A THESIS SUBMITTED TO
THE GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES
OF ÇANKIRI KARATEKİN UNIVERSITY

CORRELATION OF PLASMA ASPROSIN AND INSULIN RESISTANCE IN IRAQI PATIENTS WITH IMPAIRED FASTING GLUCOSE

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

BY

NEHAD RASHEED SALMAN SALMAN

ÇANKIRI

2022

CORRELATION OF PLASMA ASPROSIN AND INSULIN RESISTANCE IN IRAQI PATIENTS WITH IMPAIRED FASTING GLUCOSE

By Nehad Rasheed Salman SALMAN

Jun 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

Advisor **:** Prof. Dr. Volkan EYÜPOĞLU
Co-Advisor **:** Asst. Prof. Dr. Raid D. HASHIM

Examining Committee Members:

Chairman **:** Prof. Dr. Volkan EYÜPOĞLU
Chemistry
Çankırı Karatekin University

Member **:** Asst. Prof. Dr. Ümit YIRTICI
Medical Laboratory
Kırıkkale University

Member **:** Assoc. Prof. Dr. Şevki ADEM
Chemistry
Çankırı Karatekin University

Approved for the Graduate School of Natural and Applied Sciences

Prof. Dr. İbrahim ÇİFTÇİ
Director of Graduate School

I hereby declare that all information in this document has been obtained and presented in accordance with academic rules and ethical conduct. I also declare that, as required by these rules and conduct, I have fully cited and referenced all material and results that are not original to this work.

Nehad Rasheed Salman SALMAN

ABSTRACT

CORRELATION OF PLASMA ASPROSIN AND INSULIN RESISTANCE IN IRAQI PATIENTS WITH IMPAIRED FASTING GLUCOSE

Nehad Rasheed Salman SALMAN

Master of Science in Chemistry

Advisor: Prof. Dr. Volkan EYÜPOĞLU

Co-Advisor: Asst. Prof. Dr. Raid D. HASHIM

Jun 2022

According to their fasting blood glucose levels, the participants were separated into two groups in this research. Group we enrolled 120 adult participants with impaired fasting defined as fasting blood glucose ≥ 100 mg/dL. Group 2 enrolled 120 adult participants with normal fasting blood glucose (< 100 mg/dL). Both groups included age, length, sex and body mass index matched to eliminate any possible effect on the measured parameters. Each participant's weight and height be measured in order to determine their BMI. study included estimate plasma Asprosin, plasma insulin by ELISA technique (human company), plasma Glucose in full automated Integra (Roche company) and calculate HOMA-HOMA-IR according to the main equation. There was no significant difference in the mean of BMI (26.87) between the control and IFG group. In respect to Asprosin there was a significant difference in its mean (3.06) between the control group and IFG group. Regrading insulin plasma level, there was a significant difference in its mean (9.14) between the control group and IFG group, Furthermore, a significant difference was estimated in the mean (2.48) of HOMA-IR between the control group and IFG group.

2022, 36 pages

Keywords: Enzyme kinetic, Diabetes, Insulin, Asprosin, IR, IFG

ÖZET

IRAKLI HASTALARDA AÇLIK GLİKOZ BOZUKLUĞU OLAN HASTALARDA PLAZMA ASPROSIN VE İNSÜLİN DİRENCİ İLİŞKİSİ

Nehad Rasheed Salman SALMAN

Kimya, Yüksek Lisans

Tez Danışmanı: Prof. Dr. Volkan EYÜPOĞLU

Eş Danışman: Dr. Öğr. Üyesi Raid D. HASHIM

Haziran 2022

Bu çalışmada katılımcılar açlık kan şekerlerine göre 2 gruba ayrıldı. Açlık kan şekeri ≥ 100 mg/dL olarak tanımlanan açlık bozukluğu olan 120 yetişkin katılımcıyı gruba dahil ettik. Grup 2, normal açlık kan şekeri (< 100 mg/dL) olan 120 yetişkin katılımcıyı kaydetti. Her iki grup da ölçülen parametreler üzerindeki olası herhangi bir etkiyi ortadan kaldırmak için yaş, uzunluk, cinsiyet ve vücut kitle indeksi eşleştirildi. BMI'larını belirlemek için her katılımcının kilosu ve boyu ölçülecektir. çalışma, plazma Asprosin'i, ELISA tekniği (insan şirketi) ile plazma insülini, tam otomatik Integra'da (Roche şirketi) plazma Glikozu tahmin etmeyi ve ana denkleme göre HOMA-HOMA-IR'yi hesaplamayı içeriyordu. Kontrol ve IFG grubu arasında VKİ ortalamasında (26.87) anlamlı bir fark yoktu. Asprosin ile ilgili olarak, kontrol grubu ve IFG grubu arasında ortalamasında (3.06) önemli bir fark vardı. İnsülin plazma düzeyi yeniden düzenlendiğinde, kontrol grubu ile IFG grubu arasında ortalamasında (9.14) anlamlı bir fark vardı, ayrıca kontrol grubu ile IFG grubu arasında HOMA-IR ortalamasında (2.48) anlamlı bir fark tahmin edildi.

2022, 36 sayfa

Anahtar Kelimeler: Enzim kinetiği, Diyabet, İnsülin, Asprosin, IR, IFG

PREFACE AND ACKNOWLEDGEMENTS

I would like to thank my thesis advisor, Prof. Dr. Volkan EYÜPOĞLU and Asst. Prof. Dr. Raid D. HASHIM, for his patience, guidance and understanding.

Nehad Rasheed Salman SALMAN

Çankırı-2022

CONTENTS

LIST OF SYMBOLS

%	Percent
±	Plus-minus
°C	Degrees Celsius
dL	Deciliter
g	Gram
L	Liter
m^2	Square-meters
mg	Milligram
mL	Milliliters
ng	Nanogram
nmol	Nanomoles
U	Unit

LIST OF ABBREVIATIONS

ADA	American diabetes association
BMI	Body mass index
ELISA	Enzyme linked immune surbant assay
EMRO	Eastern mediterranean region
EVOO	Extra-virgin olive oil
HOMA-IR	Homeostasis model assessment of insulin resistance
IDF	International diabetes federation
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
IR	Insulin resistance
NAFLD	Non-alcoholic fatty liver disease
NGT	Normal glucose tolerance
NIH	National institutes of health
OGTT	Oral glucose tolerence test
T1DM	Type I diabetes
T2DM	Type II diabetes
WHO	World health organization

LIST OF FIGURES

LIST OF TABLES

1. INTRODUCTION

Asprosin is a newly discovered protein produced primarily by adipocytes from white adipose tissue during fasting conditions. It increases the release of glucose from hepatic cells as a glucogenic peptide by binding to the OLFR734 receptor and activating the G protein-cAMP-PKA pathway(Mazur-Bialy, 2021). During the process of the secretory route, the C-terminal peptide of the extracellular matrix protein fibrillin-1 is cleaved off and becomes asprosin. This process is catalyzed by the propeptide convertase furin (Janoschek *et al.* 2020). This adipokine has an effect on the control of glucose homeostasis, as well as the regulation of food intake and energy balance. However, there is ongoing discussion over the significance of asprosin in the control of glucose homeostasis, especially in youngsters (Corica *et al.* 2021). Insulin is a peptide hormone made up of 51 amino acids produced by the pancreas'-cells. Insulin peptide is primarily formed as preproinsulin, which is fractionated into proinsulin and then separated into two peptides, C-peptide and insulin. Insulin creation is influenced by a variety of circumstances.The metabolism of glucose is the only and most important physiological technique that drives the transcription and translation of insulin and RNA, respectively. Insulin is produced in two phases in response to high blood glucose levels following food consumption and absorption, and it links to insulin receptors found in muscle, liver, and adipose tissue.Insulin secretion from pancreatic -cells is triggered by an increase in glucose(Al-Khafajy *et al.* 2021).

