RSSDI

Indian Diabetes

EDUCATOR JOURNAL

Theme of the Month

Diabetes and Bone Health

To keep Members Diabetes Care team abreast about
DSME /DSMS - (Diabetes Self management Education / Support) Concepts

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To keep the members of diabetes care team abreast with DSME and DSMS concepts

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*DSME: Diabetes Self-Management Education, DSMS: Diabetes Self-Management Support

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FOREWORD

Research Society for the Study of Diabetes in India (RSSDI) founded by Prof MMS Ahuja in the year 1972 is the biggest scientific association of healthcare professionals involved in promoting diabetes education and research in India. RSSDI is happy to collaborate with USV to support their endeavour to make India the 'Diabetes care capital of the world'. Through this collaboration, RSSDI would like to strengthen the cadre of diabetes educators by empowering them with recent updates in diabetes management helping bridge the gap between the physician and the patient. Today, the rule of 50% is prevailing in terms of awareness, detection, treatment and control in T2DM.Our aspiration is to achieve 90-90-90-90 i.e.90% of people with diabetes should be made aware, 90% should be detected, 90% of those detected should be treated, and 90% of those treated should reach their goals.

Indian Diabetes Educator Journal (IDEJ) is the first of its kind in India, and the longest running monthly diabetes educator journal since April 2015 & continues its endeavour to spread awareness, knowledge and enable healthcare teams to manage individuals with diabetes and empower them for self-care. RSSDI IDEJ will continue to keep the members of diabetes care team abreast with concepts of Diabetes Self-Management Education/Support (DSME/S) with a reach of 44000 doctors and diabetes educators digitally.

Diabetes increases the risk of various bone and joint disorders. There are several factors which play a role in bone quality deterioration. The muscular strength also gradually reduces with insulin resistance and hyperglycemia. This month's IDEJ aims to propagate information about how diabetes affects bone health. Understanding the impact that diabetes can have on the musculoskeletal system will help the diabetes educators to counsel people with diabetes on taking measures to prevent this complication and thus reduce the risk of functional disabilities and falls.

We sincerely thank our contributors for making this issue delightful reading for our readers. We dedicate this journal to all the healthcare professionals who are working relentlessly towards making "India–The Diabetes Care Capital of the World."

Sincere Regards,

Dr. Sanjay Agarwal
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*DSME: Diabetes Self-Management Education, DSMS: Diabetes Self-Management Support

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Article: Effect of Exercise on Bone Health in People with Diabetes

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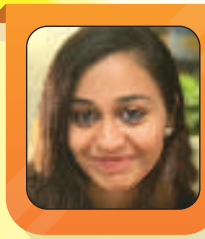
Article: Insulin Resistance and Glucose Uptake - Role of Skeletal Muscle



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Article: Impact of Diabetes Medications on Bone Health

RSSDI Indian Diabetes
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Cover Story: Impact of Diabetes Mellitus on Bone Health

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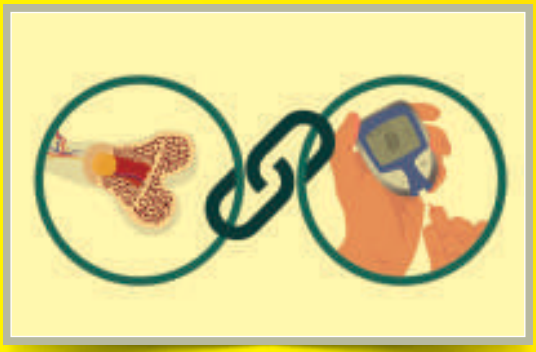
Uncontrolled diabetes has a detrimental effect on most parts of the body. Cardiovascular diseases, nephropathy, retinopathy, neuropathy and diabetic foot are commonly known complications of diabetes. It's interesting to note that diabetes may potentially affect bone health as well. In people living with type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM), there are a number of changes in bone strength, bone turnover, and stem cell differentiation that affect bone mineral density (BMD) and bone shape.

Bone Health and Diabetes

The continuing, cyclical process of bone remodelling is typically characterized by a close relationship between osteoblasts, which build new bone, and osteoclasts, which break down existing bone. The underlying causes of metabolic bone disease are assumed to be abnormalities in either pathway or an imbalance between the two. By measuring the amounts of several biomarkers in the serum and/or urine, it is possible to infer the resorption and production of bones indirectly. These markers are either bone remodelling enzymes or bone matrix elements that are released into the bloodstream during the creation or resorption of bones.



T1DM

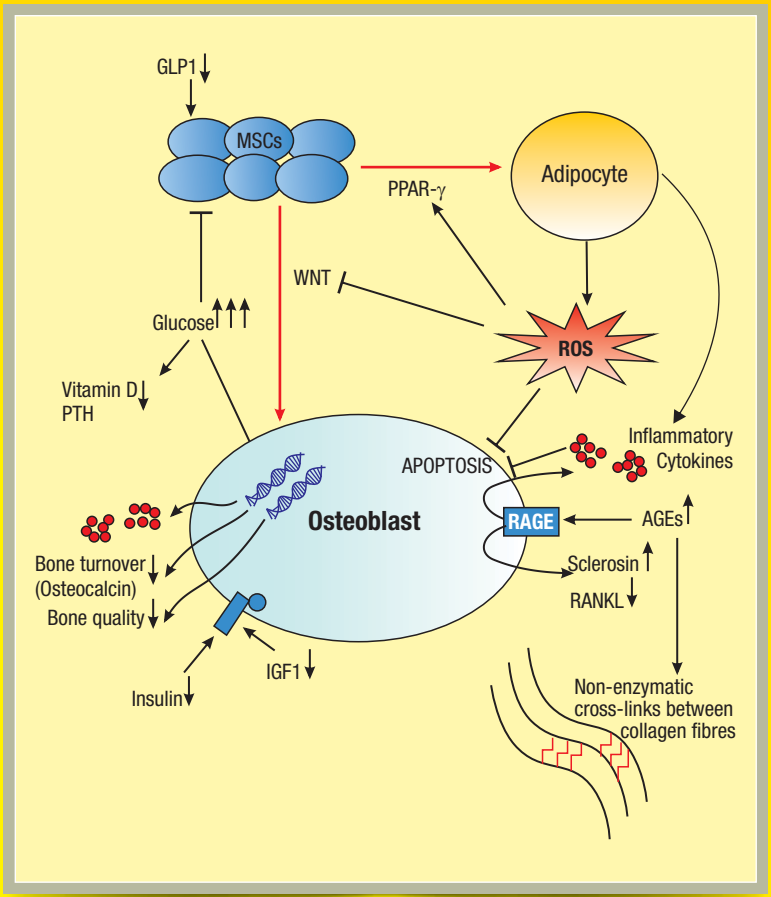
T1DM is characterized by complete lack of insulin and low insulin-like growth factor 1(IGF1) levels. Low IGF1 levels and the absence of insulin, among other pancreatic anabolic hormones, both inhibit osteoblastic activity as well as the terminal differentiation of mesenchymal stem cells (MSCs) into osteoblasts. As a result, there is an insufficient accumulation of peak bone mass and this may prevent skeletal growth at an early age.

T2DM

Diabetes negatively affects bone health in people with T2DM when a number of conditions including insulinopenia, hyperglycemia, the emergence of advanced glycation end products (AGEs), chronic inflammation, and microvascular disease all coexist to compromise the biomechanical structure and function of the bone. As a result, as T2DM progresses, the relative chance of suffering a hip fracture rises.

Mechanism of Change in Biochemical Properties of the Bone

Diabetes mellitus modifies the relationship between osteoblasts, adipocytes, MSCs, and the marrow environment. Inhibiting MSC maturation and metabolism causes hyperglycemia to directly alter gene expression linked to osteoblast activity. It also indirectly affects bone metabolism by messing with the parathyroid hormone and vitamin D systems. In various phases of diabetes mellitus, insulinopenia and low IGF-1 levels have an extra inhibitory effect on osteoblasts. Adipocyte production is increased, and by releasing reactive oxygen species (ROS) and inflammatory cytokines, which trigger osteoblast death, they contribute to the cycle of chronic inflammation. ROS supports this procedure by promoting MSC differentiation into adipocytes through the mediating effects of peroxisome proliferator-activated receptor gamma and inhibiting WNT transcription. Increased AGE formation also causes collagen fibres to cross-link without the aid of enzymes, which increases inflammation by activating receptors for advanced glycation end products. In diabetes mellitus, the buildup of these patho-mechanisms ultimately results in poor bone quality and bone turnover.



