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Study of Some Biochemical Parameters and Trace Elements in Female with Type-2 Diabetes in Maysan Province

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By

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﴿بِسْمِ اللَّهِ الْرَّحمَنِ الْرَّحَيمِ﴾

﴿ أَمْ حَسِبْتَ أَنَّ أَصْحَاب الْكَهْف وَالرَّقِيمِ كَانُوا مِنْ آيَاتِنَا عَجَبًا﴾﴿إِذْ أَوَى الْفِتْيَةُ إِلَى الْكَهْفِ فَقَالُوا رَبَّنَا آتِنَا مِنْ لَدُنْكَ رَحْمَةً وَهَيِّئْ لَنَا مِنْ أَمْرِنَا رَشَدًا﴾

صدق الله العلي العظيم

[الكهف:9,10]

Dedication

To the ray of light that illuminated my path and provided me with the reasons for success, to my support in life, my pride, and my pride..... My father, may God extend his life.

To the light of my eyes and the mirror of my soul, to the sea of tenderness and love, to giving and sacrifice... my mother, then my mother, then my mother.

To my joy and pride...my loved ones...my companions...my brothers.

To everyone who encouraged me and urged me to continue on this path despite the many obstacles I faced when preparing this research.

To everyone who taught me a letter.....appreciation and respect.....my teachers.

I dedicate my humble effort

Zainab

Acknowledgement

Praise be to God as he deserves it, and praise be to God who had mercy on us with Muhammad, his Prophet, may God's prayers and peace be upon him and his family. And after:

For those who have given me their righteousness in completing this work, there is a heavier debt than the issue of gratitude. However, gratitude is directed first to the Lord (Glory be to Him), then to those who extended a hand of guidance and assistance to me, and I especially thank my parents - may God prolong their lives.

I also extend my thanks and appreciation to my supervisor, the honorable .

Asst. Prof. Dr. Yusra Sabri

For suggesting the research project and providing moral support to me, I extend my thanks to my supervisor, the honorable.

Asst. Prof. Safaa Sabri Najim

For his efforts in this work, may God protect them and reward them on my behalf.

I also extend my thanks to **Prof Dr. Asaad Yahya** for his cooperation in conducting the statistical analysis. Ialso extend my sincere thanks to the Deanship of the College of Science and to the presidency of the Department of Chemistry and the official of the free library and my colleagues in postgraduate studies.

Zainab

Supervisor Certification

We are the supervisors of **Ms. Zainab Ali Khalaf**, certify that the thesis **(Study of Some Biochemical Parameters and Trace Elements For Women With Diabetes Mellitus on Misan Governorate)** was done and written under our supervision as a fulfillment of the requirement for the master degree of science in chemistry.

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Abstract

Diabetes mellitus is a chronic condition that affects the entire body and can cause a wide range of consequences, including as osteoporosis, cardiovascular disease, and neuropathy. Despite having fairly different underlying mechanisms, Type1Diabetes Mellitus (T1DM) and Type2 Diabetes Mellitus (T2DM) both increase the risk of fracture, which is brought on by a variety of reasons and can be partially explained by Bone mineral density (BMD) loss.

This study aims to evaluate some biochemical variables for diabetic patients (Calcitonin, Thyroid Stimulating Hormone (TSH), Estradiol (EII), Cancer Antigen 125 (CA125), Vitamin D_3, Calcium (Ca), Creatine Kinase (CK), Alkaline Phosphatase (ALP), Triglycerides (TG), High-Density Lipoprotein cholesterol (HDL), Low-Density Lipoprotein cholesterol (LDL), Glycated Hemoglobin (HbA1c) and estimate some trace elements (Fe^{+2}, Mg^{+2}, Mn^{+2}, Zn^{+2}, Cu^{+2}, K^{+1}, Na^{+1}, Li^{+1}) To achieve this goal, the study included blood samples of 120 women, after the samples were classified into two groups, (a control group) of 40 samples, and (a group of diabetic patients) of 80 samples. The results of the current study revealed the existence of significant effect (p=0.000) in Calcitonin in DM patients were detected in comparison with control group. While The results show non–significant (p=0.794) in TSH concentration in patients with DM were detected in comparison with control group.

The results showed non–significant (P= 0.245) in (E II) concentration in patients with DM, were detected in comparison with control group. As well, the results show significant effect(p=0.012) in (CA-125)

concentration in DM patients were detected in comparisons with control group. The results showed non–significant (P=0.933) in (Vitamin D) concentration in patients with DM were detected in comparison with control group. The results indicted significant (p=0.032) in Calcium concentration in DM patients, were detected in comparisons with control group. There were no statistically significant differences at the significance level ($p>0.05$) in the average concentration of (Creatine kinase, Alkaline phosphatase, High density lipoprotein, Low density lipoprotein), While there were statistically significant differences at the level ($p<0.05$) in the levels of (total cholesterol, triglycerides, Glycated hemoglobin). The results also, appeared non–significant (P=0.200) in (Iron) concentration in patients with DM, were detected in comparisons with control group, And The results showed statistical significance at the level of significance ($P < 0.05$) in the average concentration of each of (magnesium, manganese, zinc, copper, potassium, sodium). In addition to that the results showed non-significant (p=0.055) in Lithium concentration in DM patients, were detected in comparisons with control group.

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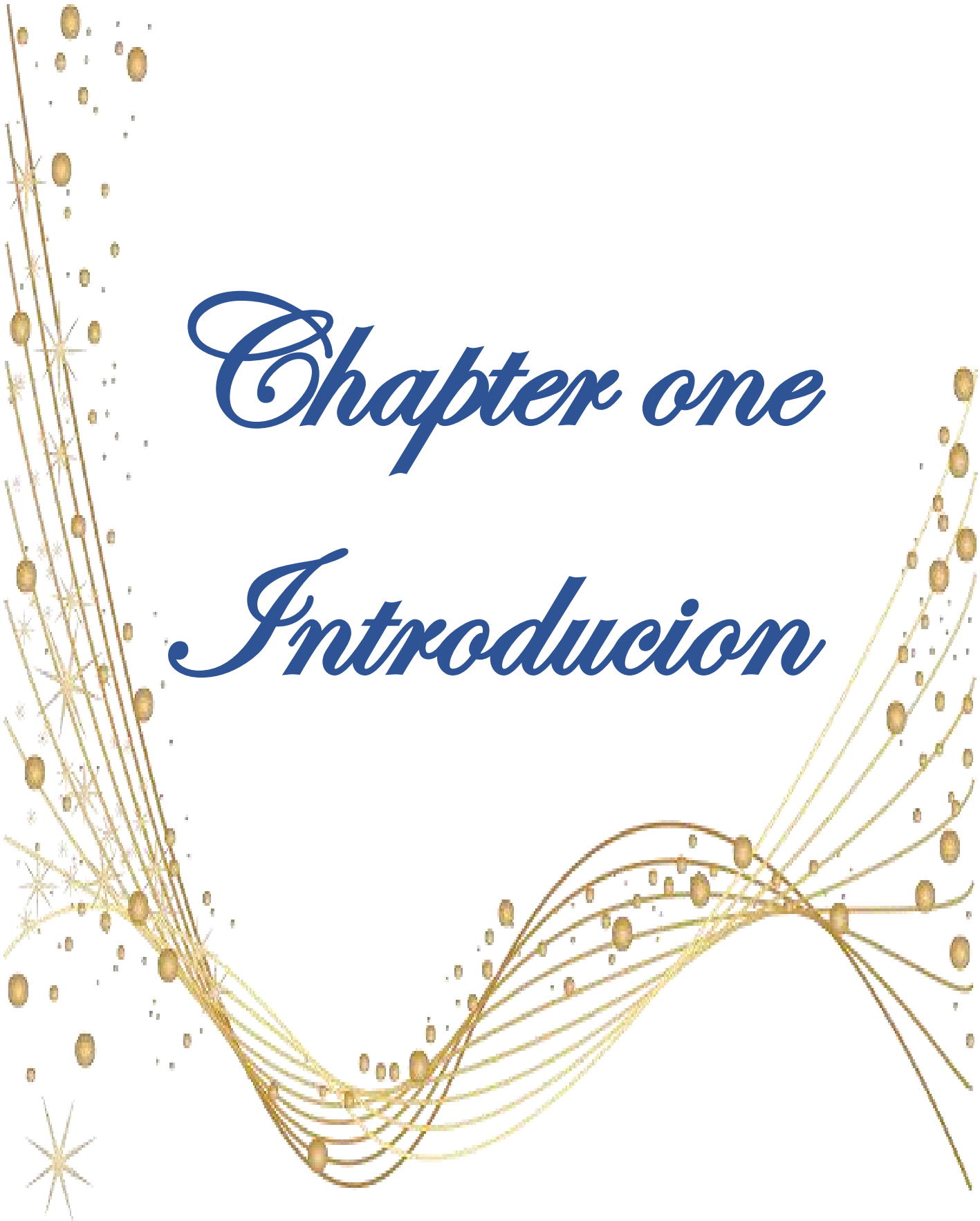
List of Abbreviations

Abbreviations	Key
A/T	Appendicular skeletal muscle mass/Trunk fat mass ratio
ACCORD	Action to Control Cardiovascular Risk in Diabetes
AGEs	Advanced Glycation End products
ALP	Alkaline phosphatase
ATP	Adenosine TriPhosphate
BAP	Bone specific alkaline phosphatase
BMD	Bone Mineral Density
BMI	Body Mass Index
BP	Blood pressure
CA125	Cancer Antigen125
CEA	Carcinoembryonic antigen
CGRP	Calcitonin Gene Related Peptide
CK	Creatine Kinase
CK1	Creatinine Kinase in the brain
CK2, CK3	Creatinine Kinase in skeletal and heart muscles
CKMB	Creatine kinase-MB isotype
CTx	C-terminal telopeptide
CVD	Cardio Vascular Disease
DKA	Diabetic Ketoacidosis
DKD	Diabetic Kidney Disease
ECM	Extra Cellular Matrix
EII	Estradiol
ELISA	Enzyme –Linked Immunosorbent Assays
EREs	Estrogen Responsive Elements
ESCs	Embryonic Stem Cells
ESR1	Estrogen Receptor 1

Abbreviations	Key
ESr1	EStrogen receptor 1
ESR2	Estrogen Receptor 2
FAAS	Flame Atomic Absorption Spectroscopy
FNBMD	Femoral neck BMD
FT4	Free thyroxine
G6P-DH	Glucose-6-phosphate dehydrogenase
GLUT4	Glucose transport Type 4
GPER1	G-protein coupled Estrogen Receptor 1
HbA1c	Glycated hemoglobin
HDL-c	High-density lipoprotein cholesterol
HE4	Human Epididymis protein 4
HF	Heart failure
HHS	Hyperglycemic hyperosmolar state
HK	Hexokinase
hMSCs	Human bone marrow-derived stromal stem cells
HOMA-IR	Homeostasis Model Assessment of Insulin Resistance
IO	Iron overload
LDL-c	Low-density lipoprotein cholesterol
M/F	Muscle/fat mass ratio
MENA	Middle East and North Africa
MI	Myocardial infarction
Mn-SOD	Manganese superoxide dismutase
MSCs	Mesenchymal stromal cells
OPG	OsteoProteGerin
OS	Oxidative stress
PTH	Para Thyroid hormone
RAGE	Receptor for AGEs
RANKL	Receptor Activator of Nuclear factor Kappab ligand
ROS	Reactive oxygen species

Abbreviations	Key
SD±	Standard Deviation
T1DM	Type1 Diabetes Mellitus
T2DM	Typ2 Diabetes Mellitus
TC	Cholesterol Total
TG	Triglycerides
THs	Thyroid Hormones
TNF	Tumor Necrosis Factor a
TSH	Thyroid Stimulating Hormone
UAE	United Arab Emirates
VCAM-1	Vascular Cell Adhesion Molecule1
VDR	Vitamin D Receptors
VIDAS	Vitek Immuno Diagnostic Assay System
WHO	World Health Organization
Wnt5	Wingless/integrated



Chapter one

Introducion

1.1 Diabetes Mellitus (DM)

Diabetes mellitus is a disorder of macromolecule metabolism marked by a reduction in the body's ability to create or react to endocrine hormones, which are necessary to keep blood sugar (glucose) levels in check. Malady is a chronic illness that arises when the body is unable to use the endocrine that the duct gland generates, or when the gland can no longer produce endocrine [1].

Due to the fact that there are 200 million diabetics worldwide, it is one of the most prevalent metabolic syndromes, which increases interest in understanding its causes and potential treatments[2].

The Diabetes mellitus is a chronic condition that affects the entire body and can cause a wide range of consequences, including as osteoporosis, cardiovascular disease, and neuropathy. Despite having fairly different underlying mechanisms, Type1Diabetes Mellitus (T1DM) and Type2 Diabetes Mellitus (T2DM) both increase the risk of fracture, which is brought on by a variety of reasons and can be partially explained by Bone mineral density (BMD) loss. The most frequent consequence is an increased risk of hip or spine fracture, which is between 2.4 and 7 times larger in T1DM and between 2-3 times greater in T2DM than in the general healthy population[3]. By understanding the factors that affect patients with DM, bone health can be improved [4].

A decrease in BMD, alterations to the microarchitecture, and an increased risk of fracture as a direct result of these changes are all signs of the dangerous health condition osteoporosis. Numerous people of various racial and gender identities are affected by osteoporosis. With age, the condition is anticipated to worsen. It is

a condition that goes unnoticed until fractures happen, at which point it can have major secondary health effects. problems, including death. Patients with T2DM have repeatedly demonstrated the link between osteoporosis and diabetes mellitus. The causes of greater bone mineral density loss include diabetes mellitus diagnosis at an earlier age, longer duration and higher insulin dosages, and extended periods of poor glycemic control[3].

1.2 Types of Diabetes Mellitus

1.2.1 Diabetes Mellitus (Type1)

Reaction diabetes and juvenile-onset or ketosis-prone polygenic illness are additional names for this form of diabetes. The person may also request treatment if they suffer from other autoimmune diseases such Graves' disease, Hashimoto's thyroiditis, and Addison's disease. The majority of people with TIDM, also known as insulin-dependent diabetes mellitus, are children and young adults. It usually starts off suddenly and can be fatal[5].

1.2.2 Diabetes Mellitus(Type2)

The hallmark of (T2DM) is a blood sugar that is consistently high or that rises after a meal that contains carbohydrates. Unless there has been beta cell loss, most people with T2DM have high insulin levels (fasting and/or post glucose consumption), in contrast to T1DM which is characterized by a lack of insulin. When there is no insulin deficit, the glucose levels continue to be raised, this is referred to as "insulin resistance" (IR). In-depth analyses of intracellular and molecular pathways have been used to try to identify the source of

IR, and the cause has been linked to fatty acid flux, but specialists have been unable to pinpoint the actual cause[6].

1.2.3. Gestational diabetes

1.2.4. Specific diabetes types with known causes

– Diseases involving a pancreatic exocrine deficiency (e.g. pancreatitis, cystic fibrosis, hemochromatosis)

– Endocrinopathies (e.g. Cushing syndrome, acro- megaly, pheochromocytoma).

– Drug or chemically induced (e.g. glucocorticoids, neuroleptics, interferon alpha, pentamidine), genetic defects of the β cell function (e.g. MODY types).

– Genetic defects of insulin action.

– Other genetic syndromes which can be associated with diabetes.

– Infections – Rare forms of autoimmune-mediated diabetes[5].

1.3 Risk factors of Diabetes Mellitus

1.3.1 Family history of diabetes

For prognosis/diagnosis purposes and public health, family history information can be a useful tool. In contrast to just genetic and environmental factors, family history of diabetes represents both environmental and genetic factors and can improve predictions of the occurrence of T2DM. A study by Tsenkova et al. (2021) found a strong correlation between a family history of diabetes and an elevated chance of developing the condition. Having a parent with diabetes is a risk factor for developing the disease, according to a second study.. a family history of diabetes in first degree relatives

(parents, children, and siblings) is a significant and independent risk factor for the prevalence of impaired fasting glucose (prediabetes) in children and adolescents, according to research by Rodrguez-Moran et al. in the absence of obesity, this is true. The findings show that when screening for diabetes in children and adolescents, it is crucial to take the parents' diabetes history into account. This is because merely screening for obesity could result in underestimate. Additionally, it was discovered that the prevalence of T2DM is significantly influenced by the family history of diabetes in at least two first-degree relatives or one first-degree relative and at least two second-degree relatives[7]. Family history is a significant risk factor for T2DM, as is widely known. Having first-degree relatives who have T2D increases your risk of getting the condition; new research has indicated that T2DM is more commonly transmitted by mothers than by fathers. The lifetime risk of having T2DMfor people with two diabetic parents is much higher (70%) than for people with one diabetic parent (40%) according to previous studies' estimates that heredity varies between 25% and 80% across different groups[8].

1.3.2 Obesity

Obesity prevalence has been rising globally, particularly in the (MENA) region, as a result of the adoption of poor eating habits and food preferences as well as the major decline in physical activity. Obesity is well-known to be a substantial risk factor for diabetes, with numerous studies demonstrating a link between body mass index (BMI) and the prevalence of diabetes. Data from the (WHO) risk surveillance program has revealed a marked increase in the prevalence of obesity worldwide. The most severely impacted nations

are the high-income Gulf nations, along with Egypt, Libya, Lebanon, and Iraq, where rates reach 30%. It's interesting to see that women were disproportionately more affected than men, with prevalence rates that are 1.5 to 2.0 times higher. Particularly, several Gulf nations (Saudi Arabia, Kuwait, Qatar, and UAE), in addition to Egypt and Jordan, had an incidence of female obesity that exceeded 40%[9].

