Musculoskeletal effects of diabetes mellitus
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Abstract
People with diabetes show higher prevalence of rheumatic diseases as compared to general population. Diabetes affects all components of musculoskeletal system viz. muscles, bones and connective tissue. Diabetic myonecrosis is a unique condition seen only in people with diabetes. Other diseases include amyotrophy, osteoporosis and increased fracture risk, carpal tunnel syndrome, adhesive capsulitis of shoulder, trigger finger and limited joint mobility. Like all other chronic diseases, musculoskeletal diseases impact quality of life negatively.

Keywords: Rheumatological manifestations, Type 1 diabetes, Type 2 diabetes, Osteoporosis.

Introduction
Impact of musculoskeletal complications on quality of life of people with diabetes is tremendous. There is a large epidemiological data associating these complications with diabetes, but pathogenesis and causative factors have not been elucidated yet. Musculoskeletal complications are frequently found in persons with diabetes mellitus. In a study from Karachi,1 54% of 210 patients had musculoskeletal abnormality whereas 30% of patients had upper limb musculoskeletal manifestations on examination. In the hand region, limited joint mobility (9.5%), carpal tunnel syndrome (9%), trigger finger (3.8%), and Dupuytren’s contracture (1%) were found more frequent as compared to controls, while in shoulder region of diabetic subjects, adhesive capsulitis and tendonitis was found in 10.9% and 9.5% respectively as compared to 2.5% and 2% in controls. For pedagogic simplicity, musculoskeletal complications of diabetes can be categorized largely into two categories:

1. Effect of diabetes on Muscle tissues
2. Effects of diabetes on joint and connective tissue.

Effects of Diabetes on Muscle
Diabetic Myonecrosis
Diabetic myonecrosis, a rare manifestation unique to DM, entails spontaneous infarction of muscle. Approximately 200 cases have been reported so far. The underlying pathophysiology is thought to be ischaemic, though no obvious atheroembolism/vascular occlusion has been documented. Myonecrosis has been shown to be associated with 2 year mortality rates of 10%, due mainly to cardiovascular disease.

Patients with diabetic muscle infarction usually present with acute pain with swelling (and a palpable mass in 34-44% of the patients) in an extremity, which persists at rest, worsens with exercise and expands during a period of days/ weeks without any prior history of trauma.2 The thigh muscles are commonly involved, while calf, upper extremity and abdominal wall muscles can be affected. Markers of inflammation, i.e. ESR (Erythrocyte sedimentation rate) and CRP (C-reactive protein), are usually raised while creatine kinase, marker of muscle injury, may normalize in late stage of presentation. Normal temperature and leucocytes help in ruling out infective pathology. It is important to rule out deep vein thrombosis or major arterial thrombosis by Doppler. Muscle oedema can be demonstrated by ultrasonography or on magnetic resonance imaging, in which involved muscle shows hyper intensity on T2-weighted sequences, and can be delineated from normal muscle by lack of enhancement after contrast administration.2 Diabetic myonecrosis is a self-limiting disease and generally remits by 6-12 weeks. Symptomatic management of pain and rest are mainstay of therapy.2 Compartment syndrome may occur due to excessive muscle oedema. Antiplatelet agents are generally co-prescribed as there is evidence of microangiopathy. However, little can be done to prevent recurrence in approximately 50% patients.

Diabetic Amyotrophy
Diabetic amyotrophy or diabetic lumbosacral plexopathy is a predominantly neural pathophysiology in contrast to direct muscle damage in diabetic myonecrosis. Amyotrophy occurs more commonly in well controlled or recently diagnosed T2DM. Presentation is similar to myonecrosis with acute onset proximal leg pain followed by muscle weakness, but may include loss of muscle mass. Disease generally starts unilaterally, but involves other limb simultaneously or later, in majority of patients. Amyotrophy may be associated with new onset

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autonomic symptoms in up to 50%, and significant weight loss in 80% patients. Ischaemic neural injury due to microvasculitis is the most likely pathophysiology.

Diagnosis is confirmed by electro diagnostic studies, in presence of relevant clinical finding.

Natural history of amyotrophy demonstrates a self-limited course with spontaneous resolution over months. Muscular weakness or pain may persist. Mainstay of treatment is pain relief along with supportive management. There is paucity of data to support treatment with steroids or immunosuppressive therapies.

**Effect of Diabetes on Joint and Connective Tissue**

People with diabetes show higher prevalence of joint and connective tissue diseases as compared to general population. There is no clear pathophysiological mechanism explaining the joint and connective tissue effects of diabetes. However, the proposed mechanism is accumulation of advanced glycation end products (AGEs), with cross-linking of collagen and other macromolecules in connective tissue (tendon sheath and palmar fascia) and around joints.

**Adhesive Capsulitis of the Shoulder (Frozen Shoulder Syndrome, Shoulder Periarthritis)**

Adhesive capsulitis is characterized by gradual development of global limitation of active and passive shoulder motion where radiographic findings other than osteopenia are absent. The prevalence of frozen shoulder is estimated to be 2-5% in the general population and 10-30% in diabetics, being more common in long-standing diabetes. The exact pathophysiology is not clear with both inflammatory and fibrosing elements being present. Clinically, adhesive capsulitis exhibits three distinct phases: initial painful phase with gradually increasing stiffness, followed by progressive severe limitation of shoulder movements and disappearance of pain, followed finally by gradual complete or incomplete resolution. The entire course spans over one to four years.
with an average of 30 months. Treatment of adhesive capsulitis involves analgesics, physiotherapy, glucocorticoid injection and intra-articular dilatation. Patient education regarding disease process is paramount. There is lack of consensus regarding selection of patients for glucocorticoid injection, but it is accepted that glucocorticoids are more effective when given early in course of disease. Arthroscopic capsular release is only indicated for refractory shoulder adhesive capsulitis.

