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Epidemiology and clinical profile of common musculoskeletal diseases in patients with diabetes mellitus at Tikur Anbessa Specialized Hospital in Addis Ababa, Ethiopia

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Abstract

Background: ***Diabetes mellitus (DM) affects connective tissues in many ways and causes different alterations in periarticular and skeletal systems.***

Methods: ***A cross-sectional study was conducted by interviewing and examining 402 consecutive diabetic patients followed at Tikur Anbessa Hospital OPD. Evaluation was performed according to the Short Musculoskeletal Function Assessment Questionnaire (SMFA). The diagnoses were established by Consultant Orthopedic Surgeon.***

Results: ***Average duration of diabetes is 143 months (12 Years) and majority, 66.7% (268/402) of them are currently on insulin therapy. Mean current FBS is 245mg%. Excluding OA (47, 11.7%) and CLBP (78, 19.4%), overall prevalence of 1 or more of musculoskeletal Diseases (MSD) is 41.5 %. Hands were the most affected (74, 18.5 %). Five had amputation. Hand involvement and sex of the patient and Type of diabetes is significantly associated, Duration of DM and shoulder involvement are significantly related.***

Conclusions: ***Musculoskeletal manifestations are very high in adult diabetic patients at the centre and need multidisciplinary clinical attention. Physicians should always consider examining the periarticular regions of the joints in the hands and feet. Duration of diabetes is associated with development of shoulder complications.***

Recommendations: ***Routine MSD screening, establishing a foot care clinic and strengthening diabetic education may prevent development or worsening of MSD.***

Keywords: musculoskeletal complications, diabetic foot, foot care, trigger finger, Dupuytren's contracture, stiff frozen shoulder

Introduction

Diabetes mellitus (DM) is a disorder of carbohydrate metabolism caused by relative or absolute deficiency of insulin, hyperglycaemia and end-organ complications, including vasculopathy, nephropathy, retinopathy, and accelerated atherosclerosis. It approximately affects 6% to 10% of the U.S. population and became an alarming epidemic. According to Enrico, the incidence of diabetes is also increasing in developing countries, owing to life style changes. The incidence of diabetes in Ethiopia is not known. Diabetes may affect the musculoskeletal system in a variety of ways. The metabolic perturbations in diabetes (including glycosylation of proteins, microvascular abnormalities with damage to blood vessels and nerves, and collagen accumulation in skin and periarticular structures) result in changes in the connective tissue. Musculoskeletal complications are most commonly seen in patients with a longstanding history of type 1 diabetes, but they are also seen in patients with type 2 diabetes. Some of the complications have a known direct association with diabetes, whereas others have a suggested but unproven association. DM affects connective tissues in many ways and causes different alterations in periarticular and

skeletal systems. Moreover, many of these rheumatological complications are treatable to varying degrees, with resultant improvements in quality of life and more independence in activities of daily living. In our hospital, 2 studies done have shown that complicated diabetes was responsible for 17% of all major limb amputations in the years 1988 to 2005.[1] It is also a leading cause of preventable major amputations-responsible for 24 of the 32 major amputations indicated in vascular insufficiency patients in the year 2002.[2] Another study conducted in our hospital demonstrated that the direct cost of hospitalisation of diabetic patient is significantly higher than non-diabetics.[3]

The short musculoskeletal function assessment (SMFA) format can possibly be a useful tool used to screen musculoskeletal complications.[4-9] Several musculoskeletal disorders have been described in these patients which can be divided into 3 categories[10,11]:

A. disorders which represent intrinsic complications of diabetes, such as limited joint mobility or diabetic cheiroarthropathy, stiff hand syndrome, and diabetic muscular infarction, [12-15]
B. disorders with an increased incidence among diabetics, such as Dupuytren's disease, shoulder capsulitis, neuropathic arthropathy, osteopenia (in type 1 DM), flexor tenosynovitis, septic arthritis, acute proximal neuropathy, proximal motor neuropathy, pyomyositis and the diffuse idiopathic skeletal hyperostosis (DISH) syndrome, the diagnosis of which depends on the radiographic recognition of a minimum of 2 bridges connecting 3 consecutive vertebrae in diabetics usually complaining of back pain.[16-17]
C. Disorders for which a possible association with diabetes has been proposed but not proven yet, such as osteoarthritis and the carpal tunnel syndrome.[18-20]

Objectives

The general objective of this study was to assess the epidemiology profile, clinical manifestation and risk factors of musculoskeletal disease in diabetic patients followed at Diabetes Center of Tikur Anbessa Specialized Hospital (TASH), a tertiary referral hospital.

