Ibn Al-Haitham Journal for Pure and Applied Sciences
Journal homepage: jih.uobaghdad.edu.iq
PISSN: 1609-4042, EISSN: 2521-3407
IHJPAS. 2025, 38(2)

Comparison of Serum Apelin-36 and Insulin Resistance between Male and Female Type 2 Diabetics

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Received: 3 June 2023 Accepted: 19 November 2023 Published: 20 April 2025
doi.org/10.30526/38.2.3571

Abstract

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia. It may be due to impaired insulin secretion, resistance to insulin's peripheral actions, or both. The aim of this study was to estimate the percentage impact of obesity on the incidence of DM, as well as compare the levels of Apelin-36, glutathione-S-transferase, and insulin resistance (IR) in subjects with and without DM for both sexes. This study included 120 subjects, divided into 60 as a control group and 60 as a patient group of both sexes; all were adults between the ages of 30 and 65. The participants with fasting blood sugar, lipid profile, glycated hemoglobin (HbA1c), apelin-36, body mass index, insulin hormone, and IR were tested. The results showed a significant difference in the males' age and body mass index but a non-significant difference for females. Fasting blood sugar, HbA1c and Apelin-36, insulin hormone, and IR for both sexes have a significant difference ($P \leq 0.05$). There is no relation between glutathione-S-transferase activity, insulin, and IR for both sexes' correlation; the area under the curve in the study= 0.993, indicating a perfect ROC test for correctly identifying individuals. An important role is played by higher levels of Apelin-36, which directly increase obesity and DM. This study concluded that Apelin-36 serves as a reliable indicator for both male and female patients with type 2 DM (T2DM); while women are less likely to develop DM, they are more likely to experience common complications such as cardiovascular disease. Men are more likely to develop T2DM due to their age and higher weight than women.

Keywords: Apelin-36, Glutathione-S-transferase, Insulin, Insulin resistance, Type 2 diabetes mellitus.

1. Introduction

Type 2 diabetes mellitus (T2DM) is previously known as adult-onset diabetes, maturity onset diabetes, or non-insulin dependent diabetes mellitus (NIDDM). This disease results from loss of responsiveness (sensitivity) of target tissues to insulin; impaired removal of glucose from blood produces hyperglycemia even in the presence of higher insulin levels (1). The main risk factor for the development of T2DM is obesity because of a variety of variables, including

age and genetics, which can induce risk for T2DM. There is a wide range of body mass at diagnosis (2). Properly the number of people with T2DM has tripled due to the rise of obesity, idle lives, high-calorie foods, and the aging of the population (3, 4). In obesity, fat cells reach a limit in storing excess energy, leading to increased release of free fatty acids into the bloodstream through lipolysis. This can result in insulin resistance (IR) and the development of T2DM. T2DM patients often have excess body fat, particularly in the abdominal area, contributing to insulin resistance through inflammatory processes (5). Insulin resistance is one of the first metabolic problems that can lead to T2DM. Because of this, it is thought to be a key factor in how the disease develops (6). It is a significant risk factor for T2DM and metabolic syndrome, a group of diseases that often go together (7). Insulin is a hormone secreted from cells in the islets of Langerhans. It controls how carbohydrates, proteins, and fats are broken down by helping glucose become fat, muscle, and liver cells (8). Glucose provides energy to cells or is stored as fat. The release of abnormal insulin caused by β-cell loss, a damaged pancreas, or IR decreases the amount in circulation and inhibits glucose uptake by cells (9). Glutathione-S-transferase (GSTs) are phase-II cleaning enzymes in all living things and are essential for keeping cells in balance. They defend cells by speeding up the process between harmful electrophiles made by cytochrome P450 metabolism and reduced glutathione (GSH) to form GSH conjugates (10). GST is thought to significantly contribute to determining the sensitivity of cells that show a wide range of spectrum toxins (11). Glycosylated hemoglobin (HbA1c) provides essential information about blood glucose values over a few weeks. It is also the primary way that people with DM keep track of glycemia (12). Some studies have shown that HbA1c could be used as a possible measure to identify cholesterol and cardiovascular disease (CVD) (13). Apelin-36 was found to be the natural ligand for the APJ receptor, which had not been known before (14). This study aims to clarify the percentage effect of obesity incidence and CVD and the levels of Apelin-36, GST, and IR in people with and without DM for both genders.

