Article

Assessment of the correlation of lipasin levels with HOMA-IR score as an index of insulin resistance in type 2 diabetic Iraqi patients

Seenaa B. Mohammed[1], Alaa. J. Mahrath[2], Tariq. R. Abd[3]

1. Department of Chemistry and Biochemistry, College of Medicine, University of Babylon, Iraq. Email: badr.seenae@uobabylon.edu.iq,
2. Department of Chemistry and Biochemistry, College of Medicine, University of Babylon, Iraq. Email: jafermohrath.alaa@uobabylon.edu.iq,
3. Department of Chemistry and Biochemistry, College of Medicine, University of Babylon, Iraq. Email: Tqchemist@gmail.com

Abstract

Lipasin, a hormone found in the liver and adipose tissue, is involved in glucose homeostasis and lipid metabolism. Lipasin levels in plasma are controlled by food and rise after glucose consumption. Because plasma glucose and insulin levels both rise after eating, The study aims to elucidate if lipasin increases insulin sensitivity.

According to this study, the patient group's lipasin concentration increased significantly (p-value< 0.05) in comparison to the control group, and the area under the curve (AUC) for lipasin was 75.75 %.

The levels of insulin and glucose and also for the BMI were higher (p-value< 0.05) in patient group in comparison to control group.

The results emphasize that Lipasin may play a crucial role in T2DM development.

Keywords: Lipasin, Insulin, glucose, ROC-Curve, Diabetes HOMA-IR.

Introduction

The chronic metabolic disease known as diabetes mellitus (DM) is characterized by hyperglycemia, or increased blood glucose levels. It is typically associated with certain conditions, like growth hormone insufficiency or insulin resistance (IR). Severe issues, including the kidneys, eyes, heart, and neurological system, can result from long-term diabetes mellitus (1) .

The most common kind of diabetes mellitus (DM), type 2 diabetes mellitus (T2DM), accounts for around 90% of cases globally. It is characterized by inadequate insulin synthesis by pancreatic β-cells and/or poor insulin response (IR) in body cells (2).

A recently identified hormone, lipasin, is expressed in adipose tissue and the liver (3). has a major impact on the metabolism of fats. Environmental elements like cold weather and food factors like consuming a lot of fat might affect how it expresses itself (4).

The aim of the study is to determine if HOMA-IR score, an indicator of insulin resistance and lipasin levels are correlated in patients with T2DM. Comprehending this correlation might offer valuable perspectives on the pathogenesis of T2DM and identify future treatment targets aimed at enhancing glycemic management and preventing complications.

Materials and Methods

This case-control research had 90 participants: 45 with T2DM (23 females and 22 men) comprised the patient group, whereas 45 individuals in apparent good health comprised the control group (19 females and 26 males).

The patient group was split into two subgroups based on their body mass index (BMI): those who were obese (BMI > 30 kg/m2) and those who were not obese (BMI = 18.5-29.9 kg/m2).

The samples were collected throughout August and October of 2023.

The ages of the study Participants range from 35 to 55 years old. The data collected in this study include, the patient's history, kind of therapy, weight, height, sex, and age.

Inclusion criteria:

Patients who have T2DM with a history less than 1 year.

Exclusion Criteria:

T2DM patients with diabetic complications, Cushing syndrome, dyslipidemia, growth hormone deficiency, liver dysfunction and thyroid dysfunction.

venous blood samples were drawn from all participants. Serum separator (SST) tubes were filled with blood, which is then centrifuged at 3000 xg for 10 minutes after coagulating for 10-15 minutes at room temperature. After the separation of serum, glucose levels were estimated. The remainder sera were kept in Eppendorf tubes at -20 C until the time came to assess the levels of insulin and lipasin.

Serum lipasin levels were measured using the commercially available enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturers' (Bioassay Technology Laboratory) instructions. Lipasin levels ranged from 0.5 ng/mL to 100 ng/mL (5).

