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Study on the correlation between PPARγ, Aβ1-42, miR-155 and the occurrence and development of diabetes

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ABSTRACT

The objective of this research was to study the correlation between PPARγ, Aβ1-42, miR-155 and the occurrence and development of diabetes. For this purpose, 52 patients with diabetes who were hospitalized from September 2019 to May 2021 were selected as the research objects. They were grouped according to the severity of the disease, which was pre-diabetes (n=16), mild (n=25), and moderate (n=16). =11), another 20 healthy subjects were taken as the control group, and the levels of PPARγ, Aβ1-42, miR-155 in each group were measured, and the correlation between changes in the levels of various indicators and the occurrence and development of diabetes was explored. Results showed that comparison of age, gender, course of disease, BMI, living habits, comorbidities, and high-density lipoprotein among the groups of diabetic patients (P>0.05); the levels of total cholesterol, triglycerides and low-density cholesterol decreased with the development of diabetes (P<0.05)); Compared with the healthy group, the levels of PPARγ and miR-155 were significantly reduced, and the levels of Aβ1-42 were significantly increased (P<0.05); compared with the prediabetes, the levels of mild and moderate PPARγ and miR-155 showed a downward trend, and Aβ1 -42 level showed an upward trend (P<0.05); PPARγ and miR-155 levels were negatively correlated with pre-diabetes, mild, and moderate; Aβ1-42 was positively correlated with pre-diabetes, mild, and moderate (P<0.05) ; PPARγ, Aβ1-42, miR-155 levels can effectively predict the occurrence and development of diabetes, and the sensitivity, specificity and accuracy of the detection of diabetes by various indicators, positive predictive value and negative predictive value are significantly higher. It is concluded that PPARγ, Aβ1-42, miR-155 are closely related to the occurrence and development of diabetes, and there are many influencing factors of diabetes. Clinical intervention measures can be taken according to specific conditions.

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Introduction

Changes in living standards and dietary habits lead to an increase in the incidence of diabetes year by year. According to the data of the International Diabetes Federation, it is expected that the number of adult diabetes patients in China will increase to 578 million by 2030, among which the number of patients in China ranks first. Type 2 diabetes is a common type, accounting for more than 90% of the total number of diabetes patients (1). Type 2 diabetes is mainly caused by insulin resistance combined with a deficiency of relative insulin secretion and occurs at all ages. After 40 years of age, the incidence of the disease increases with age. There is no significant feature of the disease in the early stage and only occasional detection of hyperglycemia. With the development of the disease, patients typically present with polyuria, polydipsia, weight loss, etc. There is no specific drug treatment before delivery, and long-term continuous control of blood glucose levels and metabolic disorders is required, which seriously affects the family and social-economic burden (2-3).

Most scholars believe that insulin resistance is the main pathogenesis of type 2 diabetes, leading to excessive insulin content in the body and difficulty in glucose metabolism and utilization, resulting in elevated blood glucose, metabolic disorders in the body, hyperglycemia and obesity (4). Central obesity, cognitive dysfunction and blood circulation disorders are related to diabetes or pre-diabetes, which can effectively predict the occurrence and development of the disease (5). Peroxisome proliferator-activated receptor γ (PPARγ) is a ligand-activated nuclear receptor factor that not only participates in lipid

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metabolism balance but also increases insulin sensitivity and effectively improves cardiovascular circulation. Amyloidβ-protein 1-42 (Aβ1-42) exists in small amounts in normal brain tissue and is widely used in clinical cognitive disorders. However, related studies have shown that increased blood lipids and atherosclerosis in diabetic patients can also cause abnormal expression of the Aβ1-42 level. Peripheral blood microRNA-155 (Mir-155) is one of the inflammatory genes with many target genes in vivo, and plays an important role in vascular diseases and the immune system, providing a reference for the development of diabetes (6-8). At home and abroad, diabetes is mainly focused on continuous treatment, new drug research and development and nursing, but there is limited research on related factors of disease occurrence and development (9-10). This study aims to explore the correlation between PPARγ, Aβ1-42, Mir-155 and the occurrence and development of diabetes mellitus, as reported below.