1.4 Complications with Diabetes Mellitus

1.4.1Osteoporosis

Diabetes mellitus has been linked to osteoporosis in a number of prior studies, and it is now well known that both T1DM and T2DM are linked to an increased risk of osteoporotic fractures. Complex factors underlie diabetes mellitus's increased bone fragility. Low bone turnover and the buildup of advanced glycation end products (AGEs) can both affect bone fragility. Fig. (1- 1, anomalies in micro- and macro-architecture, and tissue material degradation. Reduced bone strength, which increases the risk of fracture and causes pain, diminished function, a lower quality of life, and debilitation, is a prevalent skeletal illness called osteoporosis [10]. According to recent research, T1DM impacts bone health and increases the risk of osteoporosis and osteoporotic fractures. Hip fracture risk is thought to be three to six times higher overall than in the general population, affects people of all sexes and ages, and is present from an early age. One of the key risk factors for fractures at the spine and hip is low BMD, and T1DM patients were shown to have lower BMD than nondiabetic people. Furthermore, research in children with T1DM

discovered that a low for age BMD may exist early on, following the diagnosis of the condition[11].

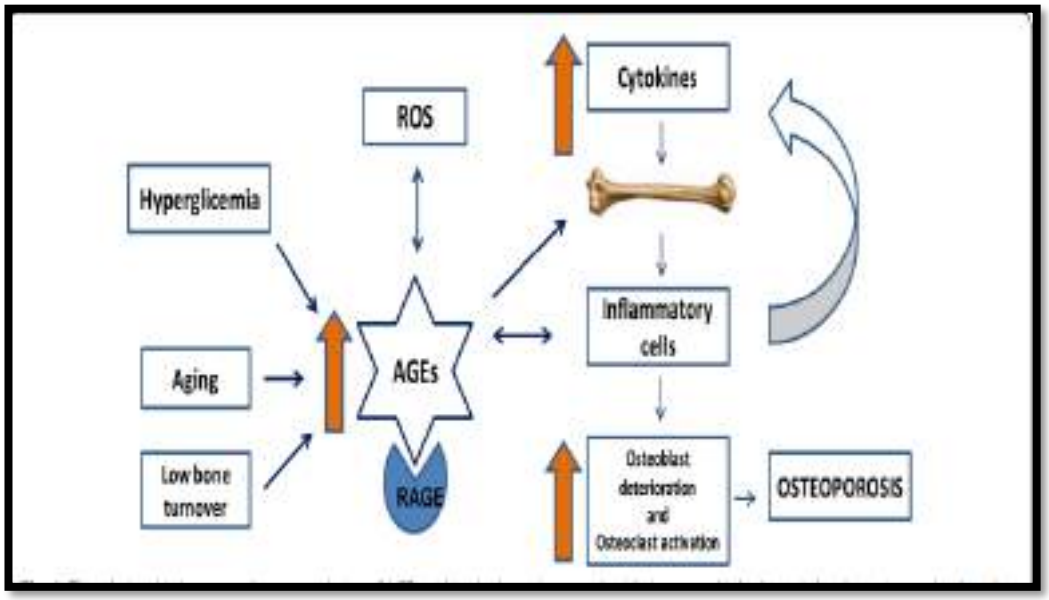


Fig. (1- 1) The relationship between the accumulation of AGEs within the bone[12]

Increased oxidative stress, high glycemic levels, ageing and reduced bone turnover are the main contributors to increased formation and accumulation of AGEs in bone. They induce an infammatory process that results in activation of osteoclastogenesis, osteoblast dysfunction and accelerated development of the osteoporosis process[12].

1.4.2 Cardiovascular disease

The most frequent cause of mortality and morbidity among diabetic people is cardio vascular disease (CVD). Nearly half of T2DM deaths are caused by cardiovascular problems, which affect more than 30% of T 2 DM patients result from CVD[13]. The term "CVD" refers to a wide range of cardiovascular system dysfunctions, such as atherosclerosis, myocardial infarction, heart failure, and

cardiomyopathy. Despite the exponential growth in studies investigating the link between diabetes and CVD, the precise pathogenic processes are still unknown. One of the most prevalent types of CVD in people with T2DM is atherosclerosis, which is the process of plaque formation inside the arteries. Atherosclerosis development is complex and involves a variety of pathogenic triggers and several varieties of cells. By encouraging endothelial cell dysfunction, a crucial stage in the formation of atherosclerotic plaques, hyperglycemia poses a significant risk factor for atherosclerosis. When blood glucose levels are high, AGEs are produced, which nonenzymatically bond to proteins or lipids and change how they function. For instance, AGE-modified proteins or lipoproteins bind to and activate the receptor for AGEs (RAGE), increasing the production of vascular cell adhesion molecule1(VCAM-1) and improving the binding of monocytes that infiltrate into the extra cellular matrix (ECM) between the endothelial cells and smooth muscle cells[14].

1.4.3 Cancer and Diabetes

The diabetes increased the chance of dying from digestive cancers, especially those of the liver, colon, and pancreas; and in women, the risk of dying from these cancers was higher. Diabetes greatly increased the probability of dying from ovarian and breast cancer. Fig. (1-2) illustrates the Pathophysiological links between obesity/insulin resistance, T2DM, inflammation and cancer. These abnormalities may play a significant part in the development of carcinogenesis. A powerful growth agent and an energy source, respectively, insulin and glycemia at supraphysiological

concentrations are present in human tissues and are necessary for the development of cancer and the neoplastic process[15].

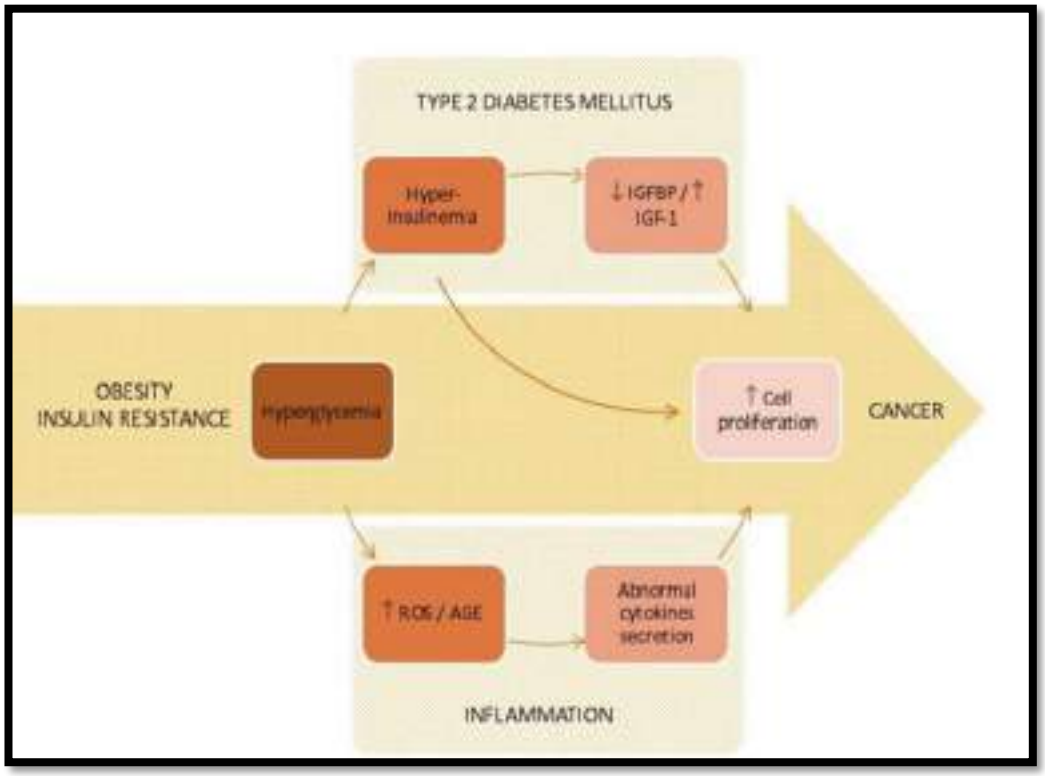


Fig. (1-2) Pathophysiological links between obesity/insulin resistance, T2DM mellitus, inflammation and cancer [16]

Oxidative stress and DNA damage are brought on byhyperglycemia, which may cause the early stages of carcinogenesis. High glucose concentrations have the ability to alter the expression of genes involved in cell adhesion, migration, and proliferation, according to in vitro research on tumor cell lines. A further effect of hyperglycemia may be the creation of AGEs, which promote the synthesis of reactive oxygen species and inflammation. Epithelial cell tumorigenesis and tumor cell tolerance to oxidative stress have both been demonstrated to be enhanced by persistent activation of the AGEs pathway[17][18].

1.5 Biochemistry Parameters

1.5.1 Calcitonin

The single-chain polypeptide hormone, calcitonin is made from thirty two amino acids , the physiological effects of calcitonin are known to be mediated by receptors, and interactions between the C-terminus and N-terminal ring appear to be important for receptor binding and signal transduction. In humans, the para-follicular or C cells of the thyroid gland release calcitonin when the amount of serum calcium rises. In the bone, where it acts primarily, calcitonin greatly lowers osteoclast activity and bone resorption, Fig (1-3) [19].

Given that calcitonin lowers blood calcium levels, it has been hypothesized that one of its physiological functions in hypercalcemia is to bring serum calcium levels back to normal When hypercalcemia was directly induced by calcium injection or infusion, the thyroid gland's existence was required to lower the levels of circulating calcium. The skeleton, the stomach, and the kidney all contribute significantly to the maintenance of calcium homeostasis. Together, these organs maintain blood calcium levels between a predetermined range of 8.5 and 10.5 mg/dL (2.12-2.62 mM). The exact control of circulating calcium levels is necessary for important physiological processes such muscle contraction, neuronal excitation, glycogen metabolism, and coagulation. Ions of calcium are necessary for key biological functions like cell adhesion and division. a hormone called parathyroid thyroid hormone (PTH), which responds to low calcium levels and works to bring them back within the normal range, is secreted by the gland, an endocrine organ. With the advent of PTH extraction techniques, the mechanism of action of PTH could be

further investigated, and it was found that the hormone takes calcium from the bone. The amount of calcium in the blood fell quickly (within 15 minutes) after high quantities of calcium were perfused into the thyroid and parathyroid glands. The only hormone known to be released from the gland is PTH, thus the researchers postulated that the high calcium concentrations in the perfused tissues reduced PTH secretion, which led to the observed decline in systemic calcium levels. The researchers tested this theory by removing the thyroid and parathyroid from the dogs, anticipating the same impact on the levels of circulating calcium in the absence of PTH. They were shocked to find that systemic calcium levels stayed high. They came to the conclusion that hypercalcemia drives the release of a hormone that decreases blood calcium levels in addition to suppressing PTH production. [20]

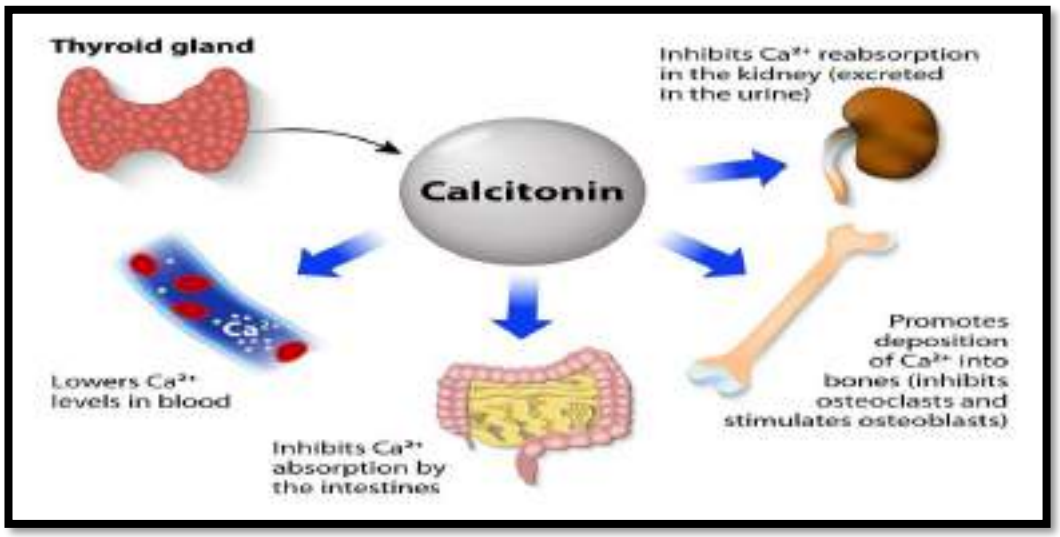


Fig (1-3) In the extracellular fluid, calcium serves as a reservoir for circulating calcium[21]

This calcium enters the extracellular fluid via the gastrointestinal tract where it is absorbed from the food a person has eaten. Calcium

also becomes available through a process called bone resorption, which is the breakdown of bone tissue by cells called osteoclasts[21].

1.5.2 Thyroid Stimulating Hormone (TSH)

Thyroid Stimulating Hormone influences bone homeostasis independently of thyroid hormones (THs) since it has receptors in osteoclasts, osteoblasts, and the thyroid. The TSH exhibits active effects on osteogenesis and inhibitory effects on bone resorption. Research showed that as the concentration of recombinant human thyroid-stimulating hormone (rhTSH) increased, the formation of osteoclasts was inhibited, and the mechanism by which TSH inhibits osteoclastogenesis was increasing the expression of osteoprotegerin (OPG) and decreasing the expression of receptor activator of nuclear factor kappab ligand (RANKL) on osteoblasts. Additionally, TSH reduced the expression of tumor necrosis factor ὰ (TNFὰ), which prevents osteoclastogenesis and reduces the number of osteoclasts. On the other hand, adding TSH to osteogenic media enhanced the amount of wingless/integrated(Wnt5) a and boosted the expression of osteogenic markers in embryonic stem cells (ESCs). Excessive THs and low TSH are characteristics of hyperthyroidism, which is in line with the finding that these individuals have lower BMD since TSH protection isn't present in their condition [22].

1.5.3 Estradiol (E2)

In addition to being involved in both male and female reproduction, the hormone estradiol (E2) also plays a part in metabolism. E2 specifically impacts the risk of the metabolic syndrome and T2DM and has an impact on the development of

adipose tissue, dyslipidemia, IR, and inflammation. Increased Glucose transporter type4**(**GLUT4**)** expression and glucose absorption in muscle and adipose tissue are regulated by E2 as part of insulin signaling, and GLUT4 is regarded as a hallmark of differentiation. Estrogen receptor 1 (ESR1, formerly ER-alpha), estrogen receptor 2 (ESR2, formerly ER-beta), and the G-protein coupled estrogen receptor 1 (GPER1) are the three receptors via which E2 exerts its effects. A complex is created when E2 binds to ESR1 and/or ESR2, recognizing estrogen responsive elements (EREs) in mitochondrial and genomic DNA and controlling the transcription of target genes involved in a variety of biological consequences, such as cell proliferation and death. The number of cells each receptor has and where they are located in various target organs determine the part, they play in controlling metabolic activity. Adipose tissues have a higher level of ESR1 expression than skeletal muscle does, and the opposite is true for ESR2. When compared to male adipose tissue, female adipose tissue has higher ESRs, which is hypothesized to be associated with greater insulin sensitivity in women. Mice lacking estrogen receptor1(Esr1)throughout their bodies and specifically in adipocytes exhibit insulin resistance, which is more evidence of Esr1's crucial role in adipose tissue and metabolic function[23].

1.5.4 Cancer Antigen125 (CA125)

Protein biomarkers linked to endometrial cancer include cancer antigen 125 (CA125) and human epididymis protein 4 (HE4). It is known that the tubal, endocervical, and endometrial epithelium express the transmembrane protein and high-molecular-weight mucin

CA125. CA125 is clinically useful as a diagnostic biomarker and for recurrence surveillance in malignancies of the ovary, pancreatic, and particularly the breast. Additionally, CA125 has shown promise as a predictive biomarker for endometrial cancer. There is mounting evidence that CA125 may be useful for the early identification of endometrial cancer when combined with HE4. The HE4, a member of the whey acidic protein family that was first discovered in the distal epididymis, is expressed by a number of tissues, including those of the female reproductive tract. Several cancers, including those of the ovary, lung, and breast, have increased HE4 gene expression. Though HE4's biological role is yet unknown, the fact that it is overexpressed in >90% of endometrial malignancies has generated interest in its potential as a diagnostic biomarker for the condition[24].

1.5.5 Vitamin D_3 (1,25- di hydroxycholecalciferol)

Clinical research data suggested that calcium and vitamin D supplements may have a positive impact on glucose metabolism [25]. Calcium is absorbed more quickly in the intestine thanks to vitamin D, which also lowers the risk of fractures while increasing bone mineral density. Additionally, vitamin D benefits both strength and muscle mass[26]. By utilizing the Vitamin D Receptors (VDR), vitamin D exerts its insulinotropic effect, increasing calcium influx through the cell membrane. By encouraging insulin production in pancreatic beta cells, vitamin D has an impact on insulin secretion[27].

1.5.6 Creatinine Kinase (CK)

An intramuscular enzyme called creatinine kinase (CK) catalyzes the conversion of creatinine to phosphocreatine from adenosine triphosphate (ATP). CK and other enzymes including lactate dehydrogenase, aldolase, myoglobin, and troponin are nonspecific but important markers of muscle integrity since they are released into the bloodstream during muscular stress and damage. High CK emia is typically explained by a myopathic mechanism. According to previous research, hyperCKemia and peripheral neuropathy may be related [28].

1.5.7 Alkaline phosphatase (ALP)

The tissue non-specific alkaline phosphatase (ALP), is a hydrolase enzyme that is widely expressed in human tissues, particularly the liver, bone, and kidney. It is regularly evaluated in clinical practice for the diagnosis and monitoring of bone and hepatobiliary illnesses. In addition, A common clinical indicator of liver or bone illness is ALP. It was demonstrated that high ALP served as a predictive marker of poor survival in diabetic individuals with acute myocardial infarction (MI), probably in conjunction with decreased renal function in male patients. Additionally, in a single case-control research, ALP in T2DMappeared to be marginally linked with men's CVD risk and stroke incidence. Only a small number of prior prospective studies have examined the link between ALP and incident diabetes, and they have produced mixed findings [29].

