Alaa Monjed

21.1 Introduction

Diabetes mellitus (DM) is a chronic disease characterized by persistent hyperglycaemia that happens as a result of a pancreatic insulin deficiency and/or insulin resistance. Its morbidity and mortality are primarily related to the resultant microvascular and macrovascular complications. Its prevalence has grown widely, which will result in higher rates of diabetic complications including rheumatic manifestations.

An improved understanding of the mechanisms through which diabetes alters connective tissue metabolism should lead to better preventive and therapeutic interventions. In this chapter, a brief summary about the pathophysiology of rheumatological manifestations in diabetes is outlined. A schematic classification of rheumatological manifestations in diabetic patients is demonstrated according to the region and according to the presence or absence of pain. This is followed by summarized review of these rheumatological manifestations of diabetes mellitus. It is obvious that these are not unique to diabetes mellitus as it may affect normal individuals, as well.

21.1.1 Objectives

The reader of this chapter should be able to:

1. Identify different diabetes related rheumatic complications.
2. Differentiate between rheumatic complications related to diabetes and those associated with other diseases.
3. Classify these rheumatic diseases based on the involved region and the underlying pathophysiology.
4. Assess diabetic patients with rheumatic complications clinically and select the appropriate diagnostic tests.
5. Manage diabetic patients with rheumatic complications.

21.2 Pathophysiology

The high glucose, high insulin milieu of diabetes affects many of the key cells and matrix components of connective tissues. For example, reactive oxygen species are increased in diabetes and certainly may mediate tissue damage [1]. Advanced glycosylation end products (AGEs) tend to accumulate in the long-lived proteins of connective tissues and may alter both extracellular matrix structure and function as well as cell viability [2]. Early glycosylation of skin collagen can be decreased by improving glycaemic

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control [3, 4]. However, the long-term, cumulative damage due to the binding of advanced glycosylation end products to collagen is probably irreversible.

21.2.1 Classification of Rheumatological Manifestations in Diabetic Patients

Rheumatological diseases associated with diabetes mellitus can be classified according to:

1. The involved musculoskeletal structures as shown in the Fig. 21.1.
2. Painful or painless rheumatic diseases as shown in the Fig. 21.2.

21.3 Carpal Tunnel Syndrome

Carpal tunnel syndrome (CTS) is an entrapment neuropathy caused by compression of the median nerve resulting in pain and/or paraesthesia in thumb, index and middle finger.

21.3.1 Epidemiology

- *In diabetic patients*: CTS is common and estimated to occur in **14%** in patients without diabetic polyneuropathies and up to **30%** in those with diabetic polyneuropathies [5].
- It may be more common in those with prediabetes [6].
- More common in women than men [7].
- *In nondiabetics* with life expectancy of 70 years: **3–5%** in Men and **11%** in women are expected to develop CTS [7].

21.3.2 Approach to CTS

21.3.2.1 History

- *Numbness and tingling sensation*: it should be localized to the palmar aspect of the first to the fourth fingers and the distal palm. These symptoms usually happen at night and resolve by shaking (shake sign).
- *Pain*: usually at night, and over the ventral aspect of the wrist and radiated distally to the palm and fingers or proximally to the ventral forearm, resolved by flicking (flicking sign).

The musculoskeletal structures involved in diabetes-associated rheumatological diseases

Fig. 21.1 The musculoskeletal structures involved in diabetes-associated rheumatological diseases

Fig. 21.2 Painful and painless rheumatic diseases associated with diabetes mellitus

- *Autonomic symptoms:* temperature and colour changes in the hand.
- *Weakness of thumb* abduction and opposition.

To exclude other causes of CTS, the following should be assessed for establishing the diagnosis (Table 21.1):

21.3.2.2 Physical Examination

- **Motor Examination:** wasting and weakness of the median-innervated hand muscles (LOAF); *first and second lumbricales*, *opponens pollicis*, *abductor pollicis brevis* and *flexor pollicis brevis* may be detectable and resulting in weak thumb abduction.
- **Sensory Examination:**
 - Decreased sensation in the median nerve distribution (from thumb through the middle of the fourth finger).