During the OGTT, those with isolated IFG and those with IFG/IGT had higher fasting insulin levels compared to individuals with NGT. There was no difference between the groups after 30 minutes, but the people who had impaired glucose tolerance had greater insulin levels than those who had normal glucose tolerance at all subsequent time periods. During the OGTT, there was no discernible difference between the groups in terms of the ratio of glucose to insulin AUC (Laakso *et al.* 2008). The homeostasis model assessment of insulin resistance (HOMA-IR) approach is used to determine an individual's level of insulin resistance. The (HOMA-IR) cut-offs for detecting metabolic syndrome may differ depending on the demographic and BMI level. to look into which HOMA-insulin

resistance cut-offs best distinguish people with insulin resistance and metabolic syndrome in each BMI group of persons without diabetes (Diniz *et al.* 2020). PCOS is a complicated and heterogeneous endocrine condition marked by oligo-anovulation, metabolic abnormalities, and hyperandrogenism, such as excessive weight or obesity, insulin resistance, T2DM, dyslipidemia, and an elevated risk of cardiovascular disease (Zeng *et al.* 2020). The body mass index, often known as BMI, is a statistical indicator that measures the amount of body fat in both men and females of any age by using a person's height in addition to their weight. To calculate a person's body mass index, or BMI, just divide their weight in kilograms by the square of their height in meters. After that, the person's body mass index is determined by applying this equation. BMI, or body mass index, is a more accurate method than traditional height vs. weight charts for determining if a person is underweight, normal weight, overweight, or obese. These categories of body mass index (BMI) are used for persons of White, Hispanic, and Black ancestry by the National Institutes of Health (NIH) and the World Health Organization (WHO) (Weir and Jan 2021). as a consequence, there was a fast release of glucose into the circulation. Asprosin levels in the plasma of humans who have insulin resistance are abnormally high, and removing its ability to function, whether by immunologic or genetic methods, has a significant impact on glucose and insulin levels due to a reduction in the amount of glucose released by the liver. Therefore, it was necessary to conduct research and studies to find out the extent of the relationship investigate asprosine as an indicator of insalin resistance (Aim).

2. LITERATURE REVIEW

2.1 Impaired Fasting Glucose

Impaired fasting glucose (IFG) is described as a type II diabetes prodrome (T2D). Obesity, an insufficient physical activity, and poor meal planning are all known risk factors for both illnesses. Although it is widely known that a balanced food and lifestyle can considerably lower the incidence of both IFG and T2D, current researchers have highlighted the significance of genetic predisposition during development of DM (Dong *et al.* 2019). Diabetes mellitus is a common side effect that may occur when high blood sugar levels go untreated. This condition is connected to long-term organ damage, dysfunction, and failure. Since 1980, there has been a roughly twofold increase in the number of adults throughout the world who have diabetes. The continued considerable growth in diabetes will have dire effects for the health and longevity of the global population, as well as on the global economy, unless comprehensive preventive and management programs are implemented (Ota and Ulrih 2017).

2.1.1 Epidemiology

The (IDF) has estimated that around 96,000 new cases of type 1 diabetes are diagnosed annually among children and adolescents less than 15 years old all over the globe. These patients are located in every region of the world. The United States, India, Brazil, China, the United Kingdom, the Russian Federation, the United Arab Emirates, Saudi Arabia, and Nigeria are among the top ten countries with the highest number of newly reported cases. Together, these countries account for more than sixty percent of all newly reported cases. Germany is the eleventh country on the list with a newly reported case. There is an approximately 400-fold increase in the prevalence of type 1 diabetes in children across countries (Mirzaei *et al.* 2020). It is anticipated that 8.5% of people over the age of 18 will have diabetes in 2014; this represents a significant increase over the course of the preceding three decades, especially in nations with a low and moderate income. The EMRO had the greatest incidence of diabetes in comparison to other areas in 2014, with an average prevalence of 13.7% in the adult population. This was the highest rate among

all regions (Mirzaei *et al.* 2020). Irregular fasting glucose (IFG), undiagnosed diabetes, and confirmed diabetes all have high incidence rates, as well as the correlations between these conditions and occupational categories, were investigated using a sample of the working population in Spain that was intended to be representative of the country as a whole. The following are the materials and procedures: A cross-sectional survey of employees who had regular medical checkups in 2007 was carried out beginning in January and continuing through December. Along with a structured interview, we also did physical tests and regular testing of the biochemical composition of the blood. A prior diagnosis of type 1 diabetes, therapy with oral anti-diabetic medications or insulin, or fasting glucose levels of (126 mg/dL) were the three criteria that were used to establish type 1 diabetes in accordance with ADA guidelines. According to the criteria established by the ADA, T2DM was classified as having a prior diagnosis of T2DM, being treated with oral antidiabetic medications or insulin, or having fasting glucose readings of (126 mg/dL) (Reviriego *et al.* 2016). From NGT to T2DM, there is a development in glucose homeostasis, the American Diabetes Association (ADA) established a separate intermediate state called impaired fasting glucose (IFG). Because people who have IFG also have a significant risk of acquiring type 2 diabetes, the diagnostic criteria for IFG were established to be very similar to those of IGT. In epidemiological research, participants with isolated IGT and those with isolated IFG were shown to have comparable chances of acquiring type 2 diabetes. IFG was only present in 45% of the participants who also had IGT, while IGT was only present in 25% of the patients who also had IFG. Due to the fact that IFG and IGT only share a small amount of common ground, it may be deduced that the disturbances in glucose homeostasis are brought on by distinct pathophysiological mechanisms. IFG must be separated from IGT, and the combined IFG/IGT secretion as well as insulin resistance must be analyzed separately (Abdul-Ghani *et al.* 2006). In this particular research, there were a total of 319 participants who were diagnosed with either NGT, IFG, or IGT, and 58 of these participants participated in an insulin clamp study under euglycemic conditions (Abdul-Ghani *et al.* 2006). In 2045, the prevalence of prediabetes, which comprises impaired fasting glucose (IFG) and impaired glucose tolerance, may reach an epidemic level of 8.6%, with 72 percent of those affected coming from LMICs(Orazumbekova et al., 2022).

2.1.2 Risc factors

Impaired fasting glucose levels are a precursor to diabetes, a well-known risk factor for atrial fibrillation (AF), which is one of the most prevalent causes of AF (IFG). IFG is a prevalent condition, but few treatments are available for it since it is often considered to be clinically normal. It was discovered that IFG and pre-hypertension are substantial risk factors for atrial fibrillation in healthy Asian persons who do not have any other comorbidities. IFG was related with a higher diastolic blood pressure (hazard ratio = 1.16), and the likelihood of atrial fibrillation (hazard ratio = 1.11) was a stronger predictor of atrial fibrillation than systolic blood pressure (HR, 1.11). The risk of atrial fibrillation increased in parallel with the risk of intraventricular fibrillation (IFG), pre-hypertension, and a body mass index (BMI) of less than 25 kg/m2. Persons who had all three risk factors had a significantly higher risk of atrial fibrillation (HR, 1.5) than those who didn't have any of them, even in a sample of people who were otherwise healthy. Subjects who had a body mass index of (25 kg/m^2) had a higher risk of atrial fibrillation (HR, 1.18) in comparison to those who had a BMI of (25 kg/m^2), and subjects who had both insulin resistance and pre-hypertension had a higher risk of atrial fibrillation (HR, 1.27) in comparison to those who do not have either of these conditions. In a population of healthy people, the BMI-dependent effects of pre-hypertension and IFG revealed a pattern that was comparable to that seen for AF-related stroke, mortality, and HF(Joung, 2019). IFG determines a person's risk for developing diabetes, cardiovascular disease, or dying too soon. Asymptomatic IFG determination Individuals enables the implementation of prophylactic measures that can postpone or stop the beginning of T2D. Overall IFG has been found to have a prevalence of 5.0 percent or higher, with differences between age groups and between individuals.popula- tions World prevalence of IFG, adjusted for age In 2011, the African region of the World Health Organization was 9.7%.compared to estimates for the entire world of 6.5%(Kufe et al., 2015).

2.1.3 Prognosis

The patients had an average age of 57 years old (interquartile range of 38–66), with 172 of them being female (55 percent of the total). At the time of admission, there were 166

patients whose fasting glucose levels were within the normal range (NFG), while there were 62 patients who had impaired fasting glucose (IFG) and 84 patients who had diabetes (of whom 36 had only just been diagnosed). Those who had both IFG and diabetes had a greater risk of events that make up the main composite endpoints, Multivariable Cox regression analyses revealed that diabetes was linked to an increased risk of primary composite end-point events and mortality, and that IFG was linked to an increased risk of mortality. This was the case despite the fact that age, sex, hospitals, and comorbidities were all taken into consideration (Zhang *et al.* 2020).

2.1.4 Treatment

Because prediabetes (IGT and IFG) and diabetes are a continuum of dysglycemia and cardiovascular risk, the same ideas that apply to type 2 diabetes diagnostic and therapy should also apply to the prediabetic condition (DeFronzo and Abdul-Ghani 2011).