1.5.8 Lipid profile

Low-density lipoprotein cholesterol (LDL-c) levels that are abnormally high and low levels of high-density lipoprotein cholesterol (HDL-c) and triglycerides (TG) are known as dyslipidemia. An increased risk of diabetes is linked to any type of dyslipidemia, either separately or in combination [30].

Triglyceride-to-high-density lipoprotein cholesterol (TG/HDL-c) ratio, a marker of atherogenic dyslipidemia, has recently been linked to (IR), cardiovascular events, incident hypertension, and fatty liver[31]. The relationship between the TG/HDL-c ratio and the prevalence of diabetes has been studied in few research. Although their data point to a link between the TG/HDL-c ratio and diabetes, the impact sizes of these findings are mixed [32] .

Additionally, the general population was included in earlier studies looking into the relationship between diabetes and the TG/HDL-c ratio[30].

1.5.9 Glycated Hemoglobin (HbA1c)

According to current recommendations, glycated hemoglobin (HbA1c) levels are used to measure glycemic management since they indicate average glycemia over around three monthsHbA1c, on the other hand, does not offer a gauge for hypoglycemia and glycemic fluctuation. Variations in blood glucose levels are referred to as glycemic variability. The potential dangers of glycemic variability appear to be linked to both an increased risk of hypoglycemia and its consequences as well as the potential for vascular damage brought on by excessive glucose swings [33] [34].

Short-term glycemic fluctuation, which includes within-day and between-day glycemic variability, may eventually lead to higher HbA1c levels. The variation in HbA1c between visits is related to variations in glycemic control across longer time periods. Therefore, the most popular method for evaluating long-term glycemic fluctuation is HbA1c variability. The link between HbA1c variation and mortality as well as micro- and macrovascular issues has been demonstrated in numerous research. A new meta-analysis looked at the connection between changes in HbA1c and diabetes-related morbidity and mortality in patients with DM. [35].

1.6 Trace Elements

These metal ions play a number of biochemical roles that are crucial for the various stages of bone regeneration because they affect the balance between osteoblasts, osteoclasts, and osteocytes. Therefore, it is important to address metals and the ions that belong to them since they affect how bones repair. (Fig1-4)[36].

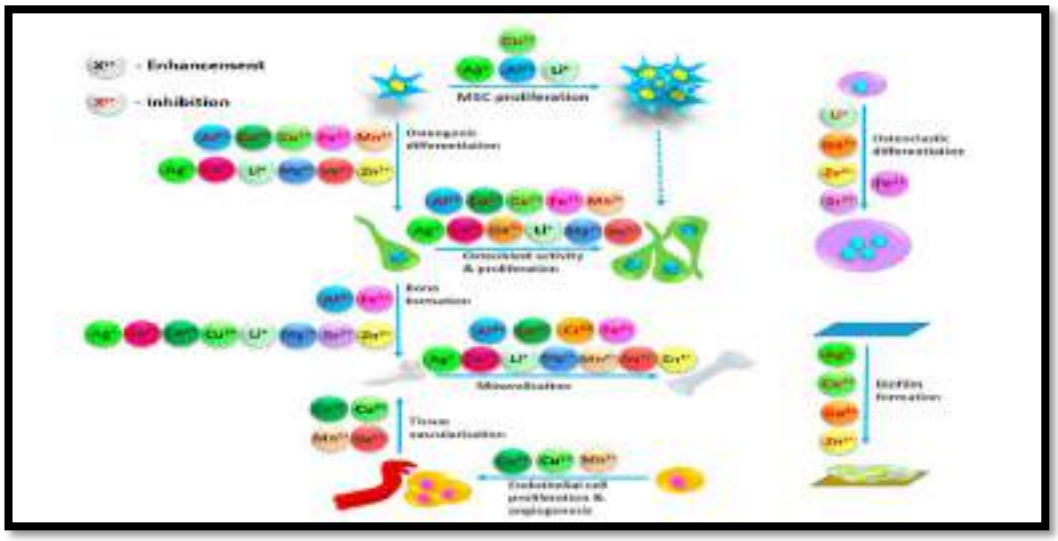


Fig. (1-4) Influence of metal ions on the variety of processes involved in bone regeneration[36]

1.6.1 Iron(Fe^{+2})

Metabolism of glucose is impacted by iron. Impairment of iron uptake may be a factor influencing glucose metabolism. Insulin sensitivity, vascular resistance, viscosity, and oxidative damage may all be impacted by the serum ferritin content in T2DM patients[37]. Numerous studies have also shown that a much milder condition of Iron overload (IO), caused by an excessive amount of dietary iron or a variety of other reasons, is also a risk factor for the development of T2DM and gestational diabetes. Possible justifications for the link between IO and diabetes development include: (too much iron can increase the production of reactive oxygen species (ROS) and cause hepatic steatosis; too much iron can result in improper glucose and lipid metabolism; and too much iron can cause beata -cell compensatory mechanisms to go awry and result in functional failure)[38].

1.6.2 Manganese (Mn^{+2})

manganese has also been linked to the regulation of blood sugar, cellular energy, immune system activity, and mechanisms for protecting against free radicals. Poor glucose metabolism may be caused by Mn^{+2} deficiency. It functions as a cofactor in several enzymes, including those responsible for mitochondrial glycoprotein synthesis. These enzymes' activity is decreased by a lack of Mn^{+2}, which changes how cartilage is produced [39].

Additionally, Mn^{+2} functions as a cofactor for the enzyme pyruvate carboxylase, which converts a variety of non-sugar molecules into glucose in a process known as gluconeogenesis.

Another study using animal models demonstrated that Ni can cause hyperglycemia via increasing hepatic glycogenolysis, increasing pancreatic glucagon release, gluconeogenesis, or decreasing peripheral glucose uptake. Numerous studies have connected circulating Ni with a higher risk of T2DM [40]. However, the redox potential of Mn^{+2} is also addressed as a potential factor in oxidative stress, which could harm beta cells. In addition, it has recently been discovered that Mn^{+2} affects the iron redox equilibrium, which in turn increases oxidative stress. Mn^{+2} has a long history of being a neurotoxic substance. Specific Mn-species affect neuronal tissue damage and other harmful consequences[41].

1.6.3 Zinc (Zn^{+2})

Zinc is a crucial trace element that plays a direct role in the production, storage, and release of insulin. It is found in secretory vesicles in the pancreatic cells, where it helps insulin crystallize. As a result, it is released into the plasma along with insulin. also is involved in more than 300 enzymatic reactions, may play a part in the pathophysiology ofT1DM. In particular, zinc is transported into cells more easily by the solute carrier family 30 member 8(SLC30A8) zinc transporter (ZnT8), which encourages the maturation and crystallization of insulin. Additionally, ZnT8 antibodies, which were very recently discovered, are found in 60 to 80 percent of T1DM patients. In fact, a zinc shortage may accompany diabetes, and zinc supplementation can prevent experimental T1DM from developing in mice. As a result, low Zn levels could affect how T1DM develops.[42] Zn deficiency disturbs the homeostasis of insulin, causing cells to secrete less insulin. Zn supplementation has been shown to lower the

likelihood of developing T2DM and improve insulin and glucose levels in diabetic patients. Zn levels in diabetics, both with and without problems, were shown to be lower than in the control group in a study by Devi et al. [43].

1.6.4 Copper ($Cu^{+2)}$

The third most common essential transition metal in humans is copper (Cu^{+2}), an essential trace metal[44], is a necessary mineral that functions as a pro-oxidant and an antioxidant as well as a catalytic cofactor of enzymes including cytochrome c oxidase and Cu/Zn superoxide dismutase[45]. Copper is one of these ions that plays a role in the pathophysiology of systemic illnesses like T1DM. By increasing sensitivity to oxidative damage, an imbalance of Cu has been linked to the etiology of DM in a prior study, and a meta-analysis found a link between serum Cu^{+2} concentrations and the risk of T2DM. In addition to being involved in several physiological pathways and biological processes, including as angiogenesis, response to hypoxia, and neuromodulation, copper also plays a significant role in the control of multiple enzymes and the creation of structural components. Additionally, slight copper deficiency may speed up the development of a number of diseases, including diabetes. To ensure cardiovascular health, Cu^{+2} is crucial. According to some studies, a lack of this ion may increase the chance of developing CVD, especially in patients with T2DM with and without Diabetic Kidney Disease (DKD). Hyperglycemia, serum heavy metal concentrations, and their binding proteins all support oxidative stress (OS) [44].

1.6.5 Lithium(Li^{+1})

Lithium was shown to have an antidiabetic action and to enhance glucose tolerance in diabetic individuals. In order to do this, short term lithium medication was linked to an insulin-like effect and lower blood sugar levels**.** T1DM sufferers must take exogenous insulin for the rest of their lives since they have an utter lack of insulin, which is uncomfortable and worsened by a variety of side effects. Lithium has been used as a successful treatment for bipolar psychiatric disorders since the late 1940s. It was unexpected to see that some manic-melancholic individuals' glucose tolerance improved while on lithium. The precise chemical mechanism underlying lithium's ability to mimic the effects of insulin is largely unknown. In contrast, stopping lithium medication in mental patients has been linked to temporary hyperglycemia. It is unclear what chemical process underlies lithium's hypoglycemic or anti-diabetic effects. Early research suggested that lithium may have a direct impact on β -cells[46].

1.7 Electrolytes

1.7.1 Potassium (K^{+1})

In fact, almost 98% of the body's potassium (K^{+1}) is found in intracellular fluid, making it one of the primary intracellular cations in human body. The K is essential for many physiological processes, particularly the neuro-endocrine system and the control of blood pressure (BP) [47]. Hypokalemia is one of the most common electrolyte abnormalities in clinical practice. It is often caused by insufficient glycemic control brought on by polydipsia and polyuria,

especially diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS), as well as polydipsia and polyuria in general. Atrial fibrillation, respiratory muscle dysfunction, an increase in the time between the beginning of the Q wave and the end of the T wave interval, torsade des pointes, ventricular fibrillation, as well as higher morbidity and mortality in diabetics with heart failure (HF) and CKD are clinical issues linked to hypokalemia[48].

1.7.2 Sodium (Na^{+1})

People with T2DM may experience osmotic diuresis as a result of the hyperglycemia brought on by the illness, which raises sodium excretion in the urine and results in hyponatremia. Sodium is an essential component for healthy physiological activities. Such hyponatremia is associated with a number of detrimental clinical symptoms and pathophysiological changes in T2DM patients. Although sodium is important for the endocrine and circulatory systems, little is known about the connection between serum sodium and new-onset diabetes, especially in hypertensive people. Sodium and glucose are the primary regulators of neurohumoral regulation and maintain a stable osmolality range[49]. In bones, where about 40% of it may be easily converted to sodium in the blood, sodium is a mineral that is abundant. As a result, in hyponatremia patients, bone-derived salt can enter the bloodstream, preserving blood pressure, blood volume, and tissue perfusion as well as perhaps inducing some bone resorption. People with fractures had considerably higher incidence of hyponatremia than people without fractures in a case-control study[50].

1.7.3 Magnesium (Mg^{+2})

Many clinical illnesses with a chronic inflammatory component have a low Mg status, which is very commonIt is important to remember that even a subclinical Mg deficit could cause the release of inflammatory cytokines and free radicals, leading to a chronic low-grade inflammatory condition. This chronic state of inflammation serves as a common substrate for many non-communicable diseases, including cardiovascular issues, metabolic syndrome, hypertension, and type 2 diabetes. Mg deficiency in T2DM and metabolic syndrome, which may take the form of a latent subclinical Mg deficiency rather than a less frequent overt hypomagnesemia, may have physiopathological and clinical significance because the Mg ion is an essential cofactor for many enzymatic reactions involved in a variety of metabolic processes. Magnesium is the fourth most prevalent mineral in the human body, after only calcium, sodium, and potassium The second-most prevalent intracellular cation after potassium is magnesium. Hundreds of biological and enzymatic processes require the cofactor magnesium, and current estimates place this number at over 600. For numerous carbohydrate-related metabolic pathways, cellular Mg+2 is an essential cofactor. Due to its vital involvement in the Mg-ATP complex, which is a crucial component for all of the glycolysis' rate-limiting enzymes, the Mg specifically regulates the activity of all enzymes involved in phosphorylation processes[51].

1.7.4 Calcium (Ca)$^{+2}$

The most recent meta-analysis showed that calcium and vitamin D_3 supplementation significantly lower fasting glucose, homeostasis model assessment of insulin resistance (HOMA-IR), and insulin levels [25]. The human body uses calcium for a variety of biological functions, including heart pumping, neurotransmission, and bone mineralization. Calcium, the most prevalent mineral in the human body, is also necessary for biologic functions like insulin release and retinal function. A higher risk of type 2 diabetes (T2D) has been linked to higher serum calcium levels in several large cohort studies[52]. Consuming calcium may help prevent obesity and overweight, which are risk factors for type 2 diabetes mellitus. A negative correlation was shown by Varenna et al. between increased dairy intake and BMI. According to their research, eating enough calcium may help prevent osteoporosis and being overweight or obese. Additionally, Patients with type 2 diabetes experience more weight reduction when they consume dairy calcium, and dairy products may aid in maintaining weight loss[53].

1.8 Research objectives

1. Taking into account these variables as an indication of osteomyelitis in diabetics.
2. follow some of the biochemical variables for diabetics Compared to healthy individuals.
3. Measuring the concentration of some trace elements in the blood sera of diabetics compared to healthy individuals.

Chapter Two

Materials and Methods

2.1 Subject

The current study was conducted in the Endocrinology and Diabetes Center and some private laboratories in Maysan Governorate during (January 2023- April 2023). The whole blood sample included 120 women aged 20- 65years, divided into two groups:

- Control group 40 (healthy females).
- Diabetic group (T2DM) 80 females.

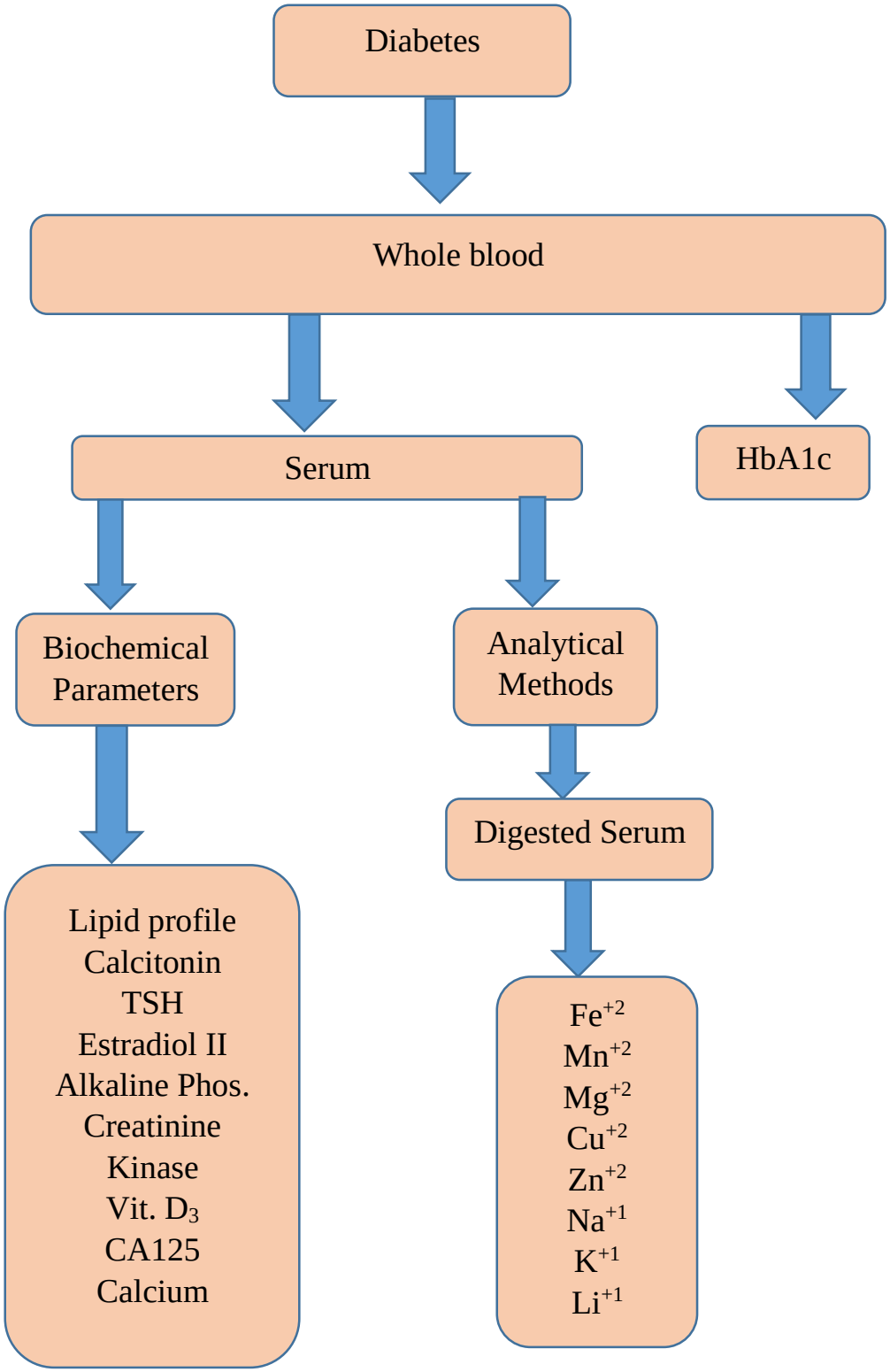
The women samples have been checked medically by Diabetes specialist and has been diagnosed with diabetic and some of them are obesity according to (BMI and HbA1c) levels. Pregnant women and smokers have been excluded. A questionnaire has been designed to obtain the actual information about the sample individuals in Maysan Governorate.

2.2 Sample's Collection

Blood samples of healthy individual were collected, forty female samples from different age groups (20-65) years, and eighty blood samples form diabetic patients (20-65) years. The veins' blood was drawn in a volume of 8 mL at (8-11) am to obtain the sample., using the disposable plastic syringe for each female (without tourniquet).