2. Materials and Methods

This work was done at the Department of Chemistry/ College of Sciences for Women/ University of Baghdad and Mustansiriyah University/ National Diabetes Centre for Treatment and Research. Two groups of 120 subjects participated in the study; group 1 included 60 T2DM patients. The study divided the T2DM patients into 31 males and 29 females. Group 2 consisted of 60 individuals without DM, comprising 35 males and 25 females. All groups were randomly selected, aged 30 to 65 years. Each participant (patient and control) was given a 10 mL disposable syringe. The blood was divided into two parts, and the first part was placed into a gel tube to collect the serum. The first part was put into a gel tube to collect the serum. The blood was spun at 3000 rpm for 10 minutes at room temperature to separate the serum after it had clotted, and then the serum was placed into aliquots in an Eppendorf tube and stored at -20 °C until testing. The second part was transferred into an EDTA tube. The HbA1c test was done on this sample. Medication such as metformin and sulfonylurea were administered to assist the participants. The kit from the U.S. company Biosource was used to measure the amount of insulin in the blood during the fasting period. The kit (Biosource USA ELISA kit from My Biosource, USA used to measure the amount to measure the amount of human total serum Apelin-36. The Cobas c111 Germany analyzer was used to measure the amount to measure

fasting blood sugar (FBS), triglyceride (T.G.), total cholesterol (Cho), and high-density lipoprotein (HDL-C). The Cobas c 111 Origin Germany analyzer automatically calculates the ratio between A1C and Hb of each sample. GSH (Sigma Chemistry, USA) was used to measure GST activity by hand. The Homeostasis Model Assessment (HOMA-IR) measures IR= FBS (mg/dL) X fasting insulin (mU/L) / 405 (for SI units).

2.1. Data analysis

The statistical analysis was done with SPSS, Version 26. The data was shown as a median (mean SE). The ANOVA test was used to find the difference between the factors using the T-test (P-value), LSD, and correlation coefficient (r). This study used the probability value to determine the statistical significance; if the probability value was less than 0.05, it was considered significant, and if it exceeded 0.05, it was not.

3. Results and Discussion

Table 1 shows a statistically significant difference between the male group with T2DM and the male control group without T2DM. The study showed that age, BMI, FSG, and HbA1C showed substantial differences between the groups with a p-value ≤ 0.05. Cholesterol, T.G., LDL-C, and VLDL showed non-significant differences among groups 1 and 2 ($p \geq 0.05$). However, HDL showed significant differences.

The earlier study of Suastika et al. agrees with the present study. There is a strong relationship between increased age and the incidence of DM; when the age of the infected person increases, it may be more likely to be associated with CVD (15). Taylor et al. results agreed very well with our findings. Metabolic diseases, like T2DM and CVD, are more common in older people. This could be because of age or the aging process itself or other age-related risk factors for T2DM and CVD, like central obesity, mitochondrial dysfunction, FFA and lipid metabolism disorders, inflammation, cell dysfunction, IR, metabolic syndrome, and so on. For males, the BMI showed a significant difference in high muscle mass (16).

Table 1. Mean ± SE among male with T2DM patient and male without T2DM as control.

Parameters	Male with T2DM Group (1) (n=31)	Male control Group (2) (n=35)	P-value
Age (year)	57.16 ± 1.17 (58)	42.74±1.40 (42)	**0.0001
BMI (kg/m^2) body mass index	28.84± 0.75 (28.30)	31.88±0.46 (30.30)	**0.001
FBS (mg/dL) fasting blood sugar	212.2±15.07 (195)	96.24±2.12 (101)	**0.0001
HbA1C (%) Glycated hemoglobin	8.19± 0.37 (7.70)	5.09±0.072 (5)	**0.0001
Cho (mg/dL) Cholesterol	172.53±9.29 (163)	180.180±6.24 (196)	0.489
TG (mg/dL) Triglycerides	173.03±13.96 (167)	198.16±17.66 (129)	0.277
HDL-C (mg/dL) High-density lipoprotein	40.07±1.59 (39)	35.27±1.084 (34)	*0.014
LDL-C (mg/dL) Low-density lipoprotein	96.16±6.93 (98)	106.35±4.89 (116)	0.226

Parameters	Male with T2DM Group (1) (n=31)	Male control Group (2) (n=35)	P-value
VLDL-C (mg/dL)	38.16±4.51	39.47±3.53	0.817
Very low-density lipoprotein	(36)	(38.40)	

- Data were presented as Mean ± SE (Median), ** is significant at the p value ≤ 0.001 level.

