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The relationship of Diabetes Mellitus with bone diseases for some patients in Dhi Qar

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Abstract:

Diabetes is defined as a group of metabolic disorders manifested by high blood sugar (hyperglycemia) as a result of the body not responding adequately to the natural hormone "insulin" or as a result of a defect in its production or both. The metabolic abnormalities of diabetes can latently affect bone metabolism, structure and mineral density, and thus can cause various musculoskeletal disorders.This study aimed to knowldgment relationship of diabetes mellitus with bone diseases for some patients . Measurements included, blood sugar,HbA1c, Ca++ Results indicated that bone fragility in diabetes is complex,with some alterations being common to type 1 and 2 diabetes, while other are distinct, pertaining to the Different ages of onset and underlying mechanisms of diabetes development Measures aimed at reducing overweight and obesity, and cardiovascular disease are likely to also reduce the risk of developing type 2 diabetes and its complications.

Key words: *Diabetes mellitus (DM) ,bone diseases, Osteoporosis, Vitamin D*:

علاقة مرض السكري بأمراض العظام لدى بعض المرضى في ذي قار

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خلاصة:

يُعرّف مرض السكري على أنه مجموعة من الاضطرابات الأيضية التي تتمثل في ارتفاع نسبة السكر في الدم (فرط سكر الدم) نتيجة عدم استجابة الجسم بالشكل الكافي للهرمون الطبيعي "الأنسولين" أو نتيجة خلل في إنتاجه أو كليهما. يمكن أن تؤثر الاضطرابات الأيضية لمرض السكري بشكل خفي على استقلاب العظام وبنيتها وكثافة المعادن، وبالتالي يمكن أن تسبب اضطرابات عضلية هيكلية مختلفة. هدفت هذه الدراسة إلى معرفة علاقة مرض السكري بأمراض العظام لدى بعض المرضى. وشملت القياسات نسبة السكر في الدم، HbA1c، Ca++ وأشارت النتائج إلى أن هشاشة العظام في مرض السكري أمر معقد، حيث تكون بعض التغيرات شائعة في مرض السكري من النوع الأول والثاني، في حين أن بعضها الآخر متميز، ويتعلق بالأعمار المختلفة لظهور مرض السكري والآليات الأساسية لتطور مرض السكري. ومن المرجح أن تؤدي التدابير الرامية إلى الحد من زيادة الوزن والسمنة وأمراض القلب والأوعية الدموية إلى تقليل خطر الإصابة بمرض السكري من النوع الثاني ومضاعفاته.

الكلمات المفتاحية: داء السكري، أمراض العظام، هشاشة العظام، فيتامين د:

1-1: Introduction

Diabetes mellitus and bone diseases:

One of the hallmarks of the diabetes family of illnesses is hyperglycemia. The etiology, symptoms, and long-term effects of various diabetic problems vary. The laboratory contributes to disease diagnosis, condition type identification, and tissue damage progression evaluation to help doctors select the best course of treatment. Exercise, food control, and insulin replacement therapy have all been demonstrated to lessen the effects of type 1 diabetes. The best ways to manage type 2 diabetes mellitus are to lose weight and follow a diet, and medication therapy, including metformin, thiazolidinediones, alpha glucosidase inhibitors, sulfonylureas, and analogs of benzoic acid. If other measures are not successful in achieving glycemic control for type 2 diabetics, then insulin may be administered. Glycemic control, or keeping blood glucose concentrations at or close to normal, is the therapeutic objective for people with type 1 and type 2 diabetes. The genesis of the disease is a factor in the current diagnostic criteria for diabetes.Diabetes has been divided into four categories. Type 1 forms are these four, type 2, gestational diabetes, and additional diabetes-specific conditions. An elevated risk of fracture is linked to diabetes. While commonly recognized risk factors are good predictors in persons without diabetes, they understate the increased fracture risk. Patients with diabetes have an understated risk of fracture from bone mineral density measures used in osteoporosis diagnosis. Low bone turnover is a feature of diabetes that may exacerbate bone fragility. The altered incretin response and hyperglycemia are probably the cause of the poor bone turnover. The most prevalent diabetic complication and the primary cause of chronic kidney damage in the developed world is diabetic nephropathy. Fragility fractures of bones are becoming increasingly acknowledged as an additional consequence of diabetes. During prenatal development, bone formation occurs, and it continues to undergo a process of continuous renewal after delivery. When old bone tissue is replaced with new bone tissue over and over again, this is called bone remodelling. The process of osteoclasts taking minerals and collagen fibres from bone is called resorption. The process of osteoblasts adding minerals and collagen fibres to bone is called deposition. The extracellular matrix of bone breaks down during bone resorption, The extracellular matrix of bone is synthesised during the process of bone development. Approximately 5% of the skeletal structure of the human body undergoes continuous morphological alterations. The annual growth rate of dense bone tissue is approximately 4%, whereas the growth rate of spongy bone tissue exceeds 20%. Remodelling occurs at varying rates in different regions of the body. The distal section of the femur is replaced approximately every four months. However, the regeneration of bone in certain regions of the femur's shaft is limited and will not fully occur over an individual's lifespan. Approximately 5% of the body's bone mass undergoes continuous remodelling, even after bones have completed their growth and