- *Semmes-Weinstein monofilament testing* or *2-point* discrimination, which may be more sensitive in picking up the sensory abnormality.
- **Special tests:**
 - *Phalen test* (87% specificity and 84% sensitivity): the patient has to hold his hands against each other in full palmar flexion; paraesthesia will happen within 30 to 120 s in this position.
 - *Tinel sign* (89% specificity and 82% sensitivity): gentle tapping over the median nerve in the carpal tunnel area causes tingling in the nerve's distribution.
 - *The carpal compression test* (sensitivity 84%, specificity 82%): applying firm pressure directly over the carpal tunnel, usually with the thumbs, for up to 30 s will reproduce the symptoms.

Table 21.1 Causes of Carpal Tunnel Syndrome

Causes	Important Differentiating Tips
Diabetes	Numbness, neuropathy, retinopathy, nephropathy, and peripheral vascular disease
Rheumatoid Arthritis	Constitutional symptoms, polyarthritis, morning stiffness, positive RF and ACPA
Gout	Monoarthritis, hyperuricemia, monosodium urate crystals in synovial fluid, negative culture of joint fluid for microorganisms
Heart failure	Orthopnea, PND, ischemic heart disease, diabetes, Hypertension
Hyperthyroidism	Palpitation, heat intolerance, weight loss, goitre, suppressed TSH
Colles' fracture	History of trauma
Over use syndrome	Work related e.g. computer Users, typists, and musicians

Abbreviations: *RF*: Rheumatoid factor, *ACPA*: Anti-citrullinated protein antibodies, *PND*: Paroxysmal nocturnal dyspnea, *TSH*: Thyroid stimulating hormone

- *Hand elevation test (89% specificity and 87% sensitivity)*: asking the patient to raise the affected hand and holding it in that position for 1 min. The test is positive when tingling and numbness happen in the median nerve distribution area.

- *MRI (sensitivity 96%)*:

It demonstrates swelling of the median nerve and increased signal intensity on T2-weighted images, indicating accumulation of the axonal transportation, myelin sheath degeneration or oedema, which are suggestive of CTS.

21.3.2.3 Investigations

- Carpal tunnel syndrome is a clinical diagnosis.
- Lab tests are usually not helpful except for assessing glycaemic control.
- *Nerve conduction studies (NCS) and electromyography (EMG)*: are the diagnostic tests that usually used to confirm the diagnosis, assess severity and rule out other abnormalities or conditions such as polyneuropathy, plexopathy and radiculopathy.
- Imaging studies are not routinely used:
 - *Ultrasound (sensitivity 64%)*:
It can demonstrate the thickening of the median nerve, the flattening of the nerve within the tunnel and the bowing of the flexor retinaculum, which are all features that indicate the presence of CTS.

21.3.3 Treatment

- *Conservative treatment*:
 - **Splinting**: splinting the wrist at night-time for a minimum of 3 weeks. Many off-the-shelf wrist splints seem to help.
 - **Steroid injection, nonsteroid anti-inflammatory drug and vitamin B6**: effective in reducing inflammation and oedema [8, 9].
- *Surgical release of carpal tunnel*:
 - This is performed more frequently among *patients with DM* and is estimated to be 4–14 times higher than the general population.
 - Success rate is more than 90%.

21.4 Reflex Sympathetic Dystrophy

Reflex sympathetic dystrophy (RSD), also known as complex regional pain syndrome I (CRPS I), is characterized by localized or diffuse neuropathic pain of the upper or lower extremity usually associated with swelling, vasomotor disturbances and trophic skin changes which include loss of hair, skin colour changes, temperature changes and skin thickening (autonomic involvement) [10].

21.4.1 Pathogenesis

The pathogenesis of RSD is unclear, but there are some theories that may explain it:

- Sympathetic nervous system dysfunction.
- Neurogenic inflammation.
- Central nervous system sensitization.
- Autoimmune condition.
- Limb ischaemia or ischaemia reperfusion injury.

21.4.2 Epidemiology

Incidence of RSD is 26.2 per 100,000 person year in Netherlands 1996–2005, the highest incidence in women aged 61–70 years, with a female to male ratio 3.4:1 [11].

21.4.3 Approach to RSD

21.4.3.1 History

- *Neuropathic pain* following an injury (tissue trauma or bony fracture). It is described as burning, throbbing, aching, squeezing or shooting pain.
- *Vasomotor and sudomotor changes* in the affected limb (colour changes, temperature changes and excessive sweating).
- Ask about the possible precipitating factors or causes such as:
 - **Trauma** kor **immobilization** following trauma to limb.