The specific objectives were to:

1) Assess the epidemiology of musculoskeletal disorders in patients with type 1 or 2 diabetes mellitus followed at the Diabetes Center of TASH.
2) Evaluate the clinical manifestations of musculoskeletal disease in patients with diabetes.
3) Assess the risk factors associated with musculoskeletal disease.
4) Compare the prevalence of musculoskeletal complications in our patients and other population studies, both from developed and developing countries.

Methods

Adult diabetics, presenting for follow-up at the TASH Diabetes Center during the study were prospectively included in this cross-sectional study.

Sample size determination and sampling procedures

A single population and a single population proportion formula, $n = (Z\ \alpha/2)2\ p\ (1-p)\ /\ d2$, was used to estimate the sample size. Proportion of patients with a MSK-complication is assumed 50% ($p = 0.5$), level of significance to be 5% ($\alpha = 0.05$), and absolute precision or margin of error to be 5% ($d = 0.05$). Computing with the above formula gives a total sample size of 384. Considering a 10% non-response rate would finally may make the sample size 422. Random sampling technique

will be used and every other patient, fitting the criteria and presenting to the clinic will be interviewed.

Inclusion and exclusion criteria

All consecutive adult diabetic patients coming to the outpatient department of the Diabetes Center in the 6 months of the study period (February-July 2010) were included in the study.

Exclusion criteria included pregnancy, age less than 14 years, and diabetes secondary to another specific syndrome (Cushing's syndrome, for example). DM patients with emergencies and inpatients were also excluded.

Study design

This was a prospective cross-sectional study. Evaluation was performed according to the Short Musculoskeletal Function Assessment Questionnaire (SMFA), clinical history, physical examination and laboratory investigations. This tool was developed by Swiontkowski in 1999.[4-9] It represents a valid reliable and responsive instrument for clinical assessments and is recommended by the American Academy of Orthopedic Surgeons. The SMFA is a self-administered form but assistance could be provided by a diabetes nurse. Patients with findings on the SMFA were closely examined by a consultant to make a diagnosis. Upon completion of the questionnaire and clinical examination of the patients' laboratory tests, imaging analysis and histopathological analysis of tissue samples were requested and evaluated in selected cases.

Variables

Presence of musculoskeletal problems represented the main dependent variable. Independent variables included age, sex, occupation, religion, education, type of diabetes, and duration of diabetes.

Data collection

The SMFA questionnaire was used.

Clinical diagnoses were made based on the following definitionsd[21-23]:

1) Carpal tunnel syndrome (CTS) was defined as weakness or pain of the hand, evidence of thenar atrophy, or nocturnal paresthesia of the thumb, index, and long fingers, with or without a positive Tinel's or Phalen's sign. CTS was excluded if other causes, such as thyroid disease, acromegaly, or C5/C6 radiculopathy were suspected. We also considered a history of surgery as evidence of the disease.
2) The diagnosis of Dupuytren's contracture was based on 1 of the following features: a palmar or digital nodule; tethering of palmar or digital skin; a pretendinous band and a digital flexion contracture, palpable thickening of the palmar fascia, with a flexor deformity of the second, third, fourth, or fifth fingers.
3) Frozen shoulder (adhesive capsulitis, AC): Patients with unilateral shoulder pain for at least 1 month, an inability to lie on the affected shoulder, and restricted active and passive shoulder joint movement of less than 50% in at least 3 planes were diagnosed as so.
4) Diabetic cheiroarthropathy or limited joint mobility was evaluated by the patient 'prayer sign' in which the patient was asked to approximate the palmar surfaces of their

interphalangeal joints, with the fingers fanned and the wrist maximally extended. If they were unable to do so, the test was considered positive