attained their final sizes and shapes. The annual growth rate of dense bone tissue is approximately 4%, whereas the growth rate of spongy bone tissue exceeds 20%. Remodelling occurs at varying rates in different regions of the body. The distal portion of the femur is replaced approximately every four months. Conversely, the regeneration of bone in certain regions of the femur's shaft is limited and incomplete throughout an individual's lifespan. Even after ossification is complete and bones have attained their maximum dimensions and form.[1][5][10][12](13)

1-2: Aims of the study:

To knowldgment relationship of diabetes mellitus with bone diseases for some patients in Dhi Qar.

2-1: Diabetes and Fracture Risk

Bone tissue consists of a matrix rich in collagen, which is reinforced by mineral crystals and also contains non-collagenous organic substances. Bone strength is determined by the quantity, composition, and integrity of the bone. Osteoblasts, which are cells that make bone, and osteoclasts, which are cells that break down bone, decide and maintain these characteristics on the bone's surface. Additionally, osteocytes, which are cells embedded within the bone matrix, also contribute to these features. Cartilage cells, known as chondrocytes, are also involved in the process of bone creation and expansion. These cells do not operate independently, but instead work together in a synchronised fashion, both within each specific group of cells and across the cells of bone, as well as between these cells and other types of cells inside the bone microenvironment. **Osteoporosis** is a condition affecting the skeletal system where the strength of the bones is weakened, making them more susceptible to fractures that occur easily. The strength of bones is influenced by both their bulk and quality. If someone has osteoporosis and a real fragility fracture happens, or if they have never had one, their bone mineral density (BMD) or the Fracture Risk Assessment Tool can be used to identify them**.** (FRAX).

Diabetes is a collection of metabolic disorders marked by high levels of glucose in the blood due to deficiencies in the production or effectiveness of insulin. Diabetes is increasingly being acknowledged as a cause of fragility fractures.

2-2: Diabetes mellitus (DM):

Diabetes mellitus (DM) is a collection of metabolic illnesses that are distinguished by elevated blood glucose levels. Hyperglycemia occurs due to impairments in either insulin secretion, insulin action, or both. Diabetes causes long-term high blood sugar levels, which lead to specific long-term issues that can damage or impair multiple organs, particularly the eyes, kidneys, nerves, heart, and blood

vessels. Type 1 diabetes is characterised by the lack of insulin production and secretion by the beta cells in the pancreas. The presence of an autoimmune reaction that leads to the destruction of the beta cells in the pancreas is a key element in the development of high blood sugar levels seen in type 1 diabetes mellitus. The cell-mediated reaction causes it to enter the pancreas and cause beta cells to shrink in size. Even though insulin is a protein hormone, it works by chemically interacting with receptors on cells in certain target areas. Insulin helps cells take in glucose and makes glycogenesis better in muscles. Insulin makes it easier for cells to take in glucose and makes fatty tissue make more fat. In the liver, insulin has a limiting effect by slowing down the processes of gluconeogenesis and glycogenolysis. A lot of people who have been labelled with type 1 diabetes have autoantibodies in their blood. The chance of having autoantibodies is affected by genetics, and people with type 1 diabetes are more likely to have specific histocompatibility antigens. Still, the development of disease is complicated because it may need things like rubella, mumps, other viral illnesses, and chemical exposure to start.**(1)(3)**