2.2 Asprosin

Asprosin is a recently found peptide hormone produced by white adipose tissue. Asprosin activates the G protein-cAMP-PKA pathway, which promotes glucose production from the liver. Elevated asprosin levels are linked to insulin resistance in humans and mice, according to the study. Furthermore, recombinant asprosin injection causes blood glucose and insulin levels to rise. One of the primary reasons for future research into the treatment of numerous metabolic illnesses related with insulin resistance was the discovery of asprosin(Alan *et al.* 2019). Fasting-induced glucogenic adipokine asprosin, a 140-amino-acid C-terminal profibrillin, was first found in infant progeroid syndrome and is a newly discovered fasting-induced glucogenic adipokine. White adipose tissues produce asprosin into the blood stream, which target the liver and has a glucogenic impact via (OR4M1), an olfactory G-protein-coupled receptor. Through (PKC-activated) endoplasmic reticulum stress and (TLR4/JNK-mediated inflammatory cytokines), it also affects insulin sensitivity and secretion(Hong *et al.* 2021). the correlation between asprosin and ovarian function, particularly in men. By increasing sperm motility, asprosin counteracts the decline in reproductive potential brought on by aging and obesity. It should be noted that

physical activity can differentially affect asprosin levels in the plasma; intensive anaerobic exercise raises asprosin levels while aerobic exercise lowers them. To confirm the precise mechanisms of asprosin activity and its potential as a therapeutic target, more study is required(Mazur-Bialy, 2021).

2.2.1 Asprosin association with other conditions

Asprosin appears to play a role in the development and progression of a variety of clinical disorders, including diabetes, obesity, cardiomyopathy, cancer, and polycystic ovarian syndrome, according to a growing body of research. It controls hunger stimulation, glucose release, insulin production, apoptotic cell death, and the inflammatory response, among other cellular and physiological functions (Ovali and Bozgeyik 2022).

2.2.2 Asprosin source

White adipocytes are the main source of asprosin. In vitro, mature adipocytes generated and released asprosin, but pre-adipocytes did not. Adipose tissue ablation in mice resulted in a 2-fold decrease in circulating asprosin. FBN1 mRNA levels were shown to be substantially expressed in white adipose tissue in healthy people and animals, according to RNA sequencing and qPCR results. Glucose stops the formation of asprosin in white adipose tissue in vitro and in vivo. In comparison to glucose-free settings, high glucose treatment of mature adipocytes lowered asprosin synthesis (Muthu and Reinhardt 2020).

2.3 Insulin resistance

Insulin is an anti-diabetic hormone created as a big proinsulin by the pancreatic B cell (containing of 109 amino acids). Cleavage converts this peptide to proinsulin quickly (containing of 86 amino acids). Proteolytic cleavage produces equimolar amounts of insulin and C-peptide, which are then released together with a little amount of proinsulin(Placzkowska *et al.* 2019). In certain clinical kinds of diabetes, autologous insulin secretion is basically non-existent or faulty and, in these circumstances, the level

of glucose is naturally increased. The amount of IRI is evaluated over time to detect the state of insulin secretion as part of an oral glucose tolerance test (OGTT). On the other hand, in the case of fasting hypoglycemia, insulin assay is critical for determining the etiology and is used for the diagnosis Insulin assay, on the other hand, is critical for determining the cause of fasting hypoglycemia and is used to diagnose insulinoma (pancreatic islet tumor) (Mirabelli *et al.* 2020).

IR which is defined as a reduced biological response to circulating insulin, is a key component of obesity and (T2D), as well as a variety of other diseases and disorders, such as (NAFLD), cognitive impairment, (CKD), endothelial dysfunction, (PCOS), and certain endocrine tumors, such as breast cancer. Insulin resistance is a reduced In obese persons, an uneven production of pro- as well as anti-inflammatory adipocytokines may contribute to the development of insulin resistance (IR) and the metabolic difficulties that are associated with it. These problems, however, can be corrected by following weight-loss programs. The (MedDiet), which includes a high intake of (EVOO), almonds, red wine, as well as other polyphenol-rich ingredients, vegetables, has been linked to a higher improvement in insulin resistance (IR) in obese people when compared to other dietary therapies (Mirabelli *et al.* 2020).

2.3.1 Insulin resistance prognosis

The evidence on the relationship between PH and IR prognostic variables and/or bad outcomes is mixed. Despite the fact that patients with IR had a lower survival rate in the current research, no link was established between clinical and IR, haemodynamics, 6MWT distance, prognostic variables, or mortality risk in earlier investigations. However, a major portion of our research sample was classified as having a high risk of death, which might explain the lack of a link between IR and mortality risk. According to Zamanian et al. patients who had IR had a worse six-month event-free survival rate, although there was no correlation found between NYHA class and IR, haemodynamic, or 6MWT distance parameters. There was no change in survival or other PH-related parameters in a trial conducted by Pugh et al such as NYHA class, 6MWT distance, or haemodynamic parameters between IR and IS patients. However, an obese woman with

IPAH lost 20% of her body weight. The same research group exhibited considerable improvement in haemodynamic parameters of PH, including mean of (PVR and PAP), which was related with a significant drop in IR (2.6 - 1.2) as evaluated by the HOMA-IR. In the Heresi et al. investigation, there were no significant relationships between the NYHA class and the IR, haemodynamic variables, and echocardiography data. Nonetheless, this research group was able to find a small association between 6MWT and IS distance (P = 0.05, r = 0.55). During the study's subsequent phase (26 months), no deaths were reported. They also discovered no link between an increased risk of hospitalization and IR (Zare *et al.* 2022).

2.3.2 Treatment

The phosphorylation of SHC activates another insulin receptor-activated pathway. The stimulation of this route causes cell proliferation and protein synthesis in normal settings. In reaction to insulin, hundreds of proteins are phosphorylated, and it has been demonstrated that tyrosine phosphorylation of the insulin receptor and IRS happens within a minute after insulin secretion/treatment(Yaribeygi *et al.* 2019).

2.4 Asprosin and impaired fasting glucose association

Asprosin is a new adipokine that is produced and acts specifically on the liver. It raises the amount of glucose that is released from the liver by activating a pathway involving G protein, cyclic AMP, and protein kinase. Fasting causes the release of asprosin, which in turn triggers the release of asprosin. There is a path. Plasma asprosin levels are pathologically elevated in humans and animals with insulin resistance. Reducing the activity of asprosin through genetic methods or immunological has a significant impact on insulin and glucose levels due to decreased hepatic glucose release. This is the case because asprosin inhibits glucose release from the liver. As a result, therapeutically targeting asprosin may be useful in people with T2DM. The quantity of circulating asprosin in patients with T2DM has been the subject of many studies, and these studies have all come to the same conclusion: the concentrations of circulating asprosin when the patients are fasting are much greater. In addition, the levels of circulating asprosin show

a diurnal oscillation in healthy persons and mice, with a sudden drop in levels that corresponds with the beginning of mealtimes. However, it is unknown whether persons suffering from type 2 diabetes still experience this circadian oscillation (Zhang *et al.* 2020). Obesity in adults is linked to asprosin, an adipokine. Its functions in kids are little known. TNF-, leptin, adiponectin, and asprosin levels were measured, as were anthropometric parameters, and circulating (TNF-), clinical data, adiponectin, and asprosin levels. The amounts of asprosin that may be found in the plasma of obese children and adolescents, were significantly greater as compared to those of children who were normal weight. IR children had increased asprosin levels than non-IR children. WHR, (HOMA-IR), diastolic blood pressure, leptin-to-adiponectin ratio, and TNF- were all significantly linked with asprosin, regardless of body mass index, SDs score, or age. The circulating amount of asprosin was linked to WHR and HOMA-IR in a multivariable linear regression analysis. Conclusions: Circulating asprosins are higher in obese children and are linked to IR (Wang *et al.* 2020).

2.5 Insulin Resistance and Impaired Fasting Glucose

IFG a kind of prediabetes, is defined by a significant increase in hepatic insulin resistance and can be detected by simply measuring fasting glucose levels. (IGT), a kind of prediabetes, meanwhile, is defined by a significant increase in skeletal muscle insulin resistance, as well as high postprandial glucose levels. These diverse routes in prediabetes pathophysiology may have different effects on resistance arteries and blood pressure. However, the various processes through which hypertension develops in each kind of prediabetes are still unknown. Little is known about how insulin resistance, hyperglycemia, and hyperinsulinemia affect hypertension as people advance from healthy to prediabetes and diabetes mellitus (Sasaki *et al.* 2020).

2.6 Asprosin and Insulin Resistance

Attenuating the effects of asprosin, may be useful in the treatment of T2DM, metabolic syndrome, and obesity with hyperinsulinemia. This is so that researchers can investigate the orexigenic, hormonal, as well as glucogenic activities of asprosin, as well as its

relationship with inflammation. This can be accomplished in order to study the asprosin (Duerrschmid *et al.* 2017). T2DM is defined by chronic hyperglycemia and insulin resistance, as well as persistently high blood glucose as well as non-esterified fatty acids, which cause greater damage to pancreatic-cell function and apoptosis. As a result, there is a larger release of inflammatory factors. Furthermore, in excremental research, It has been shown that insulin resistance and T2DM are both associated with an increase in the amount of asprosin found in the blood (Montane *et al.* 2014).