There was a significant difference in HOMA-IR between the male patients (0.91±150.7) group and the control group (0.11±0.008) at P-value (≤ 0.05). The HOMA-IR had a moderately significant correlation with the increase of the BMI percentile in the study population, which is why the current study can serve as evidence to propose an early diagnosis of IR as a preventive measure for the development of T2DM and CVD in the Chiapas adolescent population (17), and this agrees with the current study. Insulin showed a significant difference (1.84 ±0.290) for patients and (0.483±0.038) for the control group at P-value ≤ 0.05). The Apelin-36 showed a significant difference between male patients (22.01±1.20) and the male control group (10.41± 0.32). Previous study indicated a significant relationship between Apelin-36 and T2DM, which have reduced body weight and blood glucose while improving glucose tolerance and lipid profile (18).

For the GST activity, there was a non-significant difference between male patients (6.66±0.73) and the male control group (6.68 ± 0.944). It has been showed that diabetic patients have lower levels of antioxidant power, which is related to an increased chance of developing DM. The GST play an essential role in the defense of cells against ROS because of their ability to employ a diverse array of oxidative stress products as substrates (19), as revealed in **Table 2**.

Table 2. Mean ± SE values between Apelin-36, insulin and HOMA IR for male patient and control.

Parameters	Male with T2DM Group (1) (n=31)	Male control Group (2) (n=35)	P-value
Apelin-36 (nmol/mL)	22.01±1.20 (21.25)	10.41±0.32 (10.12)	**0.0001
Insulin (ng/mL)	1.84±0.290 (0.844)	0.483±0.038 (0.55)	**0.001
HOMA-IR Insulin resistance	0.91±150.7 (0.58)	0.11±0.008 (0.126)	**0.0001
GST activity (IU/L) Glutathione-S-transferase	6.66±0.73 (5.20)	6.68±0.944 (5.20)	0.984

- Data were presented as Mean ± SE (Median), ** is significant at the p value ≤ 0.001 level.

Table 3 displays the mean standard error (SE) values for BMI, age, cholesterol, TG, HDL-C, and VLDL-C. The results indicate a non-significant difference between the female patients and the control group, with a p-value of less than 0.05. However, the mean SE value for LDL was significantly different, ranging from 96.37 to 6.94 for diabetic females to 121.73 to 7.34 for the control group, with a p-value of less than 0.05.

Table 3. Mean ± SE between female diabetics and female as controls.

Parameters	Female with T2DM Group (1) (n=29)	Female control Group (2) (n=25)	P-value
Age (year)	52.68±1.47 (53)	51.04±2.17 (53)	0.524
BMI (kg/m^2) body mass index	33.01±1.19 (34)	32.30±0.55 (31.1)	0.609
FBS (mg/dL) fasting blood sugar	218.68±15.89 (200)	95.11±1.87 (96)	**0.0001
HbA1C (mg/dl) Glycated hemoglobin	8.381±0.264 (8.20)	5.39±0.078 (5.50)	**0.0001
Cho (mg/dL) Cholesterol	191.20±14.18 (173)	191.92±9.53 (201)	0.968
TG (mg/dL) Triglycerides	160.96±16.69 (133)	165.18±9.43 (181)	0.834
HDL-C (mg/dL) High-density lipoprotein	44.06±2.59 (44)	41.80±2.63 (37)	0.544
LDL-C (mg/dL) Low-density lipoprotein	96.37±6.94 (97)	121.73±7.34 (124)	*0.015
VLDL-C (mg/dL) Very Low-density lipoprotein	33.24±3.39 (27)	35.164±3.37 (36.2)	0.691

- Data were presented as Mean ± SE (Median), ** is significant at the p value ≤ 0.001 level.

The FBS and HbA1C gave a significant difference between the groups ($p \leq 0.05$). FBS's mean ± SE values were (218.68±15.89) for T2DM patients and (95.11±1.87) for control and for the HbA1C was (8.381±0.264) for patients with DM and 5.39±0.078 for controls, as shown in **Table 3**.