Type 1 diabetes is characterised by the lack of insulin production and secretion by the beta cells in the pancreas. The presence of an autoimmune reaction that leads to the destruction of the beta cells in the pancreas is a key element in the development of high blood sugar levels seen in type 1 diabetes mellitus. People with metabolic syndrome may exhibit abdominal obesity and hypertension. These individuals have a higher likelihood of developing cardiovascular disease. The aetiology of type 2 diabetes is complex and multifaceted. Substantial data exists that demonstrates a strong association between obesity and the development of type 2 diabetes. Other contributing variables, such as a genetic susceptibility to type 2 diabetes and lack of physical activity, have also been linked to the condition.(2) A prior diagnosis of gestational diabetes increases the likelihood of developing type 2 diabetes. Other risk factors include advancing age, hypertension, and dyslipidemia. Membership in specific racial and ethnic groupings is also linked to an elevated chance of having the disease. Type 2 diabetes and gestational diabetes are both caused by the same thing. Gestational diabetes, on the other hand, only happens during pregnancy. Tissue cells are less likely to respond to insulin when they are pregnant. Women who are pregnant will usually react by making more insulin, but some may get gestational diabetes if they can't. After giving birth, the elevated blood sugar levels associated with gestational diabetes decrease. However, Individuals with a history of gestational diabetes have an increased likelihood of developing type 2 diabetes in the future. The fourth categorization of diabetes is known as other specific causes of diabetes, previously referred to as secondary diabetes. This form of hyperglycemia can arise as a secondary result of factors unrelated to insulin. Endocrine disorders, such as Cushing's syndrome, and exocrine disorders, such as cystic fibrosis, and some medicines, such as protease inhibitors and glucocorticoids, can cause an

increase in blood glucose levels. Additional factors contributing to this type of diabetes include genetic abnormalities impacting pancreatic beta cells or insulin function. The manifestations and causes of diabetic problems vary. Around 10% of individuals with diabetes have type 1 diabetes. Type 1 disease typically manifests as an acute illness, but type 2 diabetes develops gradually over a period of time.[5][4]

Typically, type 1 glucose blood levels exhibit more severity compared to type 2. Ketoacidosis is more likely to happen to people with type 1 diabetes than to people with type 2 diabetes. Patients with type 1 diabetes need insulin to treat their disease because of how it works, However, the majority of individuals with type 2 diabetes do not. Individuals with type 1 diabetes typically receive a diagnosis at a younger age, typically before reaching 18 years old, and they generally have a lower body weight. Regardless, type 2 diabetes is commonly diagnosed in individuals who are older than 40 years and are more prone to being overweight or obese. All of that being said, these symptoms don't always show up in people with type 1 and type 2 diabetes. People who are at least 18 years old can be identified with type 1 diabetes. Type 2 diabetes is more likely to happen in kids who are overweight. People with Type 2 diabetes may need insulin if they can't control their blood sugar levels properly with other methods.[6][7]

The endocrine system regulates carbohydrate metabolism, particularly the metabolism of glucose, Through a sequence of acts and corresponding reactions. Insulin and glucagon have a substantial influence on the pathways of glucose metabolism. The actions of these two hormones have contrasting impacts. Insulin is secreted when blood glucose levels rise. Insulin binds to the receptors on the cell membrane, facilitating the transport of glucose into the cell. Insulin additionally promotes the formation of glycogen, fat, and glucose breakdown, while preventing the breakdown of glycogen. Glucagon is secreted when there is a demand for elevated levels of blood glucose. Glucagon promotes the breakdown of glycogen and the production of new glucose. The pancreas produces both insulin and glucagon, mostly in the beta and alpha cells of the islets of Langerhans, respectively.[1][2][8]

There are other hormones that affect how glucose is metabolised. Stressful events cause the adrenal medulla to release the hormone epinephrine, which inhibits insulin release and speeds up the breakdown of fat and glycogen. The adrenal cortex secretes glucocorticoids, like cortisol, to lower blood glucose levels by inhibiting gluconeogenesis and the absorption of glucose from food. The thyroid gland secretes the hormone thyroxine, which encourages the body to break down glycogen and create glucose from non-carbohydrate sources. Furthermore, it prevents the intestines from absorbing glucose from the food.