Serum insulin levels were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturers' (Bioassay Technology Laboratory) instructions. Insulin levels ranged from 0.2 mIU/L to 60 mIU/L (6).

The serum glucose levels were determined by using the Genx Smart-150 Chemistry Analyzer. This instrument uses a glucose determination kit from Giesse Diagnostics that uses an enzymatic colorimetric method called the Glucose-Oxidase (GOD) method (7).

Statistical Analysis

The results of the current comparative study of the patient and control groups were performed by using the IBM Statistical Package for the Social Sciences (SPSS V. 26). The students t-test was used to determine the difference in mean between the control and diabetic groups, where (p-value≤ 0.05) considered significant and correlation between studied parameters were done by using Pearson correlation. The ROC Curve analysis for lipasin levels had been performed to reveal its sensitivity and specificity.

Results and Discussion

The age range for this study was (35-55) years. The result showed that the age range of the control group does not match that of the patient group (p-value> 0.000), because

this study aims to explore the correlation between age and lipasin. It has been shown that there is no relationship between lipasin levels and age.

Table 1: means and standard deviations of the age of the studied groups

Parameter	Group	No	Mean ± SD	p-value
Age (Years)	Patient	45	48.87 ± 6.104	0.000
	Control	45	42.24 ± 5.236	

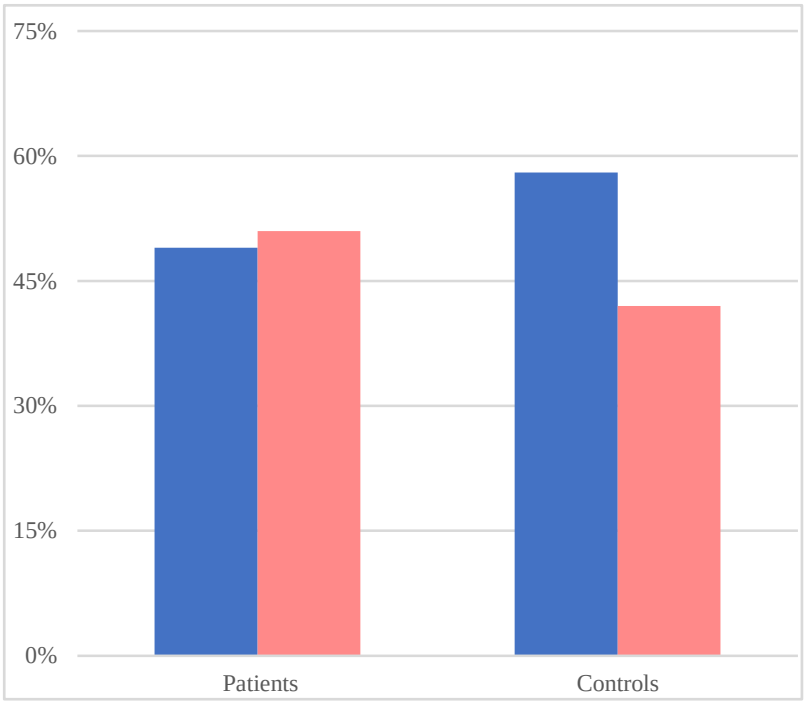

Figure 1: Sex distribution of the studied groups

Sex distribution in both groups (Patients and controls) is shown in (Figure 1), patient group composed of (22 males and 23 females), while the control group composed of (26 males and 19 females).

The number of female patients with T2DM tend to be higher than that of male patients, which agrees with the results of the national stepwise survey in Iraq performed in 2015 (8).

The Body Mass Index was higher in patient group in comparison to control group (p-vale= 0.000) as displayed in Table 2.

There is a significant difference (p-value = 0.000) between the BMI means of the studied groups. This is probably due to the difference in T2DM prevalence, which is related to overweight and obesity in comparison to normal weight in T2DM patients. This is consistent with a study by Pengpid et al. that found that overweight and obese T2DM patients had a higher prevalence of diabetes (8).