5) Diabetic sclerodactyly was defined as thickening of the skin on the dorsal aspect of the hand in association with limited joint mobility in the absence of Raynaud phenomenon, calcinosis, and telangiectasia.
6) Flexor tenosynovitis or stenosing tenosynovitis or trigger finger was diagnosed by palpating a nodule or thickened flexor tendon with locking phenomenon during finger flexion or extension.
7) Reflex sympathetic dystrophy (RSD) was defined as unilateral, localised, or diffused pain associated with swelling or trophic changes and vasomotor disturbance with impaired mobility of the affected limb.
8) Diabetic amyotrophy was defined as wasting of the proximal upper or lower extremity muscles or the paraspinal muscles, preceded by severe pain and dysesthesia of the involved part.
9) Diabetic osteolysis was characterised by osteoporosis of the proximal phalanges in the hands and feet, documented by x-ray radiographs.
10) Diffuse idiopathic skeletal hyperostosis syndrome (DISH) was diagnosed based on the classification criteria set by Resnick and Niwayama, which requires radiographically recognised bridges connecting at least 4 contiguous vertebrae of the thoracic spine, with preservation of the intervertebral disk space and absence of apophyseal joints or sacroiliac inflammatory changes. Only those with back pain had an x-ray of the spine.
11) Diabetic muscle infarction was defined as a palpable painful mass with swelling and induration of the surrounding tissue without systemic symptoms, in addition to evidence of oedema in the muscle on magnetic resonance imaging. A history of surgery for was also considered as evidence of the disease.
12) Charcot joint or neuropathic arthropathy was defined as painless swelling and deformity at the weight-bearing joints and the classical finding of articular surface destruction, dislocation, disorganisation, and increased density of the involved joint on x-rays.
13) Diabetic neuropathies were diagnosed and documented at neurology clinic when a particular patient visits the clinic during the follow up.
14) Microvascular complications like retinopathy and nephropathy were not included.

Statistical analysis

Data analysis was carried out using SPSS version 16. Means and standard deviations (SDs) were calculated for quantitative data, and percentages for categorical variables. Numbers and percentages were compared using Pearson Chi-square test. The association of MSK manifestations with the various covariates was calculated using multivariate odds ratio, with a 95% confidence interval. Results were considered significant if the P-value was < 0.05.

Results

During the 6 months study period, 402 adult outpatient diabetic patients were interviewed. Their ages ranged from 18 to 78 years, with a mean age 48 $\pm$ 12 years. Table 1 shows the age distribution. Most patients, close to 29% (115 of 402) were in the age group 50 to 59years. 56.2% (226 of 402) were female, while 43.8% (176 of 402) were male. Type 1 DM accounted for 32.6% (131) of the patients, and 171 patients (67.4%) had type 2 DM. The majority of patients on follow-up were from Addis Ababa (82.8%; 333 of 402). Figure 1 shows that most patients had some education and only 13.9% (56 of 402) were not able to read or write, while 28.9% (116 of 402) had completed secondary school. Figure 2 shows 63.6% of the patients were employed, while 36.3% were housewives.

Table 2 shows the different treatment regimens. Most patients, 268 (66.7%), were on insulin. The current fasting blood sugar (FBS) level was assessed for 388 patients, as shown in Figure 3 and Table 3. Mean FBS level was 245 mg%.

As listed on Table 4, nearly half, 49.5 %(199 of 402) of the patients on follow-up had 1 or more chronic medical illnesses. 29.6% (59 of 199) of these patients had more than 1 chronic medical illness. Hypertension was the commonest comorbidity detected; it was found in 39.6% of patients (159 out of 402).

Table 5 shows that 126 of 402 patients (31.3%) were clinically demonstrating at least 1 musculoskeletal condition that commonly exists with DM. The hands were most commonly affected. The hands were involved in 18.5% (74 of 402) of the patients, with 5 patients having more than 1 hand complication. In descending order, other body parts affected were: the shoulder (4.4%; 18 of 402), the feet (4%; 16 of 402), the lumbar skeleton (4%; 16 of 402), and muscles (0.5%; 2 of 402). Coexisting MSK conditions that were seen included: chronic low back pain with no lateral lumbar x-ray finding in 19.4% (78 of 402 patients), any joint osteoarthritis in 11.7 % (47 of 402), symptoms of peripheral neuropathy in 7.2% (29 of 402), radiculopathy in 0.7% (3 of 402), and other conditions accounted for 2.2% (9 of 402). Table 6 shows odds ratios (ORs), and statistical significance tests were performed to establish associations between the variables listed and MSK complications.