Table 2-1: **Etiologic Classification of Diabetes Mellitus** [5]

1. Type 1 diabetes (beta cell destruction, usually leading to absolute insulin deficiency)
   - Immune mediated
   - Idiopathic
2. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)
3. Gestational diabetes mellitus (GDM)
4. Other specific types
   - Genetic defects of beta cell function
   - Genetic defects in insulin action
   - Diseases of the exocrine pancreas
   - Endocrinopathies
   - Drug- or chemical-induced
   - Infections
   - Uncommon forms of immune-mediated diabetes

2.3: Pathophysiology of bone fragility

Diabetes-related bone fragility has multiple underlying causes. Certain changes between type 1 and type 2 diabetes are similar, but some are distinct due to the age differences at which they begin and the methods in which the disease worsens.An autoimmune condition known as type 1 diabetes (T1D) results in the death of cells and the inability of the body to produce insulin. It is also sometimes called childhood diabetes. When insulin is present, it raises the activity of Runx2, which then causes osteoblasts to multiply. Besides that, insulin increases the intake of carbohydrates and the production of collagen. Through the use of animal models of type 1 diabetes (T1D), such as nonobese diabetic (NOD) mice and streptozotocin-induced diabetic mice, it has been demonstrated that insufficient insulin is associated with decreased bone turnover, trabecular and cortical bone mineral density (BMD), and weaker bones. Furthermore, there is a correlation between reduced levels of insulin-like growth factor 1 (IGF-1) and type 1 diabetes (T1D), an important substance that helps osteoblasts build bones. Besides that, Inflammation and poor diet, such as not getting enough calcium and/or protein, are two things that define this disease. Low peak bone mass may occur more frequently in children and teenagers with T1D if they engage in both less physical activity and lower levels of physical exercise.Thus, in children with diabetes, the levels of P1NP and osteocalcin are inversely correlated with the degree of chronic hyperglycemia, which is determined by measuring the glycated haemoglobin (HbA1C) levels.

In young people with T1D, Both the cortical and trabecular bone volumes are decreased, as demonstrated by HRpQCT. This is particularly true for people who suffer from a grave illness characterised by microvascular issues. These individuals have fat in their bone marrow, according to a micro-MRI. It's

significant to remember that a study on bone biopsies in young individuals with T1D that was well-controlled did not discover any decreased indicators of bone formation than in the control group. But the study did find that pentosidine and other AGEs raised the amount of nonenzymatic collagen cross-linking. This could change the way bone material works.

The most common type of diabetes is type 2 diabetes (T2D), which usually starts in adults. People who have type 2 diabetes (T2D) often are overweight and have insulin resistance. Their bone mineral density (BMD) is also usually normal or high, which is influenced by increased weight-bearing, elevated oestrogen levels, and excessive insulin levels. Over time, the function of β-cells decreases and the management of glucose worsens, leading to a state of long-term high blood sugar levels that can damage organs and increase the risk of consequences, such as bone problems.[1,2,13,14]

Like type 1 diabetes, type 2 diabetes (T2D) is also linked to reduced bone turnover, which can be measured through biochemical markers and bone biopsies. T2D is also associated with both trabecular and cortical deficits, including a significant increase in cortical porosity. This is especially observed in individuals with fragility fractures and microvascular complications. Furthermore, a study conducted on 60 postmenopausal women, including 30 patients who have been diagnosed with type 2 diabetes for more than 10 years, has used in vivo microindentation testing on the tibia to show a decrease in bone mineral strength (BMS). Like type 1, the latter disorder could be brought on by an accumulation of AGEs in the bone and a reduction in enzymatic collagen cross-links. Hyperglycemia and advanced glycation end products (AGEs) can potentially impair bone strength by affecting the actions of osteoblasts and osteocytes. Therefore, both laboratory studies conducted outside a living organism and those conducted within a living organism have shown elevated levels of sclerostin in this particular situation. Furthermore, Maintaining the proper balance between osteoblastogenesis and adipogenesis is crucial, as both processes are primarily regulated by the PPARγ and Wnt pathways.Increased levels of PPARγ2 in bone tissue, decreased bone formation, and increased fat accumulation in the bone marrow are observed in diabetes-model mice. In overweight postmenopausal women with (T2D), a correlation has been observed between the quantity of fat in the bone marrow and bone mineral density (BMD).[13,14]

