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# BIOCHEMICAL COMPARATIVE STUDY FOR SOME INFLAMMATORY FACTORS IN TYPE 2 DIABETIC PATIENTS WITH HYPERURICEMIA

**IN PARTIAL FULFILLMENT OF THE REQUIREMENTS**
**FOR**
**THE DEGREE OF MASTER OF SCIENCE**
**IN**
**CHEMISTRY**

**BY**

**AMER OKAB ABDULRIDHA ABDULRIDHA**

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BIOCHEMICAL COMPARATIVE STUDY FOR SOME INFLAMMATORY FACTORS IN TYPE 2 DIABETIC PATIENTS WITH HYPERURICEMIA

By Amer Okab Abdulridha ABDULRIDHA

June 2022

We certify that we have read this thesis and that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science

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**ABSTRACT**

# BIOCHEMICAL COMPARATIVE STUDY FOR SOME INFLAMMATORY FACTORS IN TYPE 2 DIABETIC PATIENTS WITH HYPERURICEMIA

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Master of Science in Chemistry

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June 2022

One of the research plans is to study the relationship and possible relationships between uric acid levels and each of the studied inflammatory factors. This prognostic role of uric acid would serve as one of the early problems of a common complication of uncontrolled diabetes. In this study, 90 patients will be tested for varied degrees of disease activity, with the other 25 healthy persons matched for age, gender, and body mass index serving as the control group. The results indicate that age has a clear importance, as the higher the age, the higher the disease rate. There was no statistical significance for weight and height when performing the statistical analysis. The uric acid had great statistical significance among the study groups, which indicates the influence of its levels between groups. Also for the erythrocyte sedimentation rate test, hsCRP, RF, interleukin-6 and interleukin-8, which indicate inflammation increases in diabetic patients with changes in the levels of uric acid. The study concluded that it is possible that changes in uric acid levels with diabetes may lead to the development of the disease.

**2022, 35 pages**

**Keywords:** C-reactive protein, Diabetes, ESR, High sensitivity CRP, Hyperuricemia

## ÖZET

# HİPERÜRİSEMİ OLAN TİP 2 DİYABETİK HASTALARDA BAZI inflamatuar FAKTÖRLER İÇİN BİYOKİMYASAL KARŞILAŞTIRMALI ÇALIŞMA

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Haziran 2022

Araştırma planlarından biri, ürik asit seviyeleri ile çalışılan inflamatuar faktörlerin her biri arasındaki ilişkiyi ve olası ilişkileri incelemektir. Ürik asidin bu prognostik rolü, kontrolsüz diyabetin yaygın bir komplikasyonunun erken problemlerinden biri olarak hizmet edecektir. Bu çalışmada, 90 hasta çeşitli derecelerde hastalık aktivitesi için test edilecek ve yaş, cinsiyet ve vücut kitle indeksi açısından eşleştirilmiş diğer 25 sağlıklı kişi kontrol grubu olarak görev yapacak. Sonuçlar, yaşın belirgin bir önemi olduğunu, yaş arttıkça hastalık oranının da arttığını göstermektedir. İstatistiksel analiz yapılırken ağırlık ve boy için istatistiksel bir anlamlılık yoktu. Ürik asit, çalışma grupları arasında, düzeylerinin gruplar arasındaki etkisini gösteren büyük istatistiksel öneme sahipti. Ayrıca eritrosit sedimantasyon hızı testi için hsCRP, RF, interlökin-6 ve interlökin-8, ürik asit düzeylerindeki değişikliklerle diyabetik hastalarda inflamasyon artışını gösterir. Çalışma, diyabetli ürik asit seviyelerindeki değişikliklerin hastalığın gelişimine yol açabileceği sonucuna varmıştır.



**2022, 35 sayfa**

**Anahtar Kelimeler:** C-Reaktif Protein, Diyabet, ESR, Yüksek hassasiyetli CRP, Hiperürisemi

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**Amer Okab Abdulridha ABDULRIDHA**

**Çankırı-2022**

**CONTENTS**

## LIST OF SYMBOLS

| | |
|---|---|
| - | Minus |
| % | Percent |
| / | Divide |
| + | Plus |
| < | Less-Than |
| = | Equal |
| > | More-Than |
| dL | Deciliter |
| G | Gram |
| mg | Milligram |
| Min | Minute |
| mL | Milliliter |
| $O_2$ | Oxygen |
| ºC | Degrees Celsius |
| β | Beta |
| γ | Gama |

## LIST OF ABBREVIATIONS

| | |
|---|---|
| CRP | C-Reactive Protien |
| DM | Diabetes Mellitus |
| ELISA | Enzyme-Linked Immunosorbent Assay |
| ESR | Erythrocyte Sedimentation Rate |
| FDA | Food and Drug Administration |
| IFG | Impaired Fasting Glucose |
| IL-1 | Interleukin-1 |
| IL-6 | Interleukin-6 |
| IL-8 | Interleukin-8 |
| RBS | Random Blood Sugar |
| SD | Standard Deviation |
| T1DM | Type 1 Diabetes Mellitus |
| T2DM | Type 2 Diabetes Mellitus |
| UA | Uric Acid |

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## 1. INTRODUCTION

The results of a number of clinical studies showed that uric acid was strongly linked to type 2 diabetes. An investigation of 3,200 randomly chosen northern Italians between the ages of 25 and 74 found that people with higher median uric acid levels were more probable to have insulin resistance and diabetes than people with lower median uric acid levels (Bădescu *et al.* 2016).

Women who had blood levels of uric acid in the normal range had a greater risk of having new-onset diabetes than those who had low-normal levels, according to the findings of this research. The metabolic syndrome and type 2 diabetes were found to be more common in adults aged 75 to 84 who had high levels of uric acid (6.0 mg/dl for males and 5.5 mg/dl for women) (Katsarou *et al.* 2017). Blood uric acid concentration was found to be a strong predictor of whether or not an adult male will get the metabolic syndrome, diabetes, or high blood pressure. Type 1 diabetics had a lower connection than healthy volunteers between high blood UA and impaired insulin sensitivity, according to the findings of this research (Stringer *et al.* 2021).

Each of the inflammatory variables under investigation will be examined in order to throw light on any potential correlations between uric acid levels and each of them. Because of its predictive value, uric acid will act as an early warning system for common problems associated with uncontrolled diabetes. In this study, 90 patients will be tested for varied degrees of disease activity, with the other 25 healthy persons matched for age, gender, and body mass index serving as the control group. The following parameters will be examined in the patients: fasting blood glucose, HbA1c, uric acid, CRP, HSCRP, ESR, and indicators of disease.

Aim of study: Biochemical comparative study for some inflammatory factors in type 2 diabetic patients with hyperuricemia.

## 2. LITERATURE REVIEW

Uric acid was shown to be highly associated with diabetes in several clinical investigations. Consider, for example, a poll of 3,200 randomly chosen northerners. High uric acid levels were linked to an increased risk of IFG, metabolic syndrome, and diabetes among Italians ages 25 to 74, compared to those with lower median UA levels, researchers found. Studies reveal that women with serum uric acid (SUA) levels in the normal range are at an increased risk of developing type 2 diabetes. More than half of 75-84-year-old men and women had elevated levels of uric acid (6.0 mg/dl for males and 5.5 mg/dl for females). Males with high levels of serum UA were considerably more likely to develop the metabolic syndrome, diabetes, and hypertension. Type 1 diabetics have a weaker link between high blood UA levels and insulin resistance than healthy people, according to these new studies (Szmuilowicz *et al.* 2019). TNF-alpha and interleukin-1 (IL-1) are two of the several cytokines that are generated when UA levels are raised in the bloodstream (TNF-alpha). Excessive production of TNF- and activation of the classical inflammatory system have been reported to be linked to an impaired ability of insulin to enter the cells. TNF-a, interleukin-6, and C-reactive protein have been demonstrated in human research to be associated to serum UA in healthy individuals (Piero *et al.* 2015).

### 2.1 Diabetes Mellitus

Blood glucose levels are unusually high in people with diabetes, which is a metabolic condition. Diabetic mellitus may manifest itself in a variety of ways, such as type 1 or type 2 diabetes, gestational diabetes, or diabetes in infants. Endocrinopathies and steroid use are secondary causes of diabetes. It is the most common kind of diabetes, with type 1 accounting for the majority of cases. Type 1 diabetes (T1DM) and type 2 diabetes (T2DM) are the two most common kinds of diabetes (DM). Unlike other kinds of diabetes, type 1 diabetes mellitus (T1DM) is caused by a deficiency in insulin synthesis or function (T2DM). When it comes to type 2 diabetes (T2DM) and type 1 diabetes (T1DM), the latter is more prevalent among middle-aged and older adults with a chronically elevated blood sugar level. Therefore, the pathophysiology of Type 2

Diabetes and Type 1 Diabetes are significantly different. Every kind has its unique symptoms and causes, as well as treatment options. We'll go into further detail regarding the two forms of diabetes in the next sections (Landon *et al.* 2018).