The current results are consistent with the results of Salmeron et al., who found no connection between total fat consumption and the risk of T2DM in their sizeable prospective study of women (20). Another study found that DM raises the risk of heart failure, and women with T2DM are much more likely to have heart failure than men with T2DM (21). This is due to the increased LDL and its relationship to CVD. LDL rises, indicating diabetic dyslipidemia and a higher risk of CVD. Likewise, the current study agrees with previous study (22). **Table 4** displays all the parameters that significantly differed in mean SE values between the female patient and control groups at a p-value of less than 0.05. The mean ± SE value for Apelin-36 was (23.80±1.20) for patients and (9.99±0.53) for control, and the mean ± SE value for insulin was (2.31±0.25) for patients and (0.70±0.038) for control. The mean ± SE value for HOMA-IR was (1.21±0.15) for patients and (0.16±0.009) for controls. At last, the significant difference (mean ± SE value) for GST was (5.31±0.78) for patients and (7.97±1.37) for controls, as shown in **Table 4**.

Table 4. Mean ± SE values between Apelin-36, insulin and HOMA-IR for female patient and control.

Parameters	female with T2DM Group (1) (n=29)	female control Group (2) (n=25)	P-value
Apelin-36 (nmol/mL)	23.80±1.20 (24.21)	9.99±0.53 (9.14)	**0.0001
Insulin (ng/mL)	2.31±0.25 (2.81)	0.70±0.038 (0.77)	**0.001
HOMA IR insulin resistance	1.21±0.15 (1.29)	0.16±0.009 (0.17)	**0.0001
GST activity (IU/L) Glutathione-S-transferase	5.31±0.78 (3.64)	7.97±1.37 (4.60)	* 0.088

- Data were presented as Mean ± SE (Median), ** is significant at the p value ≤ 0.001 level

There was a significant difference in HOMA IR between females and control females; this value was higher than that of males, and the HOMA-IR index of female patients was significantly higher than that of males. These results agree with previous study (23). **Table 5** displays the correlation results for Apelin-36 in both the male and female groups.

Table 5. The correlation of Apelin-36 for male and female groups.

	Apelin-36 (nmol/mL) for male (n=31)		Apelin-36 (nmol/mL) for female (n=29)	
Parameters	**Person correlation**	**Sig.(2.tailed)**	**Person correlation**	**Sig.(2.tailed)**
Age (year)	0.034	0.856	0.010	0.957
BMI (kg/m^2)	0.582**	0.001	0.543**	0.002
Tg (mg/dL)	0.150	0.420	-0.084	0.665
Chol (mg/dL)	-0.165	0.375	-0.054	0.779
HDL (mg/dL)	-0.32	0.865	-0.092	0.634
LDL (mg/dL)	-0.274	0.137	-0.287	0.131
VLDL (mg/dL)	-0.080	0.670	-0.067	0.729
FBS (mg/dL)	-0.276	0.133	-0.151	0.433
Insulin (ng/mL)	0.533**	0.002	0.719**	0.000
IR	0.433**	0.015	0.537**	0.003
GST (IU/L)	-0.012	0.950	-0.129	0.506
HbA1C (%)	-0.316	0.083	0.136	0.483

** correlation is significant at the 0.001 level (2-tailed).

When comparing the correlation result values for all parameters for the two groups, there was no correlation found between Apelin-36 and age, lipid profile, FBS, GST, and HbA1C, but a positive correlation between Apelin-36 and BMI, Insulin, and IR. In this aspect, current results confirm that Apelin-36 has a significant relationship with obesity and DM for both sexes. Also, obesity has a substantial relationship with DM, and the HOMA-IR index of female patients was significantly higher than that of males. Therefore, Apelin-36 is a good indicator of DM in males and females. **Table 6** displays the correlation results for insulin resistance (HOMA-IR) for both male and female groups. Upon comparing the correlation values for all parameters, no correlation was found between the HOMA-IR and age, lipid profile, FBS, GST, and HbA1C for either group. However, there was a positive correlation between the HOMA-IR and BMI,

Insulin, and Apelin-36 for both groups. In this aspect, current data also confirmed that IR is present in subjects with DM and high obesity and that Apelin-36 is a significant indicator for DM in both females and males. BMI exhibits a positive correlation with insulin and HOMA-IR, as the IR increases in obese with DM. In another study, increased HOMA-IR gives rise to a hyperglycemic state and is a significant risk factor for the development of T2DM. Based on current results, it can be concluded that obesity is a risk factor for the development of T2DM (24).

Table 6. The correlation of HOMA-IR for male and female groups.