Transferring 5mL of blood in to a gel tube, left for proximately twenty minutes until the blood coagulation, centrifuged at 4000 revolutions/minute for 5 minutes to obtain blood serum and transfer the serum into a plane tube and abandaruff tube, stored at a temperature of -4 °C before laboratory testing is done and 2mL of whole blood was transferred to an EDTA tube (containing Anticoagulant) for HbA1c test.

2.3 Experimental Design



2.4 Instruments and Equipment

The tools and equipment that used in this study together with their countries of the origin were shown in Table (2-1).

Table (2-1): The instruments and equipment used in the study.

No.	Instrument	Origin
1	A 15 Bio system	Spain
2	Centrifuge	Japan
3	Cold box	China
4	EDTA tubes	China
5	Electronic balance	China
6	Enzyme –Linked Immunosorbent Assays (ELISA)	China
7	Eppendorf tubes (1.5ml)	UK
8	Flame atomic absorption spectroscopy, Aurora, AI-1200	Canada
9	Flame photometer- PFP7	Ireland
10	Frozen deep freeze	Germany
11	Gel tubes	China
12	Hot plat	Korea
13	Micro pipet (0.5ml)	Germany
14	Nomination paper	Germany
15	Plain tubes	China
16	Stature meter	China
17	Syringe	China
18	Tips(0.5ml)	China
19	VIDAS	France

2.5 Laboratory Kits

The laboratory kits, used in this study are shown in Table (2-2)

Table (2-2): The laboratory kits used in the study.

No.	Material (kits)	Origin
1	ALP	Spain
2	Ca	Spain
3	Ca125	Italy
4	Calcitonin	China
5	CK	Spain
6	E II	France
7	HbA1c	Bio Lab / France
8	HDL	Spain
9	LDL	Spain
10	TC	Spain
11	TG	Spain
12	TSH	France
13	Vitamin D_3	France

2.5.1 ELASA Kit

The contents of ELASA kits are shown in the following

Table (2-3): (Human calcitonin ELASA kit Components

No.	Materials provided with the kit	Determinations
1	User manual	1
2	Closure plate membrane	2
3	Sealed bags	1
4	Micro Elisa strip plate	1
5	Standard:270 pg /mL	0.5 mL× 1bottle
6	Standard diluent	1.5mL×1bottle
7	HRP-Conjugate reagent	6mL×1bottle
8	Sample diluent	6mL×1bottle
9	Chromogen solution A	6mL×1bottle
10	Chromogen solution B	6mL×1bottle
11	Stop solution	6mL×1bottle
12	Wash solution	20 mL (30X) ×1bottle

2.5.2 VIDAS Automated Kit

The contents of VIDAS kit for TSH, EII, CA 125 II and Vitamin D are listed as the following: Materials required but, not provided:

- Pipette with disposable tip to dispense 2ml, 3ml and 200µL.
- Powderless, disposable gloves.
- Instrument of the VIDAS family.

2.5.3 A 15 Bio system

The contents of Bio system kit for Ca, CK, ALP, Lipid Profile.

2.5.3.1 S. Calcium kit

A. Reagent. 10×50 mL, Arsenazo III 0.2 m mol /L, imidazole 75 m mol / L.

2.5.3.2 S. Creatine Kinase (CK)

A. Reagent: 3 x 12 mL. Imidazol 125 mmol/L, EDTA 2 mmol/L, magnesium acetate 12.5 mmol/L, D-glucose 25 mmol/L, N-acetyl cysteine 25 mmol/L, hexokinase 6000 U/L, NADP 2.4 mmol/L, pH 6.7.

B. Reagent: 1 x 10 mL. Creatine phosphate 250 mmol/L, ADP 15 mmol/L, AMP 25 mmol/L, P1,P5-di(adenosine-5'-)pentaphosphate, 102 μmol/L, glucose-6-phosphate dehydrogenase 8000 U/L.

2.5.3.3 S. Alkaline Phosphatase (ALP)

A. Reagent: 5 x 16 mL. 2-Amino-2-methyl-1-propanol 0.4 mol/L, zinc sulfate 1.2 mmol/L, N-hydroxy ethyl ethylene diamine tri acetic acid 2.5 mmol/L, magnesium acetate 2.5 mmol/L, pH 10.4.

B. Reagent: For 2 x 10 mL. 4-Nitrophenylphosphate 60 mmol/L.

2.5.3.4 S. Cholesterol (TC)

A. Reagent. 10 x 50 mL, Pipes 35 mmol/L, sodium cholate 0.5 mmol/L, phenol 28 mmol/L, cholesterol esterase > 0.2 U/mL, cholesterol oxidase > 0.1 U/mL, peroxidase > 0.8 U/mL, 4-aminoantipyrine 0.5 mmol/L, pH 7.0.

2.5.3.5 S. Tri Glycerides (TG)

A. Reagent: 10×50 mL, Pipes 45 m mol / L, magnesium acetate 5m mol /L, 4-chlorophenol 6 m mol /L, lipase >100 U/mL, glycerol kinase >1.5 U/mL, glycerol-3-phosphate oxidase > 4 U/mL, peroxidase > 0.8 U/mL, 4-aminoantipyrine 0.75 m mol/L, ATP 0.9 m mol/L, PH 7.0.

2.5.3.6 S. Cholesterol HDL

A. Reagent. 3 x 20 mL, Good´s buffer, cholesterol oxidase < 1 U/mL, peroxidase < 1 U/mL, N, N-bis(4-sulfobutyl)-m-toluidine (DSBmT) 1 mmol/L, accelerator 1 mmol/L.

B. Reagent. 1 x 20 mL, Good´s buffer, cholesterol esterase < 1.5 U/mL, 4-aminoantipyrine 1 mmol/L, ascorbate oxidase < 3.0 KU/L, detergent.

2.5.3.7 S. Cholesterol LDL

A. Reagent. 3 x 20 mL, MES buffer > 30 mmol/L, cholesterol esterase < 1.5 U/mL, cholesterol oxidase < 1.5 U/mL, 4-aminoantipyrine 0.5 mmol/L, ascorbate oxidase < 3.0 U/L, peroxidase > 1 U/mL, detergent, pH 6.3.

B. Reagent. 1 x 20 mL, MES buffer > 30 mmol/L, N, N-bis(4-sulfobutyl)-m-toluidine (DSBmT) 1 mmol/L, detergent, pH 6.3.

2.6 Mindray Automated Kit

2.6.1 HbA1c

Table (2.4): Mindray kit Components

No.	Item	Specifications
1	Reagent	2 vials
2	Disposable stirrers	2 × 50
3	Negative control.	1 × 1 mL
4	Positive control.	1 × 1 mL
5	Test cads	3

2.7 Analytical Chemical

The chemicals used in this study were all analytical reagent grad,

Table (2-5) shows chemicals, purities, companies and origin

Table (2-5) Chemicals used and their chemicals formula, purities, companies and origin.

No.	Chemicals	Chemical Formula	Purity	Company	Origin
1	Copper sulphate heptahydrate	$CuSO_4.5H_2O$	99.99%	Pubchem	China
2	Ferrous sulphate	$FeSO_4$	99%	Thomas beaker	India
3	Hydrochloric acid	HCl	37%	Applichem	USA
4	Lithium Stock solution (1000 ppm)	Li	99.99%	Jenway	Ireland
5	Magnesium sulphate heptahydrate	$MgSO_4.7H_2O$	99%	Thomas beaker	India
6	Manganese dioxide	MnO_2	85%	BDH	South Korea
7	Nitric acid	HNO_3	69%	Applichem	USA
8	Per chloric acid	$HClO_4$	70%	GCC	UK
9	Potassium chloride	KCl	99%	Thomas beaker	India
10	Sodium chloride	NaCl	98%	Thomas beaker	India
11	Zinc acetate	$(CH_3COO)_2$ $Zn.5H_2O$	99.5%	ANALAR	China

2.8 Methods

2.8.1 Body Mass Index (BMI)

Calculated by dividing weight in kilogram by the square of height (m^2) according to (WHO 2020), obese individual has BMI over 30 kg/ m^2.

BMI to document weight status (overweight: BMI 25–29.9 kg/m2 ; obesity class I: BMI 30–34.9 kg/m2 ; obesity class II: BMI 35–39.9 kg/m2 ; obesity class III: BMI 40 kg/m2[54].

2.8.2 Determination of Hormones Assay

2.8.2.1 Determination of Calcitonin Hormones[55]

Calcitonin is evaluated by using enzyme –linked-immunosorbent-assay (ELISA) system, with human kit.

Principle of Assay

1- Dilution of Standards: First dilute the standard in tiny tubes, then pipette 50 uL from each tube to a microplate well, using two wells per tube for a total of ten wells.

2. In the Micro Elisa strip plate, Empty a well to serve as a blank control. With a dilution factor of 5, 40 l of sample dilution buffer and 10 l of sample are added to sample wells. Samples should be put onto the bottom of the wells without touching the wall. Shake gently to thoroughly combine.

3. Incubation: After the Closure plate membrane has been sealed, incubate for 30 minutes at 37°C.

4. Dilution: Distilled water should be used to dilute the concentrated washing buffer (30 times for 96 T and 20 times for 48 T).

5. Washing: Gently remove the membrane from the closure plate, aspirate, and refill with the wash solution. After the wash solution has rested for 30 seconds, discard it. Five times during the washing process.

6. Addition:50µL HRT-Conjugate reagent to each well except the blank control well.

7. Incubation as described in Step (3).

8. Washing as described in Step (5).

9. Coloring: Added 50µL Chromogen Solution A and 50µL Chromogen Solution B to each well, mix with gently shaking and incubate at 37°C for 15 minutes.(They had been stayed away from the light, while coloring).

10. Termination: Added 50µl stop solution to each well to terminate the reaction. The color in the well should change from blue to yellow.

11. Using: Microtiter plate reader, read absorbance O.D. at (450 nm). The OD value of the blank control well is set as zero. Assay should be carried out within 15 minutes after adding stop solution.

2.8.2.2 Determination of TSH Hormone[56][57]

The TSH hormone is determinate by using VIDAS system, with human TSH kit.

Principle of Assay

1- Only taken the necessary reagents out of the fridge, and give them at least 30 minutes to come to room temperature.

2- For each sample, control, or calibrator that needs to be tested, use one "TSH" strip and one "TSH" SPR. Once the necessary STRs have been taken out, make sure the storage pouch has been properly resealed.

3-The "TSH" code on the instrument designates the test. The calibrator needs to be designated as "S1" and tested twice. The control should be designated as "C1" if it will be tested.

4- Used to a vortex-style mixer to combine the calibrator, control, and sample (for serum that has been separated from the pellet).

5- The 200 l section of the exam includes the calibrator, the control, and the sample test.

6- The "TSH" SPRs and "TSH" strips should be inserted into the instrument. Make sure the SPRs' and the Reagent Strips' color labels bearing the assay code are same.

7- Start the assay according to the User's Manual's instructions. The instrument executes each assay step automatically.

8- After pipetting, seal the vials once more and bring them back to the appropriate temperature.

9- The assay will be completed within approximately 40 minutes. After the assay is completed, remove the SPRs and strips from the instrument.

10- Dispose of the used SPRs and strips into an appropriate recipient.

2.8.2.3 Determination of E II [58][59][60][61][62]

Determination by using VIDAS system, with human kits.

1. Only take the necessary reagents out of the fridge, and let them sit at room temperature for 30 minutes prior to use.
2. For each sample, control, or calibrator that needs to be examined, use one "E2I" strip and one "E2" SPR. Once the necessary SPRs have been taken out, make sure the storage pouch has been meticulously resealed.

3. The "E2" code on the instrument serves as the test's unique identifier. The calibrator must be marked with "S1" and tested three times. C1 should be used to indicate the control if it needs to be tested.
4. To increase the reproducibility of the results, combine the calibrator, control, and sample in a vortex-style mixer (for serum that has been separated from the pellet).
5. The total volume of the test's calibrator, control, and sample test is 200 l.
6. Attach the E2I SPRs and E2 Reagent strips to the device. Make that the SPRs and the Reagent strips have the same color labels with the assay code.
7. Start the assay as instructed in the user's guide. The instrument executes each assay step automatically.
8. After pipetting, seal the vials once more and store them at 2-8°C..
9. The test should be finished in about 60 minutes. Remove the SPRs and the strips from the instrument after the assay is finished.
10. Place the used SPRs and strips in the proper recipient for disposal..

2.8.2.4 Determination of CA 125 II™ (125)[63][64][65][66][67][68][69]

Determination by using VIDAS system, with human kits.

Principle of Assay

1. Only take the necessary reagents out of the fridge, and give them at least 30 minutes to come to room temperature.
2. For each sample, control, or calibrator that needs to be examined, use one "125" strip and one "125" SPR. Once the necessary SPRs

have been taken out, make sure the storage pouch has been meticulously resealed.

3. The "125" code on the instrument serves as the test's unique identifier. The calibrator needs to be designated as "S1" and tested twice. The control should be designated as "C1" if it will be tested.
4. Use a vortex-style mixer to combine the calibrator and/or the control and samples (for serum that has been separated from the pellet).
5. The 200-L calibration, control, and sample test portions are used in this test.
6. Activate the instrument with the "125" SPRs and "125" strips. Make sure the SPRs' and the Reagent Strips' color labels bearing the assay code are same.
7. Start the assay as per the User's Manual's instructions. The equipment automatically completes each assay step.
8. After pipetting, seal the vials once more and bring them back to the appropriate temperature.
9. The test should be finished in about 60 minutes. Remove the SPRs and strips from the instrument after the assay is finished.
10. Place the used SPRs and strips in the proper recipient for disposal.

2.8.2.5 Determination of Vitamin D_3[70][71][72][73][74][75][76][77][78]

Determination by using VIDAS system, with human kits.

Principle of Assay

1.Take only the necessary reagents out of the fridge. They are immediately usable.

2. For each sample, control, or calibrator that needs to be evaluated, use one "VITD" strip and one "VITD" SPR® from the kit. Once the

necessary SPRs have been taken out, make sure the storage pouch has been meticulously resealed.

3. The "VITD" code on the instrument identifies the test. It is necessary to test the calibrator twice and identify it with "S1. The control should be designated as "C1" if it will be tested.

4. If necessary, centrifugate the samples to remove any debris.

5. Use a vortex-style mixer to combine the calibrator, control, and samples (for serum or plasma that has been separated from the pellet).

6. Check for bubbles in the samples, calibrators, controls, and diluent before pipetting.

7. The total volume of the test's calibrator, control, and sample test is 100 L.

8. Place the instrument's "VITD" SPRs and "VITD" strips inside. Make sure the SPRs' and the Reagent Strips' color labels bearing the assay code are same.

9. Start the assay as per the User's Manual's instructions. The instrument executes each assay step automatically.

10. After pipetting, seal the vials once more and store them at 2-8°C.

11. It will take about 40 minutes to complete the assay. Remove the SPRs and strips from the instrument after the assay is finished.

12. Place the used SPRs and strips in the proper recipient for disposal.

2.8.3 Calcium[79]

The method's guiding principle

When arsenazo III and alcium in the sample combine, a colored complex is created that can be detected using spectrophotometry.

2.8.4 Enzymes

2.8.4.1 Determination Creatine Kinase (CK)[80]

Principle of the method

Creatine kinase (CK) catalyzes the phosphorylation of ADP, in the presence of creatine phosphate, to form ATP and creatine. The catalytic concentration is determined from the rate of NADPH formation, measured at 340nm, by means of the hexokinase (HK) and glucose-6-phosphate dehydrogenase (G6P-DH) coupled reaction.

Creatine phosphate + ADP $\xrightarrow{CK}$ creatine + ATP

ATP + Glucose $\xrightarrow{HK}$ ADP + Glucose-6-phosphate

Glucose-6-phosphate + $NADP^+$ $\xrightarrow{G6P\text{-}DH}$ 6-phosphogluconate + NADPH + H^+

2.8.4.2 Determination Alkaline Phosphatase (ALP) AMP [81]

Principle of the method

Alkaline Phosphatase (ALP) catalyzes in alkaline medium the transfer of the phosphate group form 4-nitrophenylphosphate to (2-amino-2-methyl-1-propanol) (AMP), liberating 4-nitrophenol. The catalytic concentration is determined from the rate of 4-nitrophenol formation, measured at 405 nm.

4-Nitrophenylphosphate + AMP $\xrightarrow{ALP}$ AMP-phosphate + 4-Nitrophenol

2.8.5 Lipid Profile Assay

2.8.5.1 Total Cholesterol[82][83][84]

Principle of method

Free and esterified cholesterol in the sample originates, by means of the coupled reactions described below, a coloured complex that can be measured by spectrophotometry.

$$\text{Cholesterol} + H_2O \xrightarrow{\text{Cho. Esterase}} \text{Cholesterol} + \text{Fatty acid}$$

$$\text{Cholesterol} + \tfrac{1}{2}O_2 + H_2O \xrightarrow{\text{Chol. Oxidase}} \text{Cholestenone} + H_2O$$

$$2H_2O + \text{4- Amino antipyrine} \xrightarrow{\text{Peroxidase}} \text{Quinonimine} + 4H_2O$$

Reagent preparation

Reagents were ready to use.

2.8.5.2 Determination of Tri Glycerides[85][86]

Principle of the method

Tri glycerides in the sample originates, by means of the coupled reactions described below, a coloured complex that can be measured by spectrophotometry.

$$\text{Tri glycerides} + H_2O \xrightarrow{\text{lipase}} \text{Glycerol} + \text{Fatty acids}$$

$$\text{Glycerol} + ATP \xrightarrow{\text{glycerol kinase}} \text{Glycerol-3-P} + ADP$$

Glycerol-3-P + O_2 $\xrightarrow{\text{G-3-P-oxidase}}$ Dihydroxyacetone-P +4H_2O

2H2O2 + 4- Amino antipyrine + 4-Chlorophenol $\xrightarrow{\text{peroxidase}}$ Quinonimine + 4H_2O

2.8.5.3 Determination Cholesterol HDL Direct[87]

Principle of the method

The cholesterol from low density lipoproteins (LDL), very low density lipoproteins (VLDL) and chylomicrons, is broken down by the cholesterol oxidase an enzymatic accelerated non-color forming reaction. The detergent present in the reagent B, solubilizes cholesterol from high density lipoproteins (HDL)in the sample. The HDL cholesterol is then spectrophotometrically measured by means of the coupled reactions described below.