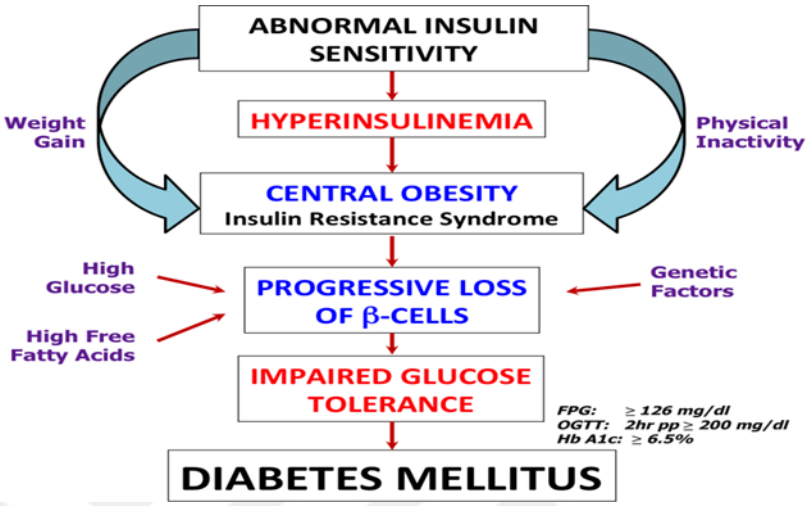


**Figure 2.1** Causes of DM (Liamis *et al.* 2014)

### 2.1.1 Type-1

T1D is also referred to as insulin-dependent diabetes in certain regions. Due to the fact that the disease is most often seen in young people, it was originally known as juvenile-onset diabetes. Type 1 diabetes is an illness that happens on its own and affects the immune system. It happens when antibodies that are made by the body attack the pancreas. Because the organ has been hurt, it can no longer make insulin. A change in the genes could cause this kind of diabetes. It can also happen when the cells in the pancreas that make insulin don't work right (Bello-Chavolla *et al.* 2017).

The nerves (peripheral neuropathy), and the kidneys (nephropathy) can result from type 1 diabetes (diabetic nephropathy), damage to the small blood vessels in the eyes (diabetic retinopathy). Heart disease and stroke are also more likely to happen to people with type 1 diabetes than to the rest of the population (Petrov 2020).

Insulin is injected directly beneath the epidermis, which is the skin's outermost layer, to treat type 1 diabetes. Insulin pens give insulin using prefilled cartridges and a tiny needle. High-pressure air is used by jet injectors to spray insulin onto the skin. Insulin is administered through a catheter implanted beneath the skin of the abdomen by pumps. The A1C blood test measures the average amount of sugar in the blood over the course of the previous three months. The doctor can find out how well the patient's blood sugar is being controlled by using this test. This helps them figure out how likely problems are to happen (Sayin vd. 2015).

### 2.1.2 Type-2

T2D is a health problem that lasts a long time. More glucose is present in the blood, which is indicative of it. Adult-onset diabetes and T2D mellitus are alternate terms for T2D. However, an increasing number of adolescents and children are becoming ill with this disease. T2D is far more prevalent than T1D and must be handled differently. But like T1D, it has high glucose levels and the problems that come with them. T2D, on the other hand, can occur in adolescents and children, primarily due to childhood obesity (Tsimihodimos *et al.* 2018).

During the digestion process, food is broken down into its basic parts. Glucose is the most common type of simple sugar, which is made when carbohydrates are broken down. The liver produces glucose, a major source of energy for the body's cells. In order for glucose to provide energy to cells, it must leave the circulation and enter the cells. Diabetic ketoacidosis is a condition in which the body cannot utilize glucose (sugar) as fuel or regulate the amount of glucose it needs. This long-term (chronic) condition causes the bloodstream to have too much blood glucose. A high quantity of glucose in the bloodstream may ultimately lead to difficulties with the circulatory, neurological, and immune systems (Spaight *et al.* 2016, DeFronzo *et al.* 2015).

When it comes to type 2 diabetes, there are two main concerns that are tied together. The amount of sugar absorbed goes down when the pancreas doesn't make enough insulin, which controls how much sugar gets into cells, and when cells don't respond

well to insulin. Even though T2D used to be called "adult-onset diabetes," both types of diabetes can manifest in childhood or adolescent. Despite the fact that T2D is more than in adults, the rise in the number of overweight adolescents and children has resulted in an increase in the number of T2D among adolescents and children (Johns *et al.* 2018).

When you have T2D, your pancreas produces very few insulin. Either it is insufficient or the body does not utilise it properly. The most common places where it can be found are in adipocytes, liver cells, and muscle cells. In general, T2D is not as bad as type 1 diabetes. The eyes are especially at risk. Heart disease and stroke are much more likely to happen to people with T2D (Bello-Chavolla *et al.* 2017).

### 2.1.3 Influence on human

T2D, previously known as adult-onset diabetes or non-insulin dependent diabetes, affects an estimated 90 to 95 percent of the 13 million men who have been diagnosed with the disease. Diabetes prevalence has climbed dramatically in every state since the early 1990s. Males had one of the most significant rises. Patients under the age of 45 who do not have any additional risk factors should begin testing as soon as they reach that age.

The generation of insulin is required in the case of T2D, as opposed to T1D. These individuals, however, either do not get enough insulin or have bodies that do not detect or use insulin adequately. In the technical world, this is referred to as insulin resistance. Sugar (glucose) cannot enter the cells to be used as fuel when there is inadequate insulin or when it is not adequately used. Sugar builds up in the bloodstream, causing the cells to become dysfunctional. Dehydration and degeneration of the body are two additional consequences connected with high blood sugar levels accumulating.

It is likely that a buildup of sugar in the bloodstream causes dehydration due to excessive urine production. Diabetic coma is caused by hyperosmolarity. This

potentially deadly disease can happen when a person with type 2 diabetes becomes very dehydrated and doesn't drink enough fluids to make up for it (Sayin vd. 2015).

The cause of body deterioration, on the other hand, is elevated blood sugar levels, which, over time, can damage neurons and small blood vessels in the eyes, kidneys, and heart. This increases the likelihood of developing atherosclerosis (the hardening of the main arteries), which can result in a heart attack or stroke. Despite advancements in therapy, diabetes management remains a challenge, which is why physicians highlight the importance of prevention.

### 2.1.4 Diagnosis and treatment

The fact that someone has diabetes is not the end of the story. In some cases, the sickness might go away completely if the person changes the way they live. Even so, many diabetics need to take pills to control their blood sugar levelsInsulin (which can be inhaled or injected) may be required if oral medications are insufficient, and it may be used with oral medications in some instances. A number of new medications that work with insulin to help regulate blood sugar levels have been approved by the (FDA) (Johns *et al.* 2018).

Acute symptoms of type 1 diabetes can come on quickly, and they are usually what make people check their blood sugar regularly. People over the age of 25 with a body mass index of over 25 and other risk factors such as abnormal cholesterol levels, a sedentary lifestyle, high blood pressure, heart disease, or a close relative, or a family history of polycystic ovarian syndrome with diabetes should be evaluated (Katsarou *et al.* 2017). If you are over 45 and haven't had one yet, you should get one as soon as you canIf the results are normal, the test should be repeated every three years. Finally, persons with prediabetes should have their blood sugar levels checked at least once a year (Tsimihodimos *et al.* 2018).

The initial glucose tolerance test was carried out. Beginning with the ingestion of a syrupy glucose solution, participants in the glucose challenge test will be evaluated. One hour later, a blood test will be conducted to determine the patient's glucose level. After a glucose challenge test, a normal blood sugar level is usually below 140 mg/dL (7.8 mmol/L) (Petrov 2020).

Glucose tolerance tests will be performed on an ongoing basis. It will be required to fast overnight before having its fasting blood sugar level measured. A woman is diagnosed with gestational diabetes if at least two of her blood sugar readings throughout each of the test's three hours are higher than the norms (Johns *et al.* 2018).

People with moderate diabetes are often instructed to begin with dietary changes, regular exercise, and diabetes education. As quickly as possible, those who are obese ought to slim down. People with high blood glucose levels, those with type 1 diabetes, and those with very high blood glucose all need medication (Sayin *et al.* 2015).