Over time, individuals with diabetes experience a decline in the beneficial effects of incretins. The incretin effect is principally influenced by two peptides, These are glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). GLP-1 receptors are present in bone marrow osteoblasts and stem cells. GLP-1 inhibits the differentiation of mesenchymal stem cells into adipocytes. Because there are fewer cortical bone mass in GLP-1 receptor-deficient mice, more osteoclasts are both active and present, as well as reduced

mechanical and material characteristics. On the other hand, when GLP-1 is given to animals, it promotes bone formation in both normal rats and rats with diabetes or insulin resistance caused by streptozocin or fructose. This indicates that the effect of GLP-1 on bone formation is not dependent on insulin. In a separate investigation, the injection of GLP-1 in an animal model with type 2 diabetes resulted in a decrease in serum levels of sclerostin and an increase in osteocalin levels.[13]

2-4: Factors Affecting Bone Growth and Bone Remodeling[8]

Normal bone metabolism requires a number of factors, including development in children and adult bone remodelling. These include getting enough minerals and vitamins in your food and making sure your hormone levels are right.

1. ***Minerals***. You need enough calcium and phosphorus, as well as smaller amounts of magnesium, fluoride, and manganese, while your bones are growing. These minerals are important for building new bones.

2. ***Vitamins***. Vitamin A makes osteoblasts work better. Making collagen, which is the main protein in bones, is impossible without vitamin C. Vitamin D improves bone growth by helping the body absorb calcium from food in the digestive system and into the bloodstream. Both vitamin K and vitamin B12 are needed to make bone proteins.

3. ***Hormones***. The insulinlike growth factors (IGFs) that are produced by the liver and bone tissue have a significant impact on the development of bones in childhood. In addition to causing cell division in the periosteum and epiphyseal plate and stimulating osteoblasts, IGFs also aid in the production of proteins required for the growth of bone. IGFs are produced when the anterior pituitary gland releases human growth hormone (hGH). The thyroid gland produces thyroid hormones (T3 and T4), which activate osteoblasts and aid in the production of new bone. Furthermore, the pancreatic hormone insulin stimulates bone development by enhancing the production of bone proteins.[18]

2-4-1: Vitamin D :

Vitamin D refers to a collection of fat-soluble chemicals that were initially identified for their ability to prevent rickets. The primary forms of vitamins relevant to human health are D2 (ergocalciferol) and D3 (cholecalciferol). Vitamin D2 is synthesised from the plant sterol, ergosterol. Vitamin D3 is synthesised in human skin by the conversion of its precursor, 7-dehydrocholesterol, upon exposure to ultraviolet (UV) radiation from sunshine. Vitamin D acquired by sunlight exposure, dietary intake, and supplementation is physiologically inactive and requires two hydroxylations within the body to become active. Since vitamin D may be produced internally, it does not fulfil the traditional definition of a vitamin. Vitamin D is classified as a hormone and is

produced in the kidney. The active form of the hormone is called 1,25-dihydroxyvitamin D [1,25(OH)2D]. It functions in various parts of the body. However, due to its initial identification as a necessary nutrient and the requirement for dietary intake in specific situations, it is categorised as a vitamin. (11) Vitamin D facilitates the absorption of calcium in the intestines and helps maintain appropriate levels of calcium and phosphate in the blood. Calcium is essential for various physiological processes, such as blood coagulation, neurotransmission, also as an enzyme cofactor and during muscle contraction. Membrane lipids, nucleic acids, and ATP include phosphorus. Multiple cellular signalling pathways are regulated in large part by the process of protein phosphorylation. Furthermore, vitamin D is necessary for the regulation of calcium and phosphorus levels in order to maintain bone mineralization and bone remodelling. A lack of Vitamin D results in bones that are thin, fragile, or malformed. Both osteomalacia in adults and rickets in youngsters are avoided by sufficient vitamin D levels. Together with calcium, it also helps shield elderly people from osteoporosis.(11) More biological functions of vitamin D are thought to include controlling insulin synthesis and function, preserving muscle function, modifying immunological and inflammatory responses, and affecting cell proliferation and differentiation. Various tissues, including cancerous cells, possess vitamin D receptors (VDRs) and exhibit the 1α,25-hydroxyvitamin The D hydroxylase enzyme is responsible for converting 25-hydroxyvitamin D [25(OH)D] into 1,25(OH)2D, which is the active form of the vitamin D hormone. 1,25(OH)2D influences several genes that encode proteins responsible for controlling cell growth, specialisation, and programmed cell death. Hence, it is now acknowledged that vitamin D holds significant significance not just for maintaining healthy bones, but also potentially for averting prevalent cancers, autoimmune diseases, diabetes, and other ailments(11)

