph shows that 58.2% people have family history of diabetes while 41.8% shows no positive family history.
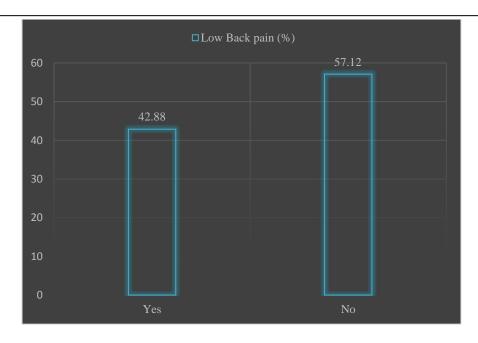
Figure 5: Distribution of low back pain or stiffness

Graph shows that 42.88% people said that they had low back pain while 57.12% says that they did not have. (Mean age: 59 years, mean duration of diabetes: four years)

Figure 6: Distribution of the shoulder pain of the study.

The above graph shows that 31.33% patients said that they have shoulder pain, while 68.07% says they did not. 0.6% patients did not respond to this question. (Mean age: 61 years, mean duration of diabetes: six years)
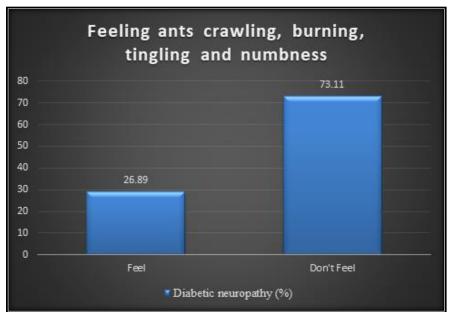

Figure 7: Distribution of percentage of Diabetic neuropathy

The graph shows that 26.89% patients feel ants crawling, burning, tingling sensations while 73.11% do not feel. (Mean age: 61 years, mean duration of diabetes: 7 years)
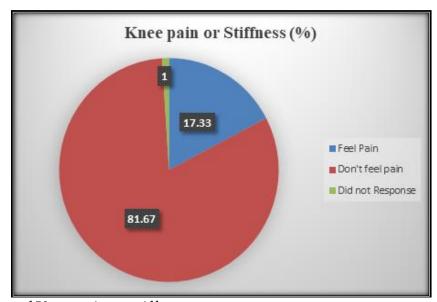

Figure 8: Distribution of Knee pain or stiffness

The above graph shows that 17.33% patients had pain or stiffness in knee while 81.67% did not. 1.0% did not response to this question. (Mean age: 63 years, mean duration of diabetes: six years)

DISCUSSION

This study was done to observe the prevalence of common musculoskeletal pain conditions in T2DM in Bangladesh. The total participants were 450. Age groups of 61-65 (24%) years were affected mostly in different pain conditions, 50.22% having blood sugar level 14-16 mmol/L, with 58.2% had family history of DM and duration of T2DM for more than 3 years. The prevalence of musculoskeletal pain condition in T2DM was 71.11%. In another Bangladeshi study revealed 77.8%,[29] and Greek study showed almost similar (82.6%) of type 2 diabetes mellitus patients suffering from musculoskeletal problemss, mainly of the degenerative, non-inflammatory type.[30] While the low back pain (42.88%), frozen shoulder was 31.33%, diabetic neuropathy was (26.89%) were the most common musculoskeletal problems, followed by knee pain (17.33%). These complications was associated with increasing mean age and prolong duration of T2DM. The most commonly used way of treatment was medications and physical therapy, whereas few received intervention.

Low back pain is discomfort felt between the 12th rib superiorly and the gluteal fold inferiorly which may or may not radiate to the lower limbs.[31] T2DM patients are more frequently affected. Present study shows high prevalence of back pain which is 42.88%. The association between low back pain and type 2 diabetes mellitus still unclear. Previous studies prooved that DM have a high prevalence of low back pain than non-diabetic patients which is 41.3%. In a different studies the prevalence of low back pain in type 2 diabetes mellitus patients was found to be 60%.[32] Such high prevalence was also found by Eivazi et al., (63.4%).[33] Although lower prevalence rates were reported by Idowu et al and Jimenez Garcia et al,[34,35] (31.5% and 37.1%, respectively). Low back pain was associated with dyslipidemia (55.4%), obesity (60.9%), moderate (56.2%) or vigorous (61.3%) physical activity and insulin therapy (100%).[36] Elderly and obesity increases the risk of low back pain by both mechanical and chemical pathways.[37] Uncontrolled diabetes contribute to low back pain due to vasculopathy that hampers the blood supply to the vertebral disc and make it more prone for prolapse.[38] Raised blood sugar and glycosylated hemoglobin (HbA1c) in T2DM causes metabolic disturbance renders neuropathy, reduction in the muscle strength and flexibility as well as increase adipose tissue deposition, intervertebral disk degeneration by cellular death due to a chronic inflammation which ultimately resulting loss of the matrix. It also increase the chance of disk prolapse and subsequently narrowing the spinal canal.[39]