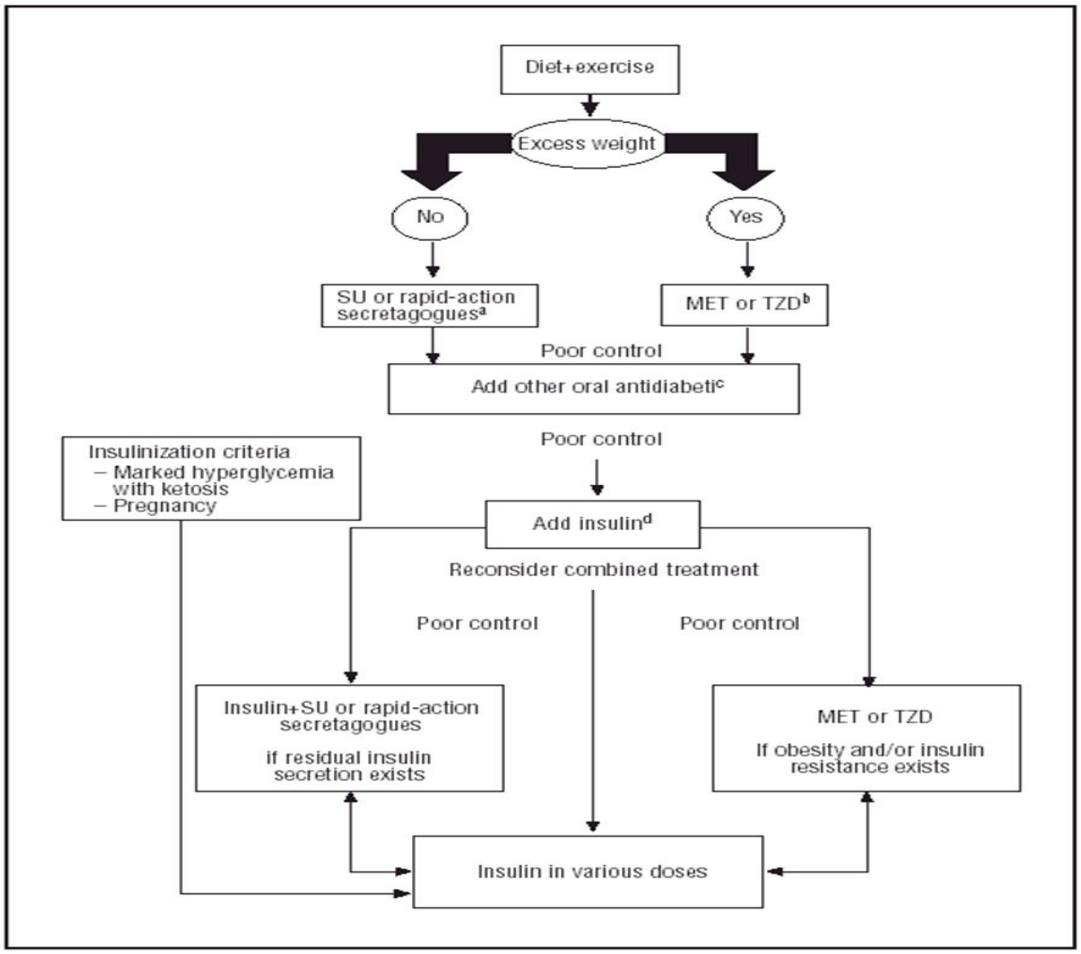


**Figure 2.2** Flowchart of DM treatment (Glovaci *et al.* 2019)

Diabetic patients are less prone to complications if they adhere to a tight blood glucose management plan, which is the primary goal of treatment. Preventing some of the consequences of diabetes may be as simple as addressing high blood pressure and excessive cholesterol. According to the American Heart Association, aspirin should be taken daily by those at risk of heart disease. All diabetics between the ages of 40 and 75 are prescribed statins, cholesterol-lowering drugs, no matter what their cholesterol level was when they were diagnosed. As an extra safety measure, people under 40 or over 75 who are more likely to get heart disease should also take a statin (Saedi *et al.* 2016).

In order to notify health care professionals to the presence of diabetes, Diabetes patients may benefit from carrying or wearing medical identification (such as a bracelet or tag). This information helps doctors and nurses start life-saving care as soon as possible,

especially if a patient has an accident or a mental change. High blood sugar levels, such as those associated with diabetes ketoacidosis and hyperosmolar hyperglycemia, may result in coma or death. Both diseases are treated in the same way: fluids and insulin are given through an IV as needed. For certain people, such as the elderly, who are especially susceptible to hypoglycemia, these goals are changed since intensive treatment to accomplish them increases the risk of blood glucose dropping too low (hypoglycemia), which is why they are modified (Al-Awar *et al.* 2016).

Keep your blood pressure under 140 and 90 mm Hg, respectively, as a precautionary measure as well. Patients with heart disease or a high risk of developing it should have blood pressure below 130/80 mmHg. Patients with diabetes gain a great deal from learning about the disease, addressing the effects of nutrition and exercise on blood glucose levels, as well as how to avoid issues. A diabetes educator, like a trained nurse, can offer dietary management advice, exercise, check blood sugar levels, and give medications (Paschou *et al.* 2018).

Controlling one's diet is essential for people suffering from any kind of diabetes mellitus. A healthy, balanced diet, as well as making an effort to maintain a healthy weight, are recommended by doctors for their patients. People with diabetes might find it helpful to work with a dietician or diabetes educator to make a diet plan that fits their needs. It is suggested that you stay away from simple sweets and processed foods, eat more fabric, and eat less carbohydrate and fat heavy foods (especially saturated fats). In order to prevent hypoglycemia, individuals on insulin should avoid fasting for lengthy periods of time between meals. Even while both protein and fat are important components of a person's calorie intake, only carbohydrates have a direct impact on blood glucose levels. Many diet-related information, including recipes. It is necessary to take cholesterol-lowering drugs even if a person follows a healthy diet in order to lessen their risk of cardiovascular disease (Petrov 2020).

## 2.2 C-Reactive Protein

The level of c-reactive protein (CRP) in your blood may be assessed by a CRP test. The liver produces CRP, which is a kind of protein. It is released into your circulation as a result of an inflammatory reaction. When you've been hurt or have an infection, your body responds by inflaming your tissues to defend them. Pain, redness, and swelling might occur in the wounded or afflicted region as a result of this condition. Inflammation may be caused by autoimmune illnesses and chronic diseases, among other things (Pathak and Agrawal 2019).

In normal circumstances, your blood contains modest quantities of c-reactive protein. Extremely high levels may indicate the presence of a significant illness or other condition. When there is an increase in inflammation in your body, the level its rises. In order to determine your C-reactive protein level, you may do a simple blood test (Sproston and Ashworth 2018).

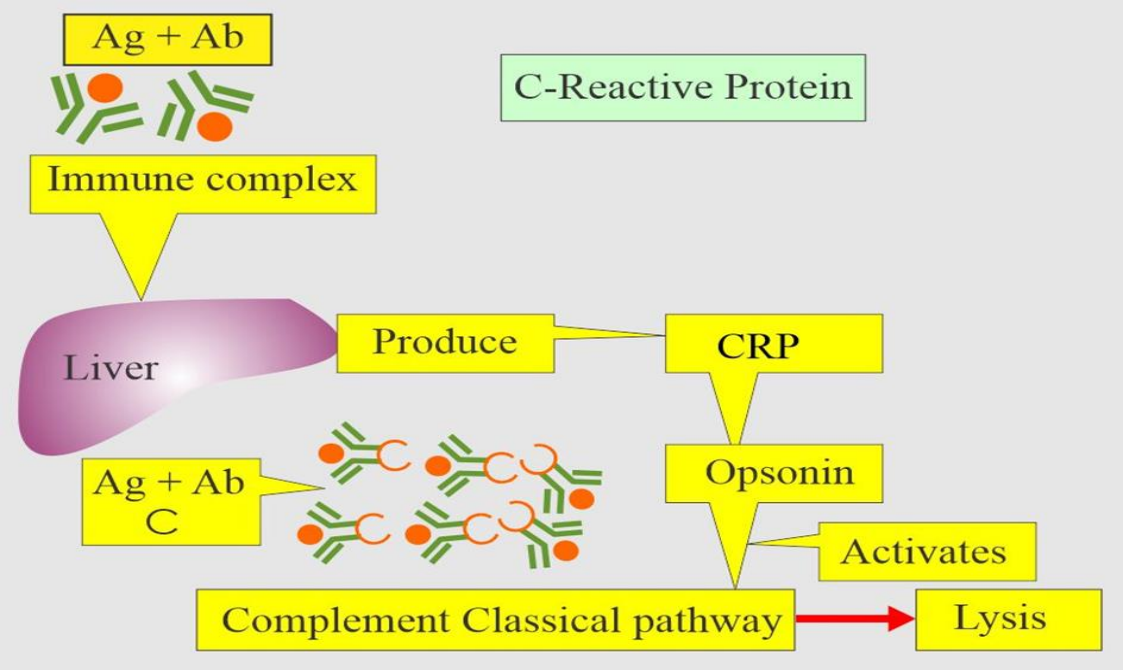


**Figure 2.3** Flowchart of CRP

Than properly identify inflammation, the high-sensitivity C-reactive protein (hs-CRP) test is superior to the normal CRP test. To put it another way, the high-sensitivity test may pick up on small changes in CRP levels that are otherwise undetectable. High cholesterol narrows the arteries of the heart, and this condition is known as coronary artery disease. The hs-CRP test may help assess whether or not a patient is at risk of acquiring this illness. A heart attack may be brought on by a condition known as coronary artery disease (Shrivastava *et al.* 2015).