Reduced bone density, poor circulation which impairs bone growth and repair, nerve damage which increases the risk of falls, chronic inflammation and impaired wound healing which are all associated with uncontrolled diabetes impact bone health. To help maintain good skeletal strength, it is important to have good glycemic control along with adequate intake of calcium, vitamin D, magnesium, regular exercise and regular bone density screenings.

Resources:

1. Murray CE, Coleman CM. Impact of Diabetes Mellitus on Bone Health. *Int J Mol Sci.* 2019;20(19):4873. Published 2019 Sep 30. doi:10.3390/ijms20194873
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Risk Assessment of Sarcopenia in Patients with Type 2 Diabetes Mellitus

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The term sarcopenia refers to age-related loss of muscle mass, muscle strength, or physical function and is an emerging health issue that mostly affects older people's quality of life. Sarcopenia occurs 3–16 times more commonly in people with diabetes. Both type 2 diabetes mellitus (T2DM) and sarcopenia become increasingly prevalent with aging and put patients at risk for long-term complications, fragility, hospitalizations, and early mortality, making prior detection essential for taking suitable preventative measures.

Diabetes and Sarcopenia

Diabetes has been reported as an influencing aspect of sarcopenia. When insulin resistance develops in skeletal muscles, glucose utilization and protein synthesis are reduced, which consecutively aggravates insulin resistance and muscle loss, thus progressing into a vicious circle. According to findings from a systematic literature review, up to 70% of adults with diabetes have difficulty carrying out routine physical tasks, particularly those with lower extremity mobility impairment. Additionally, the literature also reveals that people with T2DM have a markedly increased risk of sarcopenia.

Risk Factors for Sarcopenia

The results of the meta-analysis and systematic review which included 16 studies to analyze the relationship between diabetes and sarcopenia showed that the presence of diabetes, poor blood glucose control and related chronic complications noticeably increased the risk of sarcopenia. Elder age, male gender, chronic hyperglycemia, and osteoporosis are significant risk factors for sarcopenia.

Criteria for Assessing Sarcopenia

Various definitions and diagnostic standards have been presented since Baumgartner *et al.* first proposed the idea of "sarcopenia." Early diagnostic criteria only required skeletal muscle mass to be measured, but more recently, indications to assess muscle function and quality have come to be recognised as a significant component of sarcopenia. The gold standard for sarcopenia assessment comprises measurements of lean body mass (LBM), anthropometric measurements (such as the mid-upper arm circumference [MUAC]), and muscle strength assessments.

LBM Assessment Strategies

Imaging technique: Multiple tools available to evaluate LBM vary in cost and variability. The most common techniques include dual-energy X-ray absorptiometry (DXA), computed tomography (CT), bioimpedance analysis (BIA) and magnetic resonance imaging (MRI).

Table 1: Imaging Techniques in Sarcopenia Assessment

Mode of Measuring Sarcopenia	Method	Cut-offs	
		Male	Female
CT	Cross-sectional imaging	Cut off measures widely variable	
MRI	Cross-sectional imaging	Cut off measures widely variable	
BIA	Electric currents to evaluate total body weight (TBW)	<10.75 kg/m^2	<6.75 kg/m^2
DXA	Total body scan using X-ray technology	<7.26 kg/m^2	<5.5 kg/m^2

Anthropometric Measurement Techniques

LBM in sarcopenia can also be assessed using anthropometry. This includes calf circumference, skinfold thickness and MUAC. However, despite being relatively simple to measure, anthropometry is not always a reliable indicator of muscle mass due to the risk of human error, changes in skin elasticity, aging-related changes in body mass, and variations in user approach.

Table 2: Anthropometric Measurement Technique in Sarcopenia Assessment

Mode of Measuring Sarcopenia	Method	Cut-offs
MUAC	Measure the circumference with the arm 90 degrees bent, halfway between the olecranon process and the acromion.	<22.5 cm
Skin-fold thickness	Measured to the nearest 0.1 mm using a caliper on the posterior of the arm, halfway between the olecranon process and the acromion.	Varies depending on age and sex
Calf circumference	Maximum length of calf of lower non-dominant leg bent at 90 degrees.	<31 cm

Muscle Strength and Physical Performance Assessment

Tools to measure muscle strength include handgrip strength and the chair stand test of which the handgrip strength is measured through a dynamometer and has been shown to closely correlate with lower-extremity strength.

Validated tests to measure physical performance include the Stair Climb Power Test (SCPT), Timed Get Up-and-Go (TGUG) test, and the Short Physical Performance Battery (SPPB). Table 3 gives a detailed description of this.

Table 3: Muscle Strength and Physical Performance Technique in Sarcopenia Assessment

Mode of Measuring Sarcopenia	Method	Cut-offs
Grip strength	• Dynamometer in dominant hand with base relaxed in the palm. • Maximum isometric effort for 5 seconds.	Male - <27 kg Female - <16 kg
Chair stand	Time required to rise from seated position five times.	>15 seconds for five rises
TGUG (Timed Get Up-and-Go)	Time taken to rise from seated position and walk 3 m away and back with return to seated position.	≥20 seconds
SPPB (Short Physical Performance Battery)	• 4 m of walking time. • Feet parallel paired for 10 seconds before switching to a parallel non paired position. • Each component was graded on a scale of 0–4, with 0 representing test failure and 4 representing complete achievement.	≤8 points
SCPT (Stair Climb Power Test)	Time (calculated in watts using equation) taken to climb a flight of stairs.	Differs with age

The European Working Group on Sarcopenia (EWGS) in Older People outlined these simple tools to recognize people with sarcopenia. These tools help people with T2DM to be screened for sarcopenia in order to implement early prevention or treatment strategies.

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Effect of Exercise on Bone Health in People with Diabetes

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Diabetes mellitus (DM) is a global public health issue which affects millions of people of all age, racial and ethnic groups. Chronic hyperglycemia is linked to both microvascular and macrovascular issues which results in long-term damage and organ system failure, but recently it is also found that long term exposure to a diabetic environment alters bone metabolism and impairs bone micro-architecture. These modifications put the bone at higher risk for fracture and hinder osseous healing. Therefore in order to avoid damaging effects on bone health, optimal blood glucose control is important through diet, medication and exercise. Exercise plays a very important role for preservation of musculoskeletal and bone health.

Exercise Programs which Helps to Preserve and Improve Bone Health

- Static weight-bearing exercises like single-leg standing.
- High-impact weight-bearing exercises like jogging, running, dancing, jumping, and vibration platform.
- Low-impact weight-bearing exercises like walking and Tai Chi.
- High-impact non-weight-bearing exercise like progressive resistance exercise.
- Low-impact non-weight-bearing exercise like swimming.

Among these exercises, resistance training has been identified as the most promising strategy to preserve or increase bone mass and density among individuals. It generates stimuli and encourages an osteogenic response in the bone as various muscular loads are applied to the bone during the activity.

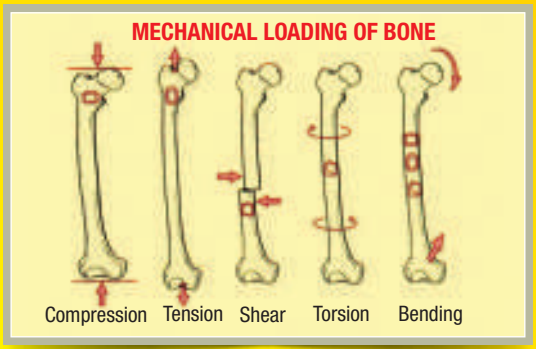
Mechanism Associated with Musculoskeletal Effects of Resistance Exercise (RE)

Skeletal Muscle Preservation

Long-term inactivity and/or a state of muscle wasting can lower the contractility of skeletal muscles, which has a significant negative impact on their myofibrillar mass, muscle strength, and mobility. Muscular protein synthesis (MPS), which is involved in muscle contraction, is preferentially stimulated by the tensile and/or compressive stress produced during RE. There is strong evidence linking RE to muscle hypertrophy by enhancing the production of systemic growth factors like insulin-like growth factor 1, which

in turn activates the PI3K-Akt-mTORC1 signalling pathway to accelerate MPS. Recent research, has shown growth factor-independent mTORC1 activation, suggesting that intrinsic mechanosensitive molecules play a significant role in driving the accretion of muscle protein. RE substantially improves the cross-sectional area of trained muscles, which boosts their force and power.