- **Bone fractures of extremities.**
- **Diabetes mellitus.**
- **Hyperthyroidism.**
- **Hyperparathyroidism.**
- **Nerve injury.**
- **Medications**, e.g. ACE inhibitors.

21.4.3.2 Physical Examination

- **Skin:** may be shiny, swollen, thinned, erythematous or cyanotic, with scaling. Temperature may be increased or decreased.
- **Extremities:**
 - Joint may be stiff with decreased range of motion.
 - Signs of chronic lymphoedema.
- **Neurologically:**
 - Sensory changes and weakness may be present.
 - Tremor or dystonia in the affected limb.

21.4.4 Diagnosis Criteria (Table. 21.2)

21.4.5 Treatment

There are different medical and surgical treatment modalities, but they have no strong evidence to support their use.

- The best treatment of RSD is prevention by early mobilization following an injury or stroke and use of supplemental vitamin C for patients with wrist fractures [14, 15]. A typical dose is 500–1500 mg daily, and the duration is 50 days.
- Physical therapy.
- Medical therapy:
 - Analgesics, e.g., topical capsaicin cream.
 - Bisphosphonates.
 - Anticonvulsants, e.g., gabapentin.
 - Tricyclic antidepressant.
 - Vasodilator medication or percutaneous sympathetic blockades.
 - Glucocorticoids.
- Invasive therapy for non-improving on non-invasive therapy.
 - Regional sympathetic nerve block.
 - Electrical nerve stimulation.

Table 21.2 Diagnostic criteria of reflex sympathetic dystrophy, also known as complex regional pain syndrome

Bruehl's criteria ^[12]
<p>Continuing pain disproportionate to any inciting event.</p> <p>1. Patient must report at least 1 symptom in each of the 4 following categories</p> <ul style="list-style-type: none">a) Sensory: hyperesthesiab) Vasomotor: temperature asymmetry, skin color changes or skin color asymmetryc) Sudomotor/edema: edema, sweating changes or sweating asymmetryd) Motor/trophic: decreased range of motion, motor dysfunction (weakness, tremor, dystonia) or trophic changes (hair, nail, skin) <p>2. Must display at least 1 sign in 2 or more of the following categories</p> <ul style="list-style-type: none">e) Sensory: evidence of hyperalgesia (to pinprick) or allodynia (to light touch)f) Vasomotor: evidence of temperature asymmetry, skin color changes or asymmetryg) Sudomotor/edema: evidence of edema, sweating changes or sweating asymmetryh) Motor/trophic: evidence of decreased range of motion, motor dysfunction (weakness, tremor, dystonia) or trophic changes (hair, nail, skin)
Veldman's criteria ^[13]
<p>1. Presence of 4 out of 5 symptoms:</p> <ul style="list-style-type: none">a) Diffuse pain during exerciseb) Temperature differences between affected and unaffected extremityc) Color differences between affected and unaffected extremityd) Volume differences between affected and unaffected extremitye) Limitations in active range of movement of the affected extremity <p>2. Occurrence or increase of symptoms during or after use</p> <p>3. Symptoms in an area larger than the area of the primary injury</p>

- Sympathectomy.
- Spinal cord stimulation.

its entrance into the base of flexor tendon sheath, accompanied by constriction of the sheath. Flexors are stronger than extensors, so finger gets locked in a flexed position, as extensors cannot overcome the resistance of constriction.

21.5 Flexor Tenosynovitis

Flexor tenosynovitis, also known as trigger finger, is a non-infectious inflammation of the flexor tendon sheath of the finger leading to finger blocking in flexion with failure of active extension.

21.5.1 Pathogenesis

Inflammation causes thickening of flexor tendon of the digit over metacarpal head and resistance to

21.5.2 Epidemiology

The prevalence of flexor tenosynovitis is estimated at 11% in diabetic patients, compared with less than 1% in nondiabetics [16]. The occurrence of flexor tenosynovitis correlates significantly with the duration of DM, but not with glycaemic control [16].

21.5.3 Approach to Flexor Tenosynovitis

21.5.3.1 History

- Locking of finger in a flexed position with a resistance to re-extension. It commonly involves thumb, the middle and ring fingers.
- Clicking of the locked digit and finger pain.