3. MATERIALS AND METHODS

3.1 Sample Collection and Storege

The samples were collected and examined in the Gideon Specialist Laboratory in Baghdad, which is one of the oldest private laboratories in Iraq, and is licensed by the Iraqi Ministry of Health. this research by selecting people who randomly do not suffer from any symptoms related to diabetes, in particular impaired fasting glucose Where all people were asked about their medical history and samples were selected based on that no type of diabetes treatment is taken for all people. 240 samples were collected within two months from January 2022 until the end of March 2022. Using a sterile disposable syringe, 10 mL of venous blood will be drawn from each patient participating in this study and placed in a vacutainer tube. When the blood has been allowed to coagulate at room temperature for the appropriate amount of time, the tubes will be centrifuged at a speed of 3000 revolutions per minute, and the supernatant plasma will be removed. After that, it will be portioned out into aliquots, placed in Eppendorf tubes, and kept at a temperature of -20 degrees Celsius until the time when plasma samples from both the patients and the controls will be analyzed for:

- Fasting blood glucose
- Insulin
- Aasprosin

The formula that will be used to determine insulin resistance is as follows: fasting insulin (microU/L) x fasting glucose (nmol/L)/22.5.

Mean plasma asprosin will be statistically correlated with insulin resistance in both studied groups.

3.2 Study Design

This study will be conducted in Baghdad, enrolling 200 randomly selected participants attending 2 private clinical laboratories for routine checking. The participants will be divided into 2 groups according to their fasting blood glucose.

- Group 1 will enrol 120 adult participants with impaired fasting defined as fasting blood glucose (≥ 100 mg/dL).
- Group 2 will enrol 120 adult participants with normal fasting blood glucose was (< 100 mg/dL).

Both groups will be age,length, sex and body mass index matched to eliminate any possible effect on the measured parameters.

3.3 Inclusion and Exclusion Criteria

A full history will be taken from each participant with more emphasis on past medical and drug history. Height and weight, will be measured to calculate the body mass index for each participant.

3.3.1 Inclusion criteria

Adults with fasting blood glucose ≥ 100 mg/dL will be included in the impaired fasting glucose group while adults with fasting blood glucose of (< 100 mg/dL) will be included in the control group, the age, weight, height and gender of each person are included.

3.3.2 Exclusion criteria

Any participant in the study who meets any of the following conditions will be disqualified from participation:

1. Diabetes mellitus
2. Any chronic illness
3. Any acute illness
4. Any drug that might affect blood glucose level (ex. Corticosteroids)
5. Age < 18 year

3.4 Equipment and Apparatuses

All Equipment and Apparatuses used in this study are listed, as shown in Table 3.1

Table 3.1 The equipment and apparatuses used in the study

NO.	Name of Equipment	Country	Company
1	ELISA, washer, reader and printer	Germany	Human
2	integra	Germany	Roche
3	centrifuge	Germany	Hettich - ROTOFIX
4	Deep Freeze	Germany	GFL

3.5 Kits Used

All kits used in this study are listed, as shown in Table 3.2

Table 3.2 The kits used and their sources are given in the table

NO.	Name of Kits	REF/LOT/ CAT	Company	Origin
1	Asprosin	[CAT] MBS2707373	MyBioSource	USA
2	Insulin	[CAT] MBS761338	MyBioSource	USA
3	Glucose	[CAT] KAC1751	Integra	Germany

3.6 Tools Used

All tools used in this study are listed, as shown in Table 3.2

Table 3.3 The tools used and their sources

NO.	Name of tools	Country	Company
1	1 ml pipette tips	Germany	-
2	Disposable syringe (5mL)	Germany	MEDECO
3	0.1ml pipette tips	Germany	-
4	0.01ml pipette tips	Germany	-
5	Plain Tube	Germany	-
6	EDTA Tube	Germany	-
7	Multichannel micropipette (0-250µL)	Germany	Titertek
8	Micropipettes (2-20, 5-50, 20-200, 100-1000 Ml)	Germany	Slamed

3.7 Estimation of Fasting Blood Glucose

3.7.1 Principle and clinical significance

Hexokinase (HK) is an enzyme that is responsible for catalyzing the phosphorylation of glucose by ATP. This process results in the formation of ADP and glucose-6-phosphate. In order to keep up with the process, a second enzyme known as (G6PDH) is employed to catalyze the oxidation of glucose-6-phosphate by NAD+. This results in the formation of NADH.

The concentration of NADH that is generated is directly proportional, to the concentration of glucose that is present in the system. The measurement of the rise in absorbance at 340 nm is what is used to establish it. n the peripheral blood, glucose is the most abundant carbohydrate. The oxidation of glucose is the primary contributor to the body's cellular energy supply. The body may either convert glucose from food into glycogen, which is then stored in the liver, or into fatty acids, which are then stored in adipose tissue. There are a number of hormones that are responsible for keeping the level of glucose in the blood within predetermined parameters. The pancreas is responsible for producing the most important of these hormones. Hyperglycemia may have a variety of causes, the most

frequent of which is diabetes mellitus, which is characterized by insufficient insulin production or activity. Elevated blood glucose levels are caused by a variety of secondary causes. Pancreatitis, thyroid dysfunction, renal failure, and liver illness are among them.Hypoglycemia occurs less commonly. Hypoglycemia occurs less commonly. Insulinoma, hypopituitarism, and insulin-induced hypoglycemia are all disorders that can cause low blood glucose levels. Glucose readings, as shown in Equation 3.1 and 3.2, are used to diagnose and treat a variety of neurological conditions, including meningitis, neoplastic involvement of the meninges, and other conditions.

$$\text{Glucose} + \text{ATP (HK)} \rightarrow \text{G-6-P} + \text{ADP} \quad (3.1)$$

$$\text{G-6-P} + \text{NADP+ (G-6-PDH)} \rightarrow \text{Gluconate-6-P} + \text{NADPH} + H^{+} \quad (3.2)$$

3.8 Estimation of Plasma or Plasma Asprosin Hormone

This test kit is a sandwich enzyme immunoassay that may be used to quantify the amount of asprosin present in human tissue homogenates, cell culture supernates, plasma, cell lysates, plasma, and other types of biological fluids in an in vitro setting.

3.8.1 Reagents and materials provided

Provided reagents and materials are listed, as shown in Table 3.1

Table 3.4 Provided reagents

Reagents	**Quantity**	**Reagents**	**Quantity**
Detection Reagent B	1×20mL	Assay Diluent B	1×12mL
Wash Buffer (30 × concentrate)	1×20mL	Instruction manual	1
Detection Reagent A	1×20mL	Assay Diluent A	1×12mL
TMB Substrate	1×9mL	Stop Solution	1×6mL
Standard	2	Standard Diluent	1×20mL
Pre-coated, ready to use 96-well strip plate	1	Plate sealer for 96 wells	4

3.8.2 Reagent preparation

1. Before using any of the components or samples in the kit, first bring everything to room temperature (between 18 and 25 degrees Celsius). Please only remove strips and reagents that will be used in the current experiment, and ensure that the remainder of the kit's strips and reagents are kept in the proper condition. If the kit will not be utilized completely in a single usage, this warning applies.
2. Standard: Reconstitute the Standard with (1.0 mL) of Standard Diluent, allow it to sit at room temperature for ten minutes, and then give it a gentle shake (not to foam). 40 ng/mL is the amount of the standard's concentration that can be found in the stock solution. First, dilute the stock solution to a concentration of (10ng/mL). After that, make the standard that has been diluted the one that is held to the greatest possible standard, which also has a concentration of 10ng/mL. After that, stock each of the seven tubes with 0.5 milliliters of standard diluent, and make use of the standard that has been diluted in order to generate a double-dilution series in accordance with the diagram that can be seen below. Prior to moving on to the next transfer, thoroughly combine the contents of each tube. Set up 7 points of diluted standards, such as (5ng/mL), (10ng/mL), (0.625ng/mL), (2.5ng/mL), (0.312ng/mL), (1.25ng/mL), and (0.156ng/mL), then fill the final (EP) tubes with standard diluent such that they read 0ng/mL.