Increased Bone Strength from Mechanical Loading



The bone cells in this system, primarily the osteocytes, are able to sense and react to mechanical loading. By sensing mechanical loads and communicating that information to the osteoblasts and osteoclasts, which consequently maintain skeletal homeostasis, osteocytes play a crucial part in the remodelling process. Sclerostin is a protein made by osteocytes that is essential for controlling bone formation. Sclerostin expression in bones is down regulated by mechanical loading, which increases osteoblastic bone formation and decreases bone resorption by inhibiting osteoclast activity. At areas of high strain, especially the periosteal bone surface, bone formation is increased while bone turnover and porosity are decreased. In turn, mechanical loading results in an increase in the cross-sectional area and tissue density of bones. As per research, bone adaptation to mechanical loading influences geometric markers of bone strength as well as bone mineral density (BMD).

After reaching skeletal maturity at 18 to 25 years, bones become less responsive to mechanical strain. When compared to adulthood and old age, the skeleton responds to exercise more readily in childhood. Therefore, engaging in RE right from an early age can help to build and maintain strong bones in people with diabetes.

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4. Murray CE, Coleman CM. Impact of Diabetes Mellitus on Bone Health. *Int J Mol Sci.* 2019;20(19):4873. Published 2019 Sep 30. doi:10.3390/ijms20194873
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Insulin Resistance and Glucose Uptake - Role of Skeletal Muscle

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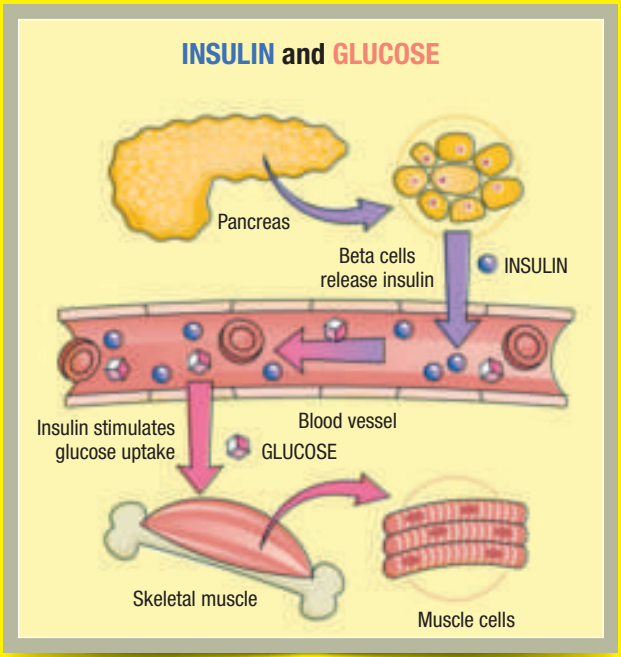
Muscle mass is crucial for metabolism because of its function in absorbing glucose as well as its significance in metabolic disorders like diabetes (insulin resistance).

Skeletal Muscle – Glucose Uptake

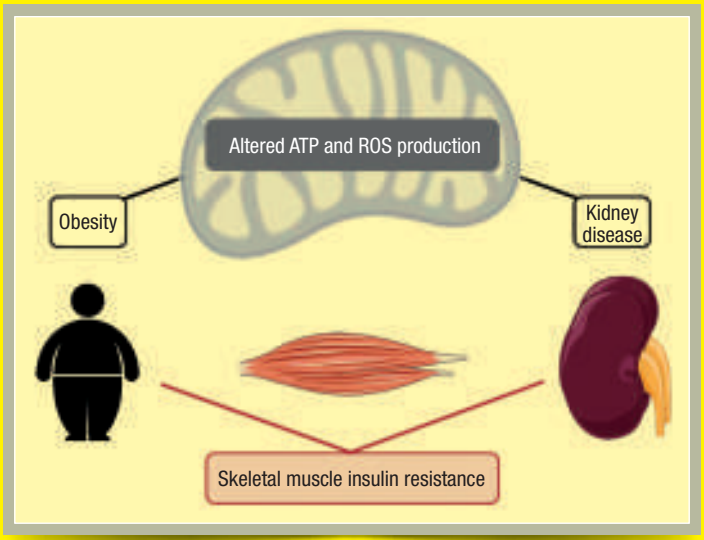
The plasma membrane can carry glucose more easily thanks to several glucose transporters (GLUTs). In order of abundance, the three GLUTs that mediate glucose absorption in skeletal muscle are GLUT4, GLUT3 and GLUT1. GLUT4 is incredibly prevalent in skeletal muscle & adipose tissue and is expressed by the SLC2A4 (solute carrier family) gene. GLUT4 needs a stimulus such as insulin or physical activity to go to the cell membrane and promote glucose absorption. Glucose enters the muscle through facilitated diffusion with help of the GLUT4 glucose transporter which moves from intracellular storage depots to the plasma membrane and T-tubules upon muscle contraction.



Skeletal Muscle – Insulin Resistance

Over 80% of the postprandial glucose absorption from a glucose load occurs in the skeletal muscle, which is crucial for glucose clearance. High blood glucose levels are a result of insulin resistance, which is brought on by the desensitization of muscle towards the insulin. A function for insulin resistance as an early stage in the development of T2D has also been supported by reports of significant skeletal muscle insulin resistance in lean, non-diabetic, normoglycemic individuals. Skeletal muscle is thought to be the main cause of overall insulin resistance as it is the main site of insulin-stimulated glucose absorption. Restoring insulin resistance in the muscles alone is adequate to restore whole-body glucose homeostasis when skeletal muscle is the major problem. Although insulin resistance in skeletal muscle can be reversed, β-cell death cannot. The rate and timing of glucose absorption into skeletal muscle are both hampered by insulin resistance. Postprandial glucose absorption into muscle rises linearly with time under typical circumstances. However, insulin action & glucose absorption are delayed in people with T2D and insulin resistance, which results in less total skeletal muscle glucose uptake.

Insulin action on skeletal muscle mass is critical in metabolic homeostasis. Insulin action in skeletal muscle is a crucial factor in generating therapeutic protocols that can prevent metabolic disease. Other than insulin, muscle contraction and exercise increase glucose uptake into skeletal muscle.



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Whats Trending?
Sarcopenia – Chronic Complication of Type 2 Diabetes Mellitus

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Uncontrolled diabetes has been known to cause several debilitating complications. Another complication coming into light in the last few years is "Sarcopenia." Sarcopenia refers to a progressive and generalized loss of muscular mass accompanying a decline in muscle performance. It is also associated with loss in muscle strength inherent to the aging process. Individuals with type 2 diabetes mellitus (T2DM) are reported to have a higher prevalence of sarcopenia than the general population.

T2DM is characterized by inflammation, insulin resistance, accumulation of advanced glycated end-products and increased oxidative stress. Insulin resistance and poor glycemic control are most likely to be associated with poor muscle health. This is because they cause increased protein degradation and decreased protein synthesis, leading to loss of muscle mass and strength. Increased inflammation in T2DM has also shown to accelerate loss of muscle mass as compared to normal population. Inflammatory markers are also negatively associated with muscle strength, which is considered a principal component of sarcopenia. Increased oxidative stress leads to myopathy. Mitochondrial dysfunction due to elevated oxidative stress in T2DM deteriorates muscle health. Figure 1 illustrates pathways that accelerate muscle loss in T2DM.

Thus, reduced muscle mass and impaired muscle function contribute to increased sedentary behaviour in individuals with T2DM leading to functional impairments followed by metabolic impairments, and vice versa. This loop can be broken using dietary and lifestyle interventions for improving metabolic and musculoskeletal health.

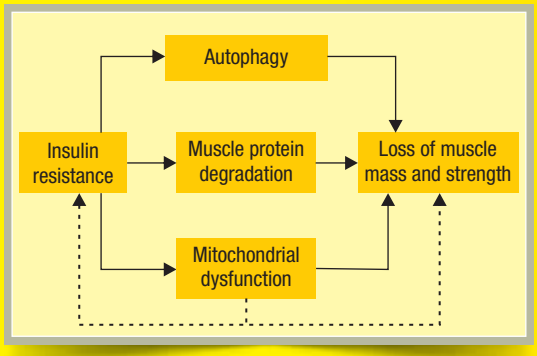

Figure 1: Pathways that accelerate muscle loss in T2DM

First and foremost, the goal is glucose control. This can be achieved by dietary intervention and physical activity. The International Clinical Practice Guideline for Sarcopenia (ICFSR) recommends protein rich diet or protein supplementation ensuring optimal intake of 1-1.2g/kg BW/day protein along with physical activity in sarcopenia. Along with protein, the beneficial role of vitamin D has also been observed in individuals with insufficient levels. Individuals with T2DM are often seen to have low vitamin D levels. Intervention with vitamin D and whey protein oral nutritional supplements has shown to improve muscle mass and lower-extremity function among sarcopenic older adults. This may also have an implication in diabetes associated sarcopenia. Protein supplementation in individuals with T2DM has shown a significant increase in appendicular muscle mass, total lean mass and insulin sensitivity (Matsuda index) as well. Maintaining muscle strength, and muscle mass is particularly important in individuals with T2DM to sustain independent mobility and healthy aging. Hence, management of sarcopenia, a chronic complication should be given adequate importance in addition to routine diabetes care.