21.5.3.2 Physical Examination

- Local tenderness and palpable swelling at the base of the finger, where the tendon crosses over the metacarpal head.
- Pain usually gets worse by stretching the tendon in extension or by resisting flexion isometrically.
- *Prayer sign test*: the ability to flatten the hands together as in prayer, facilitating recognition of contractures in the metacarpophalangeal, proximal interphalangeal and distal interphalangeal joints.
- *Table top test*: assesses the ability to flatten the palm against the surface of a table, facilitating recognition of contractures in the metacarpophalangeal joints.

21.5.3.3 Investigations

- It is a clinical diagnosis.
- *Plain radiographs* are rarely done unless there is a history of trauma or inflammatory diseases. They may show calcification of the tendon but rarely occurs.

21.5.4 Treatment [17]

- Activity modifications to avoid the triggers.
- Splinting.
- NSAIDs.
- Steroid injections into tendon sheath.
- Surgical release.

21.6 Diabetic Muscular Infarction

It refers to spontaneous ischemic necrosis of skeletal muscles, unrelated to athero-embolism

or occlusion of major arteries. Diabetic muscle infarction (DMI) is a rare but life threatening complication seen in patients with long-standing and poorly controlled diabetes. It is considered as one of the micro- and macrovascular complications of Diabetes.

21.6.1 Pathophysiology

DMI is more common in type I diabetes and most of the affected patients have multiple microvascular complications. Hyperglycaemia, with or without insulin resistance, has many potentially adverse effects on the arterial vasculature. It may also affect platelets functions and the levels of coagulation and thrombolytic factors leading to occlusion of arterioles and capillaries resulting in muscles necrosis and oedema.

21.6.2 Epidemiology

- More common with type I diabetes.
- Usually affecting women more than men.
- Usually associated with other complications of diabetes as nephropathy (70%), retinopathy (57%) and neuropathy (55%) [18]

21.6.3 Approach to DMI

21.6.3.1 History

- *Tender and swollen leg.*
- *Pain of an acute onset in the thigh and less commonly in the calf muscles over days.*
- *Autonomic symptoms: mild fever.*
- Ask about trauma: usually there is no history of trauma in DMI.
- Ask about suspected complications as recurrence or staph sepsis.
- Ask about the diabetes control and medication use.
- Ask about symptoms of nephropathy and retinopathy, e.g. urinary symptoms and vision problems.

21.6.3.2 Physical Examination

- Assessing the leg swelling: site, size, shape, tenderness and temperature.
- Any associated leg ulcers?
- Check the leg and upper limb arterial pulses.
- Look for signs of DM-related micro- and macrovascular complications such as retinopathy, neuropathy and cardiovascular abnormalities.

21.6.3.3 Imaging Studies

- **MRI:**
 - Shows a high intensity in the involved muscle as well as subcutaneous oedema and subfascial fluid (in T2-weighted sequences), in addition to loss of the normal fatty intramuscular septa with T1-weighted images (common finding) [19].
 - It is the diagnostic test of choice.
- **Ultrasonography:**
 - Finding of internal linear echogenic structures, absence of a predominant anechoic area and no evidence of internal motion can discriminate a diabetic muscle infarction from an abscess.
 - Venous Doppler ultrasound with compression to rule out venous thrombosis.
- **Arteriography:**
 - It may show atherosclerotic luminal narrowing. Generally, it is not used for diagnosis.

21.6.3.4 Muscle Biopsy (for Confirmation)

The primary pathological findings are muscle necrosis and oedema, but occlusion of arterioles and capillaries by fibrin may also be seen. It should be reserved for patients with atypical presentation, uncertain diagnosis or those who do not improve with medical treatment [20].

21.6.4 Treatment

- Rest and analgesics.
- Anti-platelet agents (ASA) and/or anti-inflammatory drugs.
- Surgical excision.

21.7 Adhesive Capsulitis (Frozen Shoulder)

Adhesive capsulitis, also known as frozen shoulder, is characterized by progressive painful restriction of the shoulder movements, especially external rotation and abduction. Typically, the pain of frozen shoulder in diabetics is less than that of nondiabetic patients.

21.7.1 Pathogenesis

The exact mechanism is unknown. It is thought that hyperglycaemia can lead to a faster rate of collagen glycosylation and cross-linking in the shoulder capsule, which will cause thickening and contraction of the capsule that result in a substantial decrease in capsular volume capacity.