Frozen shoulder or adhesive capsulitis, is a condition characterized by painful and limited active and passive range of motion of the shoulder.[40] It is a one of the most common musculoskeletal complication of DM patients. In this particular study, 31.33% patients had frozen shoulder, 0.6% patients did not respond to this question. (Mean age: 61 years, mean duration of diabetes: six years). Range of motion is decreased in abduction and external rotation mainly. Though exact mechanism is unknown,

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increased glycosylation of collagen protein and increased formation of abnormal glycation end products, increased connective tissue deposition due to myofibroblasts proliferation, neuropathy, vascular insufficiency and abnormal levels of insulin and insulin-like growth factors in the body and their accumulation and abnormal collagen repair predisposes patients to adhesive capsulitis.[41] One study showed, T2DM patients had prevalence of 22.4% which is higher than T1DM patients which is 10.3% of frozen shoulder.[29] Ramchurn et al. (2009) did a study with 96 people during the period January to March 2007 found prevalence of 39% frozen shoulder in T2DM.[42] In another study, the prevalence of FS was found out to be 41.3%, as 33 patients complained of pain during movement of the shoulder and had consistent radiologic findings. A total of 12 of them had bilateral shoulder pain.[43]

T2DM for long time, specially if poorly controlled, may develop peripheral neuropathy. It causes sensory, motor and autonomic symptoms, especially in the lower limbs which may cause foot ulcers, sometimes leading to amputations and disabilities. Recent studies showed that neuropathic changes may also occur even in the early stage.[44] The prevalence of diabetic neuropathy in this study was (26.89%) (Mean age: 61 years, mean duration of diabetes: 7 years). Previous studies showed, DPN prevalence of 32.1% (mean age: 63 years, mean duration of diabetes: six years);[45] 35.4% (mean age: 61.3 years, mean duration of diabetes: 9.7 years) and 60.0% (Mean±SD age: 57.2±10.3, Mean±SD duration of diabetes: 8.52±7.13 years) among T2DM hospital outpatients.[46,47] In a previous study it showed that prevalence of DPN in patients having DM <5 year was 20.8% which increases to 36.8% with duration >10 years.[25] Current study also revealed that peripheral neuropathy prevalence is high with prolong duration and poor control of blood glucose. T2DM rate is increasing day by day due to sedentary life, lack of physical exercise, genetic predisposition and inappropriate nutrition. Perkins et al reported that CTS is common in 30% diabetic neuropathy.[36]

T2DM plays a role on the development and progression of OA knee. It causes hyperglycemia, release inflammatory cytokines and adipokines, oxidative and osmotic stress, production of reactive oxygen species and oxidants and promotes matrix catabolism and AGEs collectively inhibit osteocyte function, alter bone turnover, and degrade collagen properties. Significant synovitis occurring in OA may be exacerbated by the increased levels of inflammatory cytokines, adipokines, and prostaglandins seen here.[48] High glucose levels may affect cell function and alter extracellular matrix components of the connective tissue producing damage and reduce space of the joint.[22,23] This is aggravated by obesity, increased age, female sex, trauma etc. Current study showed that 17.33% patients had pain or stiffness in knee while 81.67% did not feel pain and 1.0% did not respond to this question. (Mean age: 63 years, mean duration of diabetes: six years). In another study in Bangladesh, 43.9% had osteoarthritis of knee.[49]

CONCLUSIONS

It is concluded that the prevalence of different pain conditions are high among patients of T2DM and commonly affects low back, shoulder, peripheral neurons and knee. These are most commonly manageable with medications and followed by physical therapy.

Recommendations

It is recommended to investigate further on the topic with large sample size across the whole country to get the more precise prevalence.

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