Cholesterol esters + H_2O $\xrightarrow{\text{Cho. esterase}}$ Cholesterol + Fatty acid

Cholesterol + 1/2 O_2 +H_2O $\xrightarrow{\text{Cho. oxidase}}$ cholestenone + H_2O

$2H_2O_2$ + 4-Aminoantipyrine + DSB m T $\xrightarrow{\text{Peroxidase}}$ Quinonimine + $4H_2O_2$

2.8.5.4 Determination Cholesterol LDL Direct [88]

Principle of the method

Cholesterol from chylomicrons, very low density lipoproteins (VLDL), and high density lipoproteins (HDL) is solubilized by a particular detergent. Cholesterol esterase and cholesterol oxidase break down the cholesterol esters in a non-color-forming process.

Low density lipoproteins (LDL) in the sample are solubilized by the second detergent, which is a component of reagent B. Following that, the coupled reactions listed below are used to perform a Spectrophotometric measurement of the LDL cholesterol.

Cholesterol esters + H_2O $\xrightarrow{\text{Chol. esterase}}$ Cholesterol + Fatty acid

Cholesterol + 1/2 O_2 + H_2O $\xrightarrow{\text{Chol. oxidase}}$ Cholestenone + H_2O_2

2 H_2O_2 + 4-Aminoantipyrine + DSB m T $\xrightarrow{\text{Peroxidase}}$

Quinoneimine + 4H_2O

2.8.6 HbA1c[89]

HbA1c was evaluated by using Mindray system, with human HbA1c kit.

Principle of Assay

1. The HbA1C kit put out of refrigerator for 10 min.
2. The reagents are placed in their place on the side of the external device.
3. The two milliliters (2ml) of blood were taken by medical syringe and place it in EDTA tube and then, the sample mixed gently by inverting the tube.
4. The sample tubes allowed to reach the room temperature (25 c) before performing assy.
5. The sample tube is loaded into the D-10sample rack and put it in the place known inside the device D-10 .
6. Patient QC ID was appearing on the screen after they have been acanned by the barcode reader.
7. The DONE button was press after you have entered each patient ID.
8. The START button was press to begin the analysis.
9. The steps for the device followed to start the calibration process automatically.

Assay range: 4.2 – 6.4.

2.9 Determination of the Elements

2.9.1 Digestion Procedure of samples

The samples were digestion by adding (10mL) of mixture containing (HNO_3:$HClO_4$) mixed at 4:2 ratio to (0.5mL) serum in beaker 10 mL, heated for (1 hr.) at (120 ℃) by a hot plate, until the volume became (1mL) and clear (if it is not, it must be filtering), cooling to room temperature, transferred quantitatively to volumetric flask 25 mL, diluted with deionized water up to the mark[90].Fig (2-1).

Fig. (2-1) Digestion of samples

2.9.2 Preparation of Standard Solutions[91]

2.9.2.1 Stock solution of Iron(1000µg/mL)

Stock solution of Iron was prepared by dissolving (0.027g) of $FeSO_4$ in small volume of 5% HCl, transferred quantitively to volumetric flask (100 mL) filled to the mark with deionized water. The working standard solutions (0.5-2 µg/ml) were prepared by serial dilution of the stock solution, as shown in Fig (2-2).

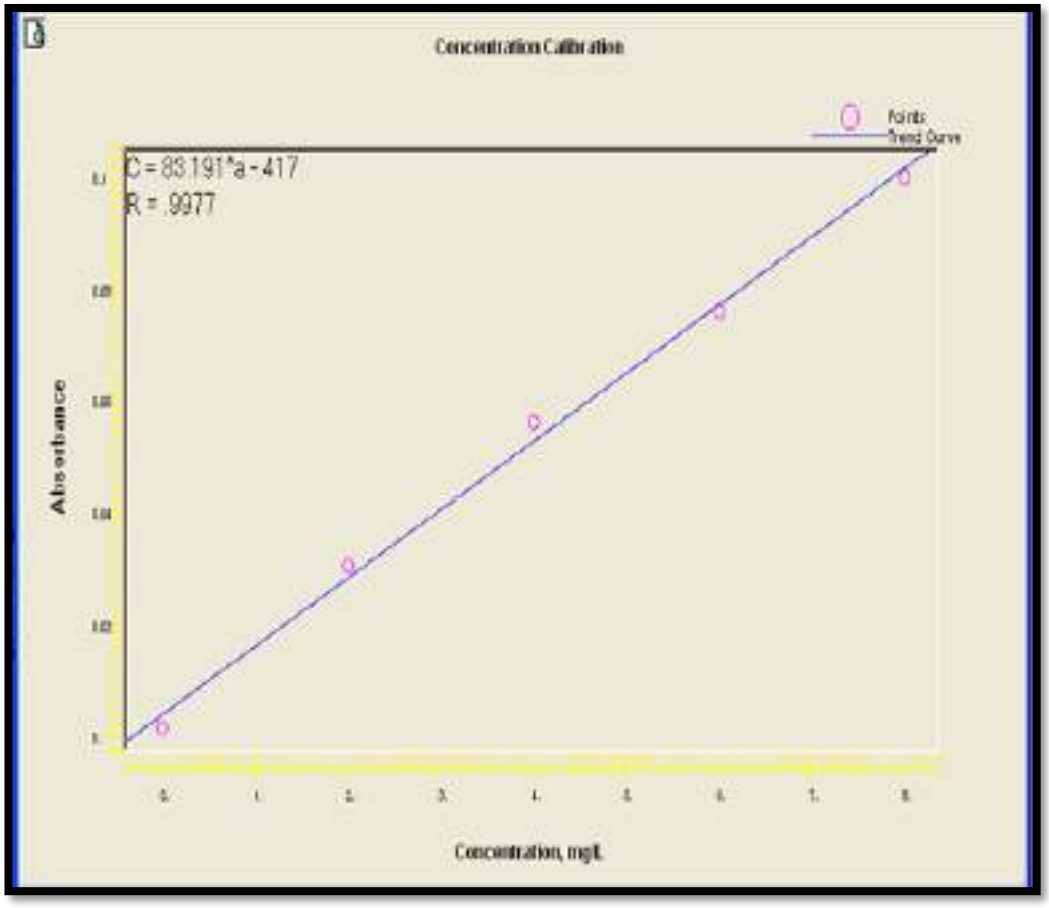


Fig. (2-2) Standard calibration curve of Fe^{+2} by Flame atomic absorption spectroscopy

2.9.2.2 Stock solutions of Magnesium(1000µg/mL)

Stock solution of Magnesium was prepared by dissolving (1.0143g) of $MgSO_4.7H_20$ in small volume of 5% HCl, transferred quantitively to volumetric flask (100 mL) filled to the mark with deionized water. The working standard solutions (0.5-2 µg/mL) were prepared by serial dilution of the stock solution, as shown in Fig.(2.3).

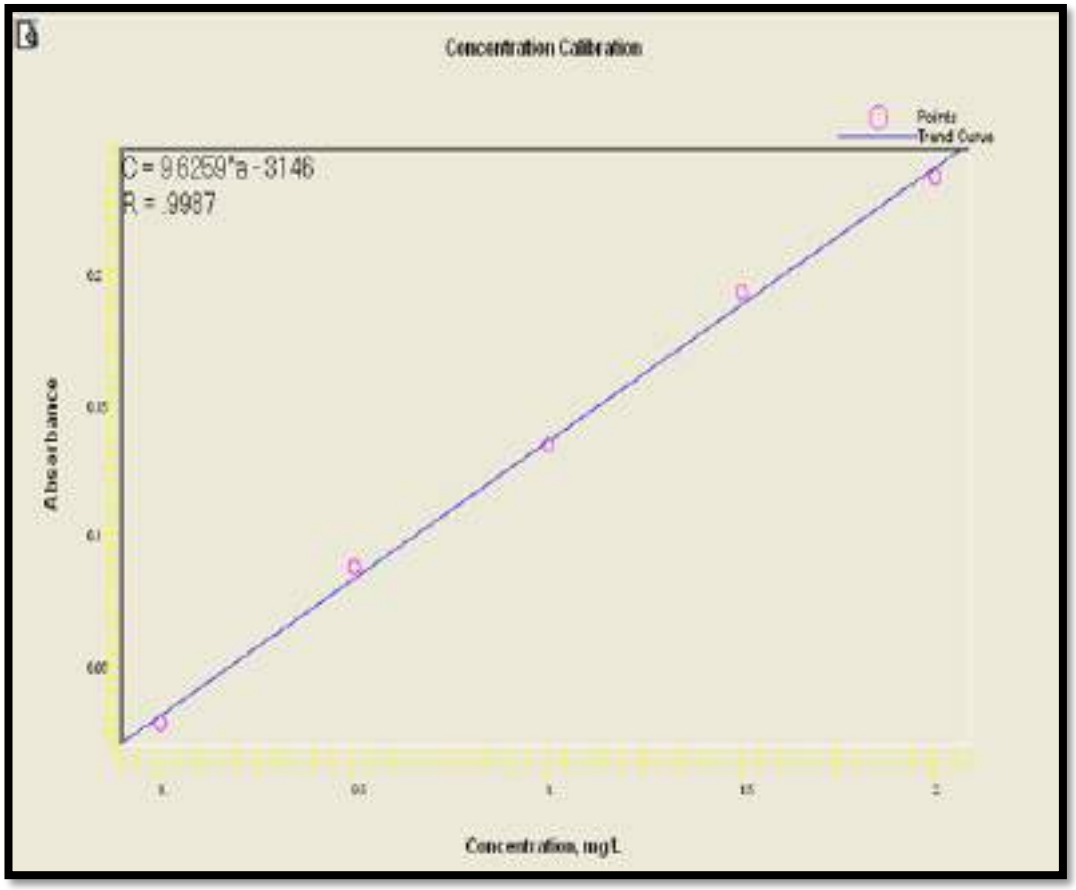


Figure (2-3) Standard calibration curve of Mg^{+2} by Flame atomic absorption spectroscopy

2.9.2.3 Stock Solutions of Manganese (1000µg/mL)

Stock solution of manganese was prepared by dissolving (0.1582 g) of MnO_2) in a small amount of 5% HCl, transferred quantitively to volumetric flask (100 mL) filled to the mark with deionized water. The working standard solutions (0.5-2 µg/ml) were prepared by serial dilution of the stock solution, as shown in Fig. (2-4).

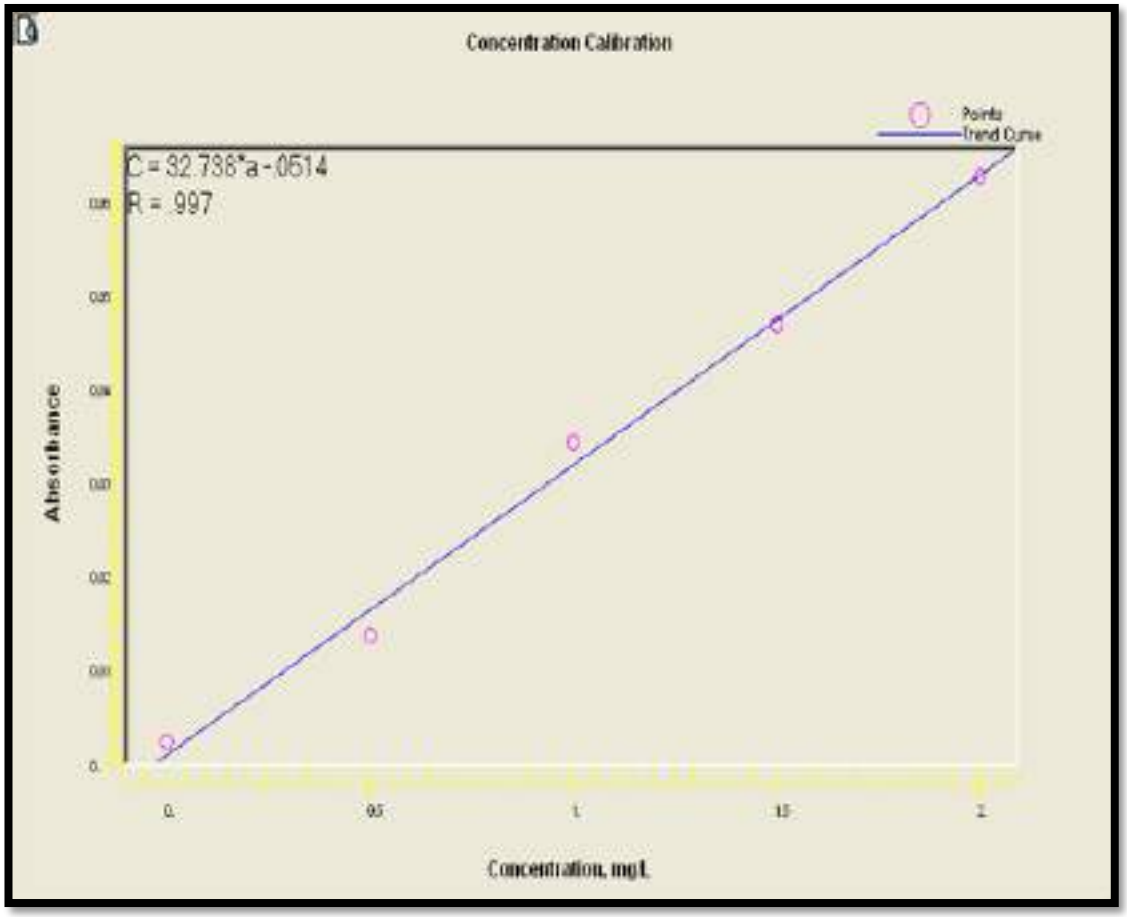


Fig. (2-4) Standard calibration curve of Mn^{+2} by Flame atomic absorption spectroscopy

2.9.2.4 Stock Solutions of Zinc (1000µg/mL)

Stock solution of zinc was prepared by dissolving (0.2469 g) of $ZnSO_4$ in small amount of 5% HCl, transferred quantitively to volumetric flask (100 mL) filled to the mark with deionized water. The working standard solutions (0.5-2 µg/mL) were prepared by serial dilution of the stock solution, as shown in Fig (2-5).

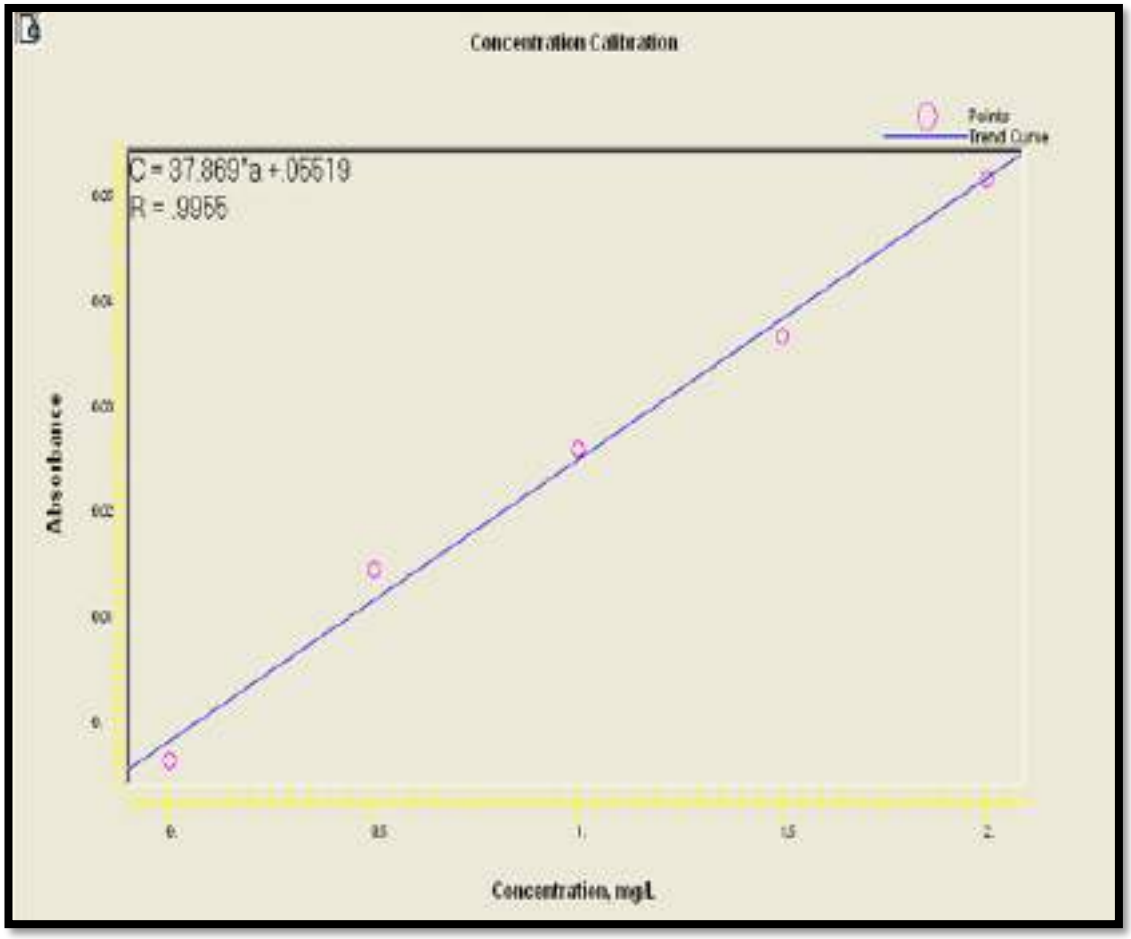


Fig. (2-5) Standard calibration curve of Zn^{+2} by Flame atomic absorption spectroscopy

2.9.2.5 Stock Solutions of Copper (1000µg/mL)

Stock solution of Cupper was prepared by dissolving (0.3927 g) of $CuSO_4.5H_20$ in small volume of 5% HCl, transferred quantitively to volumetric flask (100 mL) filled to the mark with deionized water. The working standard solutions (0.5-2 µg/ml) were prepared by serial dilution of the stock solution, as shown in Fig. (2-6).