21.7.2 Epidemiology

- The prevalence of frozen shoulder is estimated to be 2 to 5% of the general population [21, 22].
- Patients with diabetes mellitus are at a greater risk of developing frozen shoulder, with prevalence of 10 to 20% [23–25].
- Bilateral involvement is more frequent in diabetic patients than in nondiabetic subjects (33 to 42% vs. 5 to 20%) [26].
- Women are more often affected than men [27].

21.7.3 Approach to Frozen Shoulder

21.7.3.1 History

- Shoulder stiffness.
- Diffuse severe pain, even at night.
- Limitation of shoulder motion.
- *The followings should be obtained:*
 - Duration and location of pain.
 - Precipitating and relieving factors.
 - One shoulder or both are affected.
 - Any other joints involved.
 - Any strain, overuse or trauma.

Table 21.3 Frozen shoulder progression phases [22, 28]

Painful freezing phase	Adhesive phase	Resolution phase
<ul style="list-style-type: none">▪ 10-36 weeks▪ Pain and stiffness around the shoulder with no history of injury▪ Constant pain with little response to NSAIDs	<ul style="list-style-type: none">▪ 4-12 months▪ Pain gradually subsides but still apparent at extremes▪ Stiffness continues▪ Near total loss of external rotation	<ul style="list-style-type: none">▪ 12-42 months▪ Spontaneous improvement in the range of motion▪ Mean duration of overall impairment > 30 months

- Prolonged immobilization.
- Neck pain or radiation of pain into arms.
- Neurologic symptoms in arms.

Frozen Shoulder May Progress Through Three Theoretical Phases [22, 28] (Table. 21.3).

21.7.3.2 Physical Examination

A stiff and painful glenohumeral joint makes it difficult to perform a complete shoulder examination.

- Look for swelling, redness and warmth.
- Check distal strength, sensation and pulses.
- Check for diffuse tenderness over anterior and posterior aspect of the shoulder.
- Look for loss of active and passive motion in all planes especially on external rotation and abduction.
- Diagnosis is unlikely if complete abduction present on passive motion.

21.7.3.3 Imaging

- **Plain radiographs** are usually normal, so had limited diagnostic use.
- **Ultrasonography** is used either to confirm the diagnosis of frozen shoulder or to rule out other pathology of the rotator cuff and bursa. Findings associated with frozen shoulder may include [29]:
 - Thickening of the coracohumeral ligament and the soft-tissue structures in the rotator cuff interval.

- Increased fluid in the tendon sheath of the long head of the biceps.
- Increased vascularity around the intra-articular portion of the biceps tendon and the coracohumeral ligament.

- **MRI** shows a thickening of the joint capsule and the coracohumeral ligament. It is useful in some conditions like rotator cuff tendinopathy and concomitant glenohumeral osteoarthritis for accurate diagnosis.

21.7.4 Treatment

In most cases, frozen shoulder is a self-limited condition, although a complete resolution does not occur in many patients.

- Physical therapy.
- Nonsteroidal anti-inflammatory drugs (NSAIDs) and analgesics.
- Intra-articular steroid injections.
- Surgery in severe non-responding cases.

21.8 Neuropathic Osteoarthropathy (Charcot Joint)

Neuropathic osteoarthropathy, also known as Charcot osteoarthropathy, is a progressive destructive process affecting the bone and joint structures associated with various diseases in

which neuropathy occurs. However, DM is by far the most common aetiology.

decreased sensation due to a sensory neuropathy, which results in increased damage with microfractures (Fig. 21.3).

21.8.1 Pathogenesis

The pathogenesis remains uncertain, but it is probably due to an underlying diabetic peripheral neuropathy and a combination of mechanical trauma and vascular factors. It may result from repeated trauma, often minor, in the setting of

21.8.2 Epidemiology

- Among the general diabetic population, neuroarthropathy is uncommon, affecting approximately 1 in 700 diabetic patients [30, 31].