Heart attacks and strokes are more likely in those with high levels of hs-CRP in their blood. To put it another way, those who have had heart attacks are more likely to have another heart attack than individuals with normal levels of hs-CRP. Everyone should avoid a hs-CRP test since it may be harmful. It is possible that a high level of inflammation might signal that your heart is unaffected by the inflammation, especially if the amount is much higher than normal (Moutachakkir *et al.* 2017).

When it comes to your heart health, it doesn't matter what your hs-CRP level is. People who are at moderate or high risk of having a heart attack during the next decade may benefit the most from having a hs-CRP test performed (Ridker 2016).

CRP levels that are elevated suggest that you are suffering from some kind of inflammation in your body, which is likely to be chronic. The results of a CRP test do not provide information on the source. Consequently, if your findings are abnormal, your health-care provider may conduct more tests to determine the cause of your inflammation (Tang *et al.* 2017).

A CRP test is commonly mistaken with a high-sensitivity (hs) CRP test, which is more sensitive. Despite the fact that they both detect CRP, they are used to diagnosis quite different diseases. An hs-CRP test detects substantially lower levels of CRP than a standard CRP test. It is used to determine whether or not a person is at risk for heart disease. The researchers discovered that persons with higher levels of CRP were two to three times more likely than those with lower levels of CRP to have a heart attack (Ahnach *et al.* 2020).

A research conducted on 100 persons with cardiovascular risk factors found that they were all healthy. Researchers discovered that a CRP level greater than 10 mg/L was associated with a 4 percent increased risk of acquiring a fatal cardiovascular disease after ten years of testing (Smilowitz *et al.* 2021).

Additionally, more recent study reveals that CRP may be utilized as a predictor of health outcomes associated with chronic obstructive pulmonary disease (COPD) in some circumstances. It is possible that your doctor may request a regular CRP test to identify you if they are worried that you are experiencing symptoms of other inflammatory disorders in addition to cardiovascular difficulties (Miller *et al.* 2014).

## 2.3 Hyperuricemia

### 2.3.1 Overview

High amounts of uric acid in the blood define hyperuricemia. You may get it via your body breaking down purines, a chemical component contained in certain foods. Hyperuricemia is the medical term for an unusually high quantity of uric acid in the blood. Gout, a severe type of arthritis that may be very painful, can be caused by high uric acid levels. It has been shown that high uric acid levels have been connected to several health issues, including kidney illness (Bardin and Richette 2014).

Long before the discovery of gout, individuals thought that hyperuricemia was the same condition as the arthritis in their joints. However, We now know that hyperuricemia may or may not lead to the development of gout in certain individuals. In reality, the vast majority of persons with elevated uric acid levels show no signs or symptoms at all (Kubota 2019).

It may arise as a consequence of your body creating excessive amounts of uric acid or excreting insufficient amounts. It arises as a result of an excessive amount of uric acid

in the circulation. It does not create any symptoms, but it may develop to illnesses such as gout or kidney stones, among others (Gliozzi *et al.* 2016).

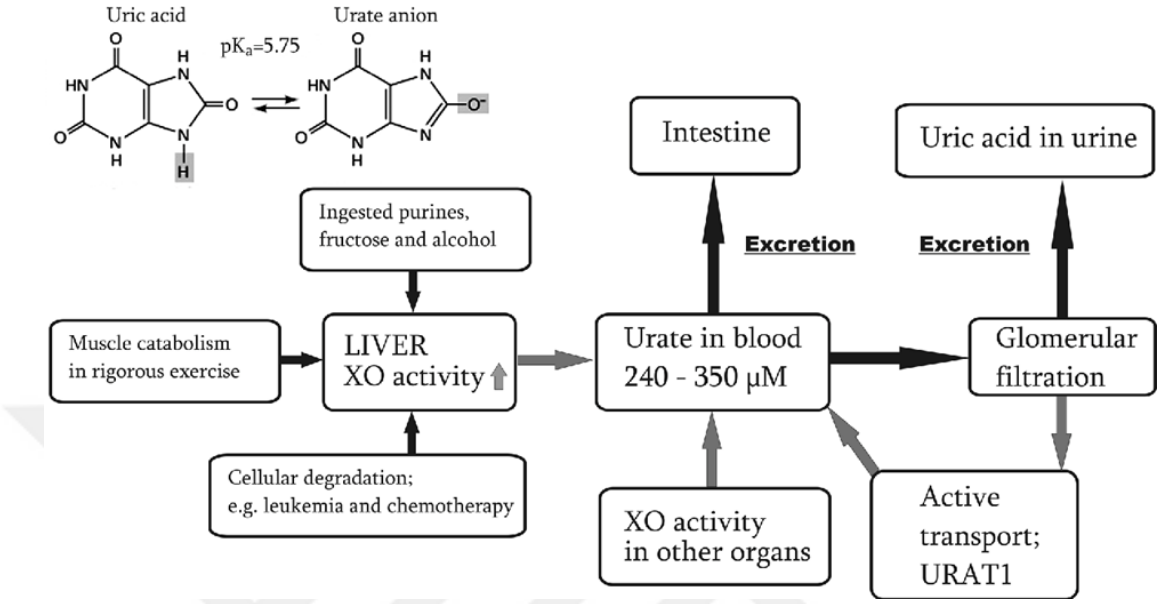


**Figure 2.4** The chemical structre and treatment of hyperuricemia (Billiet *et al.* 2014)

The body makes uric acid when it breaks down purine, which is a molecule that can be found in many different foods. The kidneys are in charge of getting rid of uric acid from the blood. Hyperuricemia happens when the amount of uric acid in the body is too high for the kidneys to work well. If you don't treat hyperuricemia, it can lead to more serious health problems like gout or kidney stones. These medical conditions need to be treated and cared for right away.

### 2.3.2 Symptoms and causes

When this happens, it is either because a person's kidneys are unable to expel enough uric acid or because they have an excessive amount of it in their system. This accumulation is often caused by a diet that is rich in purine, a chemical that may be found in a variety of foods and beverages (Li *et al.* 2020).

When the body breaks down purine as part of the digestive process, it generates uric acid as a byproduct of the process. Uric acid is released into the circulation as a result of this metabolism. The kidneys then filter it out of the bloodstream, allowing the body to eliminate it via the urine stream. Individuals who eat high purine diets may have renal failure as a result of their inability to filter uric acid out of the blood at a sufficient rate. This results in elevated quantities of uric acid in the blood, resulting in hyperuricemia (Kuwabara 2015).

The majority of persons who have hyperuricemia do not have any symptoms and do not need long-term treatment. Both the general population and hospitalization patients have asymptomatic hyperuricemia, meaning they do not exhibit any signs or symptoms of the illness. Most people with hyperuricemia end up with gout, which affects 3.9% of the general population in the United States. Urticaria is a condition in which uric acid builds up in the blood and tissues, making the joints, especially the big toe, hurt (Stewart *et al.* 2019).

One of the most frequent symptoms of hyperuricemia is the production of kidney stones, which may cause severe abdominal or side discomfort as well as nausea and vomiting. Hyperuricemia is a condition in which only roughly one-third of the population has symptoms. Asymptomatic hyperuricemia is the medical term for this condition. Although hyperuricemia is not a disease, if uric acid levels stay elevated for an extended period of time, they may contribute to a variety of illnesses (Borghi *et al.* 2014).

### 2.3.3 Diagnosis and treatment

Because hyperuricemia is such a prevalent illness, it is not routinely tested for in patients. If you're experiencing symptoms of gout or kidney stones, your doctor will most likely order a blood test to check for hyperuricemia. Physical examination, laboratory testing, and ultrasounds are all likely to be used by the team (Chalès 2019).

An examination of the body's functions. A swollen and hot joint is a sure sign that you have gout. Any joint in the body may be affected by gout, however it is most common in the great toe. Usually, only one joint is affected at a time. This area of your lower back will be sore to the touch if you have kidney stones. The results of research conducted in a lab Blood tests to measure your uric acid content may be ordered by your doctor. In addition, they may check your CBC, lipid profile, CMP, calcium and phosphate levels, and other tests to establish the source of your increased uric acid levels (Maruhashi *et al.* 2018).

Your physician may ask you to collect 24 hours' worth of urine so he or she may test it for uric acid. The diagnosis may be influenced by your gender, age, and nutritionIf you have kidney stones, your physician may recommend a kidney or renal ultrasound. Your doctor may request blood and urine tests to detect the levels of creatinine in your blood, which is used to indicate kidney function, as well as the levels of uric acid in your blood (Mallat *et al.* 2016).