Table 2: means and standard deviations of the BMI of the studied groups

Parameter	Group	No	Mean± SD	p-value
BMI (Kg/m^2)	Patient	45	30.86 ± 5.49	0.000
	Control	45	23.20 ± 1.24	

Patients' group was divided according to BMI into two, obese and non-obese (overweight and normal). There were (53%) obese and (47%) non-obese patients. There was no significant difference between lipasin levels of the obese and non-obese subgroups. This may be due to merging normal and overweight patients together in one group (non-obese).

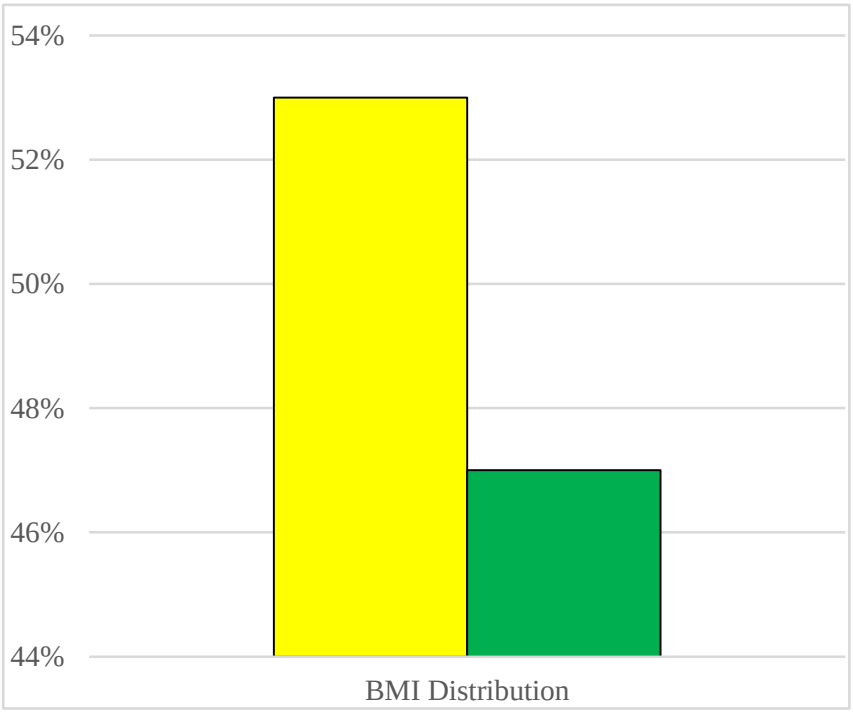

Figure 2: BMI distribution in Patient Group

This shortage of normal BMI T2DM patients in our study agrees with the findings of the national stepwise survey conducted in 2015, which summarized the higher prevalence of overweight (29%) and obese (52%), as well as diabetes, in diabetic patients in the Iraqi population compared to normally weighed (17.4%) T2DM patients (9)

Some factors that lead to an increase in BMI, such as unhealthy dietary habits or sedentary life style. These may be related to the increased incidence of IR over time. This interpretation can be augmented by finding a positive correlation between lipasin levels and the BMI in this study. This may be attributed to the role of lipasin in lipid metabolism, where lipasin inhibits lipoprotein lipase (LPL) activity (4,10). This finding agrees with the discovery reached by Zheng et al., who also revealed a positive correlation between lipasin levels and BMI (11).

Lipasin levels between studied groups show significant difference (p-value = 0.000). as in table 3.

Table 3: Mean of lipasin levels of studied groups

Parameter	Group	No	Mean ± SD	p-value
Lipasin (ng/ml)	Patient	45	8.7545 ± 2.145	0.000
	Control	45	6.7680 ± 2.265	

However, Lipasin levels among BMI subgroups show no difference (p-value = 0.444), as in table 4.