Fig. 21.3 Pathogenesis of diabetic neuropathic arthropathy

Table. 21.4 The Modified Eichenholtz System to Stage Charcot Joint Progression

Inflammatory (Stage 0)	Development (Stage 1)	Coalescence (Stage 2)	Remodeling (Stage 3)
<ul style="list-style-type: none"> ▪ Localized swelling, erythema, and warmth ▪ No radiological abnormalities 	<ul style="list-style-type: none"> ▪ Persistent swelling, redness, and warmth ▪ Bony changes such as fracture, subluxation, dislocation ▪ Bony debris starts to appear radiologically 	<ul style="list-style-type: none"> ▪ Inflammatory signs decrease ▪ Radiological signs of fracture healing, bony debris resorption ▪ New bone formation 	<ul style="list-style-type: none"> ▪ Clinical inflammatory signs have settled ▪ Bony deformity ▪ Radiologically, may show mature fracture and decreased sclerosis

- Patients at risk are usually those who have longstanding diabetes (average duration 15 years) with peripheral neuropathy and are in their sixth or seventh decade [30, 31].

21.8.3 Approach to Charcot Joint

21.8.3.1 History

- Arthritis and swollen foot or ankle (although may occur in any joint).
- The **modified Eichenholtz system** was developed to stage the progression of Charcot joint and to recommend treatment based on the clinical stage and radiographic changes [32] (Table. 21.4).

21.8.3.2 Physical Examination

- **Serial X-rays with different findings according to the stage.**
 - Inflammatory stage: no radiological abnormalities.
 - Development stage: joint effusion, subluxation, bone destruction and osteochondral fragmentation.
 - Coalescence stage: periosteal new bone formation, subchondral sclerosis, resorption of debris, marginal osteophytes.
 - Remodelling stage: ankylosis or rounded bone ends, decreased sclerosis, decreased swelling.
- **MRI:** may show bone marrow oedema, bone bruising or microfractures.

21.8.4 Treatment

- Avoidance of weight bearing is the mainstay of treatment. It should be for at least 3 months or until erythema and oedema resolve accompanied by radiographic improvements.
- NSAIDs.
- Calcitonin and bisphosphonates may be added on to limb offloading. Their use has not been approved yet in the treatment of Charcot neuroarthropathy [35, 36].
- Surgical treatment may only be required when the conservative treatment fails or severe deformities developed.

(Table 21.5) Summary of the Most Common Rheumatological Diseases/Complications in Diabetic Patients.

21.9 Diabetes and Osteoporosis

Both diabetes and osteoporosis are prevalent diseases with significantly associated mortalities and morbidities. It has been well established that diabetic patients are at increased risk of osteoporosis and fractures, particularly at the hip.

Osteoporosis is defined as a combination of reduced bone mass and altered bone quality, with microarchitectural abnormalities, resulting in decreased bone strength with an increased risk of fractures [37, 38]. At present, the diagnosis of osteoporosis rests on bone mineral density

(BMD) measurement using dual-energy X-ray absorptiometry (DXA). The results are reported as the difference, in standard deviations (SDs),

with the peak bone mass (–score). The World Health Organization (WHO) defines osteoporosis as a BMD –score of –2.5 or less [37–39].

Table 21.5 Summary of the Most Common Rheumatological Diseases/Complications in Diabetic Patients