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Association Between Muscle Mass and Osteoporosis in Diabetes

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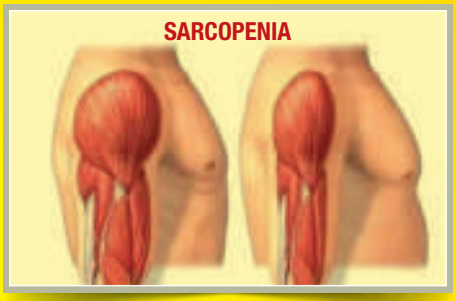
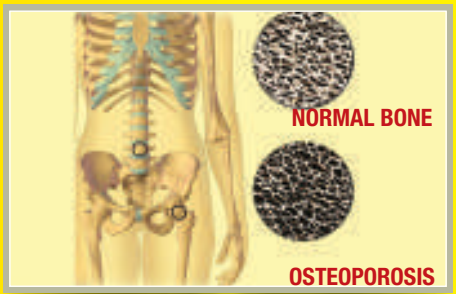
Diabetes mellitus (DM) is a chronic condition that if left untreated and uncontrolled, can weaken bones and reduce muscle mass. Loss of muscle mass (sarcopenia), and osteoporosis, have emerged as global public health issues as a result of the rise in life expectancy. People with type 2 diabetes mellitus have a greater prevalence of sarcopenia, which can range from 7% to 29.3%, because of their decreased insulin sensitivity. Numerous studies have revealed that people with type 2 diabetes mellitus are known to lose skeletal muscle mass more quickly and have an increased risk of osteoporosis. High glucose level and the metabolic products of diabetes are risk factors of fragility fractures, while insulin resistance or oxidative stress result in muscle loss. Bone fragility is caused by advanced glycosylated end products and osmotic stress due to hyperglycemia. On the other hand, insulin resistance can cause muscle atrophy by reducing protein synthesis and increasing protein breakdown.



Sarcopenia has been linked to decreased insulin signalling and elevated levels of inflammatory cytokines such interleukin -1 (IL-1), interleukin - 6 (IL-6), and tumour necrosis factor alpha. Chronic inflammation, oxidative stress, and mitochondrial dysfunction have all been associated with sarcopenia in people with diabetes. There is growing evidence that sarcopenia and osteoporosis share a number of similar pathways and a large proportion of people suffer from both these conditions. The elderly population is more likely to experience sarcopenia, low bone mineral density, diminished muscle mass and strength, and other conditions that might impair physical performance. The connection between osteoporosis and sarcopenia in people with type 2 diabetes mellitus has been unidentified so far. Several studies have concluded that people with sarcopenia, especially those with type 2 diabetes mellitus, might have a high risk for osteoporosis. A recent study by Pan Y, Xu J.(2022) showed that appendicular skeletal muscle (ASM) adjusted by height (ASM/height^2)which is a marker for sarcopenia is strongly associated with osteoporosis and low BMD in people with type 2 diabetes mellitus. The risk of osteoporosis was more when the diagnostic cut-off value of sarcopenia was 7.87 kg/m^2 in men and 5.94 kg/m^2 in women, respectively.



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Frequently Asked Questions on Diabetes & Bone Health

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1. My mother is 50 years old and was diagnosed with diabetes 12 years ago, and has recently entered 'Menopause'. I came across an article online which stated that most menopausal women, especially those with diabetes are at a risk of various bone related disorders. Is this true?

Ans. Despite appearing to be solid, bones are constantly changing. In diabetes, the body does not produce enough insulin or is resistant to it, thus interfering with the growth of new bone structures, resulting in brittle bones and weak muscles and a higher risk of fracture. High blood glucose levels in the blood may lead to - reduced release of insulin-like growth factor-1 (IGF-1) which promotes the growth of healthy bones and muscles, poor absorption of calcium, increased oxidative stress, increased glycation etc. These factors impair the nerves as well as the quality of the bones and muscles in the body. Menopause also is a phase which increases the risk of osteoporosis. As hormones adapt to accommodate typical menopausal changes, oestrogen levels start to fluctuate and then plummet. Because oestrogen slows the natural breakdown of bone, it helps keep bones from weakening. Therefore, its reduction during menopause causes a dramatic acceleration of bone loss. Thus, diabetes and menopause, together have a detrimental effect on the bone health of women.

2. I am a 59-year-old woman, with diabetes, since the past 19 years. I have noticed that my blood glucose levels, have been slightly erratic and I have developed ankle and knee pain. How do I manage these bone health issues, especially with diabetes?

Ans. As diabetes can result in osteoporosis and other bone problems as well as permanent damage and deterioration of bones and tissues, it is essential for those with diabetes to:

Control blood glucose levels: People with diabetes should always try to control their blood glucose levels. This will help to prevent nerve damage, circulation issues, and muscle loss, which can otherwise result in the weakening of bones and a markedly increased risk of bone-related ailments.

Nutrition: Diabetes, causes the body to absorb calcium less effectively. Therefore, including foods high in calcium and vitamin D is very important. Calcium rich sources like milk products, sesame seeds, finger millet (ragi), soya, and green leafy vegetables should be part of the diet.

Regular exercise: Similar to muscle, bone is a living substance that gets stronger with exercise. Bone strength can also be increased by resistance training, such as weightlifting. By improving balance and flexibility, regular exercise can help prevent bone loss and lower the risk of falling and fracturing a bone.

Lifestyle changes: Smokers have trouble absorbing calcium from their diets. Alcohol consumption can harm bone health as well. Due to poor nutrition and a higher chance of falling, those who consume large amounts of alcohol are more likely to experience bone loss and fractures. Avoiding drinking and smoking can aid in managing diabetes.

Bone mineral density test: Bone mineral density (BMD) exams, which are specialized examinations, gauge bone density in distinct body regions. These examinations can identify osteoporosis before a bone fracture occurs and forecast a person's future fracture risk. Your hip and spine's bone density can be measured. People with diabetes should discuss the possibility of a bone density test with their medical professionals.

3. I am 62-year-old, I was diagnosed with diabetes almost 20 years ago. I am recovering from a leg fracture. I read an article on the importance of calcium, and have made an effort to include foods rich in calcium in my diet. Are there any other nutrients which are beneficial and will help improve my bone health?

Ans. Yes, while calcium is an important nutrient and plays a major role in bone formation, there are also other nutrients such as magnesium and vitamin K which aid in bone formation.

Vitamin K is a crucial vitamin for bone health because it aids in the carboxylation of numerous proteins connected to bones, controls the genetic transcription of osteoblastic markers, and controls bone reabsorption. Food sources of vitamin K are dark green leafy vegetables, soybean and nuts.

Magnesium plays a role in bone formation (increases production of osteoblasts and reduced production of osteoclasts). It also aids in the synthesis and activation of vitamin D which plays a role in bone formation. Food sources of magnesium are whole grains and cereals, whole pulses, peanuts, and dark green leafy vegetables.

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A A1C REDUCTION
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R RENAL BENEFITS

E ENSURES ADHERENCE

Abridged Prescribing Information

Indication: It is indicated as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus.
Dosage and Administration: The recommended dose is one tablet daily. Each tablet contains a fixed dose of dapagliflozin, Sitagliptin and Metformin Hydrochloride.
Adverse Reactions: Most common adverse reactions reported are: Dapagliflozin- Female genital mycotic infections, nasopharyngitis, and urinary tract infections. Sitagliptin- Upper respiratory tract infection, nasopharyngitis and headache. Metformin- Diarrhea, nausea/vomiting, flatulence, asthenia, indigestion, abdominal discomfort, and headache.
Warnings and Precautions: Dapagliflozin: Volume depletion; Ketoacidosis in Patients with Diabetes Mellitus; Urosepsis and Pyelonephritis; Hypoglycaemia; Genital Mycotic infections
Sitagliptin: General- Sitagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Acute pancreatitis: Hypoglycaemia when used in combination with other anti-hyperglycaemic medicinal product; Renal impairment; Hypersensitivity reactions including anaphylaxis, angioedema, and exfoliative skin conditions- Stevens-Johnson syndrome; Bullous pemphigoid. Metformin Hydrochloride: Lactic acidosis; In case of dehydration (severe diarrhoea or vomiting, fever or reduced fluid intake), metformin should be temporarily discontinued and contact with a healthcare professional is recommended.
Contraindications: Hypersensitivity to the active substance of Dapagliflozin, Sitagliptin & Metformin or to any of the excipients listed. Any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis). Diabetic pre-coma; Severe renal failure (eGFR<30mL/min); Acute conditions with the potential to alter renal function such as: Dehydration, Severe Infection, Shock; Acute or chronic disease which may cause tissue hypoxia such as: Cardiac or respiratory failure, Recent myocardial Infarction, Shock, Hepatic Impairment, Acute Alcohol intoxication, alcoholism
Use in a special population: Pregnant Women: Due to lack of human data, drug should not be used during pregnancy. Lactating Women: It should not be used during breastfeeding. Paediatric Patients: The safety and efficacy of drug has not yet been established. No data are available. Geriatric Patients: In Patients > 65 years, it should be used with caution as age increases.