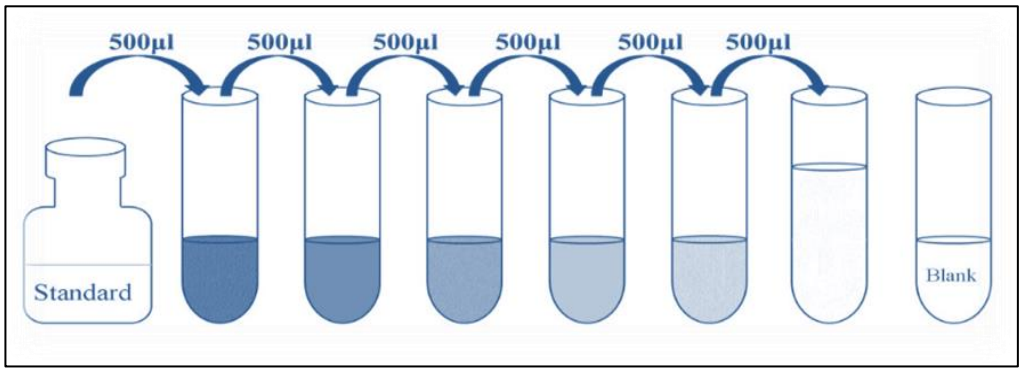

Figure 3.1 Add solutions

3. Detection Reagent B and Detection Reagent A - Before using the stock Detection A and Detection B, give them a quick spin in the centrifuge or give them a brief spin. They need to be diluted to a working concentration that is one hundred times lower using Assay Diluent B and A, respectively.
4. Wash Solution To make (600 mL) of wash solution at a concentration of one part per thousand, dilute 20 mL of wash solution concentrate at a concentration of thirty times with 580 mL of deionized or distilled water.
5. When using (TMB) substrate, aspirate the required dose of the solution using tips that have been sanitized, and do not pour any of the remaining solution back into the vial.

3.8.3 Assay Procedure

1. Locate the wells that will hold the diluted standard, the blank, and the sample. Make sure you have 7 wells ready for the standard, and 1 well ready for the blank. In the appropriate wells, add a total of one hundred microliters (L) of dilutions of the standard, the blank, and the samples. Utilize the Plate sealer to cover the plate. Incubate for a full hour at a temperature of 37 degrees Celsius.
2. Pour out the liquid from each well, but do not wash the wells themselves.
3. Pour one hundred microliters of the detection reagent into the well. Putting a workable solution in each well, sealing the wells with a plate sealer, and observing the results, and incubating at 37 degrees Celsius for one hour is the procedure.
4. Aspirate the solution and wash each well with (350 L) of (1 M). Wash Solution using multi-channel pipette, a squirt bottle, autowasher, or manifold dispenser, and then let it rest for 0.5 minutes. Snapping the plate into a piece of absorbent paper allows you to fully empty any wells that still contain liquid. Complete the washing process three times. After final wash, any residual Wash Buffer must be removed by decanting and either aspirating it. Turn the plate upside down and dab it against some absorbent paper.
5. Pour one hundred microliters (L) of the Detection Reagent (B), working solution into each well, after that cover the wells use the plate sealer and place the plate in an incubator set to 37 degrees Celsius for half an hour.

6. In all, you will need to carry out the steps of aspiration and washing five times, as outlined in step 4. 6. For a total of five times, repeat the operation of aspiration and washing, as outlined in step 4.
7. Pour ninety microliters (L) of substrate solution, into each well. Replace the cover, with a brand replacement plate sealer. At 37 degrees Celsius, incubate the mixture for ten to twenty minutes (the total time should not exceed thirty). Avoid direct sunlight whenever possible. The addition of Substrate Solution will cause the liquid to take on a bluish hue.
8. Pour a total of fifty microliters of the Stop Solution into each well. The addition of the Stop solution will cause the liquid to take on a yellow color. The liquid should be mixed by tapping the side of the dish. If the shift in hue does not seem to be consistent, give the plate a few light taps to confirm that everything has been well mixed.
9. Wipe away any traces of water or fingerprints that may have been left on the underside of the plate, as well as check to see that there aren't any bubbles on the top of the liquid. Microplate reader should then be started, and measurements should start at 450 nm as soon as possible.

3.8.4 Asprosin test principle

This kit comes with a microplate that has already had an antibody that is specific to asprosin coated onto it for you. After that, a biotin-conjugated antibody specific to asprosin is inserted into either standards or samples are put into the appropriate wells of the microplate.

Following this step, After adding an antibody that has been modified such that it is coupled to horseradish peroxidase to each well of the microplate, the plates are placed in an incubator. After adding a solution of sulfuric acid, the enzyme-substrate reaction is halted, and the spectrophotometric examination of the color change is carried out at a wavelength of (450 nm ± 10 nm). Next, A comparison of the samples' optical densities (O.D.) to the standard curve enables the computation of the samples' asprosin concentrations.

3.9 Estimation of Plasma Insulin

3.9.1 Principle of the assay

The sandwich enzyme-linked immune-sorbent assay technology was used in the development of this product. Anti-INS antibody was used to cover the wells of 96-well plates before use. Anti-INS antibodies that had biotin attached to them were used in the detection process. Following that, the wells were cleaned with wash buffer, and then the standards, test samples, and biotin-conjugated detection antibody were added. Following the addition of HRPStreptavidin, the wash buffer was used to remove any unbound conjugates. TMB substrates were used in the experiment, and the HRP enzymatic process was observed. After being subjected to an acidic stop solution, the blue product that was produced as a consequence of the catalysis of TMB by HRP turned into a yellow color. There is a correlation between the quantity of material that was collected in the plate and the density of the color yellow. Take a reading of the optical density absorbance at 450 nm using a microplate reader, and then calculate the INS concentration.

3.9.2 Assay procedure

Before introducing any chemicals to the wells, the TMB Substrate should be allowed to acclimate at 37 degrees Celsius for half an hour. When diluting samples and reagents, it is essential that they be thoroughly and uniformly combined. It is strongly suggested that a standard curve be constructed for each test.

1. First, we place standard wells, test sample wells, and control (zero) wells in the plate that has been pre-coated, and then we note where each of those wells is located. It is advised to do two separate measurements for each sample and standard. Wash the plate twice before adding the standard, the sample, and the control (zero) wells!
2. Aliquot (0.1mL) of (2.5ng/mL), (0.312ng/mL), (10ng/mL), (0.625ng/mL), (5ng/mL), (1.25ng/mL), (0.156ng/mL), standard solutions into the standard wells.

3. We start by pouring 0.1 milliliters of sample as well as standard dilution buffer into the well designated as the control (zero).
4. We next pour 0.1 milliliters of a sample that has been suitably diluted into each of the test sample wells. This sample may consist of human plasma, tissue homogenates, plasma, or other types of biological fluids.
5. We put the plate in an incubator at 37 degrees Celsius for an hour and a half and cover it.
6. After removing the lid and emptying the plate's contents, we wash the plate twice with the Wash Buffer. Under NO circumstances should you allow the wells to go totally dry.
7. We proceed to pour (0.1 mL) of biotin-labeled antibody, working solution into each of the wells that have been prepared. Place a little of the solution in the bottom of each well, making sure to avoid coming into contact with the walls.
8. In step eight, we make a cover for the plate, then incubate it at 37 degrees Celsius for an hour.
9. We begin by removing the lid and washing the plate three times with wash buffer, pausing each time to allow the wash buffer to remain in the wells for one minute.
10. After covering the plate, we incubate the mixture at 37 degrees Celsius for half an hour while adding (0.1 mL) of SABC Working Solution to each well.
11. We begin by removing the lid and washing the plate five times with Wash Buffer. Each time, we allow the wash buffer, to remain in the wells for (1-2) minutes.
12. After covering the plate, we incubate it at 37 degrees Celsius in the dark for 15-30 minutes after adding 90 microliters of TMB Substrate to each well. The first three to four wells (with the most concentrated INS standard solutions) will see a change to a blue tint, whereas the remaining wells may not show any visible color change.
13. Pour 50 l of Stop Solution into each well, and thoroughly combine the contents of all of the wells. Instantaneously, the hue transforms into a bright yellow.
14. Immediately after adding the stop solution, read the absorbance of the optical density reading at 450 nm in the microplate reader. The standard curve may be shown graphically by plotting the relative optical density (O.D.) 450 of each standard solution (Y) against the relevant concentration of the standard solution (X). Interpolation from the standard curve allows for the INS concentration of the samples

to be determined. It is strongly suggested that you utilize a professional piece of software called curve expert 1.3.

3.10 Data Analysis

SPSS version 23 was used for statistical analysis. The t-test is a statistical test. It was chosen to use the formula to express continuous variables. A 0.05 or lower p-value was judged significant.

4. RESULTS AND DISCUSSION

4.1 Age

In this study, the level of mean ± SD in age of Control group is (36.900 ±8.902) compared with IFG group is (45.808 ±14.365) And the results proved that no significant deferent between control group and IFG group in the age (P 0.19) as shown in Figure 4.1 and Table 4.1.