A vein in the arm, usually on the inside of the elbow or the back of the hand, is used to draw blood. Because uric acid is expelled by the body, it might be found in the urine. When uric acid levels in the blood are high, a 24-hour urine collection may be recommended by your doctor if necessary. Any fluid that has accumulated in your joints will be tested by your doctor if you are suffering from the signs and symptoms of gout. This is accomplished by the use of a tiny needle to remove fluid from the joint. It will be transported to a laboratory, where it will be analyzed for the presence of uric acid crystals and other contaminants. The presence of these crystals implies that the person has gout (Abeles 2015).

The therapy for hyperuricemia will be determined by the underlying reason. If your hyperuricemia is asymptomatic, it is not suggested that you get therapy. In this case, there is no evidence that giving uric acid reducing medications will be of any help (Maharani *et al.* 2016).

# 3. MATERIALS AND METHODS

For this study, 115 blood samples were collected from individuals with hyperuricemia and type 2 diabetes, as well as individuals without type 2 diabetes and hyperuricemia, who were categorised as follows.

Group A: 25 healthy individuals without diabetes or hyperglycemia (control group).

Group B: consists of thirty patients with type 2 diabetes and no hyperglycemia.

Group C: consists of 30 patients with type 2 diabetes.

Group D: consists of 30 hyperuricemic individuals without diabetes.

## 3.1 Collection of Blood Sample

Each participant provided 7 mL of venous blood, of which 5 mL was placed in a centrifuge tube and 2 mL was placed in EDTA tubes for HbA1c testing, allowing the blood thts putted in gel tube to clot at room temperature before centrifuging the blood at 3000 rpm and extracting the serum. It was then kept at- 20°C in eppendrof tubes until the findings could be evaluated. When the serums of the patients and the controls were compared.

## 3.2 Biochemical Parameters and Chemicals

Table 3.1 contains the biochemicals that were employed in this study.

**Table 3.1** Biochemical used in study

| No. | Test | Company | Origin |
|---|---|---|---|
| 1 | RBS | biosystem | Spain |
| 2 | HbA1c | Roche | Switzerland |
| 3 | SUA | biosystem | Spain |
| 4 | Albumin | biosystem | Spain |
| 5 | Protein | biosystem | Spain |
| 6 | IL-8 | Thermo | Turkey |
| 7 | IL-6 | Thermo | Turkey |
| 8 | hsCRP | Roche | Switzerland |
| 9 | RF | Thermo | Turkey |
| 10 | ESR | Citotest | China |

### 3.3 Devices and Tools Used in the Study

Table 3.2 lists the devices and tools that were used in the investigation.

**Table 3.2** Tools and devices

| NO | Lists | Company | Country |
|---|---|---|---|
| 1. | Ultra violate visible Spectrophotometer | Unico | America |
| 2. | Automated ELISA system (reader, washer, printer) | Awareness | America |
| 3. | Incubator | Gallen Kamp | UK |
| 4. | Refrigerator 2-6 °C | Philips | Netherlands |
| 5. | Water bath | Memmert | Germany |
| 6. | Freezer - 20 °C | Uger | Turkey |
| 7. | Micropipettes 5-50, 0,5-10, 100-1000 µl | Eppendorf | Germany |
| 8. | Centrifuge | Sigma | Germany |
| 9. | Disposable plane tubes | Afma – Dispo | Germany |
| 10 | Disposable Syringes | Hayat | Turkey |
| 11 | Disposable micro tips | Medico | Germany |
| 12 | Gloves | Falcon | America |
| 13 | Gel tube | Sanli Medical | China |
| 14 | Eppendorf micropipettes with different sizes | Eppendorf | Germany |

### 3.4 Instrument and Materials

The instruments and materials utilised in the research are given in Table 3.3.

**Table 3.3** Instruments and materials that will be used in this study

| No | Instruments and materials | Company | origin |
|---|---|---|---|
| 1 | ELISA system Automated (Reader, Washer, printer) | Unico | USA |
| 2 | Cobas c111 | Roche | Switzerland |
| 3 | Deep Freezer (-80 °C) | Angel Antoni | Italy |
| 4 | Centrifuge | Kokusan | Germany |
| 5 | Incubator | Memmert | Germany |
| 6 | Gel Tubes | Afco | Jordan |
| 7 | Water bath | Kottermann | Germany |
| 8 | Spectrophotometer | Shimadzu | Japan |
| 9 | Micropipettes 5-50, 0,5-10, 100-1000 µl | Eppendorf | Germany |
| 10 | Disposable Syringes | Hayat | Turkey |
| 11 | Disposable plane tubes | Roche | Switzerland |
| 12 | Gloves | Falcon | USA |
| 13 | Disposable tips | Medico | Germany |
| 14 | Eppendorf micropipettes with different sizes | Eppendorf | Germany |
| 15 | ESR Tube (westergreen tube) | Citotest | China |
| 16 | EDTA Tubes | Afco | Jordan |

## 3.5 Determination of Biochemical Test

### 3.5.1 Principle of human IL-6 elisa kit

The (enzyme-linked immunosorbent assay) ELISA for Human IL-6 solid-phase sandwich detects the amount of a target bound to two antibodies. An antibody specific to the target has already been coated in each well of the given microplate. The samples, standards, or controls that bind to the immobile (captured) antibody are subsequently placed in these wells. The second (detector) antibody and a substrate solution are added to the sandwich. To generate a quantifiable signal, this solution interacts with the enzyme, antibody, and target. The amount of target in the original specimen determines the signal's strength.

### 3.5.2 Principle of human IL-8 elisa kit

The (enzyme-linked immunosorbent assay) ELISA for Human IL-8 solid-phase sandwich assesses the amount of a target bound to two antibodies. An antibody specific to the target has already been coated in each well of the given microplate. The samples,

standards, or controls that bind to the immobile (captured) antibody are subsequently placed in these wells. The second (detector) antibody and a substrate solution are added to the sandwich. To generate a quantifiable signal, this solution interacts with the enzyme, antibody, and target. The amount of target in the original specimen determines the signal's strength.

### 3.5.3 Principle of human hS CRP by cobas c111

Centrifugation separates the erythrocytes from the plasma in a capillary or venous blood sample. The plasma sample is then diluted with HEPES buffer and delivered to a reaction chamber, where it is combined with the other components. Latex reagent with CRP antibody. CRP binds to the CRP in the diluted plasma. Antibody to CRP on a latex particle. The CRP concentration is calculated. As a function of the difference in absorbance between 525 and 625 nm is proportional to the degree of agglutinationsample.

### 3.5.4 Principle of HbA1c by cobas c111

TRIS buffer is used to dilute blood and remove haemoglobin from erythrocytes. Material is transferred to a room where sodium lauryl sulphate is combined with it (SLS). The SLS-hemoglobin complex includes SLS. Using an SLS-hemoglobin combination with a 525 nm wavelength, the total hemoglobin concentration is determined. In another component of the sample, potassium ferricyanide and sucrose laurate denature hemoglobin A1c (HbA1c). HbA1c that has been denatured binds to HbA1c antibody on the latex particle. Then, to stop latex from sticking together, the agglutinator is used. It has a synthetic antigen that can link with HbA1c antibody. With a latex agglutination inhibition reaction kit, you can measure the latex agglutination inhibition response to find out how much HbA1c is in your blood.

### 3.5.5 Principle of serum protein

Copper salts bind to proteins in an alkaline solution to make a strong violet-blue complex. As an antioxidant, iodide is added. The total amount of protein in the sample is related to how bright the colour is.

### 3.5.6 Principle of serum albumin

Albumin changes the colour of the indicator from yellow-green to green-blue when bromocresol green is present and the pH is a little bit acidic. The strength of the colour is directly related to the amount of albumin in the sample.

### 3.5.7 Principle of serum uric acid

Uricase makes allantoin and hydrogen peroxide from uric acid (2H2 O2) Equation 3.1. When these are mixed with POD, 4-aminophenazone (4-AP), and 2-4 dichlorophenolsulfonate (DCPS) Equation (3.2), a red quinoneimine compound is made.

$$\boldsymbol{Uric\ acid\ +\ 2H2\,O\ +\ O2\ \rightarrow\ Allantoine\ +\ CO2\ +\ 2H2\,O2}$$

(3.1)

$$\boldsymbol{2H2O2\ +\ 4-AP\ +\ DCPS\ \rightarrow\ POD\ Quinoneimine\ +\ 4H2O}$$

(3.2)

The amount of red color generated is related to the amount of uric acid in the sample.