Additional information is available on request.
Last updated: January 03, 2023

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Metformin Hydrochloride 850 mg SR + Glimepiride 3 mg

January 2023[1]

ESC*

European Society of Cardiology[2]

Long term continuous usage of High Dose Glimepiride:

Inhibits sEH → Increases EET

Greater Cardiovascular Protection

Meta analysis of 21 well established trials[2]

5% Reduction of Weight Vs Baseline Weight[2]

100% Availability

20-50% Affordable vs other brands

Appropriate to add along with Newer AHAs

1. Glimepiride use is associated with reduced cardiovascular mortality in patients with type 2 diabetes and chronic heart failure, a prospective cohort study | European Journal of Preventive Cardiology | Oxfont Academic (oup.com) 2. Ther Adv Endocrinol Metab 2020. Vol 11:1-12 DOI: 10. 1177/2042018820926000. *Data on file * As compared to non-glimepiride group
EET: Epoxyeicosatrienoic acid; sEH: soluble Epoxide Hydrolase; AHAs: antihyperglycemic agents; T2DM: Type 2 Diabetes Mellitus

Priscribing information

Information: Metformin hydrochloride (as prolonged release) and glimepiride tablets. Glycomet-GP 0.5/Glycomet-GP 0.5 Forte/ Glycomet-GP 1/ Glycomet-GP 1/850/ Glycomet-GP 2/ Glycomet-GP 2/850/ Glycomet-GP 3/ Glycomet-GP 3/850/ Glycomet-GP 4/ Glycomet-GP 4/850/ Glycomet-GP 1 Forte/ Glycomet-GP 2 Forte/ Glycomet-GP 3 Forte/ Glycomet-GP 4 Forte Abridged Prescribing Information **Composition:** Glycomet GP 0.5mg: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500mg and glimepiride IP 0.5mg.• Glycomet GP 0.5 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 0.5mg.• Glycomet GP 1: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 1 mg. • Glycomet GP 1/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 1 mg. • Glycomet GP 2: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 2 mg. • Glycomet GP 2/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 2 mg.• Glycomet GP 3: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 3 mg. • Glycomet GP 3/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 3 mg. • Glycomet GP 4: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 4 mg. • Glycomet GP 4/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 4 mg. • Glycomet GP 1 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 1mg. • Glycomet GP 2 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 2mg. • Glycomet GP 3 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 3mg. • Glycomet GP 4 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP mg. **Indication:** For the management of patients with type 2 diabetes mellitus when diet, exercise and single agent (glimepiride or metformin alone) do not result in adequate glycaemic control. **Dosage and Administration:** The recommended dose is one tablet daily during breakfast or the first main meal. Each tablet contains a fixed dose of glimepiride and Metformin Hydrochloride. The highest recommended dose per day should be 8 mg of glimepiride and 2000mg of metformin. Due to prolonged release formulation, the tablet must be swallowed whole and not crushed or chewed. **Adverse Reactions:** For Glimepiride: hypoglycaemia may occur, which may sometimes be prolonged. Occasionally, gastrointestinal (GI) symptoms such as nausea, vomiting, sensations of pressure or fullness in the epigastrium, abdominal pain and diarrhea may occur. Hepatitis, elevation of liver enzymes, cholestasis and jaundice may occur; allergic reactions or pseudo allergic reactions may occur occasionally. For Metformin: GI symptoms such as nausea, vomiting, diarrhea, abdominal pain, and loss of appetite are common during initiation of therapy and may resolve spontaneously in most cases. Metallic taste, mild erythema, decrease in Vit B12 absorption, very rarely lactic acidosis, Hemolytic anemia, Reduction of thyrotropin level in patients with hypothyroidism, Hypomagnesemia in the context of diarrhea, Encephalopathy, Photosensitivity, hepatobiliary disorders. **Warnings and Precautions:**: For Glimepiride: Patient should be advised to report promptly exceptional stress situations (e.g., trauma, surgery, febrile infections), blood glucose regulation may deteriorate, and a temporary change to insulin may be necessary to maintain good metabolic control. Metformin Hydrochloride may lead to Lactic acidosis; in such cases metformin should be temporarily discontinued and contact with a healthcare professional is recommended. Sulfonylureas have an increased risk of hypoglycaemia. Long-term treatment with metformin may lead to peripheral neuropathy because of decrease in vitamin B12 serum levels. Monitoring of the vitamin B12 level is recommended. Overweight patients should continue their energy-restricted diet, usual laboratory tests for diabetes monitoring should be performed regularly. **Contraindications:** Hypersensitivity to the active substance of glimepiride & Metformin or to any of the excipients listed. Any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis, diabetic pre-coma). Severe renal failure (GFR<30ml/min). In pregnant women. In lactating women.Acute conditions with the potential to alter renal function (dehydration, severe infection, shock, intravascular administration of iodinated contrast agents); acute or chronic disease which may cause tissue hypoxia (cardiac or respiratory failure, recent myocardial infarction, shock); hepatic insufficiency; acute alcohol intoxication; alcoholism. **Use in a special population:** Pregnant Women: Due to a lack of human data, drugs should not be used during pregnancy. Lactating Women: It should not be used during breastfeeding. Pediatric Patients: The safety and efficacy of drugs has not yet been established. Renal impairment: A GFR should be assessed before initiation of treatment with metformin containing products and at least annually thereafter. In patients at increased risk of further progression of renal impairment and in the elderly, renal function should be assessed more frequently, e.g. every 3-6 months.

Additional information is available on request.

Last updated: March 13, 2023

*In case of any adverse events, kindly contact: pv@usv.in

For the use of registered medical practitioner, hospital or laboratory.*

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Bone and Joint Disorders Associated with Diabetes

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Diabetes affects the functioning of many organs in the human body, including the musculoskeletal system. Clinically, both type 1 (T1DM) and type 2 (T2DM) diabetes incur an increase in fracture rate as compared to those without diabetes. A few bone and joint disorders associated with diabetes are as follows:

Charcot Foot

Charcot neuropathic osteoarthropathy (CN), also known as charcot foot, is an inflammatory disorder that affects the bones, joints, and soft tissues of the foot and ankle. This serious foot problem can affect the feet of people with neuropathy (nerve damage with numbness). The foot's bones become very brittle and can start to dislocate or break in reaction to even minor forces, including response to even those forces that come with standing or walking.

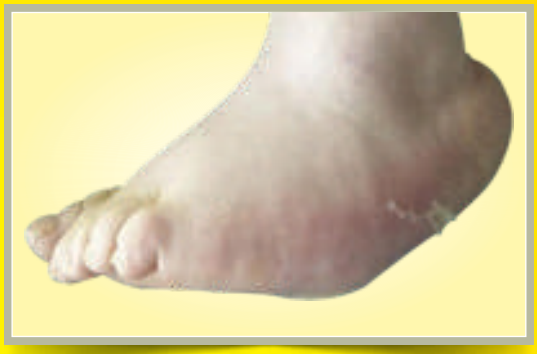

Figure 1: Charcot Foot

Figure 2: Removable walker cast

Often confused with an infection, inflammation (swelling, heat, and redness) in the affected area of the foot or ankle are the first warning indications of charcot foot. Sometimes a little injury (like tripping over something) or recent foot surgery causes it, but many times it starts without any apparent cause. If not appropriately treated early enough, the foot may become deformed. The only successful treatment is to minimize the weight on the foot along with the ankle and prevent it from moving until the inflammation has settled. This is normally done with some form of cast.