Table 1: Age distribution of adult outpatients followed at the Tikur Anbessa Hospital Diabetes Center

Age group (years)	n	%
14-19	6	1.5
20-29	51	12.7
30-29	59	14.7
40-49	72	17.9
50-59	115	28.6
60+	99	24.6
Total	402	100.0

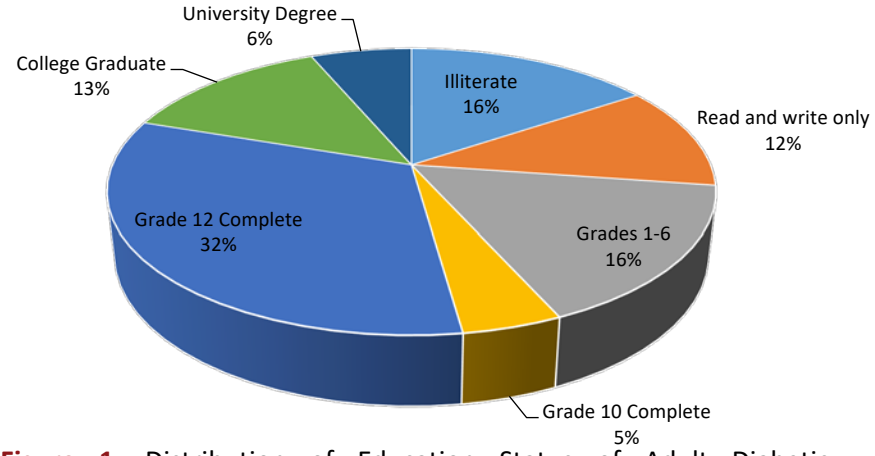

Figure 1: Distribution of Education Status of Adult Diabetic outpatients followed at the Tikur-Anbessa Hospital Diabetes Center (N = 402)

Table 2: Treatment regimens of adult outpatients followed at the Tikur Anbessa Hospital Diabetes Center

Treatment regimen	n	%
Insulin	268	66.7
Oral hypoglycaemic (OH) agents	112	27.9
Both insulin & OH agents	12	3.0
Diet alone	2	0.5
Unknown	8	2.0
Total	402	100.0

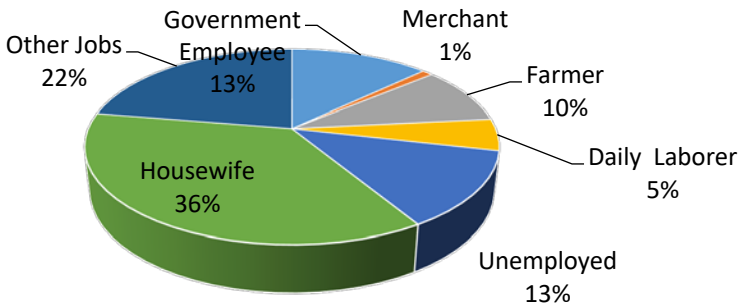

Figure 2: Distribution of occupations

Table 3: Fasting blood sugar (FBS) measurements among adult outpatients followed at the Tikur Anbessa Hospital Diabetes Center

n = 388	FBS current (mg %)	FBS highest	FBS lowest
Mean	245.2	341.1	80.5
Median	215.5	300.0	70.0
Range	719	641	385
Minimum	31	109	15
Maximum	750	750	400
Standard deviation	123.6	115.8	38.6