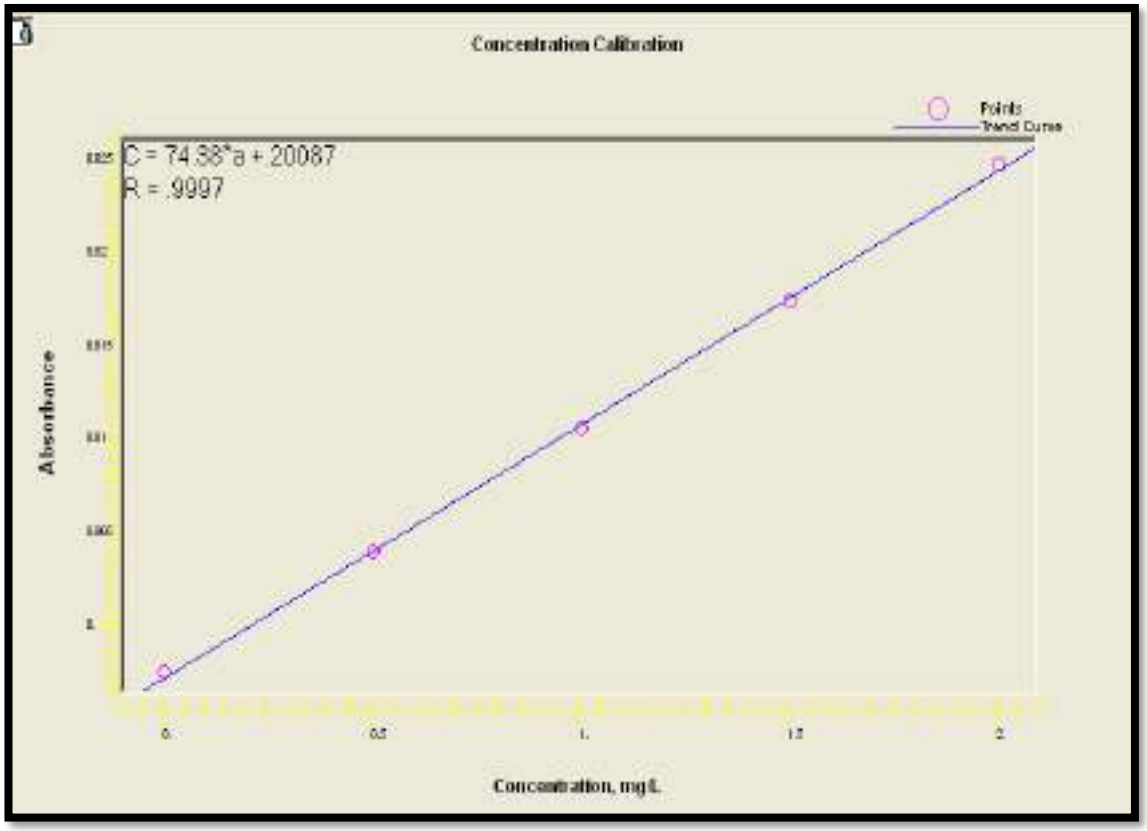


Fig (2-6) Standard calibration curve of Cu^{+2} by Flame atomic absorption spectroscopy

2.9.2.6 Stock Solutions of Potassium (1000µg/m

Stock solution of potassium was prepared by dissolving (0.1907g) of KCl, in 10 mL deionized water, transferred quantitively to volumetric flask (100 mL) filled to the mark with deionized water. The working standard solutions (1-8 µg/mL) were prepared by serial dilution of the stock solution, as shown in Fig. (2-7).

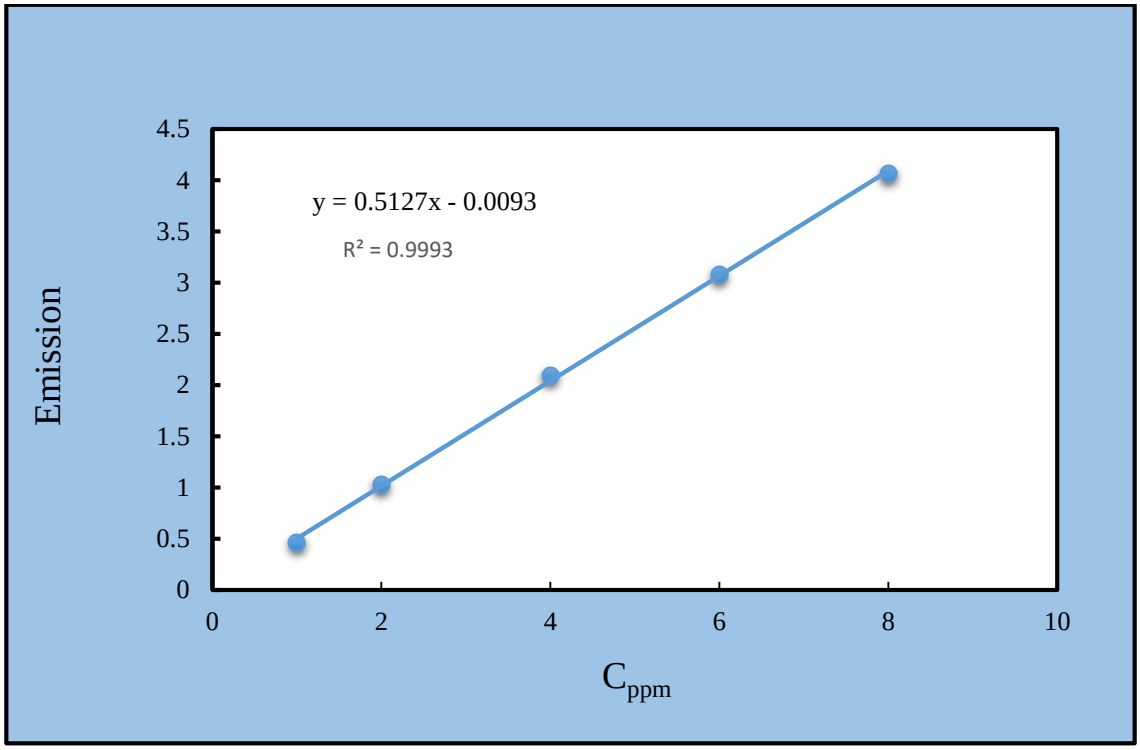


Fig (2-7) Standard calibration curve of K^{+1} by Flame photometer

2.9.2.7 Stock Solution of Sodium(1000µg/mL)

Stock solution of sodium was prepared by dissolving (0.2540 g) of NaCl in 10 mL deionized water, transferred quantitively to volumetric flask (100 mL) filled to the mark with deionized water. The working standard solutions (1-8 µg/mL) were prepared by serial dilution of the stock solution, as shown in Fig. (2-8).

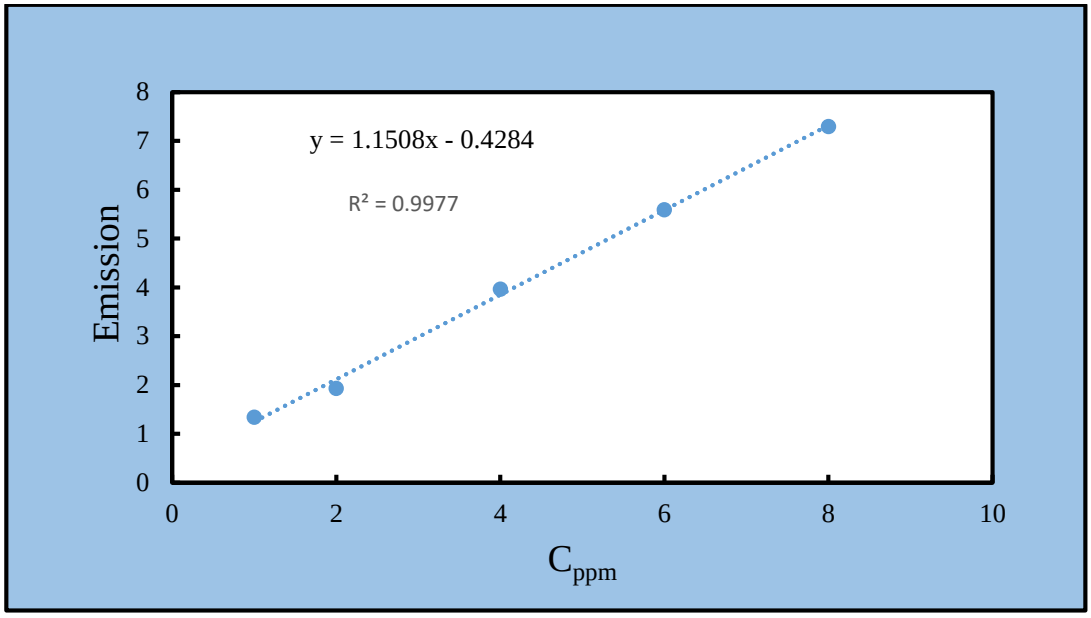


Fig (2-8) Standard calibration curve of Na^{+1} by Flame photometer

2.9.2.8 Stock Solution of Lithium(1000µg/mL)

The working standard solution of lithium (0.01-0.08 µg/mL) was prepared by serial dilution of the stock solution (1000 µg/mL), as shown in Fig. (2-9).

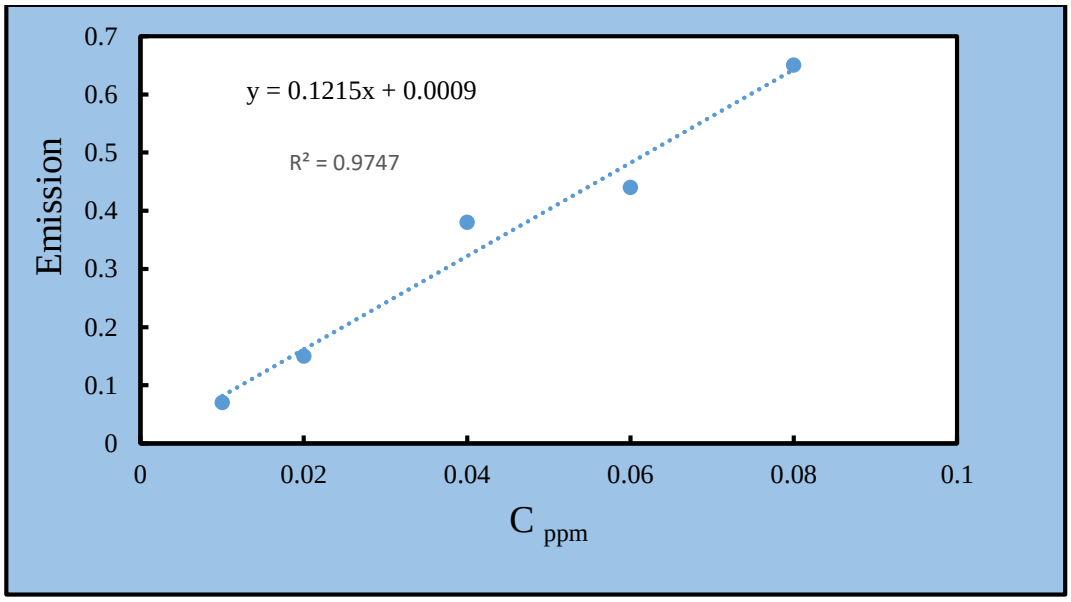


Fig (2-9) Standard calibration curve of Li^{+} by Flame photometer

2. 10 Statistical analysis

Operations in statistics were performed according to statistical analysis The study groups will be compared using the student t test in the SPSS version (24) program to see if there are any significant differences at the value of $P< 0.05$ and also the application of statistical analysis to determine the mean and standard deviation of the traits of people with diabetes and healthy people.

Chapter Three

Results and Discussion

3.1 Diabetes Mellitus

Table 3- 1 : Distribution of DM patients and control groups according to age and Duration of disease, and BMI.

Variable	Control (mean±SD)	DM (mean±SD)	P- value
Age (years±SD)	33±7.57	45.30±6.35	------
Weight (Kg)	75±10.56	78±1.519	------
Duration of disease (month)	-----	16.48±1.723	------
Height (m)	1.645±0.449	1.633±0.428	------
Body mass index (Kg/m^2)	32.035±4.326	29.93784±5.27	0.023649
Blood pressure (mmHg)	118.46±0.77	117.40±1.651	------

The results of this study are showed (45.30±6.35) years with DM group, were detected in comparison with control group (33±7.57).

These results are agree with Pouya Saeedi et al (2019). According to estimates, diabetes will be the cause of 4.2 million deaths in adults aged 20 to 79 in 2019, making up 11.3% of all fatalities. This translates to eight fatalities every minute. Nearly half of these fatalities (46.2%, or 1.9 million) are thought to include persons under the age of 60. Women (2.3 million) have a greater rate of diabetes-related mortality than men (1.9 million), with aged 60 to 69 years old having the highest rate. The highest diabetes-related death rates are found in the 60-69year age group for males and the 70-79 year age group for women, according to sex stratification of the estimates. A greater proportion of deaths linked to diabetes occur in men than in women between the ages of 30 and 59[92].

Obesity is the major risk factor for diabetes development. Hartemink et al .(2018). has out a meta-analysis that discovered a dose-response connection between BMI and T 2DM. According to research, the chance of developing diabetes rose by 18% for every kg/m2 increase in BMI. Young age is a remarkable barrier to getting diabetes by itself. T2DM prevalence has increased primarily in middle-aged and elderly people, although there is compelling evidence that it is also increasing in young adults. It has been hypothesized that the rising prevalence of diabetes in young adults can be explained, at least in part, by the rising prevalence of obesity in young people. However, there is a dearth of information on diabetes in younger groups. Recent research has demonstrated that there is a more pronounced difference between younger and older persons in the association between BMI and its effects. The risk of mortality per unit increase in BMI was higher in younger than in older adults, according to the global BMI mortality collaboration, which included 239 prospective studies across four continents.

Age appears to have the reverse effect on the relationship between BMI and renal disease, though.Only a small number of studies have evaluated the variability of age on the link of obesity and T 2DM, with mixed results. BMI was highly related with an elevated RR of developing a metabolic condition, including type 2 diabetes and cardiovascular disorders, according to data from the Third National Health and Nutrition Examination Survey. Additionally, as people aged, the link between BMI and hypertension and cardiovascular disease weakened. Age did not appear to have any moderating impact on the link between BMI and T2DM, though . In comparison to

individuals older than 70 years old, subjects younger than 60 years old showed a greater connection between BMI and the risk of diabetes, according to meta-analysis data from Japan, Australia, and New Zealand. [93].

Suggests that an SBP drop of about 130 mmHg is safe and may help to explain some of these positive outcomes. It should be noted that the 140 mmHg target for diabetics receives at least as little direct evidence-based support as the 130 or 120 mmHg targets. Even the harshest detractors of an SBP of less than 120 mmHg were unable to refute the more recent findings from studies showing that diabetics with SBP levels at least a little above 130 mmHg have a very low risk of both cardiovascular events and problems due to hypotension.Based on the foregoing, we previously suggested for at least careful reevaluation of the recommended target of 140 mmHg in diabetes because a properly planned trial comparing 130 to 140mmHg thresholds is very difficult to arise soon.[94].

3.2 Hormones and Tumor Marker

The results in table 3-2 show the ± SD of hormone levels and tumor marker level in sera of patients with DM and control group.

Table 3-2 Descriptive & Inferential statistics of hormones levels and tumor marker level in DM patients& control group.

Parameters	Diabetes (80) Mean ± SD	Control (40) Mean±SD	P- value
Calcitonin pg/mL	3.574±1.0402	5.604±3.3009	0.000
TSH µlU/mL	2.896±0.21739	3.104±0.47268	0.794
EII pg/mL	186±5.8362	49.16±3.8611	0.245
CA125 U/mL	17.240±19.9860	9.772±3.4238	0.012
Vitamin D_3 ng/mL	15.086±1.48622	15.356±0.81023	0.933

3.2.1 Calcitonin

The results show a significant effect (p=0.000) in Calcitonin concentration in DM patients (3.574±1.0402), were detected in comparison with control group (5.604± 3.3009) pg/d, and significant effect (p<0.05) in BMI (29.93784±5.27), (32.035±4.326**) Table3-1** DM and control respectively. Numerous research that looked into the connection between BMI and calcitonin levels came up with contradictory findings. The largest trial, which included 9340 T2DM patients, revealed a relationship between BMI and calcitonin levels that was favorable. Nevertheless, a research by Song et al. that included 4638 healthy people failed to find a link between BMI and calcitonin. Experimental research have demonstrated that consuming salmon

calcitonin results in weight loss, despite the fact that the relationship between calcitonin levels and BMI in humans has not been thoroughly clarified. Additionally, these authors discussed various additional drugs that target the calcitonin receptor and may be utilized to treat obesity.[95].

3.2.2 Thyroid Stimulating Hormone

The results show non–significant effect in TSH concentration in patients with DM (2.896 ±0.21739), were detected in comparison with control group (3.104±0.47268) µlU/mL, (p=0.794), it's not significant. These results are agree with Vadivelan Mehalingam et al.(2020)[96]. and Marina Gabriela Birck et al.(2022)[97].It's interesting to note that two Korean longitudinal studies found individual-level variations in TSH rather than a statistically meaningful link between diabetes incidence and reduced TSH levels. Although a cohort study from Rotterdam suggested that lower free thyroxine levels and higher plasma TSH levels within the reference range of thyroid function were linked to an increased risk of diabetes[98].

3.2.3 Estradiol

The results showed non–significant effect in (E II) concentration in patients with DM (186.50 ± 5.8362), were detected in comparison with control group (49.16 ±3.8611) pg/mL.