Rheumatological diseases		Pathophysiology	Symptoms	Investigations	Treatment
Rheumatological complication of diabetes	Syndromes of limited joint mobility	Diabetic cheiroarthropathy (Stiff-hand syndrome) (8–50% among diabetics)	Binding of advanced <i>glycosylation end products</i> to collagen that is deposited around joints	- Painless stiffness of small joints in the hand - Decreased grip strength - Prayer sign test - Table top test	- Glucose level - Imaging: U/S MRI - Improve glycemic control - NSAID - Corticosteroid injection - Physiotherapy - Surgery
		Dupuytren's contracture	Same as other limited joint, leading to fibroblastic proliferation and collagen deposition	- Finger stiffness, usually the 3 rd & 4 th digits in DM - Thickening or a palpable nodule in the palm - Loss of motion of the affected fingers	Clinical diagnosis Mild disease: - physiotherapy Moderate: - corticosteroid injection Contracture: - surgery
		Trigger finger (Stenosing flexor tenosynovitis)	Inflammation of flexor tendons in hand leading to thickening	- Finger pain - Locking of finger in flexed position	- Clinical diagnosis - X-ray - Biopsy - Active movement - Splinting - NSAIDs - Steroid injection
		Adhesive capsulitis (Frozen shoulder)	Same as other limited joint mobility	- Shoulder stiffness - Painful shoulder - Loss of motion	- Clinical diagnosis - U/S, MRI, and plain X-rays - Physiotherapy - NSAID - Steroid injection - Surgery
	Neuropathy	Neuropathic arthritis (Charcot joints)	Mechanical and vascular factors resulting from diabetic peripheral neuropathy	- Arthritis - Swollen foot - Foot arch collapse	- Clinical diagnosis - X-ray - MRI - Weight-bearing limitation - NSAIDs - Surgery
		Carpal tunnel syndrome (CTS)	Neuropathy of diabetes causes nerve compression	- Numbness - Pain - Weakness	- Phalen test - Tinnel test - Nerve conduction study+/-EMG - Splinting - NSAIDs - Steroid injection - Surgery
		Diabetic Amyotrophy	Ischemic injury from a non-systemic micro vasculitis	- Acute local pain, followed by weakness in the proximal leg - Autonomic failure and weight loss	- CBC, FBS, HbA1C, ESR - EMG, nerve conduction study - MRI and CT - Tricyclic antidepressant - Steroids - Immunotherapy
		Reflex sympathetic dystrophy	Neuropathic complication of DM with autonomic symptoms	1 st stage: burning throbbing pain & edema 2 nd stage: ↑ edema & skin thickening 3 rd stage: limitation of movement and contracture, waxy trophic skin changes, and brittle nails	- Education - Physical therapy - Analgesics, corticosteroids, oral muscle relaxants, bisphosphonates, and calcium-channel blockers - Invasive: intravenous percutaneous sympathetic blockade, surgical sympathectomy, spinal cord stimulation, and amputation

(continued)

Table 21.5 (continued)

	Rheumatologic diseases	Pathophysiology	Symptoms	Investigations	Treatment
Rheumatological complication of diabetes	Diffuse idiopathic skeletal hyperostosis (DISH) (Non-inflammatory disease with calcification and ossification of spinal ligament and entheses)	<ul style="list-style-type: none"> • Etiology: unknown, could be due to abnormal osteoblastic activity at the enthesis. • Insulin-like growth factor-1, insulin, glucose, and growth hormone are involved in the pathogenesis of osteoblastic activity in DISH. • Other factors : <ul style="list-style-type: none"> ➢ prolonged exposure to Vitamin A and fluoride. ➢ usage of Isotretinoin. ➢ Mechanical: Dextrocardia 	<ul style="list-style-type: none"> • Neck, thoracic spine, low back, or extremities pain • Disability and spinal morning stiffness • May be associated with dysphagia, stridor, apnea, hoarseness, or thoracic outlet syndrome due to large anterior cervical osteophytes • O/E: ↓ range of spinal motion with tender entheses 	<ul style="list-style-type: none"> • Radiologically: • Plain X-ray: <ul style="list-style-type: none"> ➢ Thoracic: longitudinal calcification and ossification ➢ Cervical: Hyperostosis with downward pointing spurs ➢ Lumbar: Hyperostosis with upward pointing spurs • CT: is more sensitive in detecting posterior calcifications 	<p>Symptomatic relief:</p> <ul style="list-style-type: none"> • Physical therapy • Analgesia: NSAIDs or local steroid • Surgery: If dysphagia, myopathy, or thoracic outlet syndrome developed
<p>Criteria for diagnosis of DISH:</p> <ul style="list-style-type: none"> • Resnick and Niwayama Criteria:^[31] <ol style="list-style-type: none"> 1. Presence of longitudinal ossification and calcification on the anterior surface of at least, 4 consecutive vertebral bodies. 2. Absence of degenerative radiological changes in discs involved with preservation of intervertebral space. 3. Absence of apophyseal joint bony ankylosis and sacroiliac joint erosion or sclerosis. • Utsinger Criteria:^[32] <ol style="list-style-type: none"> 1. Ossification, fine and ribbon-like wave, along the anterolateral aspect of at least 4 consecutive vertebrae. 2. Ossification on the anterolateral aspect of at least 2 consecutive vertebral bodies. 3. Presence of peripheral and symmetrical entheses pathology, involving heel, patella and olecranon, with new bone formation. <p>1 = definite, 2 or 3 = probably.</p> 					
	Diabetic Muscular Infarction	Hyperglycemia has many adverse effects on arterial vasculature as well as platelets and coagulation factors leading to occlusion of the vessels	<ul style="list-style-type: none"> • Painful and swollen leg: commonly involving thigh +/- calf muscles • Mild fever without infectious signs or symptoms • History of trauma • Compartment syndrome (less common) 	<ul style="list-style-type: none"> • CK elevation • U/S • MRI • Muscle biopsy to confirm the diagnosis 	<ul style="list-style-type: none"> • Analgesia • Anti-platelets (ASA) • NSAIDs • Surgical excision of infarcted tissues