	HOMA IR for male (n=31)		**HOMA IR for female (n=29)**	
Parameters	**Person correlation**	**Sig.(2.tailed)**	**Person correlation**	**Sig.(2.tailed)**
Age (year)	-0.172	0.354	-0.167	0.388
BMI (kg/m^2)	0.591**	0.000	0.605**	0.001
Tg (mg/dL)	0.280	0.127	0.118	0.542
Chol (mg/dL)	-0.006	0.973	-0.040	0.836
HDL (mg/dL)	-0.050	0.790	0.090	0.641
LDL (mg/dL)	-0.094	0.615	-0.138	0.475
VLDL (mg/dL)	0.036	0.850	0.101	0.604
FBS (mg/dL)	0.132	0.478	0.336	0.075
Insulin (ng/mL)	0.931*	0.000	0.844**	0.000
Apelin-36 (nmol/mL)	0.433*	0.015	0.537**	0.003
GST (IU/L)	0.240	0.193	-0.296	0.119
HbA1C (%)	-0.008	0.967	0.074	0.701

** correlation is significant at the 0.001 level (2-tailed).

For the male group, the ROC (AUC) gave a positive value for Apelin-36; the result is an excellent value (0.993) for the ROC. **Table 7** and **Figure 1** demonstrate that Apelin-36 significantly impacted with T2DM. For the female group, the ROC (AUC) gave a positive value for Apelin-36; the result is an excellent value (0.993) for the ROC. **Table 8** and **Figure 2** demonstrate that Apelin-36 significantly impacted with T2DM. The two groups had excellent results for linking Apelin-36 with DM upon rock analysis, as shown in **Figures 1** and **2** for the male and female groups.

Table 7. The result of Apelin-36 at the ROC (AUC) analysis for male group.

Cut-off point	**Sensitivity**	**Specificity**	**Std. Error[a]**	**Asymptotic Sig.[b]**	**Asymptotic 95% CI**	
					Lower Bound	Upper Bound
0.993-12.7310	1.000	0.086	0.006	0.0001	0.980	1.000

a. Under the nonparametric assumption, Null hypothesis: true area = 0.5.

Table 8. The result of Apelin-36 at the ROC (AUC) analysis for female group.

Cut-off point	**Sensitivity**	**Specificity**	**Std. Error[a]**	**Asymptotic Sig.[b]**	**Asymptotic 95% CI**	
					Lower Bound	Upper Bound
0.977-9.3430	1.000	0.320	0.016	0.0001	0.945	1.000

a. Under the nonparametric assumption, b. Null hypothesis: true area = 0.5.

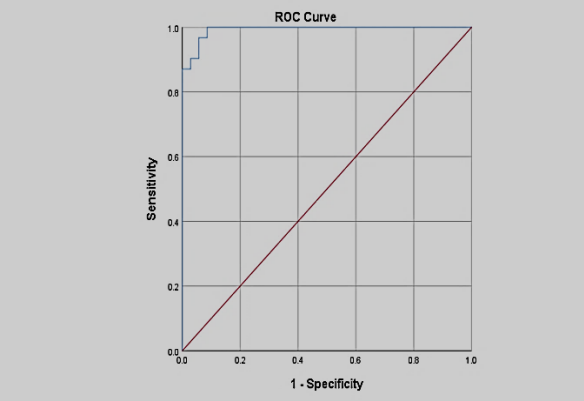

Figure 1. The ROC carve for Apelin-36 with diabetic male.

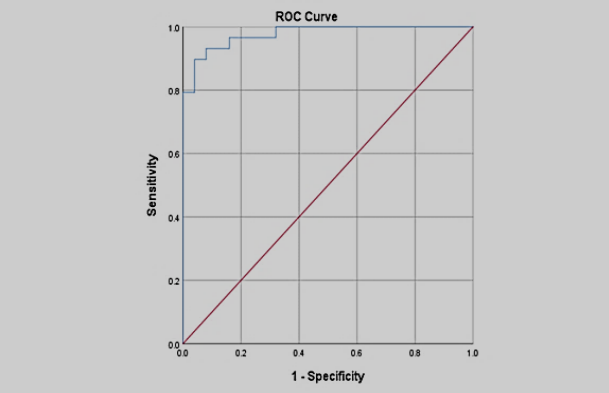

Figure 2. The ROC carve for Apelin-36 with diabetic female.