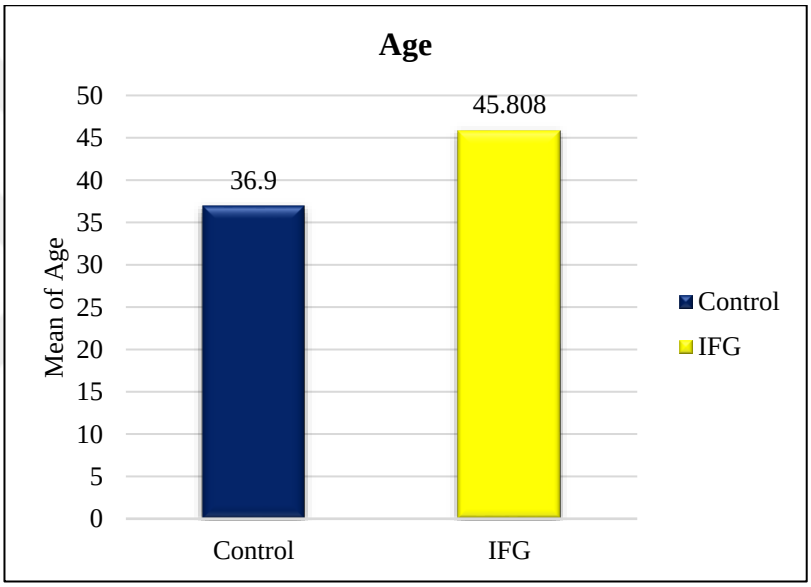

Figure 4.1 Mean of age IFG gruop and control group

4.2 BMI

The current study enrolled the mean of their BMI mean ±SD was in control group (26.009 ±2.580)compared with IFG group (26.872±2.999) relying on the results mentioned in this paragraph, it was found as no significant deferent of control group ang IFG group (p 0.14) shown in Figure 4.2 and Table 4.1.

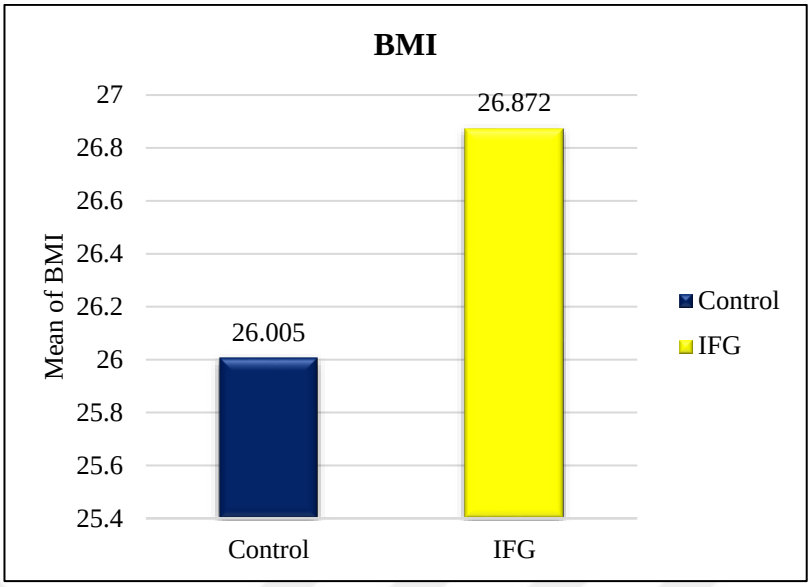

Figure 4.2 Mean of BMI IFG gruop and control group

Table 4.1 Mean±SD of IFG group and control group in age and BMI

PARAMETERS	MEAN±SD		STD. ERROR		P-VALUE
	IFG	control	IFG	Control	
Age (years)	45.808±14.365	36.900±8.902	1.311	0.812	0.19
BMI (kg/m^2)	26.872±2.999	26.005±2.580	0.273	0.235	0.14

4.3 Insulin

In insulin prevalence it was contained control group and IFG group statistics results showed in mean±SD are increased in IFG group (9.140±0.561) compared with the control group (7.007±0.229), Previously in this paragraph it was found that significant deference between control group and IFG group in Insulin (p 0.00) as shown in Figure 4.3 and Table 4.2.

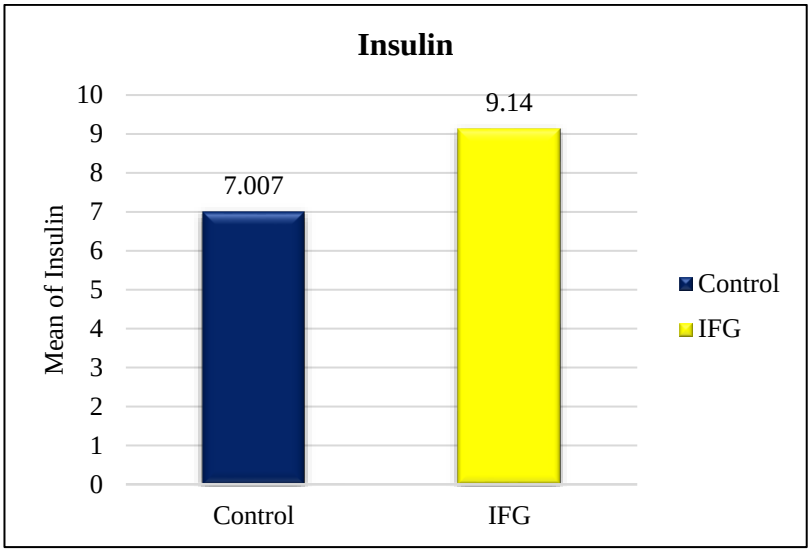

Figure 4.3 IFG level and Control leve in Insulin

4.4 HOMA-IR

Value taken mean±SD for control group (1.571±0.050) and IFG group (2.484±0.530) with HOMA-IR based on these two results, we arrive the significant deference between control group and IFG group with HOMA-HOMA-IR (p 0.00) as shown in Figure 4.4 and Table 4.2.

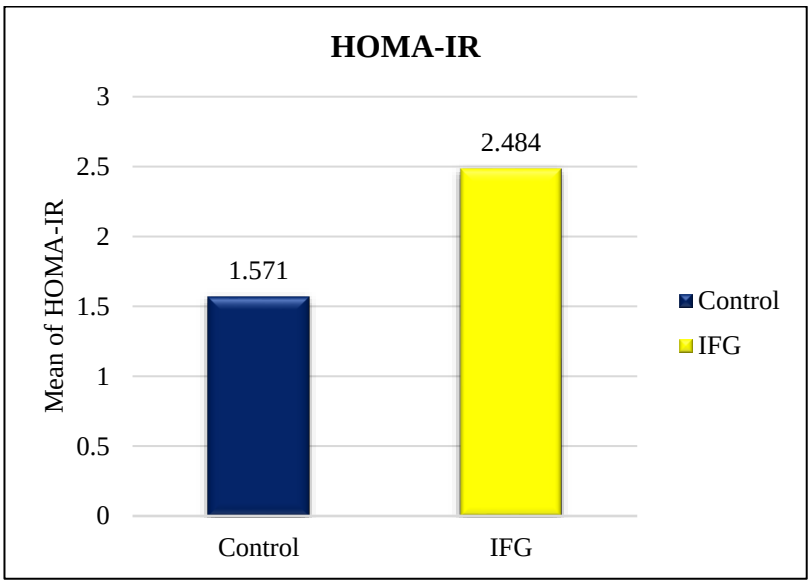

Figure 4.4 The level of IFG group and control group in HOMA-IR

Table 4.2 The level of IFG and control group in insulin and HOMA-IR

PARAMETERS	MEAN±SD		STD. ERROR		P-VALUE
	IFG	control	IFG	Control	
Insulin (ng/mL)	9.140±6.151	7.007±2.518	0.561	0.229	0.00
HOMA-IR	2.484±1.685	1.571±0.551	0.530	0.050	0.00

4.5 Asprosin

In this investigation, the mean SD of the Asprosin participant group (3.065±0.057) was higher than the result of the control group (1.655±0.257), based on these results, we conclude that there is a significant deference in Asprosin between control group and IFG group (p 0.00) as shown in Figure 4.5 and Table 4.3.

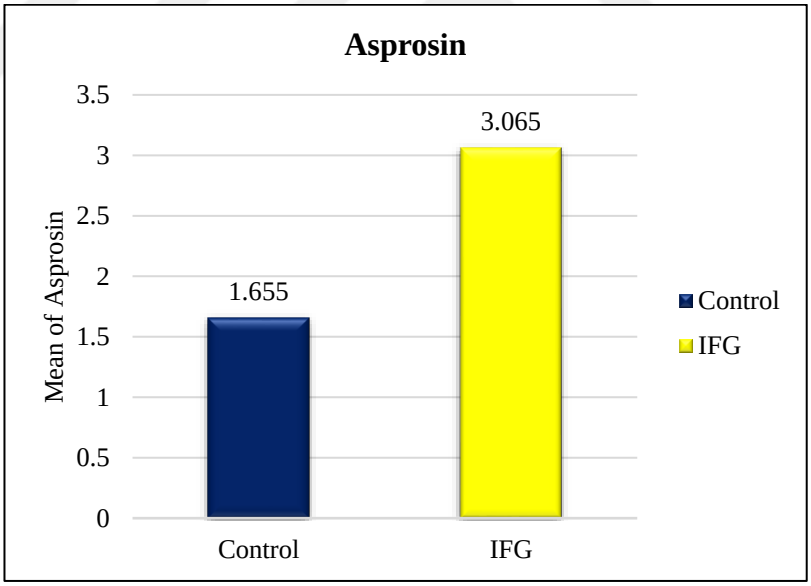

Figure 4.5 The mean of asprosin in IFG group anf control group

4.6 Glucose

By estimating the glucose level in this research maen±SD for control group (91.250±4.102) and IFG group (1110.083±5.890) based on the results mentioned in this

paragraph, it was inferred that there is significant deferent between IFG group and control group (p 0.00) as shown in Figure 4.6 and Table 4.3.