Table 4: Mean of lipasin levels according to BMI subgroups in patients

Parameter	BMI Group	No	Mean ± SD	p-value
Lipasin (ng/ml)	Non-Obese	21	8.496 ± 1.671	0.444
	Obese	24	9807. ± 2.502	

The observed noteworthy difference in lipasin levels between the research groups (patients and controls) could strengthen the hypothesis that lipasin functions as a hormone to stimulate the growth of pancreatic β-cells, thereby mitigating the IR associated with T2DM by augmenting cellular glucose uptake. This result is consistent with the findings of Abu-Farha et al., who found that after controlling for a variety of risk factors, higher lipasin levels were linked to a more than six-fold increase in the odds of having T2DM (12).

The results in Figure 3 and Table 5 show that area under curve (AUC) = (0.758), sensitivity = (77%), and specificity = (68%), which can be interpreted as; that lipasin biomarker has Fair Sensitivity and Specificity for the diagnosis of T2DM (13).

Table 5: Area Under the Curve for lipasin

Group	No	Area Under Curve	cutoff point	Sensitivity	Specificity
Patients	45	0.758	7.23	77%	68%
Controls	45				

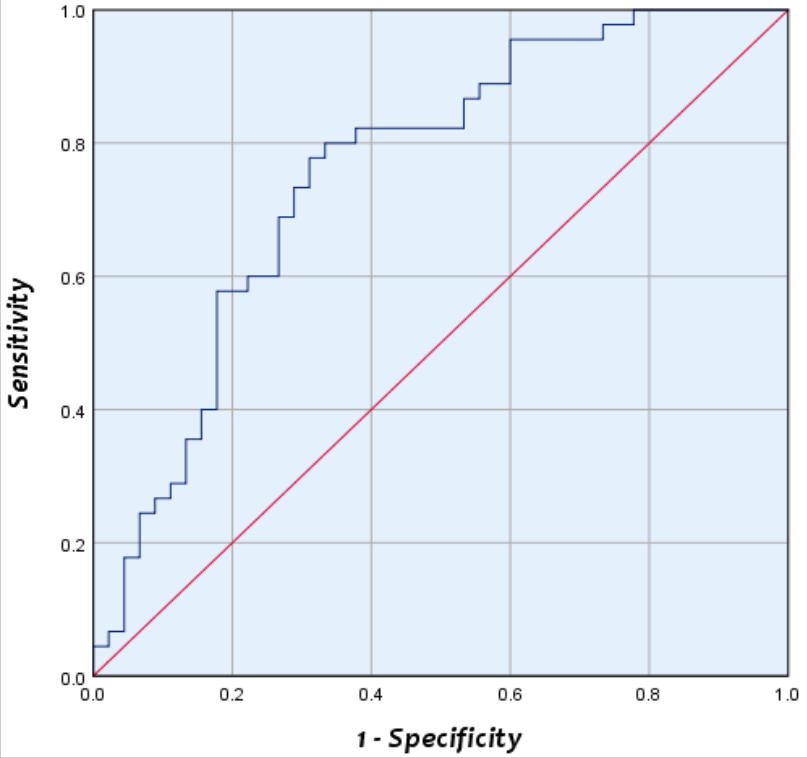

Figure 3: ROC Curve analysis for lipasin levels of the study participants

For Insulin, levels of patient and control groups show significant difference (p-value =0.008), as shown in Table 6.

Table 6: Insulin level means in both study groups

Parameter	Group	Mean ± SD	p-value
Insulin (mIU/L)	Patient	5.898 ± 0.919	0.008
	Control	4.935 ± 1.064	

Glucose levels of study groups show significant difference (p-value= 0.000), as shown in table 6. The mean of glucose levels of the patient group is higher than that of normal blood glucose (2).