The present study shows that males with advanced age and increased muscle mass and weight are more likely to develop T2DM. They may reach advanced stages of the disease early, and women are less likely to develop diabetes than men. The common element between the two sexes is obesity, which is the incidence of DM. The weights of men are less than in women, which may be attributed to the pattern of fat distribution and the extent of its role in the incidence of the disease, and Apelin-36 is a good indicator for male and female patients with T2DM. The current results agree with Delaney et al., who suggested that T2DM is more common in men than women. In middle age, more men than women have T2DM. One of the reasons that T2DM is more common in women than in men that the difference in the distribution of adipose tissue (fat) in different body regions in women than in men (25,26) indicated that the greater prevalence of T2DM in older men compared to older women was associated with a higher visceral fat percentage in men. In contrast, BMI differences were not related to this disparity. Also, sex differences have been found in the onset and development of diabetic problems, which shows how important it is to treat DM differently for men and women. As with almost all diseases, the sex of the person with DM should be taken into account when deciding how to treat them (27). Diabetes raises the risk of CVD, and women with diabetes are much more likely to have heart failure than men with DM (28). T2DM causes several problems with the large blood vessels through different pathogenic pathways, such as high blood sugar and IR. T2DM is accompanied by arterial disease (29). Age at T2DM diagnosis has predictive importance for life and cardiovascular risks, which has implications for determining appropriate treatment strategies, making clinical decisions, and giving care based on guidelines. Based on this result, T2DM is more likely to be prevented or delayed in younger people (30). In patients with T2DM, the disease becomes more complicated after a long time, for example, diseases of the liver, kidneys, heart, and retinas. Elevated serum concentrations of enzymatic and non-enzymatic markers of liver function in T2DM support the hypothesis that the liver plays a vital role in the pathogenesis of T2DM and that hepatic enzymes may be helpful to additional markers of individuals at high risk for developing DM. Elevated levels of renal profile markers in the serum were associated with an increased risk of T2DM and hyperglycemia. As DM is the primary cause of renal morbidity and mortality, sugar management can reverse the progression of kidney damage (31). Previous study showed that age plays a significant part in developing T2DM risk after 40 years (32). Adopting a healthy lifestyle is associated with a considerable reduction in the risk of T2DM and adverse long-term

outcomes among diabetic patients; reducing the global burden of T2DM should be based on addressing multiple risk factors (33).

4. Conclusion

In conclusion, Apelin-36 is a good indicator for patients with T2DM, both males and females. Although women are less likely to develop DM than men, they are more likely to experience common complications, such as CVD. On the other hand, men are more likely to develop T2DM due to factors such as age, higher muscle mass (BMI), and weight.

Acknowledgment

The authors thank the Department of Chemistry/ College of Sciences for Women/ University of Baghdad and the National Diabetic Centre/ Al-Mustansiriyah University for their support.

Conflict of Interest

There was no conflict of interest.

Funding

The research work did not include any funding or financial support.

Ethical Clearance

This study was approved by the Scientific Committee at the Department of Chemistry/ College of Science for Women/ University of Baghdad.

References

1. Abdullah A, Salh D. Determination of serum zinc, manganese, copper and cobalt traces in type two diabetic patients in Sulaimaniyah city using ICP technique. IHJPAS. 2012; 25(3):220-225. https://doi.org/ BIM-382950.
2. Logue J, Walker JJ, Colhoun HM, Leese GP, Lindsay] RS, McKnight JA, Morris AD, Pearson DW, Petrie JR, Philip S, Wild SH. Do men develop type 2 diabetes at lower body mass indices than women. Diabetologia. 2011; 54(12):3003-3006. https://doi.org/10.1007/s00125-011-2313-3.
3. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci. 2020; 21(17):6275. https://doi.org/10.3390/ijms21176275.
4. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. Lancet. 2017; 389(10085):2239–2251. https://doi.org/10.1016/S0140-6736(17)30058-2.
5. Veit M, van Asten R, Olie A, Prinz P. The role of dietary sugars, overweight, and obesity in type 2 diabetes mellitus: a narrative review. Eur J Clin Nutr. 2022; 76(11):1-5. https://doi.org/10.1038/s41430-022-01114-5.
6. Sanchez-Garcia A, Rodriguez-Gutierrez R, Mancillas-Adame L, González-Nava V, Díaz González-Colmenero A, Solis RC, Alvarez-Villalobos NA, González-González JG. Diagnostic accuracy of the triglyceride and glucose index for insulin resistance: a systematic review. Int J Endocrinol. 2020; 2020: 4678526. https://doi.org/10.1155/2020/4678526.
7. Adamczak M, Ritz E, Wiecek A. Carbohydrate metabolism in chronic renal disease. In book: Nutritional management of renal disease. Academic Press; 2022, p.29-41. https://doi.org/10.1016/B978-0-12-818540-7.00005-7.