ASA, aspirin; CBC, complete blood count; CK, creatinine kinase; CT, computed tomography; EMG, electromyography; ESR, erythrocyte sedimentation rate; FBG, fasting blood glucose; MRI, magnetic resonance imaging; NSAIDs, non-steroidal anti-inflammatory drugs; O/E, on examination; U/S, ultrasound

21.9.1 Pathogenesis

Type I diabetes is associated with bone fragility and loss of bone mass, while type II diabetes, despite having a normal or an increased bone mineral density (BMD), is associated with bone quality deterioration that cannot be diagnosed by using dual-energy X-ray absorptiometry (DXA).

Box 21.1 Risk Factors for Fractures in Diabetic Patients [37, 40]

1. Type of diabetes I or II, poor glycaemic control, and risk of drug-induced hypoglycaemia.
2. Microvascular complications of diabetes, especially nephropathy and neuropathy.
3. Type I diabetes-associated diseases such as autoimmune hyperthyroidism, amenorrhea, eating disorders and celiac disease.
4. Increased risk of falls due to diabetes-related complications such as hypoglycaemia, poor vision and/or balance, autonomic orthostatic hypotension and arthropathy.
5. Vitamin D deficiency, which is more common in diabetics than general population.

21.9.2 Challenges in Diagnosing and Treating Diabetes-Related Osteoporosis

Although the risk has been well established, it remains underappreciated in the major international diabetes guidelines and by most clinicians caring for diabetic patients. There have been also insufficient studies evaluating the effectiveness and long-term safety of the available therapeutic antiporotic modalities to reduce the risk of fracture in patients with diabetes.

21.9.3 Approach to Diabetes-Related Osteoporosis

21.9.3.1 History

- Type of diabetes and glycaemic control (frequency of hyper- and hypoglycaemia).
- Symptoms of diabetes-related microvascular complications.
- Assess any risk for falls.
- Ask about any of the following risk factors that might increase the risk of osteoporotic fractures:
 - Previous history of fracture.
 - Parental history of hip fracture.
 - Smoking.
 - Alcoholism.
 - Steroid use.
 - Hyperthyroidism, celiac disease, hyperparathyroidism, vitamin D deficiency or rheumatoid arthritis.

21.9.3.2 Physical Exam

- Height measurement for any loss of height.
- Body mass index (low BMI < 19 kg/m²).
- Back examination for kyphosis or point tenderness over a vertebra suggesting a compression fracture.
- Signs that may indicate increased fall risk (difficulty with balance or gait, orthostatic hypotension, lower extremity weakness and/or neuropathy, poor vision or hearing).

21.9.3.3 Diagnosis

- Use the current osteoporosis guidelines for screening in patients with diabetes through using dual-energy X-ray absorptiometry (DXA) to measure the bone mineral density (BMD), but keep in mind the fracture risk is high in type II diabetes despite having normal or increased bone mineral density (BMD).
- Use the fracture risk assessment (FRAX) algorithm (www.shef.ac.uk/FRAX/), which is a validated tool used to estimate 10-year risks for major osteoporotic and hip fractures even if BMD is not measured [41]. It has been developed by the metabolic bone disease unit at the University of Sheffield.

21.9.3.4 Management of Osteoporosis on Diabetic Patients

- Maintain a good glycaemic control.
- Minimize hypoglycaemia as possible.
- Screening and prevention of diabetes-related complications.
- Avoid glitazones (TZDs).
- Identify patients with high risk of falls and prevent falls.
- Good supplementation with calcium (600–1200 mg/day) and vitamin D (at least 800–1000 IU/day).
- Use of specific antiporotic medication (bisphosphonates, denosumab or anabolic agent teriparatide) based on the recommendations of good clinical practice and the patients' factors.

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