Table 7: Glucose levels means in both study groups

Parameter	Group	No	Mean ± SD	p-value
Glucose (mmol/L)	Patient	45	11.987 ± 3.695	0.000
	Control	45	6.188 ± 0.961	

By determination Insulin and Glucose levels, Insulin Resistance have been determined by the homeostatic model assessment for insulin resistance (HOMA-IR). The calculation of the HOMA-IR index was done using the following equation:

$$HOMA - IR = \frac{FastingGlucose(mmol/L) * FastingInsulin(mIU/L)}{22.5}$$

HOMA-IR value represents the level of IR (opposes insulin sensitivity). The optimal insulin sensitivity when HOMA-IR is less than 1, while Levels above 1.9 signal early insulin resistance and levels above 2.9 signal significant IR (14).

There was no correlation between lipasin levels of study participants with age (r= 0.130, p-value> 0.05).

Table 8: Correlations between Lipasin and age of the study Participants

Parameter	Correlations	Age (Years)	No
Lipasin (ng/ml)	r	0.130	90
	p-value	0.223	

On the other hand, lipasin levels of the study participants were positively and significantly correlated with the BMI, (r= 0.293, p-value= 0.05) as shown in figure 3.

The relationship between lipasin and Insulin levels of the study participants was positive significant relationship (r= 0.574, p-value= 0.000), as shown in figure 4.

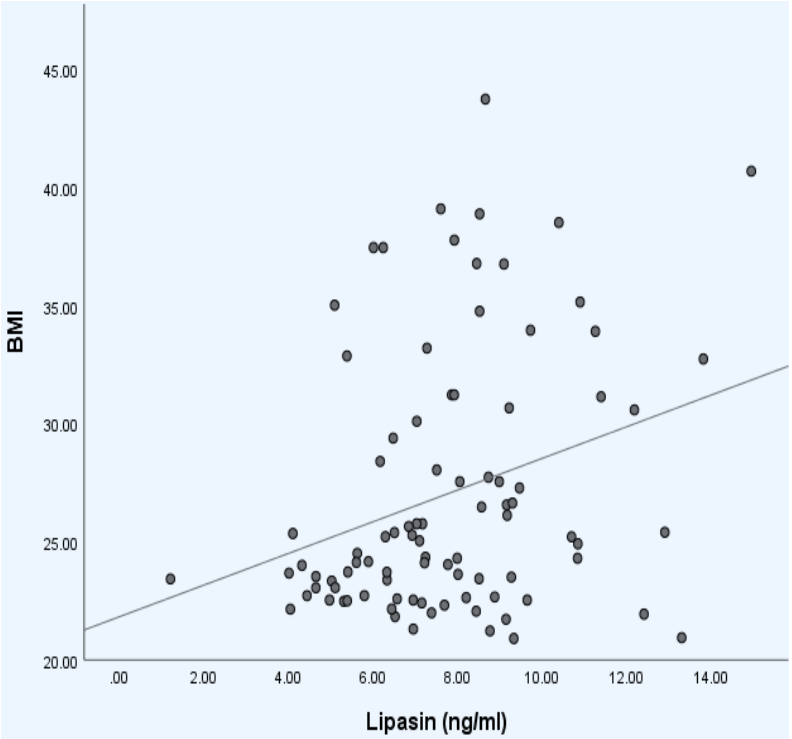

Figure 3: Correlation between lipasin levels and the BMI

The high levels of insulin in diabetic patients in this study may be attributed to the IR. It is considered a risk factor that led to the development of T2DM, in which the insulin became less effective. Eventually, this situation prompts an increase in insulin production to compensate this disturbance (2,15). Lipasin, insulin, and blood glucose may affect each other.

This could be interpreted as the increase of insulin in T2DM patients leading to an increase in lipasin levels, as Guo et al. mentioned that insulin could exert this promoting effect on lipasin only in the presence of high glucose levels (16).