2-4-2: Parathyroid hormone (PTH)

Maintaining calcium balance and bone health is mostly dependent on parathyroid hormone (PTH), PTH-related peptide (PTHrP), and other hormones that control calcium levels. All land-dwelling animals depend on parathyroid hormone (PTH) to regulate blood calcium levels. PTH is produced by the parathyroid glands, ranging from amphibians to mammals. PTHrP, a molecule somewhat larger than PTH, was found more recently during the search for the component responsible for the humoral hypercalcemia of malignancy syndrome, which occurs when certain tumours release an excessive amount of PTHrP. Unlike PTH, which is secreted by specific endocrine glands, PTHrP is created as a paracrine/autocrine factor in several adult and foetal tissues. Additionally, PTHrP has multiple roles, unlike PTH.(14)

2-4-3: Calcitonin (CT)

The mammalian thyroid gland's C cells produce calcitonin (CT), whose release is controlled by the blood's calcium content.Mammals mostly produce CT at the thyroid C cell. But across various mammalian species, these cells are distributed in rather different ways inside the thyroid gland. Furthermore, there is proof indicating that CT-producing cells may also be found in other neck regions, such the thymus, in some species.[14]

2-5: Osteoporosis

Osteoporosis is a medical disorder characterised by porous bones and low bone mass, known as osteopenia, which increases the chance of developing osteoporosis. The fundamental issue lies in the fact that bone resorption, or the breakdown of bone tissue, exceeds bone deposition, or the development of new bone tissue. Primarily, This is explained by the fact that the body excretes more calcium through urine, faeces, and sweat than it absorbs from the diet. Bones becoming so fragile they could break when their mass declines, often without any external force, due to the normal physical strains of daily activities. For instance, a hip fracture might occur as a consequence of abruptly sitting down. In the US, osteoporosis causes around 1.5 million fractures every year, mostly to the hips, wrists, and vertebrae. Osteoporosis impacts every part of the skeleton. Moreover, fractures are very common, and osteoporosis causes the vertebrae to shrink in size, loss of height, curvature of the spine, and discomfort in the bones.Osteoporosis predominantly impacts individuals in the middle-aged and older demographic, with women constituting 80% of the affected population. Older women are more prone to osteoporosis compared to men due to two factors: Firstly, women generally have less dense bones than men. Secondly, During menopause, women produce far less oestrogens than older men do, whereas older men produce testosterone, the main androgen, gradually and only somewhat less.[13]

Osteoblasts are stimulated to produce bone matrix and testosterone and oestrogens both do this. Other risk factors for osteoporosis development, besides gender, include a family history of the disease, European or Asian ancestry, a thin or small body, a sedentary lifestyle, smoking, a diet low in calcium and vitamin D, drinking more than two alcoholic beverages a day, and the use of specific medications. An osteoporosis diagnosis needs a family medical history and a bone mineral density (BMD) test. Bone mineral density (BMD) examinations quantify bone density, much as x-rays do. They might be employed to confirm an osteoporosis diagnosis as well, determine how quickly bones are deteriorating, and monitor the effects of therapy. Furthermore, there is a relatively new technique called FRAX® that accurately calculates the probability of fracture by integrating risk factors beyond bone mineral density. Patients answer an internet questionnaire about risk factors including age, gender, height, weight, ethnicity, history of fractures, hip fractures in the family, usage of cortisone and other glucocorticoids, smoking, alcohol use, and rheumatoid arthritis. FRAX® utilises the data to calculate the likelihood that

an individual would experience a hip fracture or a fracture in the spine, shoulder, or forearm as a result of osteoporosis during a ten-year period.