**Limited Joint Mobility (Diabetic Cheiro-Arthropathy)**

Limited joint mobility (LJM), known as "diabetic cheiroarthropathy", affects upper limb and hands, and is characterized by involvement of small joint of hands with markedly thick, rigid and waxy skin, especially on the dorsal aspects of finger. The prevalence of LJM in diabetes varies from 8-60% in contrast to the general population prevalence of 12-25%. Prevalence of LJM increases with duration of diabetes and may increase with poor glycaemic control, increasing age and smoking. LJM should alert the physician about higher risk for foot ulceration in these patients as well as for other microvascular complications that may be pre-existing.

LJM can be clinically screened by two simple physical examination signs. The Prayer (preacher’s) sign involves flattening the hands against one another. This test helps recognizing limited joint mobility at metacarpophalangeal and interphalangeal joints. In table top sign the patient flattens the palms on hard surface of table, and assesses mobility at metacarpophalangeal joints. The complete palmar surface of the digits and palm should touch the table, if joint mobility is normal. If mobility is limited, the digits and palm will not touch the table surface completely.

No satisfactory treatment of LJM is available at present. Cessation of smoking, optimal glycaemic control, physiotherapy and occupational therapy is suggested. Physiotherapy involves active and passive mobilization at involved joints and use of corrective splints, if required.

**Dupuytren’s Contracture (DC)**

DC is a benign, slowly progressive fibro-proliferative disorder of palmar fascia. This condition can be either painless or painful and usually starts as nodule on palmar aspect. With time, fibrosis increases and forms longitudinal bands on palmar fascia resulting in flexion deformity of one (middle finger most commonly) or more fingers. Some form of DC has been reported to occur in 15-45% of persons with diabetes. Apart from diabetes, DC is seen more commonly with smoking, alcohol consumption and work related exposure to vibratory motion.

Incidence of DC increases in males, with age, duration of diabetes, poor glycaemic control, and microvascular complications. DC runs a variable course with 40% patients reporting static disease, 50% reporting progression and 10% showing regression.

Treatment of mild DC involves optimized glycaemic control and physiotherapy. Care should be taken to avoid forceful stretching as it may actually worsen fibrosis. Topical steroid injections are recommended in patients with painful disease or if fibrosis is growing rapidly. Surgery is mainstay of treatment in moderate to severe diseases. Collagenase injection has been used, but long term results are not clear.

**Stenosing Flexor Tenosynovitis (Trigger Finger) (TF)**

Flexor tendon of each digit passes through a fibro-osseous tunnel/sheath to reach its distal attachment, the middle phalanx in case of superficialis tendon and distal phalanx for the profundus tendon. This tunnel is important for providing mechanical stability and nutrition to the tendon. TF involves nodule formation in flexor sheath or tendon, due to combination of repetitive trauma and impaired healing, which prohibits the smooth movement of tendon within flexor sheath. Patient typically presents with pain and sensation of snapping due to locking (or "triggering") of fingers in flexion, extension or both, most commonly affecting ring finger, middle finger, and thumb.

On clinical examination, locking is present both on active or passive finger flexion. The nodule in flexor sheath or tendon may be palpable at the base of affected finger. The prevalence is 5-36% among people with diabetes as compared with 2% in the general population. As in other musculoskeletal disorders in diabetes, trigger finger correlates more with duration of diabetes than metabolic control. Multiple fingers may be affected simultaneously in patients with DM.

Treatment of acute TF includes immobilization of finger, ice application and oral paracetamol. After resolution of acute symptoms, gradual stretching exercises are recommended. Intraleseional glucocorticoids with or without lidocaine can be injected in severe or refractory cases. Surgery is usually considered when intraleseional steroid has failed on two occasions.

**Carpal Tunnel Syndrome (CTS)**

Carpal Tunnel Syndrome is the most common
compression neuropathy seen in patients with diabetes. The prevalence of CTS in diabetes is shown to be around 14-20%, and it is more common in women.

This syndrome occurs as a result of compression of median nerve in carpal tunnel, which is narrowed by structural alterations of tendons, and proliferation of the peri-neural connective tissue. Patient usually presents with sensory symptoms involving median nerve territory, worsened by sleep and extremes of motion at wrist. In severe cases, patient may experience clumsiness of hand movements due to atrophy of hand muscles. Two physical signs, Tinel's sign and Phalen's test, may provide valuable clinical clue in suggesting the diagnosis. Diagnosis can be confirmed by nerve conduction studies and electromyography.

Management of mild cases is conservative with splinting, analgesics and ultrasound therapy. Local glucocorticoid injection is added in moderate cases, while surgical release of overlying fascia is indicated in severe cases with motor deficit or in refractory disease.

Table-1 summarizes the musculoskeletal complications of diabetes.

The rheumatic hand manifestations seen in persons with diabetes are summarized in Table-2.

**Conclusion**

Musculoskeletal diseases are more common in people with diabetes, and significantly affect their quality of life. Most of these problems are duration-dependent, and can be harbinger or marker of underlying microvascular complications. Early identification of musculoskeletal problems can lead to reduction in long term morbidity. A large number of these diseases run a self-limiting course, and education about course of disease and expected outcome can help in relieving psychological stress and preventing use of spurious remedies.

**References**