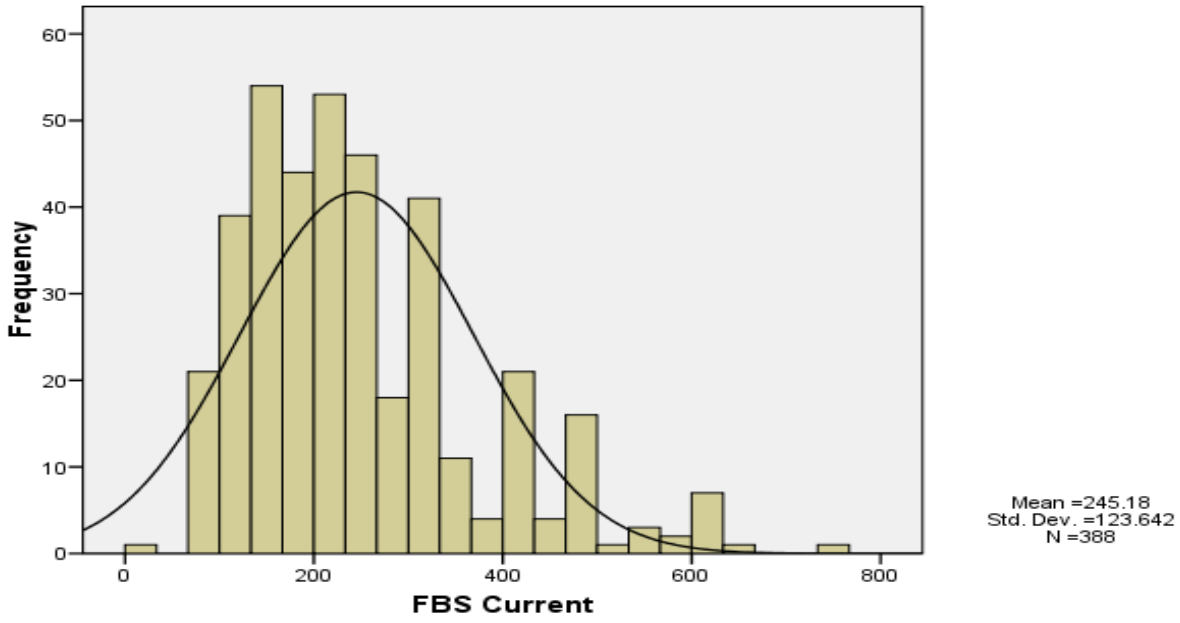

Figure 3: Histogram of current fasting blood sugar (FBS) in adults followed at Tikur Anbessa Hospital Diabetes Center (n = 388)

Table 4: Chronic medical comorbidities among adult outpatients followed at the Tikur Anbessa Hospital Diabetes Center (n = 199)

Chronic medical illness	n	% (of total N = 402)
Hypertension	159	39.6
Cardiac illness	22	5.5
HIV	5	1.2
Rheumatoid arthritis	1	0.2
Asthma	5	1.2
Nephropathy or renal failure	27	6.7
Retinopathy	13	3.2
Dyslipidaemia	19	4.7
Liver disease	3	0.5
Anaemia	1	0.2
Seizure disorder	2	0.5
Thyrotoxicosis	1	0.2
No chronic medical illness	203/402	
More than 1 chronic illness	59/199	

Table 5: Distribution of musculoskeletal diseases among adult outpatients followed at the Tikur Anbessa Hospital Diabetes Center

Musculoskeletal clinical manifestations	n	% (N = 402)
Conditions affecting hand		
Diabetic cheiroarthropathy	30	7.5
Trigger finger	36	9
Dupuytren's contracture	4	1
Carpal tunnel syndrome	4	1
Subtotal	74	18.5
Conditions affecting shoulder		
Frozen Shoulder	13	3.2
Calcific Periarthritis	5	1.2
Subtotal	18	4.4
Conditions affecting the feet		
Diabetic Osteoarthropathy	6	1.5
Plantar Fasciitis	10	2.5
Subtotal	16	4.0
DISH (back pain + x-ray finding)	16	4
Muscle infarction	2	0.5
Total	126	31.3 %
Other MSK conditions encountered		
Chronic low back pain	78	19.4
Osteoarthritis (any joint)	74	11.7
Peripheral neuropathy symptoms	29	7.2
Radiculopathy symptoms	3	0.7
Unrelated musculoskeletal conditions	9	2.2

Table 6: Study variables with statistically significant associations (at the 95% confidence level) among adult outpatients followed at the Tikur Anbessa Hospital Diabetes Center

Variables	Odds Ratio	P-value	Z-statistic
Male sex and hand complications	1.99	0.015	2.43
Type 1 diabetes mellitus (DM) and hand complications	2.36	0.009	2.62
DM duration > 10 years and hand complications	3.370	< 0.001	3.90
DM duration > 10 years and shoulder complications	5.745	0.022	2.29
Type 1 DM and neural complications	4.863	0.035	2.11
Chronic medical illness and musculoskeletal complication	4.323	< 0.001	6.21
DM duration > 10 years and chronic medical illness	2.210	< 0.001	3.81

Discussion

The percentage of any MSK manifestation in our adult outpatients with DM was 31.3% (126 of 402).

Our study reveals the following 5 important findings:

1. Hypertension being the commonest (39.6%), about half (49.5%) of the patients examined have at least 1 chronic medical illness and about 29.6% of have multiple chronic medical illnesses.
2. Overall average FBS value was 245 mg%, which is very high.
3. There was a high proportion (19.4%) of chronic low back pain, and the x-ray findings were in line with this finding.
4. There was a statistically significant association observed between clinically manifesting MSK complications and having a male sex, type 1 DM, DM for more than 10 years, and a chronic medical illness. These patents showed the highest risk for developing 1 or more musculoskeletal disorder or complication.
5. Long standing diabetes (10 years or more) was significantly associated with development of a chronic medical illness, which in turn was significantly associated with development of a MSK complication.