As stated by Guo et al., overexpression of lipasin increased the insulin-stimulated activation of the Akt-FoxO1 or Akt-GSK3β pathways regardless of whether IR was present in the cells. In contrast, lipasin knockout had no effect on the Akt-GSK3β or Akt-FoxO1 pathways unless the HepG2 cells were preset with IR (16).

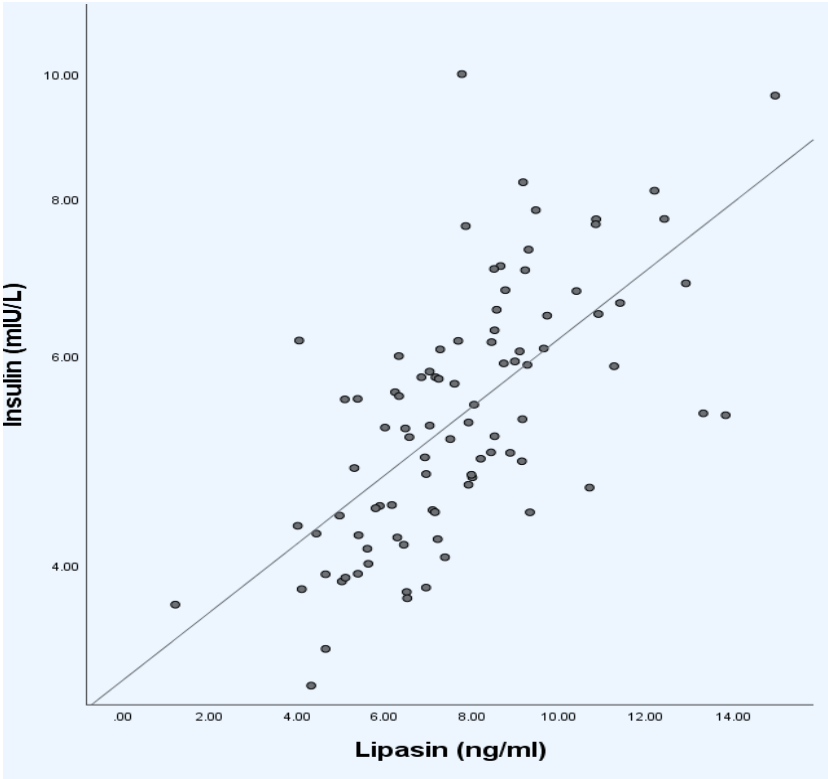

Figure 4: Correlation between lipasin levels and the Insulin

On the other hand, Abu-Farha et al. discovered that insulin was positively correlated with lipasin in a non-diabetic group but not related to lipasin in a T2DM group, although the T2DM group exhibited an increased level of lipasin (12).

A current argument about whether insulin affects the expression level of lipasin directly or indirectly through blood glucose. Although this has been examined, there is still no practical clarification for the contradictory conclusions, which still require extra efforts to be authenticated.

The relationship between lipasin and Glucose levels of the study participants (patients and controls) was shown to be a non-significant relationship.

Table 9: Correlations between levels of lipasin and Glucose

Parameter	Correlations	Glucose (mmol/L)
Lipasin (ng/ml)	r	0.028
	p-value	0.873

For the relationship between lipasin levels and IR, the study found that there is an association between lipasin levels and HOMA-IR scores in healthy individuals, but this relation seemed to be troubled when the score indicates IR.

The relation between levels of lipasin and HOMA-IR of the study participants is a positive non-significant correlation (r= 0.243, p-value= 0.167), also in case of patient group, it was a positive non-significant correlation (r= 0.317, p-value= 0.215). On the other hand, control group exhibit a positive significant correlation (r= 0.524, p-value=0.031), as shown in Table 10.

Table 10: Correlations between lipasin and HOMA-IR.