8. Ahmed B, Sultana R, Greene MW. Adipose tissue and insulin resistance in obese Biomed. Pharmacother. 2021; 137:111315. https://doi.org/10.1016/j.biopha.2021.111315.
9. Tan SY, Wong JL, Sim YJ, Wong SS, Elhassan SA, Tan SH, Lim GP, Tay NW, Annan NC, Bhattamisra SK, Candasamy M. Type 1 and 2 diabetes mellitus: A review on current treatment approach and gene therapy as potential intervention. Diabetes Metab Syndr: Clin Res Rev. 2019; 13(1):364-372. https://doi.org/10.1016/j.dsx.2018.10.008.
10. Kural C, Kocdogan AK, Şimşek GG, Oguztuzun S, Kaygın P, Yılmaz I, Bayram T, Izci Y. Glutathione S-transferases and cytochrome P450 enzyme expression in patients with intracranial tumors: Preliminary report of 55 patients. Med Princ Pract. 2019; 28(1):56-62. https://doi.org/10.1159/000494496.
11. Prysyazhnyuk V, Sydorchuk L, Sydorchuk R, Prysiazhniuk I, Bobkovych K, Buzdugan I, Dzuryak, V, and Prysyazhnyuk, P. Glutathione-S-transferases genes-promising predictors of hepatic dysfunction. World J Hepatol. 2021; 13(6):620-633. https://doi.org/10.4254/wjh. v13.i6.620.
12. Casadei G, Filippini M, Brognara L. Glycated hemoglobin (HbA1c) as a biomarker for diabetic foot peripheral neuropathy. Diseases. 2021; 9(1):16. https://doi.org/10.3390/diseases9010016.
13. Alzahrani SH, Baig M, Aashi MM, Al-Shaibi FK, Alqarni DA, Bakhamees WH. Association between glycated hemoglobin (HbA1c) and the lipid profile in patients with type 2 diabetes mellitus at a tertiary care hospital: a retrospective study. Diabetes Metab Syndr Obes. 2019; 12:1640-1644. https://doi.org/10.2147/dmso.s222271.
14. Galon-Tilleman H, Yang H, Bednarek MA, Spurlock SM, Paavola KJ, Ko B, To C, Luo J, Tian H, Jermutus L and Grimsby J, Apelin-36 modulates blood glucose and body weight independently of canonical APJ receptor signaling. JBC. 2017; 292(5):1925-1933. https://doi.org/10.1074/jbc.M116.748103.
15. Suastika K, Dwipayana P, Semadi MS, Kuswardhani RT. Age is an important risk factor for type 2 diabetes mellitus and cardiovascular diseases. Glucose Tolerance. 2012; 5:67-80. https://doi.org/10.5772/52397.
16. Taylor R, Al-Mrabeh A, Sattar N. Understanding the mechanisms of reversal of type 2 diabetes. Lancet Diabetes Endocrinol. 2019; 7(9):726-736. https://doi.org/10.1016/S2213-8587(19)30076-2.
17. Chang-Rueda C, Cañas-Urbina A, Trujillo-Murillo K, Espinoza-Ruiz M, Feliciano-Díaz J, Vázquez-Moreno M, Lugo-Trampe Á. Correlation of HOMA-IR with BMI-for-age percentile in children and adolescents from the Soconusco region of Chiapas, Mexico. Revista de la Facultad de Medicina. 2019; 67(4):447-450. https://doi.org/10.15446/revfacmed.v67n4.67159.
18. Son JS, Kim HJ, Son Y, Lee H, Chae SA, Seong JK, Song W. Effects of exercise-induced apelin levels on skeletal muscle and their capillarization in type 2 diabetic rats. Muscle & Nerve. 2017; 56(6): 1155-1163. https://doi.org/10.1002/mus.25596.
19. Alwan LH, Khaleel FM, Hameed AS, Al-Ghani A. Determination of polymorphism of glutathione S transferase (GST) in the Iraqi (diabetic and non-diabetic) acromegalic patients. Biochem Cell Arch. 2020; 20(2):6709-6714. https://connectjournals.com/03896.2020.20.6709.
20. Salmeron J, Hu FB, Manson JE, Stampfer MJ, Colditz GA, Rimm EB, Willett WC. Dietary fat intake and risk of type 2 diabetes in women. Am J Clin Nutr. 2001; 1(736):1019-1026. https://doi.org/10.1093/ajcn/73.6.1019.
21. Ohkuma T, Komorita Y, Peters SA, Woodward M. Diabetes as a risk factor for heart failure in women and men: a systematic review and meta-analysis of 47 cohorts including 12 million individuals. Diabetologia. 2019; 1(62):1550-1560. https://doi.org/ 10.1007/s00125-019-4926-x.
22. Zhang Y, Yang J, Guo Q, Wang W, Sun Y, Zeng Q. Separate and combined associations of physical activity and obesity with lipid-related indices in non-diabetic and diabetic patients. Lipids Health Dis. 2019; 18(1):49. https://doi.org/10.1186/s12944-019-0987-6.