Osteoporosis

Osteoporosis is a disorder where the bones lose density and are more prone to breaking. Osteoporosis-related fractures can cause pain and impairment. Diabetes causes an increase in osteoclast activity (increased bone resorption) and a decrease in osteoblast (decreased bone formation) activity, which accelerates bone loss and causes osteopenia and osteoporosis. The highest risk of fracture is found in individuals who take insulin and have chronic diseases with poor glycemic control. Therefore, effective glycemic control should be the hallmark for preventing and treating DM-induced osteoporosis. A diet rich in vitamin D and calcium, or supplements for the same and weight-bearing exercises can help to strengthen bones. For patients with glucocorticoid-induced osteoporosis, medications may be required.

Osteoarthritis (OA)

OA is the most common form of arthritis also known as degenerative joint disease or “wear and tear” arthritis. Diabetes can be considered as an independent predictor of severe OA necessitating joint arthroplasty. Symptoms include aches or pains, stiffness, decrease in range of flexibility and swelling. OA has no cure and there are few conservative therapy alternatives available, and in severe cases, joint replacement surgery may be required. Studies have shown that people with diabetes are more likely to have their knee and hip joints replaced.

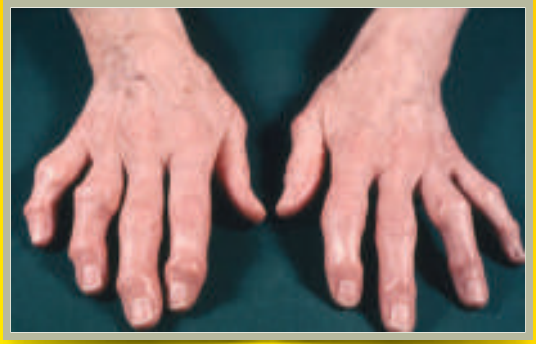

Figure 3: Hand Osteoarthritis

Diabetic Hand Syndrome or Stiff Hand Syndrome or Diabetic Cheiroarthropathy

Figure 4: Prayer Sign due to Diabetic Cheiroarthropathy

Diabetic cheiroarthropathy is a disorder in which finger movement becomes restricted as the hands become waxy and thickened. This syndrome can affect both patients with T1DM and T2DM, however, improving glucose management and physical therapy can delay the onset of this condition. Symptoms include inability of the fingers to be extended or flex properly, spontaneous extension of the fingers, and stiffness or swelling of the fingers, often associated with pain. Physical treatment and better blood glucose management can reduce the progression of this condition, but the restricted movement may not be reversible.

Diffuse Idiopathic Skeletal Hyperostosis (DISH)

This is a form of arthritis that affects the tendons and ligaments around the spine. Also known as Forestier's disease, it develops when these tendons and ligaments calcify or become hardened. The upper section of the back (thoracic) and neck (cervical spine), are commonly affected by DISH. It can also impact the hands, knees, hips, heels, and/or ankles. DISH patients often have no symptoms, thus the disease is only accidentally detected. Symptoms include pain, stiffness or reduced range of motion in any affected part of the body. For patients with back discomfort treatment include physical therapy, activity modification, bracing, NSAIDs, and bisphosphonates. For particular consequences of the disorder, such as fracture, cervical myelopathy, lumbar stenosis, neurologic impairments, infection, or painful deformity, surgical decompression and stabilization may be required.

Early detection of diabetes-related bone and joint disorders is important. Good glycemic control along with dietary modifications and physiotherapy can help treat these conditions.

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Falls and Fractures Associated with Diabetes

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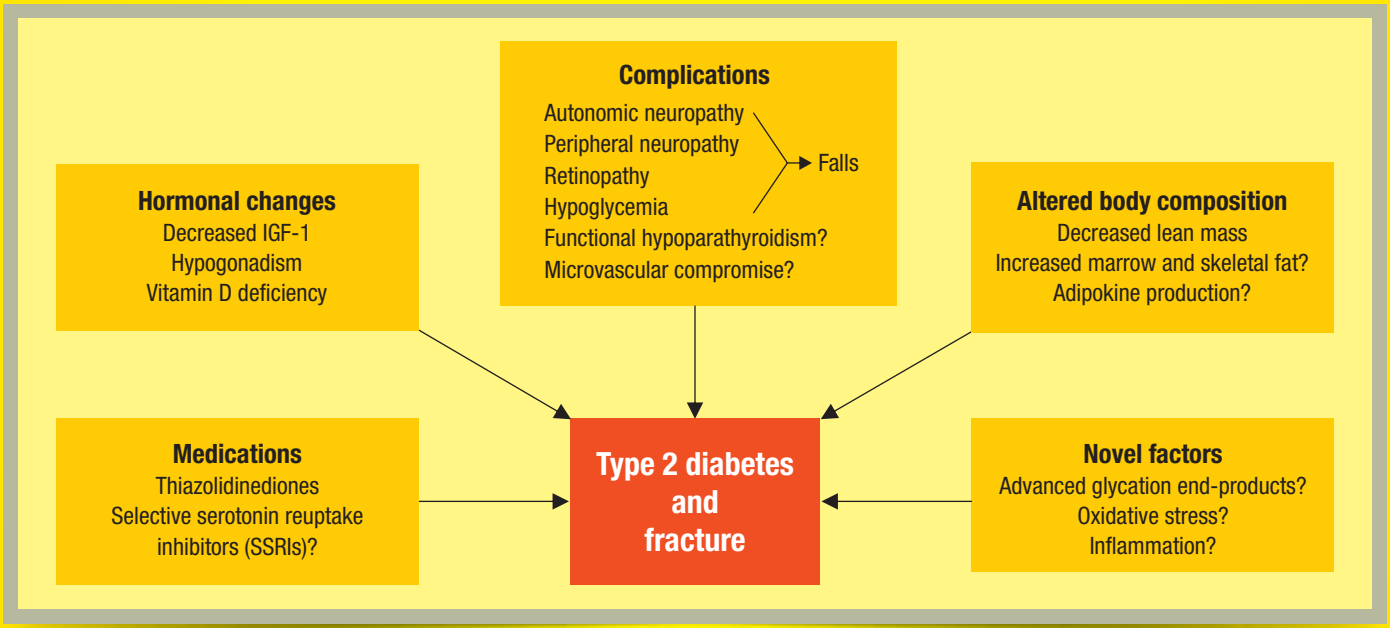
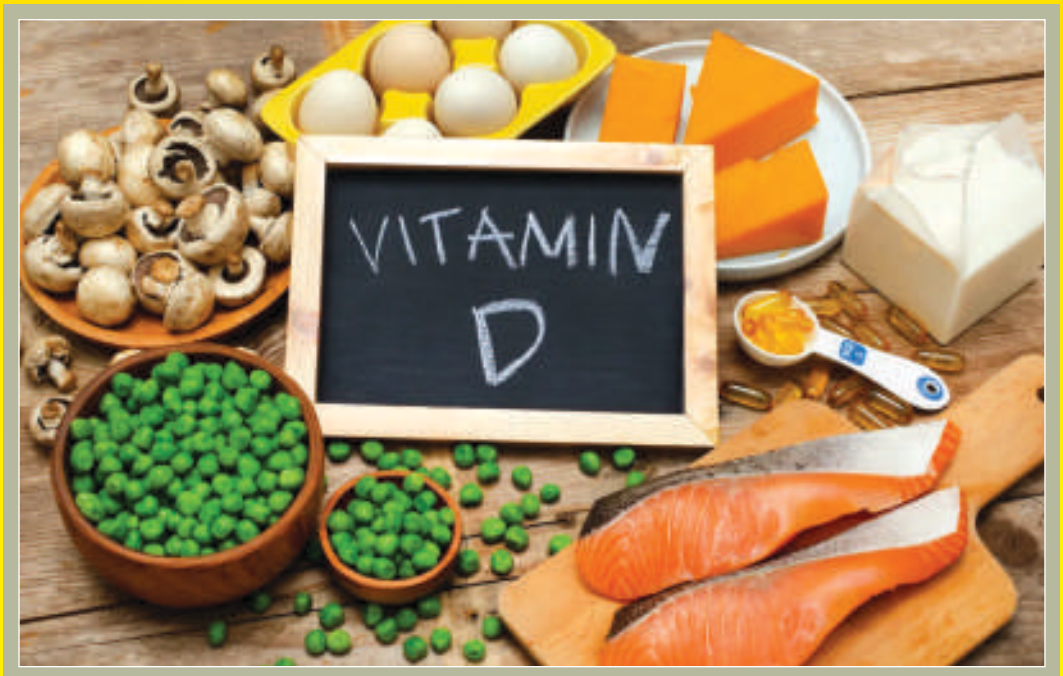
Skeletal fracture is a devastating occurrence with dire health effects. The negative consequences of diabetes on bone fragility and fracture risk have come to light in recent years. Comparing the bone mineral density (BMD) to that of their age-matched healthy counterparts, people with type 2 diabetes mellitus (T2DM) frequently have normal to high BMD. Despite having high BMD, studies have indicated that people with T2DM are more likely to fracture their bones. T2DM complications such as retinopathy and autonomic dysfunction may contribute to bone fracture. Renal osteodystrophy could be caused by nephropathy.