Materials and methods

General Information

Fifty-two hospitalized patients with diabetes from September 2019 to May 2021 were selected as the study subjects. According to the severity of the disease, the patients were divided into pre-diabetes (n=16), mild diabetes (n=25) and moderate diabetes (n=11). Another 20 healthy subjects were selected as the control group. There was no significant difference in baseline data among all groups (P>0.05), indicating comparability. This study was approved by the medical ethics committee of the hospital.

Inclusion and exclusion criteria

Inclusion criteria: ① Meet the diagnostic criteria of diabetes in guidelines for prevention and treatment of Type ii diabetes (11) and WHO[12] 1999; ② Age ≥18 years, < 80 years; ③ Receiving insulin control and hypoglycemic drugs; (4) Complete preservation of clinical data; ⑤ No mental disorders, cognitive disorders, immune system diseases and cardiovascular diseases; ⑥ Patients and their families were aware of the study content and voluntarily signed informed consent.

Exclusion criteria: ① patients with serious insufficiency of heart, liver and kidney function; ② Diabetic cerebral infarction, ketoacidosis and other complications; ③ With severe immune system disorders or malignant tumors; ④ Pregnant and lactation women; ⑤ Those who have recently received hormone therapy; ⑥ Those who participate in other research projects, quit or lose contact; ⑦ Poor compliance.

Research methods

General data were collected after admission, including age, height, weight and body mass index (BMI), medication history and living habits, and complications. 5mL of peripheral venous blood was taken from the patient in the morning and stood for 10min after centrifugation. The supernatant was taken for examination, and the total cholesterol, triglyceride, low-density lipoprotein, high-density lipoprotein, etc. of the patient were detected by an automatic biochemical analyzer (Shanghai Jumumedical Instrument Co., LTD., Model IMGIC-M7). Laboratory indicators: Serum PPARγ and Mir-155 levels were detected by QRT-PCR. Enzyme-linked immunosorbent assay (ELISA) was used to detect the level of Aβ1-42. The kit was provided by Shanghai Jinganti Bioengineering Co., LTD., and the kit instructions were strictly followed.

Observation Indicators

(i) To compare the general data of patients with different degrees of diabetes; (ii) The levels of PPARγ, Aβ1-42 and Mir-155 in each group were observed and recorded; (iii) Pearson correlation coefficient was used to analyze the correlation between PPARγ, Aβ1-42, Mir-155 levels and the occurrence and development of diabetes mellitus. (iv) The predictive value of PPARγ, Aβ1-42 and Mir-155 levels on the occurrence and development of diabetes mellitus was evaluated by receiver Operator characteristic (ROC) curve.

Statistical treatment:

SPSS 24.0 statistical software was used. The measurement data conforming to normal distribution were expressed as ± S, and a t-test was used for comparison between groups. The statistical data were expressed as the number of cases (n) and percentage (%), and the comparison between groups was performed by $\chi 2$ test, P<0.05 indicated a statistically significant difference. Pearson correlation coefficient

was used to analyze the correlation between PPAR γ , A β 1-42, Mir-155 and the occurrence and development of diabetes mellitus. The predictive value of PPAR γ , A β 1-42 and Mir-155 levels on the occurrence and development of diabetes mellitus was statistically significant with P<0.05.

Results and discussion

Comparison of basic data

The results showed that there were no significant differences in age, gender, course of the disease, BMI, lifestyle, complicated diseases and high-density lipoprotein among all groups (P>0.05). The levels of total cholesterol, triglyceride and LOW-density cholesterol decreased with the development of diabetes, and the differences were statistically significant (P<0.05), as shown in Table 1.

Comparison of PPAR γ , A β 1-42 and Mir-155 levels between the healthy group and the diabetic group

The results showed that compared with the healthy group, the levels of PPAR γ and Mir-155 were significantly decreased, and the levels of A β 1-42 were significantly increased. The difference was statistically significant (P<0.05), as shown in Table 2.

Comparison of PPARγ, Aβ1-42 and Mir-155 levels in patients with different degrees of diabetes

The results showed that compared with prediabetes, the levels of mild and moderate PPARγ and Mir-155 were decreased, and the levels of Aβ1-42 were increased, with statistical significance (P<0.05). (Table 3 and Fig. 2).