The results of this study do not agree with Carolain Felipin Vincensi Anklam et al. (2021). Estrogen, mainly 17β-estradiol (EII), is a powerful antioxidant by modulating the expression and activity ofmore

than a few antioxidant enzymes. As a result, postmenopausal hypoestrogenism degrades the redox status, which is further worse in diabetic women. Using a multivariate regression, we verified that lipoperoxidation and T2DM are related. These findings thus demonstrate a synergistic relationship between menopause and type 2 diabetes that increases the risk of oxidative damage. A persistent and low-grade inflammatory illness may develop if there is insufficient EII, which is a potent anti-inflammatory hormone. Menopause both alone and in combination with T2DM increased the leukometry in our sample, resulting in postmenopausal women with T2DM having the greatest numbers. [99].

3.2.4 Carbohydrate antigen 125 (CA-125)

The results show significant effect(p=0.012) in (CA-125) concentration in DM patients(17.240±1.99860), were detected in comparisons with control group(9.772±3.4238) U/mL.

The results of this study do not agree with Patrícia Lourenço et al(2022)[100].

The tumor markers known as glycosylation markers, such as CA125, are membrane- or secrete- shed into the blood. The majority of studies showed that tumor markers were frequently elevated in diabetes patients, particularly in those with poor blood glucose control. Within two weeks of maintaining stable blood glucose levels, carcinoembryonic antigen CEA and carbohydrate antigens such CA125 and CA15-3 recovered to normal or dramatically decreased.[10].

The results of this study do not agree with Manal Abudawood et al. (2020).

There has been a perceived link between diabetes and certain cancers, most notably pancreatic cancer. Analysis of several cancer biomarkers was carried out to clarify any potential correlation that exists between these indicators in order to clarify the relationship between HbA1c, oxidative stress, and cancer in diabetic people. possible cancer indicators, such as CA125. The CA125 levels among the groups were only marginally significant. [102].

3.2.5 Vitamin D_3

The results show non–significant effect in (Vitamin D_3) concentration in patients with DM (15.086±1.48622), were detected in comparison with control group (15.356±0.81023) ng/mL.

The results of this study do not agree with Deepak S Bhosle et al(2018). Health benefits of vitamin D are both preventative and reparative. Researchers in recent years have linked low vitamin D levels to diabetes and insulin resistance. There is evidence that vitamin D allows body to secrete more insulin and may also increase insulin sensitivity [12].

A non-significant and even inverse connection between 25(OH) D_3 and HbA1c%levels in diabetes individuals was found in the results of various earlier investigations. In a cohort research, it was discovered that there was an inverse correlation between glycosylated hemoglobin levels and 25(OH) D3 levels in patients with T2DM as compared to the control group. These findings suggest that 25(OH) D3 levels may influence the regulation of glucose in T2DM[103][104].

A non-significant negative association between the fasting blood sugar and our study's findings was found. Furthermore, there is still dispute regarding the involvement of vitamin D in the insulin pathway despite the known connections between T2DM and vitamin D insufficiency being previously noted. Preclinical research suggests that vitamin D is crucial for the regulation of calcium influx into cells, insulin production, and cell survival. Rat pancreatic beta cells' ability to secrete insulin in response to glucose is compromised by a vitamin D shortage, whereas supplementing with vitamin D appears to improve this ability[105][106]. Pancreatic cells exhibit vitamin D receptor binding of the circulating active form, 1,25(OH)2D [107], Moreover, the insulin gene was revealed to include a vitamin D response element [108], presence of vitamin D receptor in skeletal muscle[109]. Given the fact that 1,25(OH)2D increases the transcription of insulin receptor genes [110], In addition, the renin gene is suppressed, which results in a decrease in the hyperglycemia-induced rise in renin levels in pancreatic cells.A fresh target for treating diabetes has been suggested: blocking renin-angiotensin activity [108].

3.3 Enzymes

The results in table (3-3) show the ± SD of calcium level and enzymes levels expressed in mg/dL in sera of patients with DM and control group.

Table (3-3) Descriptive & Inferential statistics of calcium level and enzymes levels in DM patients& control group.

Parameters	Diabetes (80) Mean ± SD	Control (40) Mean±SD	P- value
CK U/L	109.70±6.2613	113.68±3.2471	0.767
ALP U/L	106.98±39.175	98.48±24.641	0.326

3.3.2 Creatine Kinase enzyme (CK)

The results show non–significant effect in (CK) concentration in patients with DM (109.70±6.2613), were detected in comparison with control group (113.68±3.2471) U/L.

The results of this study are agree with Mezgebu Legesse Habte et al.(2023)[111].The results of this study do not agree with Shamma AlMuraikhy et al.(2022).

The data demonstrated greater levels of both CK and CK2, in addition to the expected higher handgrip, among the common clinically important features that were linked with physical exercise regardless of insulin resistance status. The skeletal, cardiac, and muscles of the brain (CK1, CK2, and CK3) all contain the enzyme CK. Skeletal muscles account for the majority of the CK found in normal blood levels. Higher blood levels of CK are a result of damaged tissues. CK and CK2 rise

during exercise, regardless of the presence or absence of insulin resistance, as they detect muscle damage brought on by increased physical activity. [112].

Diabetes has been the focus of past study regarding the relationship between cramps and the development of neuropathy. According to a study from 2014, neuropathy is the single most significant predictor for the onset of cramps in diabetes patients. T1DM patients did not experience an increase in age-adjusted prevalence of cramping. Since we did not quantify cramping as a complaint during clinical evaluation, the prevalence of cramping in our study was lower than that in other investigations.[28].

3.3.3 Alkaline phosphatase enzyme

The results show non–significant effect in (ALP) concentration in patients with DM (106.98±39.175), were detected in comparison with control group (98.48±24.641) U/L.

The results of this study do not agree with Nishant Raizada,et al.(2023) ALPIts bone-specific component most likely contributes to vascular calcification in T2DM. ALP elevations in T2DM have been reported in the past without explanation. Furthermore, it has been observed that T2DM is associated with higher levels of bone-specific alkaline phosphatase (BAP). It's intriguing how BAP causes an increase in arterial calcification. Vascular smooth muscle cells express BAP. The matrix vesicles that are released by vascular smooth muscle cells serve as a nidus for vascular calcification. While some of these matrix-bound vesicles include calcification inhibitors such fetuin A (non-calcifying

vesicles), others have large amounts of BAP. BAP speeds up calcification in many ways. Bone Alkaline Base Phosphatase deactivates polyphosphates, particularly pyrophosphate, which prevent calcification. Dephosphorylation of osteopontin has also been hypothesized as a mechanism for osteopontin inhibition. Additionally, BAP has the ability to hydrolyze organic phosphate esters, releasing phosphate, a substrate for calcification. Even if serum phosphate levels are not increased, changes in the phosphate to pyrophosphate ratio in the vascular tissue can cause vascular calcification. [113].

The results of this study do not agree with Yuhua Wen et al.(2021). T 2 DM is now understood to represent a separate risk factor for unstable fractures. Hypoglycemia, muscle weakness, and chronic problems (such as retinopathy, neuropathy, and neuropathy) which typically occur in the patient with prolonged duration of T2DM can all contribute to the elevated fracture risk in T2DM patients. Hyperglycemia should however always be taken into consideration because it is crucial in the impaired bone metabolism experienced by T2DM patients, which results in decreased bone strength. The results of this study suggest that excessive glucose levels can harm bone metabolism even in the early stages of T2DM. The risk of osteoporosis rose after HbA1c level in newly diagnosed T2DM. The expression of genes linked to osteoblast maturation is likewise suppressed by hyperglycemia and the hyperosmolarity it causes. Causes of hyperglycemia[114].

3.4 Lipid profile and Glycated hemoglobin

The results in table 3-4 show the ± SD of lipid profile levels and glycated hemoglobin level expressed in mg/dL in sera of patients with DM and control group.

Table (3-4) Descriptive & Inferential statistics of lipid profile levels and glycated hemoglobin level in DM patients& control group.

Parameters	Diabetes (80) Mean ± SD	Control (40) Mean±SD	P- value
TC mmol/L	198.0092±5.02927	178.6400±36.96494	0.092
TG mmol/L	201.4830±13.52659	123.080±5.162	0.007
HDL mmol/L	45.92±7.42	47.50±13.48	0.587
LDL mmol/L	114.64±4.092433	112.44±3.1678	0.814
HbA1c mg/dL	10.0830±2.08591	5.4160±0.31712	0.000

3.4.1 Lipid profile

The results showed non–significant effect in TC concentration in patients with DM (198.0092±5.02927), were detected in comparisons with control group (178.6400±36.96494) mmol/L, The results showed non–significant increase in HDL concentration in patients with DM (45.92±7.42), were detected in comparisons with control group (47.50±13.48) mg/dL, and , The results show non–significant increase

in LDL concentration in patients with DM (114.64±4.092433), were detected in comparisons with control group (112.44±3.1678) mmol/L.

The data shows only significant increase (p=0.007) in TG concentration in DM patients (201.4830±13.52659), were detected in comparisons with control group (123.080±5.162) mmol/L.

The results of this study are agree with Zihui Yan et al.(2022) only (TG), but not agree with Zihui Yan in (TC, HDL, LDL). Diabetes is closely related to dyslipidemia; hence, patients with T2 DM usually present with low HDL, increased TG, and elevated levels of small dense of LDL. As a serum indicator, TG could be used to predict the risk of diabetes; hence, elevated TG levels increase the risk of prediabetes.

Because aging raised blood TG levels and altered the body's TG metabolism, elevated TG levels in our study only increased the risk of prediabetes and diabetes in the older group. As a result, metabolic illnesses like diabetes, metabolic syndrome, and non-alcoholic fatty liver disease were more prevalent in older persons than in younger ones. Additionally, our study found that among middle-aged people, unusually elevated TC levels in the blood are a risk factor for a higher risk of prediabetes. However, the older group did not exhibit the corresponding connection. According to a longitudinal analysis, TC rose with age, peaked about middle age, and then started to fall. Because of this, we hypothesized that aberrant TC levels had little of an impact on diabetes in the elderly.[115].

The results of this study do not agree with Biao Zheng et al.(2023). In older persons who have lost weight, there is a 75% chance of dying from an infection. As a result, directing the early detection and

prevention of osteoporosis risk factors solely through BMI to determining the appropriate body weight while disregarding its body composition is not complete. According to this study, the changing trend of the muscle/fat mass ratio (M/F), the appendicular skeletal muscle mass/trunk fat mass ratio (A/T), and the M/F ratio were all consistent with the femoral neck BMD (FNBMD), however the BMI ratio was not. FNBMD reduced in patients with decreased, steady, and growing BMI, while M/F and A/T similarly dropped in those with increased BMI. According to the data, BMD is influenced by body composition or constituent ratio rather than BMI. Unlike BMI, which only considers the benefits of muscle and the risks of fat, the evaluation of BMD by M/F and A/T also considers the impact of body composition ratio on BMD. Older persons who were obese and had muscle loss had a higher risk of osteoporosis and nonvertebral fractures than those who were merely obese, according to other studies [116].

3.4.2 Glycated hemoglobin (HbA1c)

The results showed significant effect (p=0.000) in HbA1c concentration in DM patients (10.0830±2.08591), were detected in comparisons with control group (5.4160±0.31712) mg/dL. The results of this study are agree with Sandra Sif Gylfadottir et al.(2022)[117].

The results of this study are agreement with Zihui Yan et al.(2022)[115].

Patients with T2DM are at an elevated risk of developing hip fractures in particular, and this risk is heightened in those who are on insulin, have poor glycaemic control (high levels of HbA1c), which may indicate the severity of the disease. Observational studies, on the other hand, have revealed a higher fracture risk with more frequent hypoglycemic episodes. According to the Rotterdam trial, people with

T2DM and a HbA1c level below 7.5% have a 62% higher risk of fracture than those with a HbA1c level. The Action to Control Cardiovascular Intensive glucose control patients (median HbA1c level 6.4%) did not have a higher risk of fractures or falls than patients receiving standard care (median HbA1c level 7.5%), according to the Risk in Diabetes trial, indicating that lowering HbA1c levels below 7.5% does not significantly contribute to fracture prevention [118].

The results of this study do not agree with Zahra Soleimania et al.(2021)[119].

3.5 Trace Elements

Table 3-5 shows the ± SD of Trace Elements levels expressed in µg/mL in sera of patients with DM and control group.

Table (3-5) Descriptive & Inferential statistics of Trace Elements levels in DM patients& control group

Parameters µg/mL	Diabetes (80) Mean± SD	Control (40) Mean± SD	P- value
Fe^{+2}	83.947±7.6631	105.020±38.074	0.200
Mn^{+2}	38.193±46.513	149.262±18.069	000
Zn^{+2}	58.475±3.0561	154.425±12.719	000
Cu^{+2}	126.595±7.2825	340.170±29.260	000
Li^{+1}	14.128±4.524	19.824±1.9751	0.055

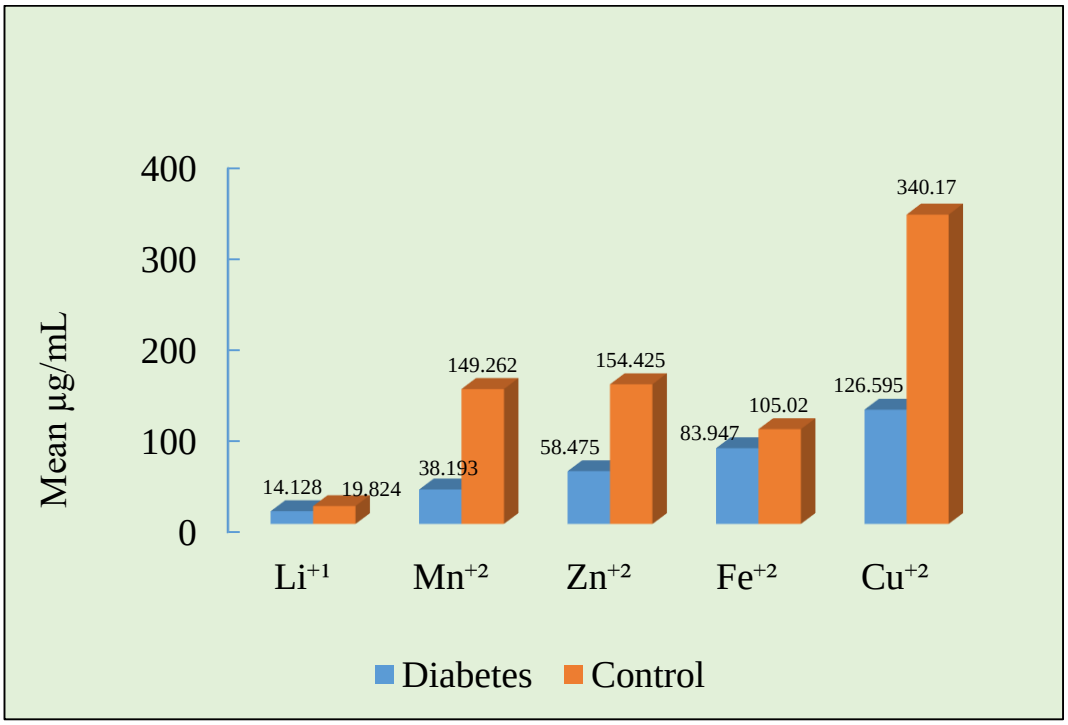


Fig. (3.1) The mean concentration of (Li^{+1} , Mn^{+2}, Zn^{+2}, Fe^{+2}, Cu^{+2}) in the blood serum of DM patients and healthy individuals

3.5.1 Iron

The results show non–significant effect in (Iron) concentration in patients with DM (83.947±7.6631), were detected in comparisons with control group (105.020±38.074) µg/ml.

The results of this study agree with M. Basaki et al.(2012) though the difference in Fe concentration was not significant. There is general agreement in the literature that homeostasis of trace elements can be disrupted by diabetes mellitus. On the other hand, alterations in the status of trace elements and increased oxidative stress in diabetes mellitus may be linked to the development of insulin resistance and diabetic complications. Reactive oxygen species (ROS) can be produced by free Fe, a molecule that is very pro-oxidant. Therefore, it

is crucial to maintain the homeostasis of free Fe because large levels of it may be detrimental. It has been shown that patients with diabetic retinopathy have greater Fe concentrations than healthy individuals. Therefore, it would appear that the pathophysiology of diabetic retinopathy involves oxidative damage brought on by a high concentration of free Fe. Despite the fact that another study revealed a rise in the Fe concentration in T2 DM, Ekin et al. reported that plasma Fe concentration is not significantly affected in DM, there were no variations in Fe concentration between the study groups[120].

The results of this study do not agree with Jun-Wei Wang et al.(2022)[121].

3.5.2 Manganese

The results showed significant effect (p=0.000) in Mn^{+2} concentration in DM patients (38.193±46.513), were detected in comparisons with control group (149.2 ± 18.069) µg/mL.

The results of this study are agree with Sobhy Yakout et al.(2022).

According to the study's findings, the diabetic group's median serum Mn levels were considerably lower than those of the control group. Our findings support those of previous researchers who discovered that T2DM patients' serum Mn concentrations were lower than those of controls. Additionally, one study found that pre-DM individuals had lower intra-arterial Mn concentrations than controls, which could lead to heart attacks and strokes. It was discovered that T2DM patients' urine Mn concentration was substantially higher than that of controls. This information backs up some writers' assertions that

people with T2DM may have lower blood Mn levels due to greater urine Mn excretion. Supplemental Mn may lower the incidence of T2DM issues by boosting the activity of the enzyme manganese superoxide dismutase (Mn-SOD). Understanding that Mn exposure should be kept to a minimum and shouldn't exceed what is commonly found in food is essential. [40].

The results of this study do not agree with Ting Wu et al.(2023).

Mn is a necessary nutrient that can also potentially be hazardous depending on the exposure level. By increasing MnSOD activity and preventing diabetes, Mn supplementation may shield mitochondria and islets from ROS. However, it has also been proposed that Mn may limit glucose-stimulated insulin production in -cells by affecting mitochondrial function. According to a cross-sectional study including coke oven employees, urine Mn levels were positively correlated with hyperglycemia but not with the risk of developing diabetes [122].