It is estimated that more than half of diabetic patients will suffer from chronic disability.[24] Some factors that contribute to chronic disability in diabetic patients include vascular complications, in addition to predisposing conditions, such as obesity and low physical activity.

Many studies have evaluated MSK manifestations in diabetic patients, but most assessed only an individual component, especially MSK involvement of the hands and shoulders.[25] Few studies have evaluated the entire MSK system, including the limbs and back. Among these was a pilot

study on 208 patients with type 2 diabetes in which MSK complications, excluding osteoarthritis, were detected in 38% of cases.[3] A higher prevalence (58%) was reported by other authors in a cohort of 80 patients with type 2 diabetes.[26] The relatively lower prevalence of MSK manifestations in our cohort could be related to the fact that we excluded osteoarthritis, which was a common finding in our study population (11.7%). We excluded osteoarthritis because there are many confounding factors that lead to osteoarthritis in our patients.

The single organ most frequently affected by MSK complications in this study was the hand. We commonly encountered trigger finger (9%) and hand stiffness (7.5%). Only 4 patients (1%) had carpal tunnel syndrome (CTS). CTS has been observed in up to 20% of patients with diabetes.[27] The lower proportion of CTS in this study could be explained by the fact that most such patients have been receiving treatment at a dedicated hand subspecialty centre in our study area. Adhesive capsulitis (frozen shoulder) was observed in 3.2% of our patients; however, this was much less than the 25% reported from studies in the West.[28]

Adhesive capsulitis is a chronic disabling condition associated with pain and requires long-term treatment (2 to 3 years) in the form of physiotherapy and repeated injections. Unfortunately, the treatment is more prolonged in patients with diabetes, and surgical intervention may be required if the condition is not treated early. The association of adhesive capsulitis with DM was disputed among researchers, but a recent huge meta-analysis has shown that patients with DM are as much as 5 times more likely than controls to have adhesive capsulitis. In the same analysis, the overall prevalence of adhesive capsulitis in patients with DM was 13.4%, and the prevalence of DM among patients with adhesive capsulitis was approximately 30%.[29,30]

In a long-standing disease, there is strong evidence that the development of 1 complication predisposes the development of another. We found a significant association between any MSK complication of diabetes and a comorbid chronic medical illness. Similarly, a Japanese group examined 302 diabetic patients in a case–control study and demonstrated a significant association between different types of complications, especially flexor tenosynovitis and limited joint mobility.

The most important predictor of MSK complications in people living with diabetes is blood glucose control.[31] In our study, there was no association between blood glucose control and MSK manifestations, although we calculated only the mean FBS and not HbA1c level. Even a single HbA1c level does not correlate with tissue levels of advanced glycosylation end products.[30] This is in line with the findings of Thomas et al. but contradicts the results obtained in a British cohort that demonstrated a strong association between MSK manifestations and poor blood glucose control.

Vascular complications are another important predisposing factor, but we did not include them in our study because there are only limited number of vascular evaluations and investigations that can be performed in our centre. Ardic et al. demonstrated that hand and shoulder syndrome was most likely associated with retinopathy but not nephropathy or neuropathy. In our hospital, patients with vascular complications are usually inpatients.

At present, there are established guidelines for the follow-up of type 2 diabetic patients, which are aimed at detecting microvascular complications, such as retinopathy, neuropathy, and nephropathy. However, no guidelines have been established to guide clinicians on the detection of MSK complications among individuals with type 2 diabetes.

Conclusions

Musculoskeletal manifestations are highly prevalent among adults with diabetes at our centre and attention must be given to these complications. Physicians should consider examining the periarticular regions of the hands and shoulders whenever an adult diabetes patient presents with MSK symptoms. There was a statistically significant association between clinically manifesting MSK complications and having a male sex, type 1 DM, DM for more than 10 years, and a comorbid chronic medical illness.

Long-standing diabetes is significantly associated with comorbid chronic medical illness and development of MSK complications.

Recommendations

The following are our recommendations:

1. Increasing patient awareness and physician detection of MSK complications in DM.
2. Identifying patients at high risk of developing MSK complications and arranging proper evaluation that may help early intervention.
3. Multidisciplinary handling of diabetic patients at our centre (including physiotherapy, foot care, a hand centre, for example)
4. Further investigation of the highly prevalent chronic low back pain without x-ray finding suggesting DISH.
5. If 1 MSK condition is clinically encountered, screening for DM is suggested.

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