The importance of the marrow microenvironment for effective bone remodelling is becoming increasingly recognized. Thiazolidinediones and selective serotonin reuptake inhibitors are two medications that may hinder bone remodelling by affecting osteoblastogenesis and mesenchymal stem cell differentiation. Systemic inflammation, the buildup of advanced glycation end products, and the production of reactive oxygen species are all significantly altered in T2DM. Moreover, these systemic alterations may have a negative impact on the remodelling process and cause bone fragility in T2DM patients.



Fracture Prevention and Treatment in Type 2 Diabetes Mellitus

The skeleton is significantly affected by glycemic control to minimize end-organ damage, possibly lowering falls and renal osteodystrophy. Men and women with T2DM should be screened for vitamin D insufficiency. To avoid subsequent hyperparathyroidism and osteomalacia, vitamin D should be replenished as needed. Patients with T2DM should also be informed about the value of a diet rich in calcium and vitamin D as well as weight-bearing exercise, which is typically emphasized in people with metabolic bone disease. The hazards and advantages of drug commencement should be carefully considered when prescribing medications that could negatively affect the skeleton.



Resources:

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Super Food: Sesame Seeds

Sesame seeds are well known for their numerous nutritional benefits. Sesame seeds have a smooth nutty flavour and an aromatic scent. Sesame seeds are divided into three categories based on the color of their germplasm: black, white, and yellow.

Nutritional Benefits

- Good source of calcium and vitamin E
- Antioxidant property
- Helps reduce cholesterol
- Anti-inflammatory
- Cardioprotective

Health Benefits

- **Hypoglycemic Effect:** Due to the presence of bioactive lignans, which enhance insulin release from the pancreatic beta cells, sesame seeds have a hypoglycemic impact.
- **Anti-oxidant Property:** Sesame seeds contain a variety of active compounds, including lignans like sesamin, sesaminol, sesamol, and sesamolin, all of which have potent anti-oxidant capabilities.
- **Cardioprotective, Lipid-regulating, and Cholesterol-lowering Effects:** Sesame seeds contain a variety of phytosterols, including stigmasterol, campesterol, sitostanol, and campesterol, which lower blood cholesterol levels as well as have anti-inflammatory, anti-bacterial, anti-oxidative, and anti-cancerous properties.
- Due to their abundance in phytosterols, lignans, PUFA, and vitamin E, sesame seeds can help lower blood pressure.
- **Anti-cancer Effect:** Sesame seeds contain significant levels of linoleic acid esters, which can specifically suppress the growth of malignant melanoma.

How to Consume?

Because of their distinct nutty flavour, sesame seeds can be roasted and added to a variety of salads and over khakhras. Tahini, also known as sesame butter, is a paste produced from ground sesame seeds that is often used to make dips like hummus. Sesame seed chikki or ladoo is traditionally made during Sankrant. Sesame oil goes very well in salad dressings and is best suited for frying.

Recommended Intake

One exchange of sesame seeds (white) equals to 15 g (1 tbsp) which gives 3.26 g of protein, 1.62 g of carbohydrates, 6.46 g of fat, 192.45 mg of calcium , 113.1 mg of phosphorous and 78 kcal of energy.

Resources:

1. L Wei P, Zhao F, Wang Z, Wang Q, Chai X, Hou G, Meng Q. Sesame (Sesamum indicum.): A Comprehensive Review of Nutritional Value, Phytochemical Composition, Health Benefits, Development of Food, and Industrial Applications. *Nutrients.* 2022 Sep 30;14(19):4079. doi: 10.3390/nu14194079. PMID: 36235731; PMCID: PMC9573514.
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Impact of Diabetes Medications on Bone Health

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As the prevalence and incidence of diabetes continue to rise, a proper understanding of the adverse effects on bone metabolism is important. Type 1 (T1DM) and type 2 (T2DM) diabetes mellitus are remarkably linked to osteoporosis and fracture risk. For diabetes patients to regulate their glucose levels, anti-diabetes medications are administered.

As these medications have their own impact on bone health, it is important to evaluate these effects when managing people with diabetes. Let's discuss impact of below diabetes medication on bone health.

Thiazolidinedione

Thiazolidinedione increases mesenchymal stem cell allocation to adipocytes and decreases differentiation to osteoblasts while increasing differentiation towards adipocytes, resulting in lower osteoblast function and increased bone loss. It activates peroxisome proliferator-activated receptor (PPAR) nuclear receptors, which increases the risk of fracture and bone loss. Additionally, it may have a detrimental effect on fracture healing due to its inhibitory effects on the production of estrogen and androgen.

Metformin

Metformin stimulates the AMP-activated protein kinase (AMPK) signaling pathway and consequent augmentation of endothelial nitric oxide synthase and bone morphogenetic protein-2 production. It induces the differentiation and mineralization of osteoblastic MC3T3-E1 cells. Metformin has positive or neutral effects on bone health and lowers the chance of fracture.

Sulfonylureas and Sodium-Glucose Co-transporter 2 Inhibitors

They have a neutral effects on bone metabolism and bone mineral density. These medications increase the risk of falling events due to increased chances of hypoglycemic episodes.

Incretin-based Therapy (DPP-4 and GLP-1)

Incretin based therapy such as dipeptidyl peptidase-4 (DPP-4) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists showed a neutral effect on the health of the bones and the risk of fracture. Incretin-based therapy has anabolic effects on bone. GLP-1 enhanced bone density by preventing bone loss and increasing bone formation.

Insulin

Insulin increases the osteoblasts activity by binding the insulin receptor, which in turn promotes bone formation. The usage of insulin may serve as an indicator for the severity or duration of T2DM, due to the existence of comorbidities, the risk of hypoglycemia, or the increased fall risk, all of which likely contribute to the higher fracture risk of patients with T2DM. It is therefore not easy to draw conclusions on whether the association between fracture risk and insulin is related to the treatment with insulin or the person's long association with diabetes. Studies convey conflicting results over insulin safety profile on bone health.

Various diabetes medications may worsen or improve bone quality. Therefore, a better comprehension of the biological mechanisms and effects of the various classes of diabetes medications on bone metabolism is crucial when developing T2DM treatment strategies. This will help clinicians make decisions about the various medications available for the treatment of T2DM.

Resources:

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Dia-Games

Word Search

Find these words in the grid horizontally, vertically or diagonally.

T	N	I	O	J	T	O	C	R	A	H	C	O	F
S	I	T	I	R	H	T	R	A	O	E	T	S	O
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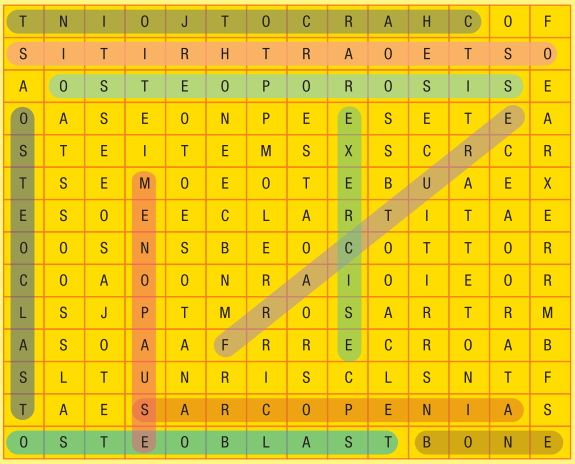
OSTEOPOROSIS
BONE
OSTEOCLAST
EXERCISE
CHARCOTJOINT
MENOPAUSE
FRACTURE
SARCOPENIA
OSTEOARTHRITIS
OSTEOBLAST