3.5.3 Zinc

The results show significant effect (p=0.000) in Zn^{+2} concentration in DM patients (58.475±3.0561), were detected in comparisons with control group (154.425±12.719) µg/mL.

The results of this study are agree with Ana Maria Dascalu et al.(2022)[43]. The results of this study are agreement with Emine Şen et al.(2021). After iron, zinc is the trace metal found in the body in the second-highest concentration. More than 300 enzymes depend on zinc for their proper function. Numerous physiological processes, including cell division, tissue repair, bone formation, membrane stability, growth and development, pregnancy, fertility, brain activity, taste, and appetite

depend on it. Different findings about serum zinc in T2DM were found in the investigations that were undertaken. In their studies, many experts discovered that diabetic patients' serum zinc levels were lower than those of the healthy controls. Additionally, they demonstrated that in the diabetic group, there was a negative association between blood zinc levels and both serum glucose levels and basal HbA1c values, demonstrating the value of zinc supplementation for enhancing glycaemic control and lowering HbA1c levels. Serum zinc levels in diabetic and hypertensive patients were shown to be greater in diabetes patients compared to control groups in research by Zhang et al. [123] .

3.5.4 Copper

The results showed significant effect (p=0.000) in Cu^{+2} concentration in DM patients (126.595 ±7.2825), were detected in comparisons with control group (340.170 ± 29.260) µg/mL.

The results of this study do not agree with Rana MW Hasanato .(2020). Serum levels of Cu were elevated among T2DM patients with poor glycemic control compared to normoglycemic T2DM patients and normal individuals. Increased Cu level among T2DM patients reported previously has been linked with the development of diabetes. Cu is a pro-oxidant and high levels of Cu induce increased production hydrogen peroxide resulting in β cell degeneration and development of T2DM. Zn on the other hand is bestowed with anti-oxidant and anti-inflammatory properties through its ability to down regulate the production of inflammatory cytokines. In diabetes mellitus, low Zn levels and high Cu levels tip the scales in favor of an inflammatory environment. Diabetes raises free Cu levels, which are toxic and

encourage pro-oxidant activity. This is due to elevated Cu levels, decreased ceruloplasmin levels, and decreased Cu binding activity. Protein glycosylation is induced by hyperglycemia, and Cu has a greater affinity for these glycosylated proteins as a result. This increased oxidative stress and free radical generation predispose T2DM patients to disease-related problems [124].

3. 5.5 Lithium

The results showed non-significant effect (p=0.055) in Li^{+1}concentration in DM patients (14.128±4.524) were detected in comparisons with control group (19.824±1.9751) µg/mL.

Since lithium is a trace non-essential element, it has no known biological roles in humans. However, lithium has been increasingly incorporated into medical applications due to its positive effects in the treatment of psychological illnesses. The stimulation of neural progenitor cell proliferation by the Wnt/-catenin pathway, which results in an increase of the brain's grey matter, is generally acknowledged as one of the several modes of action for lithium. It's interesting to note that the Wnt/-catenin pathway also controls the proliferation of other cell types, including bone marrow-derived mesenchymal stromal cells (MSCs), indicating that lithium may potentially influence the growth of these cellsIn fact, a recent study found that lithium-mediated Wnt/-catenin signaling boosted the proliferation of human bone marrow-derived stromal stem cells (hMSCs) in vitro. Furthermore, prior research indicated that this pathway was a key regulator of osteoblastogenesis, which increased the attraction of using lithium in tissue engineering. The chemical processes by which lithium promotes

these effects are still unclear, despite the fact that a few studies have shown that it has a positive effect on bone mineral density and lowers the risk of fracture.Satija and colleagues reported diminished proliferation of hMSCs treated with lithium and decreased expression of adipogenic. and osteoclastogenic factors accompanied by the induction of osteoblastogenic markers associated with collagen-1 deposition and mineralization; similar results were also reported by other groups[36]

3.6 Electrolytes

Table 3-6 shows the ± SD of electrolytes levels expressed in µg/mL in sera of patients with DM and control group

Table (3-6) Descriptive & Inferential statistics of electrolytes levels in DM patients& control group

Parameters µg/mL	Diabetes (80) Mean± SD	Control (40) Mean± SD	P- value
K^{+1}	98.965±26.774	84.917±19.798	0.023
Na^{+1}	303.126±73.407	463.732±67.660	000
Mg^{+2}	89.051±8.676	38.433±1.543	0.034
Ca^{+2}	8.956± 0.4272	9.164± 0.2914	0.032

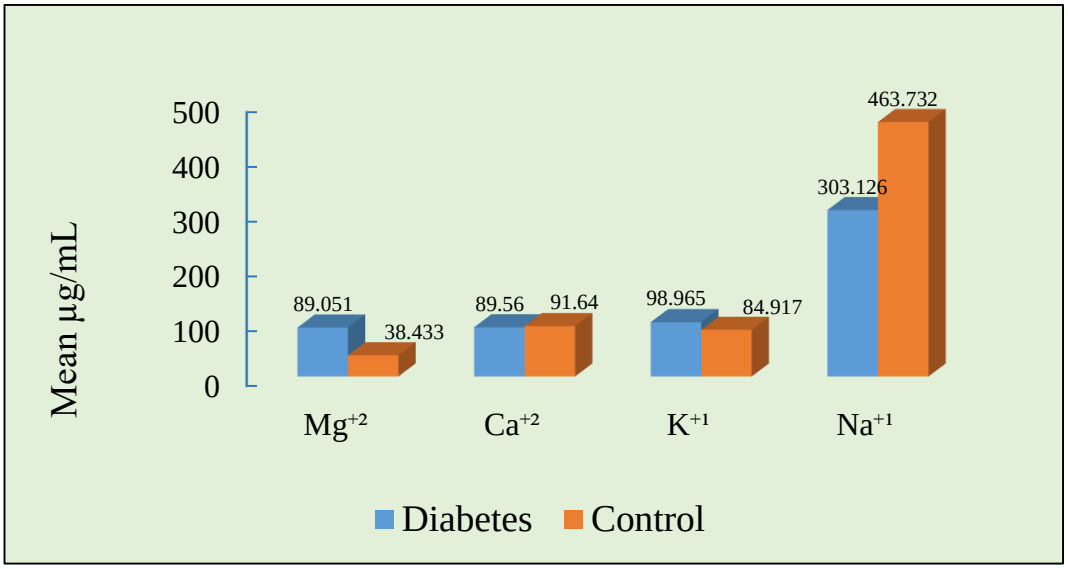


Fig. (3.2) The mean concentration of (Mg^{+2}, Ca^{+2}, K^{+1}, Na^{+1}) in the blood serum of DM patients and healthy individuals.

(∴the unit of measurement for calcium was changed from mg/dL⟶mg/L).

3.6.1 potassium

The results show significant effect (p=0.023) in K^{+1}concentration in DM patients (98.965±26.774) were detected in comparisons with control group (84.917±19.798) µg/mL.

The results of this study are agree with Allan J. Collins et al.(2017)[125]but do not agree with Qi Cheng et al.(2022) [49].

Potassium chloride (KCl), potassium bicarbonate, potassium citrate, and potassium phosphate are the four primary categories of potassium-containing preparations. When hypophosphatemia is present, potassium phosphate solutions are especially helpful, as are citrate or bicarbonate solutions when acidosis is present. But potassium chloride is typically the best solution to use. The gastrointestinal tract's mucosa may get irritated by oral KCl tablets, which typically contain 8 mmol K^{+1}. This irritation may potentially result in ulcerations or bleeding. This

necessitates consuming a lot of drink along with the medication. When using non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors (ACEi), or angiotensin receptor blockers (ARBs) in diabetic patients with reduced glomerular filtration rate (GFR), potassium-sparing diuretics can help prevent the onset of hyperkalemia. Encouragement of the consumption of foods high in potassium, such as bananas, tomatoes, lentils, almonds, fish meat, etc., while always bearing in mind the glycemic load of each food, is an intriguing strategy for diabetes patients who are prone to hypokalemia. [48].

The major adverse cardiovascular events (MACE) results presented here add to a small but growing body of evidence suggesting that serum potassium (sK+) variability may be a risk factor for unfavorable clinical outcomes. This increased risk may be concealed by analyses that only take mean sK + over time or by the evaluation of competing biomarkers. It is possible to draw comparisons, for instance, with the more well-established significance of glucose variability as a risk factor and potential surrogate marker for cardiovascular and microvascular problems in diabetes patients.[126].

3.6.2 Sodium

The results showed significant effect (p=0.000) in Na^{+1}concentration in DM patients (303.126±73.407) were detected in comparisons with control group (463.732±67.660) µg/mL.

The results of this study are agreement with Hai-yan Huang et al.(2022). These findings point to a potential role for low normal serum sodium levels in T2DM patients' impaired bone turnover. To our knowledge, no research have specifically examined the relationship between normal blood sodium levels and bone turnover in people with T2DM.

Numerous research have looked at the connection between hyponatremia and bone health in people with subarachnoid hemorrhage. Patients receiving incorrect antidiuresis syndrome treatment or antiepileptic medication. the elderly and animal model systems. In T2DM patients, serum sodium levels are related to bone turnover. In this study, blood sodium levels were found to be strongly positively linked with the markers of bone turnover, osteocalcin and the N-terminal propeptide of type-I procollagen, but not with levels of the C-terminal telopeptide (CTx) Patients with subarachnoid hemorrhages who experienced transient mild hyponatremia frequently also showed significant decreases in bone production, but not in bone resorption. The lack of a link between sodium and CTx levels could be attributed to two variables. One example is that low bone turnover in T2DM patients is mostly due to decreased bone production. Furthermore, the mobilization of bone salt stores to maintain circulation sodium concentrations is a key component of the mechanisms through which hyponatremia can accelerate bone resorption. however when sodium levels are within the usual range, this effect can be less pronounced. [50].

3. 5.3 Magnesium

The results show significant effect ($p=0.034$) in Mg^{+2} concentration in DM patients (89.051±8.676), were detected in comparisons with control group (38.433±1.543) µg/mL.

The results of this study do not agree with Nicola Veronese et al.(2021). Through a number of routes, magnesium may enhance insulin sensitivity and glucose metabolism. First, chronic Mg deficiency has been linked to reduced post-receptorial activity, which in turn causes cells to use less glucose. This is known from experimental models.

Additionally, Mg may enhance pancreatic beta-cells' ability to secrete insulin. Improvements in HOMA-IR, especially in those at high risk of diabetes, indicate that the major effect of magnesium appears to be a reduction in insulin resistance, suggesting that magnesium functions more effectively when there is an insulin deposit. Additionally, other experimental data showing that Mg is able to reduce oxidative stress and inflammatory parameters—two major causes of insulin resistance—confirm the findings about the improvement in insulin sensitivity.[127].

It has been suggested that a dietary Mg deficiency may increase the risk of developing osteoporosis and losing bone mass. Increased dietary intakes of Mg were positively and significantly associated to (BMD), according to epidemiologic research. On the other hand, postmenopausal osteoporotic women who had inadequate dietary Mg intakes had a higher rate of bone loss. In the Health, Aging and Body Composition Study, it was found that in healthy white adults aged 70 to 79 at baseline, higher Mg intakes were linked to higher BMD.

Additionally, Mg is required for the synthesis, transport, and activation of vitamin D; as a result, deficiencies in Mg would hinder the creation of 1,25-OH2 D3, the active form of vitamin D, and result in resistance to PTH and vitamin D effects. The impacts of Mg deficiency combined with decreased PTH responsiveness and low 1,25-OH2 D3 synthesis would interfere with the processes of bone formation and mineralization, lowering the quality, strength, and BMD of the bone. Anormal bone turnover can be restored by Mg supplementation, which has been proposed to limit bone loss and lower the risk of osteoporosis. It was discovered that women with higher dietary Mg intakes had a 27%

lower risk for future fractures in the cohort of the "Osteoarthritis Initiative" participants who were followed for 8 years. This finding supports the protective effect of maintaining an adequate Mg balance on the risk of osteoporosis and fragility fractures.[128].

3.6.4 Calcium

The results show significant effect (p=0.032) in Calcium concentration in DM patients (8.956± 0.4272), were detected in comparisons with control group (9.164± 0.2914) mg/dL. The results of this study do not agree with Qi Cheng et al.(2022) [49].

The finding that calcitonin reduces the amount of circulating calcium led to the theory that its physiological role in hypercalcemia may be involved in returning normal serum calcium concentrations. This idea was investigated in a number of vitro experiments using rats, many of whom had parathyroidectomies without cells that secrete PTH or thyroparathyroidectomies without cells that secrete both PTH and calcitonin (C-cells). The thyroid gland was necessary to lower the calcium concentrations in the circulation when calcium injection or infusion caused hypercalcemia.[129].

Conclusions and Recommendation

Conclusions and Recommendation

Conclusions:

1. Significant differences in the level of calcitonin, cancer antigen125 and calcium in patients with T2DM compared to healthy individuals.

2. Significant differences in the level of trace elements (zinc ,manganese, copper) in patients with T2DM compared to healthy individuals.

3. Significant differences in the level of triglyceride in patients with T2DM compared to healthy individuals.

4. Significant differences in the level of electrolytes (potassium, calcium, sodium and magnesium) in patients with T2DM compared to healthy individuals.

5. No significant differences were obtained between DM patient and healthy individuals for each of (TC, LDL, HDL, Vitamin D, CK, ALP, TSH, E II, lithium, Fe).

Recommendations:

1. Studying the relationship between calcitonin and variables (gender, age, BMI, family history, geographical location, medications taken, and nutritional supplements in the blood of diabetic patients).
2. Studying the relationship between ALP and variables (age, gender, family history of diabetes before and after taking the medication).
3. Study of trace element levels (cobalt, nickel, lead, mercury).

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Appendix

No.	The questionnaire of the study	
1	Name	
2	Age(year)	
3	Weight(Kg)	
4	Length(m)	
5	Duration of disease	
6	Family history	
7	Medication	
8	Other disease	

الخلاصة

داء السكري هو حالة مزمنة تؤثر على الجسم بأكمله ويمكن أن تسبب مجموعة واسعة من العواقب، بما في ذلك هشاشة العظام وأمراض القلب والأوعية الدموية والاعتلال العصبي. على الرغم من وجود آليات أساسية مختلفة إلى حد ما، فإن داء السكري من النوع الأول (T1DM)وداء السكري من النوع الثاني (T2DM) يزيدان من خطر الإصابة بالكسور، والذي يحدث بسبب مجموعة متنوعة من الأسباب ويمكن تفسيره جزئيًا بفقدان كثافة المعادن في العظام.

تهدف هذه الدراسة إلى تقييم بعض المتغيرات الكيموحياتية لمرضى السكري(EII, TSH، CA125، فيتامينD ، Ca، CK، ALP TC، TG، HbA1,HDL، LDL,Calcitonin وتقدير بعض العناصر النزرة(Fe ، Mg، Mn، Zn, Cu, K, Na, Li)ولتحقيق هذا الهدف شملت الدراسة عينات دم لـ 120 امرأة، بعد أن تم تصنيف العينات إلى مجموعتين، (مجموعة مراقبة) مكونة من 40 عينة، و(مجموعة من مرضى السكري). من 80 عينة. أظهرت نتائج الدراسة الحالية وجود تأثير معنوي (P=0.000) للكالسيتونين لدى مرضى السكري مقارنة مع مجموعة السيطرة. في حين أظهرت النتائج عدم وجود تاثير معنوي (P =0.794)لل TSHلدى مرضى السكري مقارنة بمجموعة السيطرة.

أظهرت النتائج عدم وجود أهمية (P= 0.245)في تركيز E II في المرضى الذين يعانون من مرض السكري، مقارنة مع مجموعة السيطرة. كذلك أظهرت النتائج وجود تأثير معنوي (p=0.012)في تركيز CA-125 لدى مرضى داء السكري عند مقارناتهم مع مجموعة السيطرة. كما أظهرت النتائج عدم وجود تاثير معنوي (P=0.933)في تركيز فيتامين (د) لدى المرضى الذين يعانون من مرض السكري مقارنة مع مجموعة السيطرة. أظهرت النتائج تاثير معنوي (p=0.032)في تركيز الكالسيوم لدى مرضى داء السكري، وذلك من خلال المقارنات مع مجموعة التحكم.

لا توجد فروق ذات دلالة إحصائية عند مستوى الدلالة ($p>0.05$)في متوسط تركيز (كرياتين كيناز، الفوسفاتيز القلوي، البروتين الدهني عالي الكثافة، البروتين الدهني منخفض الكثافة)، بينما توجد فروق ذات دلالة إحصائية عند مستوى ($p<0.05$)في مستويات (الكوليسترول الكلي، الدهون الثلاثية، الهيموجلوبين السكري). كما ظهرت النتائج غير معنوية (($P=0.200$ في تركيز (الحديد) لدى مرضى داء السكري، وقد تم الكشف عنها في المقارنات مع مجموعة السيطرة، وأظهرت النتائج دلالة إحصائية عند مستوى دلالة ($P<0.05$)في متوسط تركيز كل من (المغنيسيوم، المنغنيز، الزنك، النحاس، البوتاسيوم، الصوديوم). بالإضافة إلى ذلك أظهرت النتائج غير معنوية ($p=0.055$)في تركيز الليثيوم لدى مرضى السكري وذلك عند المقارنة مع مجموعة السيطرة.

جمهورية العراق

وز ارة التعليم العالي و البحث العلمي

جامعة ميسان

كلية العلوم

قسم الكيمياء

دراسة بعض المتغيرات الكيموحيوية و العناصر النزرة في النساء المصابات بالنوع الثاني لمرض السكري في محافظة ميسان

رسالة مقدمة الى

كلية العلوم / جامعة ميسان جزء من متطلبات نيل شهادة الماجستير

في علوم الكيمياء

الطالبة

زينب علي خلف

بكالوريوس علوم كيمياء/ جامعة ميسان (٢٠١٨)

بإشراف

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صفاء صبري نجم

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