## 4. RESULTS AND DISCUSSION

There may be a link between uric acid levels and each of the factors that cause inflammation that have been looked into. This prognostic role of uric acid would serve as one of the early problems of a common complication of uncontrolled diabetes. The relationship has been studied according to the design of the study in the practical section and divided into four groups. The results were as per the tables 4.1:

**Table 4.1** Mean and standard deviation of age, weight, RF and some biochemical markers type 2 diabetic patients with hyperuricemia

| test | Groups | N | Mean | Std. Deviation | Std. Error Mean | P-value |
|---|---|---|---|---|---|---|
| Age | Group A | 25 | 30.10000 | 7.837942 | 2.478575 | 0.006 |
| | Group B | 30 | 44.40000 | 9.070097 | 2.868217 | 0.006 |
| | Group C | 30 | 42.70000 | 10.583530 | 3.346806 | 0.006 |
| | Group D | 30 | 37.40000 | 9.418658 | 2.978441 | 0.006 |
| | Total | 115 | 38.65000 | 10.550368 | 1.668160 | 0.006 |
| Weıghr | Group A | 25 | 80.30000 | 10.133004 | 3.204337 | 0.389 |
| | Group B | 30 | 86.40000 | 9.383200 | 2.967228 | 0.389 |
| | Group C | 30 | 85.30000 | 7.888811 | 2.494661 | 0.389 |
| | Group D | 30 | 85.90000 | 7.370361 | 2.330713 | 0.389 |
| | Total | 115 | 84.47500 | 8.776389 | 1.387669 | 0.389 |
| Length | Group A | 25 | 178.70000 | 13.233375 | 4.184761 | 0.263 |
| | Group B | 30 | 177.90000 | 11.836385 | 3.742993 | 0.263 |
| | Group C | 30 | 197.80000 | 45.237153 | 14.305244 | 0.263 |
| | Group D | 30 | 183.60000 | 9.547542 | 3.019198 | 0.263 |
| | Total | 115 | 184.50000 | 25.127368 | 3.972986 | 0.263 |
| SUA | Group A | 25 | 3.99130 | 1.377993 | 0.435760 | 0.000 |
| | Group B | 30 | 4.55108 | 1.732519 | 0.547871 | 0.000 |
| | Group C | 30 | 6.93268 | 1.079929 | 0.341504 | 0.000 |
| | Group D | 30 | 8.26727 | 1.118127 | 0.353583 | 0.000 |
| | Total | 115 | 3.99130 | 1.377993 | 0.435760 | 0.000 |
| ESR | Group A | 25 | 8.50000 | 2.549510 | 0.806226 | 0.001 |
| | Group B | 30 | 15.30000 | 5.735852 | 1.813836 | 0.001 |
| | Group C | 30 | 28.40000 | 7.947047 | 2.513077 | 0.001 |
| | Group D | 30 | 20.90000 | 6.154492 | 1.946221 | 0.001 |
| | Total | 115 | 18.27500 | 9.339707 | 1.476737 | 0.001 |
| hsCRP | Group A | 25 | 5.01746 | 1.862482 | 0.588968 | 0.001 |
| | Group B | 30 | 7.96981 | 1.574970 | 0.498049 | 0.001 |
| | Group C | 30 | 8.48345 | 1.706392 | 0.539609 | 0.001 |
| | Group D | 30 | 5.53256 | 1.278805 | 0.404393 | 0.001 |
| | Total | 115 | 6.75082 | 2.173470 | 0.343656 | 0.001 |
| RF | Group A | 25 | 3.03833 | 1.920794 | 0.607408 | 0.003 |
| | Group B | 30 | 6.21749 | 2.689921 | 0.850628 | 0.003 |
| | Group C | 30 | 6.88209 | 3.110518 | 0.983632 | 0.003 |
| | Group D | 30 | 13.74055 | 5.446895 | 1.722459 | 0.003 |
| | Total | 115 | 7.46961 | 5.216251 | 0.824762 | 0.003 |

### 4.1 Age, Weight and Length

The aim and outputs of this current study included a comparison between three groups of patients, and a group of healthy people as a control group, and the study was done as follows: Age (30.10000 ± 7.837942, 44.40000 ± 9.070097, 42.70000 ± 10.583530 and 37.40000 ± 9.418658 respectivly) was studied, and the results indicated that there were statistically significant differences, in contrast to weight (80.30000 ± 10.133004, 86.40000 ± 9.383200, 85.30000 ± 7.888811 and 85.90000 ± 7.370361 respectively) and height (178.70000 ± 13.233375, 177.90000 ± 11.836385, 197.80000 ± 45.237153 and 183.60000 ± 9.547542 respectively ), which did not have any significant differences or statistical significance for the study patients when compared to control group as shown in Table 4.1 and Figure 4.1.

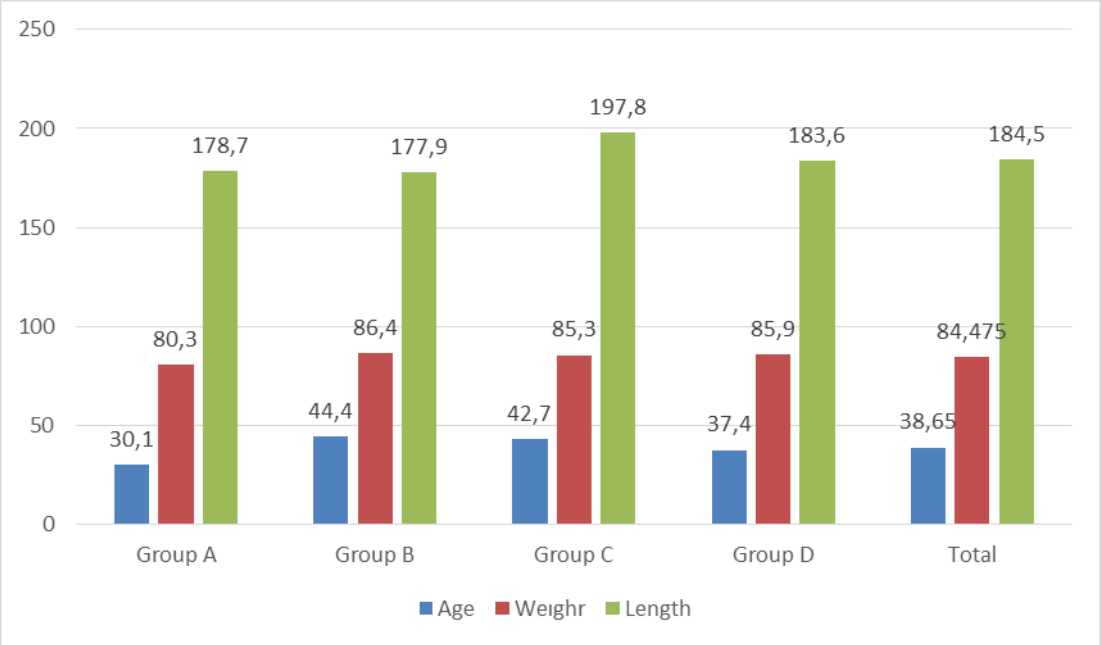


**Figure 4.1** The averages of age, weight and length for the patient compared to the control group

### 4.2 Serum Uric Acid

The serum uric acid mean in the disease targeted in our study groups recorded as (4.55108 ± 1.732519, 6.93268 ± 1.079929 and 8.26727 ± 1.118127 respectively) more than recorded in group A (control group) (5.01746 ± 1.862482), the resuls of serum uric acid intcated to high diffrence significant patients are shown in Table 4.1 and Figure 4.2.

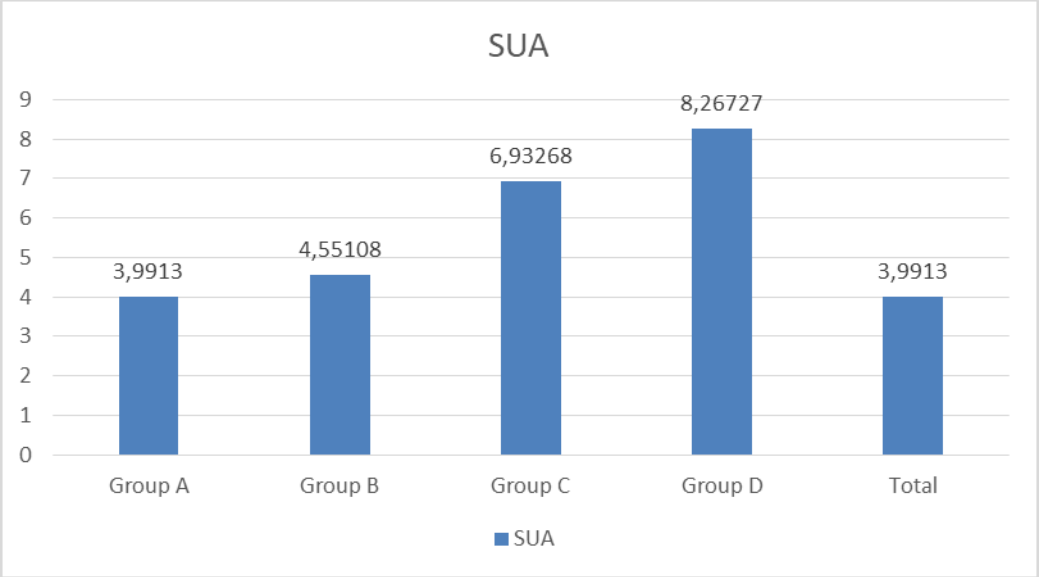


**Figure 4.2** The averages of SUA for the patient compared to the control group

### 4.3 ESR

Erythrocyte Sedimentation Rate (ESR) mean in the disease targeted in our study groups recorded as (15.30000 ± 5.735852, 28.40000 ± 7.947047 and 20.90000 ± 6.154492 respectifely) more than recorded in group A (control group) (90.3 ± 11.95), the resuls of ESR indicated to high difterince significant as shown in Table 4.1 and Figure 4.3.