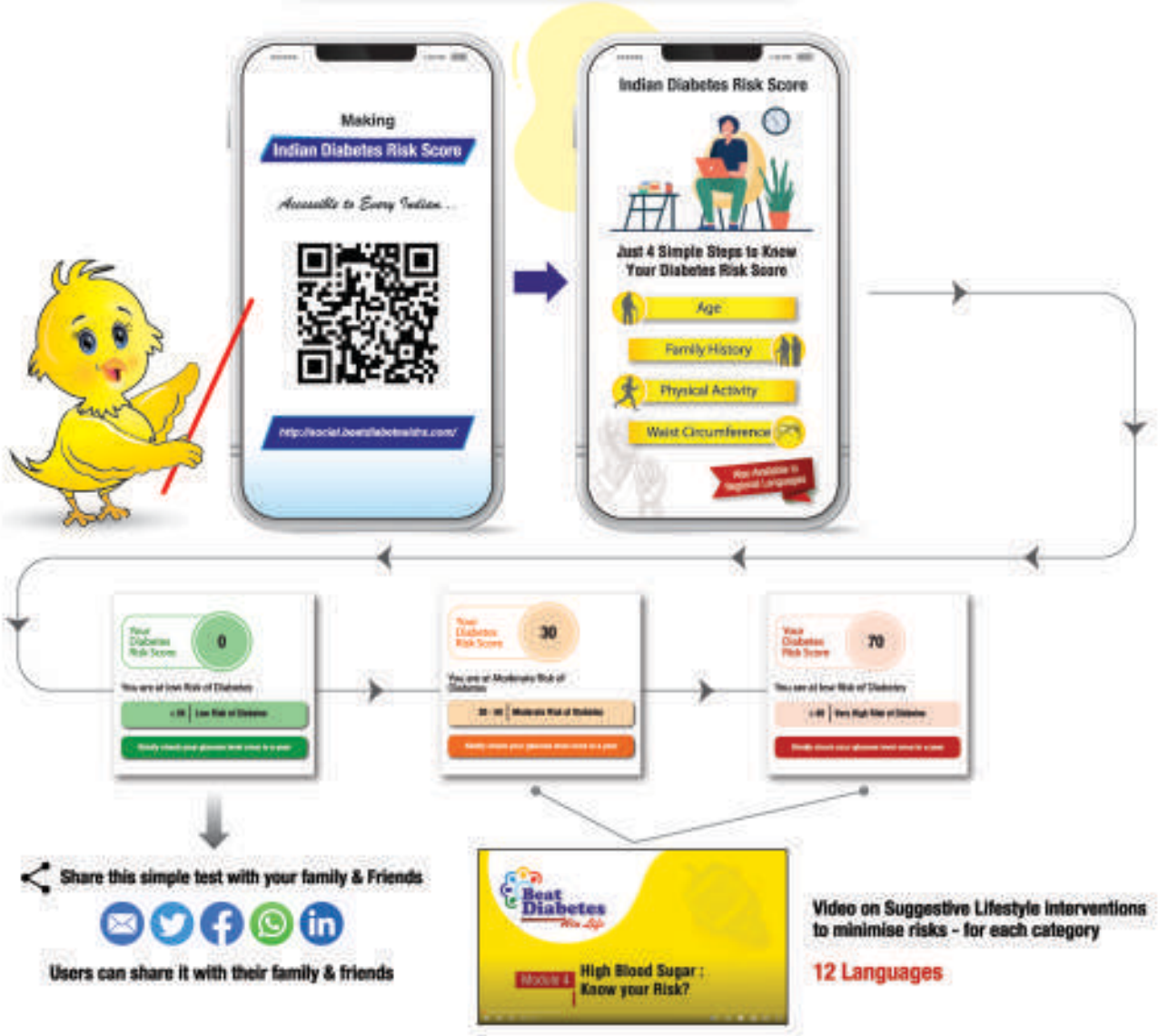


NOTES

Beat Diabetes
Win Life

For screening people with High & Moderate Risk of Diabetes

Indian Diabetes Risk Score



Share this simple test with your family & Friends

Users can share it with their family & friends

Video on Suggestive Lifestyle Interventions to minimise risks - for each category

12 Languages

An awareness initiative by USV

Complications

Stages

Ages

BMI

Comorbidities

MODY

In T2DM Across Continuum,

START with,

Glycomet®-GP 1

Metformin Hydrochloride 500 mg SR + Glimepiride 1 mg

Glycomet®-GP 2

Metformin Hydrochloride 500 mg SR + Glimepiride 2 mg

Add Early Along with other AHAs

DPP4i

SGLT2i

TZDs

Insulin

AGIs

GLP1-RAs

* Data on File

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Priscribing information

Information: Metformin hydrochloride (as prolonged release) and glimepiride tablets. Glycomet-GP 0.5/Glycomet-GP 0.5 Forte/ Glycomet-GP 1/ Glycomet-GP 1/850/ Glycomet-GP 2/ Glycomet-GP 2/850/ Glycomet-GP 3/ Glycomet-GP 3/850/ Glycomet-GP 4/ Glycomet-GP 4/850/ Glycomet-GP 1 Forte/ Glycomet-GP 2 Forte/ Glycomet-GP 3 Forte/ Glycomet-GP 4 Forte Abridged Prescribing Information **Composition:** Glycomet GP 0.5mg: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500mg and glimepiride IP 0.5mg.• Glycomet GP 0.5 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 0.5mg.• Glycomet GP 1: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 1 mg. • Glycomet GP 1/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 1 mg. • Glycomet GP 2: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 2 mg. • Glycomet GP 2/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 2 mg.• Glycomet GP 3: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 3 mg. • Glycomet GP 3/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 3 mg. • Glycomet GP 4: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 4 mg. • Glycomet GP 4/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 4 mg. • Glycomet GP 1 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 1mg. • Glycomet GP 2 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 2mg. • Glycomet GP 3 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 3mg. • Glycomet GP 4 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP mg. **Indication:** For the management of patients with type 2 diabetes mellitus when diet, exercise and single agent (glimepiride or metformin alone) do not result in adequate glycaemic control. **Dosage and Administration:** The recommended dose is one tablet daily during breakfast or the first main meal. Each tablet contains a fixed dose of glimepiride and Metformin Hydrochloride. The highest recommended dose per day should be 8 mg of glimepiride and 2000mg of metformin. Due to prolonged release formulation, the tablet must be swallowed whole and not crushed or chewed. **Adverse Reactions:** For Glimepiride: hypoglycaemia may occur, which may sometimes be prolonged. Occasionally, gastrointestinal (GI) symptoms such as nausea, vomiting, sensations of pressure or fullness in the epigastrium, abdominal pain and diarrhea may occur. Hepatitis, elevation of liver enzymes, cholestasis and jaundice may occur; allergic reactions or pseudo allergic reactions may occur occasionally. For Metformin: GI symptoms such as nausea, vomiting, diarrhea, abdominal pain, and loss of appetite are common during initiation of therapy and may resolve spontaneously in most cases. Metallic taste, mild erythema, decrease in Vit B12 absorption, very rarely lactic acidosis, Hemolytic anemia, Reduction of thyrotropin level in patients with hypothyroidism, Hypomagnesemia in the context of diarrhea, Encephalopathy, Photosensitivity, hepatobiliary disorders. **Warnings and Precautions:**: For Glimepiride: Patient should be advised to report promptly exceptional stress situations (e.g., trauma, surgery, febrile infections), blood glucose regulation may deteriorate, and a temporary change to insulin may be necessary to maintain good metabolic control. Metformin Hydrochloride may lead to Lactic acidosis; in such cases metformin should be temporarily discontinued and contact with a healthcare professional is recommended. Sulfonylureas have an increased risk of hypoglycaemia. Long-term treatment with metformin may lead to peripheral neuropathy because of decrease in vitamin B12 serum levels. Monitoring of the vitamin B12 level is recommended. Overweight patients should continue their energy-restricted diet, usual laboratory tests for diabetes monitoring should be performed regularly. **Contraindications:** Hypersensitivity to the active substance of glimepiride & Metformin or to any of the excipients listed. Any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis, diabetic pre-coma). Severe renal failure (GFR≤30ml/min). In pregnant women. In lactating women.Acute conditions with the potential to alter renal function (dehydration, severe infection, shock, intravascular administration of iodinated contrast agents); acute or chronic disease which may cause tissue hypoxia (cardiac or respiratory failure, recent myocardial infarction, shock); hepatic insufficiency; acute alcohol intoxication; alcoholism. **Use in a special population:** Pregnant Women: Due to a lack of human data, drugs should not be used during pregnancy. Lactating Women: It should not be used during breastfeeding. Pediatric Patients: The safety and efficacy of drugs has not yet been established. Renal impairment: A GFR should be assessed before initiation of treatment with metformin containing products and at least annually thereafter. In patients at increased risk of further progression of renal impairment and in the elderly, renal function should be assessed more frequently, e.g. every 3-6 months.

Additional information is available on request.

Last updated: March 13, 2023

In case of any adverse events, kindly contact: pv@usv.in For the use of registered medical practitioner, hospital or laboratory.

USV Private Limited Corvette Team

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