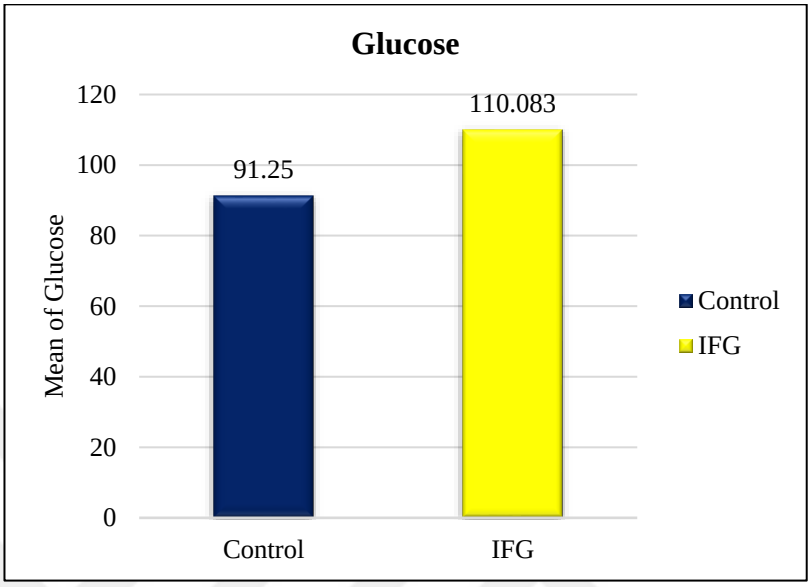

Figure 4.6 Mean of glucoce in IFG group and control group

Table 4.3 The mean±SD asprosin and glucose in IFG and control group

PARAMETERS	MEAN±SD		STD. ERROR		P-VALUE
	IFG	control	IFG	Control	
Asprosin (ng/mL)	3.065±0.633	1.655±0.257	0.057	0.023	0.00
Glucose (mg/dL)	110.083±5.890	91.250±4.102	0.537	0.374	0.00

5. DISCUSSION

The measured variables were compared between the IFG group and the control.

Between the control group and IFG group, there was no significant difference in BMI (26.87) (P 0.14) which eliminated any possible interference of BMI between the studied groups.

Concerning asprosin, there was a statistically significant gap in the mean value (3.06) between the control group and the IFG group (p value). Similarly, plasma asprosin was significantly increased in individuals with IFG as seen by Domenico Corica et al. 79 children and adolescents who did not have diabetes took part in the study that the researchers performed in to test the hypothesis of a change in the meal-related fluctuation of asprosin levels (Corica *et al.* 2021). In 2018 Wang et al. found significant increase of plasma Asprosin in both IFG and T2DM in their study that carried out in Canada and included 143 subjects where plasma Asprosin Concentrations was significantly higher in Individuals with Glucose intolerance. The same study has shown a positive correlation between HOMA-HOMA-IR and plasma (Wang *et al.* 2018). People who have HOMA-IR and/or type 2 diabetes have been demonstrated in a number of studies to have a considerably greater content of asprosin in their plasma (Corica *et al.* 2022).

Regrading insulin plasma level, Between the two groups, the control group and the IFG group, there was a statistically significant difference in its the mean (9.14) ($p < 0.05$). In Sae Aoyama-Sasabe et al. study that included 4905, of these 2046 were normal subject, 1510 with IFG and 396 with IGT, they observed a significant difference in plasma insulin concentration between IFG, IGT compared to healthy control (Aoyama-Sasabe *et al.* 2016).

Furthermore, a significant difference was estimated in the mean (2.48) of HOMA-IR between IFG group and the control group ($p <0.05$).

The current study has shown a poor correlation between plasma asprosin concentration and IR (r= 0.196).A nearly similar strength of correlation between asprosin and HOMA-IR (r = 0.296) has been found in a similar study performed by Yuren Wang et al. in their study that included 143 participants of various status of glucose regulation (Wang *et al.* 2018).

Asprosin has been linked strong behavoir and influence with to the metabolic syndrome. The overexpression of asprosin can target the beta cells in the pancereas resulting in the inhibition of insulin secrtion and induce inflammatory events, hereby, increase the levels of glucose in the circulation. Additionally, asprosin can target the skeletel muscle cells causing diverse effects that ultimatily can lead to the development of insulin resistance (Yuan *et al.* 2020).

In the research carried out by Zhang et al. the scientists discovered that the levels of asprosin in the circulation of type 2 diabetes patients were considerably elevated, both when the participants were fasting and when they were not. They have concluded that when a flactuations occurs in the level of asprosin in people with glucose intolerence, it may refere to the development of T2DM disease (Zhang *et al.* 2020).

According to the findings of Li et al. the plasma asprosin level is significantly altered in individuals who suffer from metabolic disorder. The workers have shown a significant increase of plasma asprosin levels in patients with T2DM disease, and in women with polycystic ovarian syndrome compared to normal people. This increase of plasma asprosin was correlated with the blood glucose level (Li *et al.* 2018).

6. CONCLUSIONS AND RECOMMENDATION

1. Asprosin can be used as a marker of IFG.
2. Asprosin is correlated with common biochemical marker of insulin resistance.
3. The privilege of asprosin over HOMA-IR as a marker of IR should be further investigated.
4. The association of Asprosin and progression of IFG to frank diabetes should have a special attention in the upcoming medical studies.

REFERENCES

Abdul-Ghani, M. A., Jenkinson, C. P., Richardson, D. K., Tripathy, D. and DeFronzo, R. A. 2006. Insulin secretion and action in subjects with impaired fasting glucose and impaired glucose tolerance: Results from the veterans administration genetic epidemiology study. Diabetes., 55(5): 1430–1435.

Alan, M., Gurlek, B., Yilmaz, A., Aksit, M., Aslanipour, B., Gulhan, I., Mehmet, C. and Taner, C. E. 2019. Asprosin: a novel peptide hormone related to insulin resistance in women with polycystic ovary syndrome. Gynecological Endocrinology., 35(3): 220–223.

Al-Khafajy, D. A. M., Majeed, M. J., Al-Azzawi, O. F. and Khaleel, A. I. 2021. Role of coq10 and igfbp-1 in obese male patients with diabetic mellitus type ii. Indian Journal of Forensic Medicine and Toxicology., 15(1): 2204–2209.

Aoyama-Sasabe, S., Fukushima, M., Xin, X., Taniguchi, A., Nakai, Y., Mitsui, R., Takahashi, Y., Tsuji, H., Yabe, D., Yasuda, K., Kurose, T., Inagaki, N. and Seino, Y. 2016. Insulin secretory defect and insulin resistance in isolated impaired fasting glucose and isolated impaired glucose tolerance. Journal of Diabetes Research., 2016: 1–9.

Corica, D., Aversa, T., Currò, M., Tropeano, A., Pepe, G., Alibrandi, A., Ientile, R. and Wasniewska, M. 2021. Asprosin plasma levels and glucose homeostasis in children with obesity. Cytokine., 142: 155477.

Corica, D., Pepe, G., Aversa, T., Currò, M., Curatola, S., Li Pomi, A., Alibrandi, A., Ientile, R. and Wasniewska, M. 2021. Meal-Related Asprosin Plasma Levels Are Affected by Insulin Resistance and Impaired Fasting Glucose in Children With Obesity. Frontiers in Endocrinology., 12: 805700.

DeFronzo, R. A. and Abdul-Ghani, M. 2011. Assessment and treatment of cardiovascular risk in prediabetes: Impaired glucose tolerance and impaired fasting glucose. American Journal of Cardiology., 108(3 SUPPL.): 3B-24B.

Diniz, M. de F. H. S., Beleigoli, A. M. R., Schmidt, M. I., Duncan, B. B., Ribeiro, A. L. P., Vidigal, P. G., Benseñor, I. M., Lotufo, P. A., Santos, I. S., Griep, R. H. and Barreto, S. M. 2020. Homeostasis model assessment of insulin resistance (HOMA-

IR) and metabolic syndrome at baseline of a multicentric Brazilian cohort: ELSA-Brasil study. Cadernos de Saude Publica., 36(8): e00072120.