23. Yang Y, Zhang Y, Wang J, Ning X, Zhang Y, Zhao T, Zhong Y, Liu Z, Xia L, Li W, Yao X. Sex differences in the association of HOMA-IR index and BDNF in Han Chinese patients with chronic schizophrenia. Front Psychiatry. 2021; 21(12):656230. https://doi.org/ 10.3389/fpsyt.2021.656230.
24. Abbas KM, Alaaraji SF, Alâ RS. A study of the association between IL-17 and HOMA-IR in Iraqi type 2 diabetic patients. Iraqi J Sci. 2020; 61(3):491-498. https://doi.org/10.24996/ijs.2020.61.3.4.
25. Delaney KZ, Santosa S. Sex differences in regional adipose tissue depots pose different threats for the development of type 2 diabetes in males and females. Obes Rev. 2022; 23(3):e13393. https://doi.org/10.1111/obr.13393.
26. Nordstrom A, Hadrévi J, Olsson T, Franks PW, Nordström P. Higher prevalence of type 2 diabetes in men than in women is associated with differences in visceral fat mass. J Clin Endocrinol Metab. 2016; 101(10):3740-3746. https://doi.org/10.1210/jc.2016-1915.
27. Tramunt B, Smati S, Grandgeorge N, Lenfant F, Arnal JF, Montagner A, Gourdy P. Sex differences in metabolic regulation and diabetes susceptibility. Diabetologia. 2020; 63(3):453-461. https://doi.org/10.1007/s00125-019-05040-3.
28. Ohkuma T, Komorita Y, Peters SA, Woodward M. Diabetes as a risk factor for heart failure in women and men: a systematic review and meta-analysis of 47 cohorts including 12 million individuals. Diabetologia. 2019; 62(9):1550-1560. https://doi.org/10.1007/s00125-019-4926-x.
29. Viigimaa M, Sachinidis A, Toumpourleka M, Koutsampasopoulos K, Alliksoo S, Titma T. Macrovascular complications of type 2 diabetes mellitus. Curr Vasc Pharmacol. 2020 ;18(2):110-116. https://doi.org/10.2174/1570161117666190405165151.
30. Sattar N,Rawshani A, Franzén S, Rawshani A, Svensson AM, Rosengren A, McGuire DK, Eliasson B, Gudbjörnsdottir S. Age at diagnosis of type 2 diabetes mellitus and associations with cardiovascular and mortality risks: findings from the Swedish National Diabetes Registry. Circulation. 2019; 139(19): 2228-2237. https://doi.org/10.1161/circulationaha.118.037885.
31. Balaky HM, Kakey IS. Indications of liver and kidney functions innon-insulin dependent diabetic patients. Iraqi J Sci. 2021; 62(3):769-778. https://doi.org/10.24996/ijs.2021.62.3.7.
32. Ahmed SY. A study of Hepcidin levels and other biochemical parameters in woman with osteoporosis with type 2 diabetes mellitus. IHJPAS. 2022; 35(4):183-193. https://doi.org/10.30526/35.4.2867.
33. Zhang Y, Pan XF, Chen J, Xia L, Cao A, Zhang Y,Wang J, Li H, Yang K, Guo K, He M. Combined lifestyle factors and risk of incident type 2 diabetes and prognosis among individuals with type 2 diabetes: a systematic review and meta-analysis of prospective cohort studies. Diabetologia. 2020; 63(1):21-33. https://doi.org/10.1007/s00125-019-04985-9.