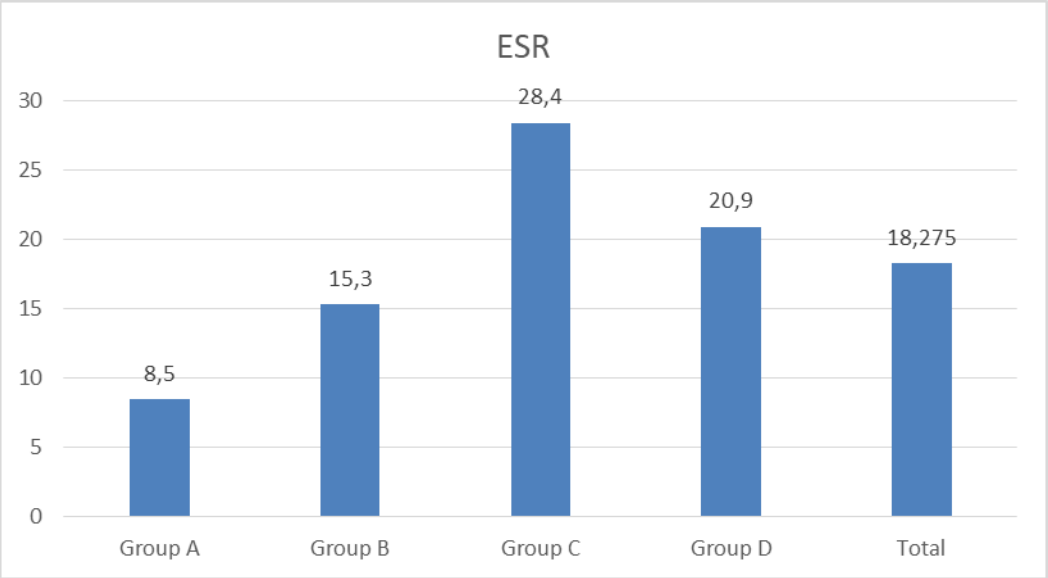


**Figure 4.3** The averages of ESR for the patient compared to the control group

### 4.4 hsCRP and RF

The level or concentration of hsCRP and RF in the disease targeted in our study groups recorded as (7.96981 ± 1.574970, 8.48345 ± 1.706392, 5.53256 ± 1.278805 and 6.21749 ± 2.689921, 6.88209 ± 3.110518, 13.74055 ± 5.446895 respectifely) more than recorded in group A (control group) (90.3 ± 11.95 and 3.03833 ± 1.920794), the resuls of hsCRP and RF indicated to low difterince significant as shown in Table 4.1 and Figure 4.4.

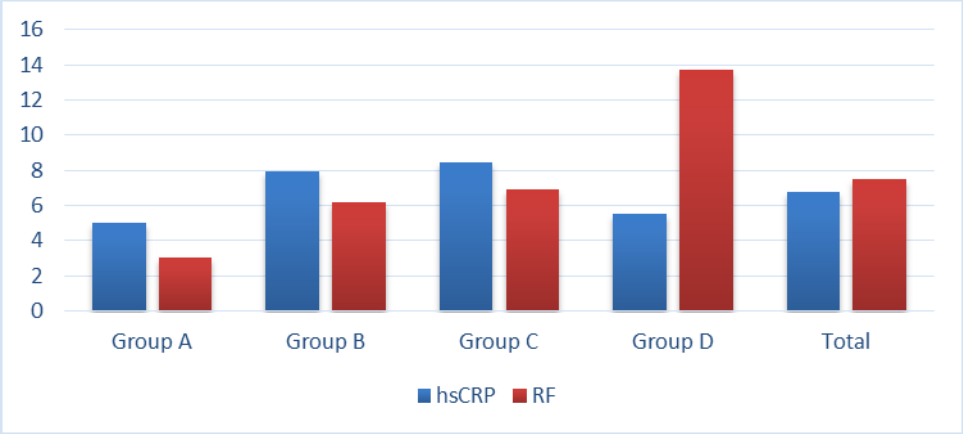


**Figure 4.4** The averages of hsCRP and RF for the patient compared to the control group

### 4.5 Random Blood Sugar and Interleukin 8

The level or concentration of glcose and HbA1c in the disease targeted in our study groups recorded as (210.10000 ± 36.915670, 189.40000 ± 14.009521, 94.80000 ± 9.908470 and 4.17459 ± 1.022694, 4.52390 ± 0.819412, 4.74084 ± 1.250304 respectifely) more than recorded in group A (control group) (95.30000 ± 11.972654 and 4.58694 ± 1.518128), the resuls of glcose and HbA1c indicated to high difterince significant as shown in Table 4.2 and Figure 4.5.

The mean of interleukin 8 in the disease targeted in our study groups recorded as (74.20027 ± 20.317766, 64.22013 ± 11.750700, 49.55456 ± 13.806527 respectively) more than recorded in group A (control group) (37.78028 ± 8.478267), the resuls of interleukin 8 indicated to high difterince significant as shown in Table 4.2 and Figure 4.5.

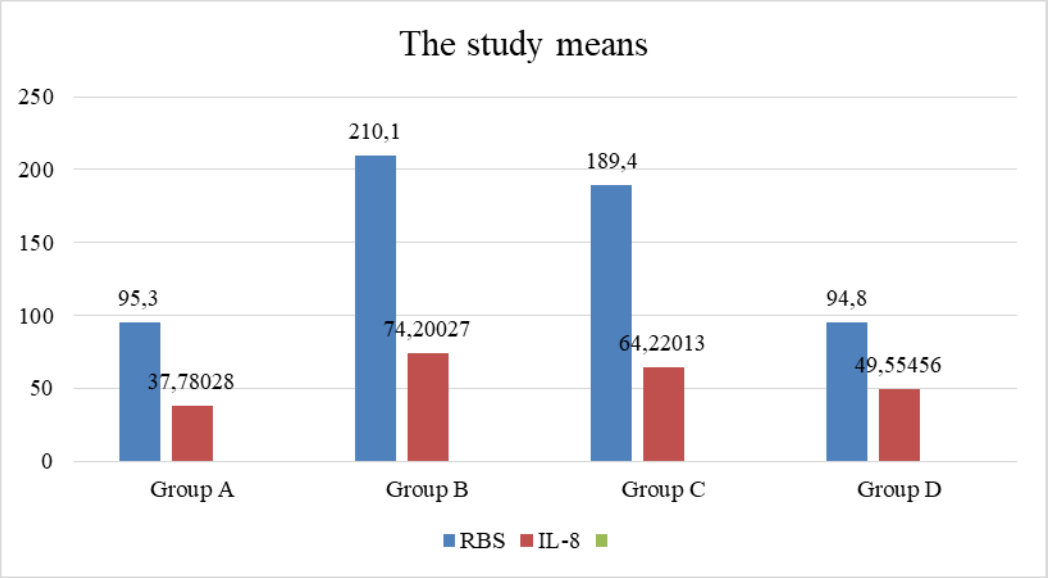


**Figure 4.5** The averages of RBS and Interleukin 8 for the patient compared to the control group

### 4.6 Albumin and Protein

The mean of serum Albumin and Protein in the disease targeted in our study groups recorded as (7.90182 ± 3.616468, 6.48864 ± 2.696070, 20.25565 ± 3.226387 and 8.26727 ± 1.118127 respectively) more than recorded in group A (control group) (16.51719 ± 3.007085 and 4.33773 ± 0.641708), the resuls of serum Albumin and Protein indicated to high diffrence significant as shown in Table 4.2 and Figure 4.6.

### 4.7 Interleukin 6

The level or concentration of interleukin 6 in the disease targeted in our study groups recorded as (7.01980 ± 1.640538, 6.13556 ± 0.579382, 7.15438 ± 1.074041 respectively) more than recorded in group A (control group) (6.53950 ± 1.431059), the resuls of interleukin 6 indicated to high difterince significant as shown in Figure 4.6 and Table 4.2.