Dong, Y., Zhang, B., Sun, W. and Xing, Y. 2019. Intervention of Prediabetes by Flavonoids From Oroxylum indicum. In Bioactive Food as Dietary Interventions for Diabetes (2nd ed.). Elsevier Inc.

Duerrschmid, C., He, Y., Wang, C., Li, C., Bournat, J. C., Romere, C., Saha, P. K., Lee, M. E., Phillips, K. J., Jain, M., Jia, P., Zhao, Z., Farias, M., Wu, Q., Milewicz, D. M., Sutton, V. R., Moore, D. D., Butte, N. F., Krashes, M. J. and Chopra, A. R. 2017. Asprosin is a centrally acting orexigenic hormone. Nature Medicine., 23(12): 1444–1453.

Hong, T., Li, J.-Y., Wang, Y.-D., Qi, X.-Y., Liao, Z.-Z., Bhadel, P., Ran, L., Yang, J., Yan, B., Liu, J.-H. and Xiao, X.-H. 2021. High Plasma Asprosin Levels Are Associated with Presence of Metabolic Syndrome.

Janoschek, R., Hoffmann, T., Morcos, Y. A. T., Sengle, G., Dötsch, J. and Hucklenbruch-Rother, E. 2020. Asprosin in pregnancy and childhood. Molecular and Cellular Pediatrics., 7(1): 18.

Joung, B. 2019. Risk factor management for atrial fibrillation. Korean Circulation Journal., 49(9): 794–807.

Kufe, C. N., Klipstein-Grobusch, K., Leopold, F., Assah, F., Ngufor, G., Mbeh, G., Mbanya, V. N. and Mbanya, J. C. 2015. Risk factors of impaired fasting glucose and type 2 diabetes in Yaoundé, Cameroon: A cross sectional study. BMC Public Health., 15(1).

Laakso, M., Zilinskaite, J., Hansen, T., Boesgaard, T. W., Vänttinen, M., Stančáková, A., Jansson, P.-A., Pellmé, F., Holst, J. J., Kuulasmaa, T., Hribal, M. L., Sesti, G., Stefan, N., Fritsche, A., Häring, H., Pedersen, O., Smith, U. and Consortium, for the E. 2008. Insulin sensitivity, insulin release and glucagon-like peptide-1 levels in persons with impaired fasting glucose and/or impaired glucose tolerance in the EUGENE2 study. Diabetologia., 51(3): 502–511.

Li, X., Liao, M., Shen, R., Zhang, L., Hu, H., Wu, J. and Zheng, H. 2018. Plasma asprosin levels are associated with glucose metabolism, lipid, and sex hormone profiles in females with metabolic-related diseases. Mediators of inflammation., 2018.

Long, W., Xie, X., Du, C., Zhao, Y., Zhang, C., Zhan, D., Li, Z., Ning, Q. and Luo, X. 2019. Decreased Circulating Levels of Asprosin in Obese Children. Hormone Research in Paediatrics., 91(4): 271–277.

Mazur-Bialy, A. I. 2021. Asprosin-A Fasting-Induced, Glucogenic, and Orexigenic Adipokine as a New Promising Player. Will It Be a New Factor in the Treatment of Obesity, Diabetes, or Infertility? A Review of the Literature. Nutrients., 13(2).

Mazur-Bialy, A. I. 2021. Asprosin—a fasting-induced, glucogenic, and orexigenic adipokine as a new promising player. Will it be a new factor in the treatment of obesity, diabetes, or infertility? a review of the literature. Nutrients., 13(2): 1–10.

Mirabelli, M., Chiefari, E., Arcidiacono, B., Corigliano, D. M., Brunetti, F. S., Maggisano, V., Russo, D., Foti, D. P. and Brunetti, A. 2020. Insulin Resistance and Related Diseases. Nutrients.

Mirzaei, M., Rahmaninan, M., Mirzaei, M., Nadjarzadeh, A. and Dehghani Tafti, A. A. 2020. Epidemiology of diabetes mellitus, pre-diabetes, undiagnosed and uncontrolled diabetes in Central Iran: Results from Yazd health study. BMC Public Health., 20(1): 1–9.

Montane, J., Cadavez, L. and Novials, A. 2014. Stress and the inflammatory process: A major cause of pancreatic cell death in type 2 diabetes. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy., 7: 25–34.

Muthu, M. L. and Reinhardt, D. P. 2020. Fibrillin-1 and fibrillin-1-derived asprosin in adipose tissue function and metabolic disorders. Journal of Cell Communication and Signaling., 14(2): 159–173.

Orazumbekova, B., Issanov, A., Atageldiyeva, K., Berkinbayev, S., Junusbekova, G., Danyarova, L., Shyman, Z., Tashmanova, A. and Sarria-Santamera, A. 2022. Prevalence of Impaired Fasting Glucose and Type 2 Diabetes in Kazakhstan: Findings From Large Study. Frontiers in Public Health., 10(February): 1–10.

Ota, A. and Ulrih, N. P. 2017. An overview of herbal products and secondary metabolites used for management of type two diabetes. Frontiers in Pharmacology., 8(JUL): 1–14.

Ovali, M. A. and Bozgeyik, I. 2022. Asprosin, a C-Terminal Cleavage Product of Fibrillin 1 Encoded by the FBN1 Gene, in Health and Disease. Molecular Syndromology., 175–183.

Placzkowska, S., Pawlik-Sobecka, L., Kokot, I. and Piwowar, A. 2019. Indirect insulin resistance detection: Current clinical trends and laboratory limitations. Biomedical Papers., 163(3): 187–199.

Reviriego, J., Vázquez, L. A., Goday, A., Cabrera, M., García-Margallo, M. T. and Calvo, E. 2016. Prevalence of impaired fasting glucose and type 1 and 2 diabetes mellitus in a large nationwide working population in Spain. Endocrinologia y Nutricion., 63(4): 157–163.

Sasaki, N., Ozono, R., Higashi, Y., Maeda, R. and Kihara, Y. 2020. Association of insulin resistance, plasma glucose level, and plasma insulin level with hypertension in a population with different stages of impaired glucose metabolism. Journal of the American Heart Association., 9(7).

Wang, M., Yin, C., Wang, L., Liu, Y., Li, H., Li, M., Yi, X. and Xiao, Y. 2020. Plasma Asprosin Concentrations Are Increased and Associated with Insulin Resistance in Children with Obesity. Annals of Nutrition and Metabolism., 75(4): 205–212.

Wang, Y., Qu, H., Xiong, X., Qiu, Y., Liao, Y., Chen, Y., Zheng, Y. and Zheng, H. 2018. Plasma asprosin concentrations are increased in individuals with glucose dysregulation and correlated with insulin resistance and first-phase insulin secretion. Mediators of Inflammation., 2018.

Weir, C. B. and Jan, A. 2021. BMI Classification Percentile And Cut Off Points. StatPearls Publishing, Treasure Island (FL).

Yaribeygi, H., Farrokhi, F. R., Butler, A. E. and Sahebkar, A. 2019. Insulin resistance: Review of the underlying molecular mechanisms. Journal of Cellular Physiology., 234(6): 8152–8161.

Yuan, M., Li, W., Zhu, Y., Yu, B. and Wu, J. 2020. Asprosin: a novel player in metabolic diseases. Frontiers in endocrinology., 11: 64.

Zare, E., Kafshbani, P., Chenaghlou, M., Noori, M., Ghaemmaghami, Z., Amin, A., Taghavi, S. and Naderi, N. 2022. Prognostic significance of insulin resistance in pulmonary hypertension. ESC Heart Failure., 9(1): 318–326.

Zeng, X., Xie, Y. J., Liu, Y. T., Long, S. L. and Mo, Z. C. 2020. Polycystic ovarian syndrome: correlation between hyperandrogenism, insulin resistance and obesity. Clinica Chimica Acta., 502: 214-221.

Zhang, J., Kong, W., Xia, P., Xu, Y., Li, L., Li, Q., Yang, L., Wei, Q., Wang, H., Li, H., Zheng, J., Sun, H., Xia, W., Liu, G., Zhong, X., Qiu, K., Li, Y., Wang, H., Wang, Y. and Zeng, T. 2020. Impaired Fasting Glucose and Diabetes Are Related to Higher Risks of Complications and Mortality Among Patients With Coronavirus Disease 2019. Frontiers in Endocrinology., 11(July): 1–11.

Zhang, X., Jiang, H., Ma, X. and Wu, H. 2020. Increased plasma level and impaired response to glucose fluctuation of asprosin is associated with type 2 diabetes mellitus. Journal of Diabetes Investigation., 11(2): 349–355.

CURRICULUM VITAE

Personal Information

Name and Surname : Nehad Rasheed Salman SALMAN

Education

MSc	Çankırı Karatekin University Graduate School of Natural and Applied Sciences Department of Chemistry	2020-2022
Undergraduate	Baghdad University College of Science Department of Chemistry	2003-2007