There are diverse treatment methods available for osteoporosis. Regarding nutrition, it is crucial to have a diet that is rich in calcium in order to minimise the likelihood of experiencing fractures. The body cannot properly use calcium without vitamin D. Bone density can be maintained and even increased by regular weight training. There include walking, running, trekking, stair climbing, tennis, and dancing exercises. Weight lifting and other resistance training improve muscle volume and bone density.[13,14,8]

2-5-1: Medications used to treat osteoporosis are generally of two types:

(1) While bone-forming drugs promote the development of bone mass, antireabsorptive drugs slow down the rate of bone loss. One type of antireabsorptive medications is bisphosphonates, which work by inhibiting osteoclasts (Fosamax®, Actonel®, Boniva®, and calcitonin); (2) Selective oestrogen receptor modulators (SERMs) are chemicals that imitate oestrogen function without causing unwanted side effects.(Raloxifene®, Evista®); The third treatment option is oestrogen replacement therapy (ERT), which involves replacing the oestrogen hormones that are lost during and after menopause (Premarin®), Hormone replacement therapy (HRT) is a treatment that replenishes the levels of oestrogens and progesterone that are diminished during and after menopause (Prempro®). ERT, or oestrogen replacement therapy, aids in preserving and enhancing muscle mass during menopause. Women who undergo oestrogen replacement therapy (ERT) have a marginally higher likelihood of experiencing a stroke and developing blood clots. Hormone replacement therapy (HRT) also aids in the preservation and augmentation of bone density. Women on hormone replacement treatment are more likely to develop heart disease, breast cancer, stroke, blood clots, and dementia.Parathyroid hormone (PTH) is one of the drugs that stimulates osteoblasts and helps build new bone (Forteo®). These days, other initiatives are being created.[13]

2-6 : Chronic kidney disease (CKD)

In these case vitamin D is low and impairment calcium absorption from GIT lead to decreased bone density. Chronic kidney disease (CKD) is diagnosed when there is a consistent occurrence of increased urine albumin excretion (albuminuria), reduced estimated glomerular filtration rate (eGFR), or other signs of kidney impairment. Diabetic kidney disease (DKD), also known as CKD due to diabetes, affects around 20-40% of individuals with diabetes. Diabetic kidney disease is the primary factor contributing to the development of end-stage renal disease (ESRD). Diabetic kidney disease is typically diagnosed through clinical evaluation, which involves identifying the presence of albuminuria and/or

lowered eGFR. This diagnosis is made when there are no signs or symptoms indicating other major causes of kidney impairment.[10][12]

2-7 : Metabolic bone diseases

Conditions that arise from changes in bone remodelling or mineralization, leading to an increased likelihood of fractures and deformities. **Osteoporosis is a prevalent disorder that can be diagnosed using either of three criteria:** A low trauma fracture, a T-score of -2.5 or below on bone mineral density tests, or a FRAX risk score of more than 3% for hip fractures or more than 20% for major osteoporosis fractures—as determined by the FRAX Risk Assessment tool—are among the diagnostic criteria for osteoporosis. By accelerating bone loss and degrading bone quality, glucocorticoid drugs cause osteoporosis and increase the frequency of fractures more than bone mineral density testing can reliably predict. The next common metabolic bone disorders are rickets or acquired or congenital osteomalacia, which are treated with vitamin D and/or phosphorus replacement treatment and result from a protracted deficiency of these nutrients. Seldom occurring congenital abnormalities that can be detected by genetic testing include osteogenesis imperfecta, osteopetrosis, and hypophosphatasia. Therapeutic development is now underway for these conditions.[12]

Materials and Method

3-1 : Subjects

In the present investigation, a total of 240 serum specimens were collected from patients with diabetes mellitus (D.M.) at Alshatrah hospital and Alrifai hospital throughout the specified period (1/2/2021 to 1/7/2021).

3-2 : Materials

The following is a list of materials and laboratory equipment utilised in the present investigation:

1- plane tube

2- syringes

3- Micropipette

4- Centrifuge

5- Cotton

6- gel tubes and EDTA tube.

7- tourniquet

8- tips

9- alcohol 70%

10- spectrophotometer

11- cuvette

12- test tubes

13- incubator

14- stop watch

15- fine care for HBA1c

16- lancets

3-3 : Methods:

For all patients and control glucose concentrations measured via lab kits.

3-3-1.Random or Fasting blood sugar :

Tube	Blank	Sample	STD (standard)
Working solution	1.0 ml	1.0 ml	1.0 ml
Sample		10 ul	
STD			10 ul

Wait 5minut at 37^{o} or 10 minute at R.T. and read at 500 nm.