		Participants' HOMA-IR		
Parameter	Correlations	All	patients	Controls
Lipasin (ng/ml)	r	0.243	0.317	0.524
	p-value	0.167	0.215	0.031

Conclusion

The results emphasize that lipasin may play a crucial role in T2DM development through its positive correlation with insulin and BMI, but it can't be used as a diagnostic biomarker because of its fair sensitivity and specificity according to its ROC curve.

References

1. Crook MA. Clinical Biochemistry & Metabolic Medicine. 8th ed. London: CRC Press; 2013.

2. IDF Diabetes Atlas 10th edition [Internet]. Available from: www.diabetesatlas.org

3. Guo Q, Cao S, Wang X. Betatrophin and Insulin Resistance. Vol. 12, Metabolites. MDPI; 2022.

4. Sylvers-Davie KL, Davies BSJ. Regulation of lipoprotein metabolism by ANGPTL3, ANGPTL4, and ANGPTL8. Am J Physiol Endocrinol Metab. 2021 Oct 1;321(4):E493–508.

5. Human Betatrophin ELISA Kit [Internet]. 1008 Junjiang Inter. Bldg. 228 Ningguo Rd. Yangpu Dist. Shanghai. China; Available from: www.bt-laboratory.com

6. Human Insulin ELISA Kit [Internet]. Available from: www.bt-laboratory.com

7. Enrico V. Glucose determination Kit by Giesse Diagnostics [Internet]. Guidonia Montecelio (RM) - Italia; 2014 Nov. Available from: www.giessediagnostics.com

8. Pengpid S, Peltzer K. Overweight and Obesity among Adults in Iraq: Prevalence and Correlates from a National Survey in 2015. Int J Environ Res Public Health. 2021 Apr 15;18(8):4198.

9. Hussein A, Ahmed I, Huwail M, Aati adnan, Al-Noori T, Al-Siraj M, et al. Non-Communicable Diseases Risk Factors STEPS Survey Iraq 2015. WHO [Internet]. 2015 Jan 1 [cited 2024 Jan 28]; Available from: https://cdn.who.int/media/docs/default-source/ncds/ncd-surveillance/data-reporting/iraq/steps/iraq-2015-steps-report.pdf?sfvrsn=5531fd55_2&download=true

10. Zhang R. Lipasin, a novel nutritionally-regulated liver-enriched factor that regulates serum triglyceride levels. Biochem Biophys Res Commun. 2012 Aug;424(4):786–92.

11. Zheng J, Liu J, Hong BS, Ke W, Huang M, Li Y. Circulating betatrophin/ANGPTL8 levels correlate with body fat distribution in individuals with normal glucose tolerance but not those with glucose disorders. BMC Endocr Disord. 2020 Apr 16;20(1):51.

12. Abu-Farha M, Abubaker J, Al-Khairi I, Cherian P, Noronha F, Hu FB, et al. Higher plasma betatrophin/ANGPTL8 level in Type 2 Diabetes subjects does not correlate with blood glucose or insulin resistance. Sci Rep. 2015 Jun 16;5(1):10949.

13. Safari S, Baratloo A, Elfil M, Negida A. Evidence Based Emergency Medicine; Part 5 Receiver Operating Curve and Area under the Curve. Emerg (Tehran). 2016;4(2):111–3.

14. Tang Q, Li X, Song P, Xu L. Optimal cut-off values for the homeostasis model assessment of insulin resistance (HOMA-IR) and pre-diabetes screening: Developments in research and prospects for the future. Drug Discov Ther. 2015;9(6):380–5.

15. Ozougwu O. The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. Journal of Physiology and Pathophysiology. 2013 Sep 30;4(4):46–57.

16. Rong Guo X, Li Wang X, Chen Y, Hong Yuan Y, Mei Chen Y, Ding Y, et al. ANGPTL8/betatrophin alleviates insulin resistance via the Akt-GSK3β or Akt-FoxO1 pathway in HepG2 cells. Exp Cell Res. 2016 Jul;345(2):158–67.