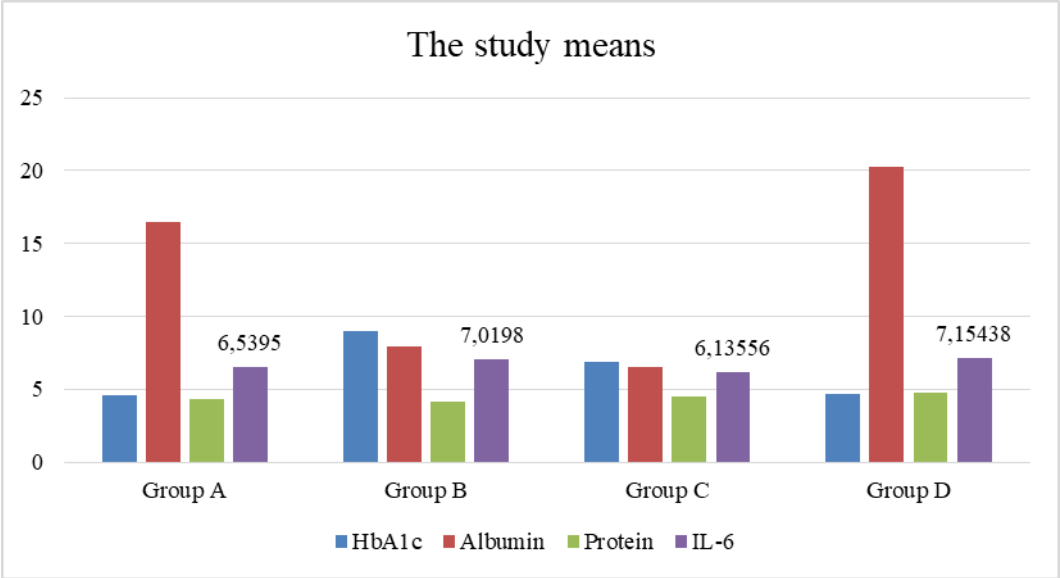


**Figure 4.6** The averages of albumin, protein, IL-6 and HbA1c for the patient compared to the control group

**Table 4.2** Mean and standard deviation of RBS, HbA1c, IL6, IL8 and some biochemical markers type 2 diabetic patients with hyperuricemia

| Test | **Groups** | **N** | **Mean** | **Std. Deviation** | **Std. Error Mean** | P-value |
|---|---|---|---|---|---|---|
| RBS | Group A | 25 | 95.30000 | 11.972654 | 3.786086 | 0.000 |
| | Group B | 30 | 210.10000 | 36.915670 | 11.673760 | 0.000 |
| | Group C | 30 | 189.40000 | 14.009521 | 4.430199 | 0.000 |
| | Group D | 30 | 94.80000 | 9.908470 | 3.133333 | 0.000 |
| | Total | 115 | 147.40000 | 57.282386 | 9.057141 | 0.000 |
| HbA1c | Group A | 25 | 4.58694 | 1.518128 | 0.480074 | 0.001 |
| | Group B | 30 | 8.94613 | 2.068303 | 0.451669 | 0.001 |
| | Group C | 30 | 6.90761 | 1.422576 | 0.449858 | 0.001 |
| | Group D | 30 | 4.65559 | 1.327564 | 0.419813 | 0.001 |
| | Total | 115 | 6.27407 | 2.282880 | 0.360955 | 0.001 |
| Albumin | Group A | 25 | 16.51719 | 3.007085 | 0.950924 | 0.024 |
| | Group B | 30 | 7.90182 | 3.616468 | 1.205489 | 0.024 |
| | Group C | 30 | 6.48864 | 2.696070 | 0.852572 | 0.024 |
| | Group D | 30 | 20.25565 | 3.226387 | 1.020273 | 0.024 |
| | Total | 115 | 12.91618 | 6.595247 | 1.056085 | 0.024 |
| Protein | Group A | 25 | 4.33773 | 0.641708 | 0.202926 | 0.604 |
| | Group B | 30 | 4.17459 | 1.022694 | 0.323404 | 0.604 |
| | Group C | 30 | 4.52390 | .819412 | 0.259121 | 0.604 |
| | Group D | 30 | 4.74084 | 1.250304 | 0.416768 | 0.604 |
| | Total | 115 | 4.43666 | 0.936985 | 0.150038 | 0.604 |
| IL-6 | Group A | 25 | 6.53950 | 1.431059 | 0.452541 | 0.048 |
| | Group B | 30 | 7.01980 | 1.640538 | 0.546846 | 0.048 |
| | Group C | 30 | 6.13556 | 0.579382 | 0.499444 | 0.048 |
| | Group D | 30 | 7.15438 | 1.074041 | 0.497755 | 0.048 |
| | Total | 115 | 6.70442 | 1.548672 | 0.247986 | 0.048 |
| IL-8 | Group A | 25 | 37.78028 | 8.478267 | 2.681063 | 0.003 |
| | Group B | 30 | 74.20027 | 20.317766 | 12.749597 | 0.003 |
| | Group C | 30 | 64.22013 | 11.750700 | 3.715898 | 0.003 |
| | Group D | 30 | 49.55456 | 13.806527 | 4.366007 | 0.003 |
| | Total | 115 | 56.43881 | 25.795270 | 4.078590 | 0.003 |

### 4.8 Correlation Among Parameters of the Study at all Groups

When doing the Pearson test, there was a correlation between uric acid with ESR, hsCRP, RF, RBSIL6 and IL8 (r = 0.504**, r = 0.616**, r = 0.675**, r =0.362*, r = 0.131*, r = 0.640*) at P = <0.05. At the same time, there was no association with age, weight, length, HbA1c, Albumin and protein as in the Table 4.3.

**Table 4.3** Correlation among parameters in all groups

| Parameters | Result = r | P -value |
|---|---|---|
| SUA - Age (Year) | 0.059 | 0.718 |
| SUA – Weight | 0.120 | 0.461 |
| SUA – Length | 0.074 | 0.651 |
| SUA – ESR | 0.504** | 0.001 |
| SUA – hsCRP | 0.616** | 0.000 |
| SUA – RF | 0.675** | 0.015 |
| SUA – RBS | 0.362* | 0.031 |
| SUA – HbA1c | 0.199 | 0.218 |
| SUA – Albumin | 0.188 | 0.251 |
| SUA – Protein | 0.030 | 0.857 |
| SUA – IL-6 | 0.131* | 0.030 |
| SUA – IL-8 | 0.640* | 0.017 |

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## 5. CONCLUSIONS AND RECOMMENDATION

One of the goals of the research is to find out if there is a link between uric acid levels and each of the inflammatory factors that have been looked at. The results indicate that age has a clear importance, as the higher the age, the higher the disease rate. There was no statistical significance for weight and height when performing the statistical analysis. The lion vein had great statistical significance among the study groups, which indicates the influence of its levels between groups. Also for the erythrocyte sedimentation rate test, hsCRP, RF, interleukin-6 and interleukin-8, which indicate inflammation increases in diabetic patients with changes in the levels of uric acid.

Type 1 and type 2 diabetic individuals had higher rates of hyperuricemia than type 0 diabetics in our research. The early detection and treatment of hyperuricemia in diabetics was made possible by systolic hypertension, a family history of diabetes, and a BMI of 25 kg/m2. Cardiovascular disease is more common in people with type 2 diabetes, in part because of risk factors such high uric acid levels (Woldeamlak *et al.* 2019).

With the enhancement and expansion of research methods and uric acid research, it has expanded, particularly in the investigation of metabolic illnesses. Gout has been linked to obesity, the human metabolic syndrome, non-alcoholic fatty liver disease, diabetes, and other metabolic disorders, according to a new study. And it's thought to be a factor in the outbreak. Uric acid generates a variety of pathophysiological changes that make it easier for diabetic people to develop and proceed with diabetes, including inflammation, oxidative stress, vascular endothelial damage, etc. This review confirmed, through aetiology and clinical research, the connection between uric acid and diabetes mellitus in patients, as well as its long-term negative effects.

Hyperuricemia, or elevated amounts of uric acid in the blood, has long been recognized as a predisposing factor to diabetes, especially type 2. However, little is understood about how changes in hyperuricemia affect diabetes risk and how inflammatory mechanisms function. People with hyperuricemia, which is caused by hyperuricemia,

were 35 to 48 percent more likely to get type 2 diabetes than people without hyperuricemia. Also, having hyperuricemia for a long time was linked to a 75 percent higher chance of getting diabetes. Compared to small changes in serum uric acid (SUA). Changes in serum or hyperuricemia, especially persistent hyperuricemia, are better indicators of the risk of developing type 2 diabetes than a single measure of hyperuricemia at baseline.

Diabetes is substantially more likely to develop in patients with hyperuricemia, even when other risk factors are taken into consideration. About 8.7% of all new occurrences of type 2 diabetes are thought to be brought on by hyperuricemia, according to research. Hyperuricemia increases the risk of developing type 2 diabetes. Hyperuricemia is statistically more common in diabetics than in non-diabetics (Krishnan *et al.* 2013).

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