[glucose] = sample ABS /STD ABS X 100.

Normal value for

Fasting (70-110 mg/dl)

Random : (70-126 mg/dl)

3-3-2 : HBA1c :

Add 10ul from whole blood to buffered wait 5 min. and read the results by fine care system.

Normal value : 4-6 %

3-3-3: Ca^{++} and phosphate :

Tube	Blank	Sample	STD (standard)
Working solution	1.0 ml	1.0 ml	1.0 ml
Sample		10 ul	
STD			10 ul

Wait 5minute at 37^{o} or 10 minute at R.T. and read at 590 nm.

Results and Discussion

4-1 Results

1. Distribution of high glucose levels in patient with bone diseases according to study groups.

Low bones density in patients with diabetes as illustrated in table 1.

Table 4-1: Comparison between patients and control in patients with bone diseases and D.M. *:*

Group	No	Mean ± SE	
		Glucose (mg/dL)	Bone diseases
Patients	240	147.40 - 614.43	78 % (193 patients)
Control	240	11.78 ± 1.87	----
T-test	----	18.047 **	
P-value	----	0.0002	

2. Distribution of glucose and HbA1c in patient with bone diseases according to gender

Gender-wise, female patients with bone diseases and type 2 diabetes mellitus (D.M.) had higher glucose levels than did male patients. Children with bone disorders and type 1 D.M. also showed this tendency, With significant variations between boys and girls ($P \leq 0.10$) as table 2 illustrates.

Table 2: Effect of gender in D.M. and bone diseases of patients

Gender		Mean ± SE		
		Glucose (mg/dL)	HbA1c %	Bone diseases %
Adult	Female	147.38 ± 199.31	7.3-7.9%	22 %
	Male	202.81 ± 214.79	8.2-8.6%	28%
Children	Female	177.38 ± 289.31	8.4-9.1%	33%
	Male	313.81 ± 614.79	10-13%	17%
T-test		87.08 *		
P-value		0.1243		

3. Distribution of Glucose and HbA1c with bone diseases according to age groups

Less than 15-year-olds with type 1DM and bone disorders had higher glucose levels. The median age range of 16 to 40 years old, however, was lower than younger age groups in the cases of bone disorders and type 2 diabetes. Table 3 illustrates the little lower concentration of the older group (over 40 years old) than the younger group, with no discernible age group disparities.

Table 3: Effect of age groups in Glucose and HbA1c of Bone diseases patients

Age groups (year)	Mean ± SE		
	Glucose (mg/dL)	HbA1c %	Bone diseases %
Less than 15	506.77 ± 88.94	12.1-14.3 %	45 %

16-40	240.00 ±113.59	8.2-11.3 %	37 %
More than 40	200.88 ± 219.53	7.7-11.1 %	18%
T-test	82.77 *	73.44*	
P-value	0.142	0.112	

Conclusion and Recommendation

1. The aetiology of diabetes-related bone fragility is complex; type 1 and type 2 diabetes share some alterations, while type 2 diabetes has unique ones related to the ages at which the disease appears and the underlying processes of diabetes progression .

2. Implementing interventions targeted at mitigating overweight and obesity, as well as cardiovascular disease, is highly probable to concurrently decrease the likelihood of getting type 2 diabetes and its associated problems. The following actions are specifically pertinent to mitigating the risk of diabetes:

3. Treatment and prevention of obesity and overweight, especially in high-risk populations.

4. maintaining an ideal body mass index, or staying below the usual range. For adults, this means maintaining a mean BMI of 21–23 kg/m2 and avoiding weight gain of more than 5 kg throughout adulthood.

5. voluntary weight loss in those who are overweight or obese and have a low glucose tolerance; nevertheless, in many countries, screening for these people may not be very cost-effectiv.

6. putting in at least an hour a day, most days of the week, of high-intensity endurance exercise, including brisk walking.

7. To maintain a healthy diet, it is important to limit the consumption of saturated fat to no more than 10% of total energy. For individuals at a higher risk, the intake of fat should be even lower, not exceeding 7% of total energy.

8. To ensure sufficient intake of dietary fibre, it is recommended to regularly consume wholegrain cereals, legumes, fruits, and vegetables. It is recommended to consume at least 20 grammes every day.

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