Correlation analysis of PPAR γ , A β 1-42 and Mir-155 on the occurrence and development of diabetes mellitus

The results showed that PPAR γ and Mir-155 levels were negatively correlated with pre-diabetes, mild and moderate diabetes, while A β 1-42 was positively correlated with pre-diabetes, mild and moderate diabetes, with statistical significance (P<0.05), as shown in Table 4.

Predictive efficacy of PPAR γ , A β 1-42 and Mir-155 levels on the occurrence and development of diabetes mellitus

The results showed that PPAR γ , A β 1-42 and Mir-155 levels could effectively predict the occurrence and progression of diabetes mellitus. In addition, the sensitivity, specificity, accuracy, positive predictive value and negative predictive value of all indicators in the detection of diabetes were significantly higher, as shown in Table 5 and Figure 1.

Diabetes is one of the chronic diseases caused by abnormal blood glucose metabolism in the body. Along with the disease process and improper drug control, it will cause disorders of the immune system and cardiovascular system, resulting in systemic organ involvement and endangering life. At present, there are no significant treatment methods and drugs, so early detection and treatment are particularly important for the development and control of diabetes (13). Insulin resistance is one of the main pathogenesis of type 2 diabetes. In recent years, studies have found that lipid metabolism, cognitive level and vascular sclerosis all affect the disease of diabetes, and PPAR γ , A β 1-42 and Mir-155 play an important role in this process (14). Studies have shown that the levels of PPAR γ , A β 1-42 and Mir-155 in patients with hyperlipidemia are significantly changed, so it is speculated that they are closely related to the occurrence and development of diabetes (15-16). Domestic and foreign scholars mostly conducted a factor analysis on a single aspect of diabetes but did not jointly analyze the occurrence and development of diabetes with multiple indicators. This study analyzed the correlation between PPAR γ , A β 1-42 and Mir-155 levels in different periods and the occurrence and development of diabetes.

Chen et al. (17) explored the association between A β 1-42 in diabetes mellitus and Alzheimer's disease, and the results showed that the continuous increase of A β 1-42 in the body can significantly promote the pathological changes of Alzheimer's disease in diabetic patients. Akhbari et al. (18) investigated the level of free Mir-155 in patients with different degrees of diabetes.The results showed that the level of Mir-155 in serum of diabetic patients was significantly lower than that of the healthy group, and there was no significant difference in the level of Mir-155 in patients with different degrees of diabetes. The results of this study showed that compared with the healthy group, the levels of PPAR γ and Mir-155 were

significantly decreased, and the levels of Aβ1-42 were significantly increased.

Table 1. Comparison of basic information

Group		Prophase (n=16)	Mild (n=25)	Medium (n=11)	Statistics	P
Gender (case)	Male	9（56.25）	14（56.00）	6（54.55）	5.053	0.067
	Female	7（43.75）	11（44.00）	5（45.45）		
Age (years)		64.13±7.49	67.42±6.91	68.82±4.24	2.181	0.052
Course of disease (years)		0.91±0.18	4.78±1.27	6.71±1.25	3.027	0.064
BMI（kg/mL）		23.49±0.73	23.58±0.67	24.29±0.81	0.164	0.051
Living habits (case)	Smoking	1（6.25）	3（12.00）	2（18.18）	4.052	0.117
	Drinking	6（37.50）	1（4.00）	0（0.00）		
	Insomnia	2（12.50）	3（12.00）	3（27.27）		
Merger disease (case)	Hyperlipidemia	1（6.25）	2（8.00）	0（0.00）	2.398	0.204
	Hypertension	0（0.00）	0（0.00）	2（18.18）		
	Kidney disease	1（6.25）	0（0.00）	1（9.09）		
	other	0（0.00）	1（4.00）	0（0.00）		
Total cholesterol (mmol/L)		5.49±0.92	4.67±0.82	4.38±0.76	0.429	0.016
Triglyceride (mmol/L)		2.23±0.79	1.87±0.78	1.57±0.65	0.370	0.042
Low density lipoprotein (mmol/L)		3.84±0.94	3.43±0.81	2.96±0.92	0.519	0.004
High-density lipoprotein (mmol/L)		1.08±0.51	1.12±0.46	1.19±0.32	0.461	0.053

Table 2. Comparison of PPARγ, Aβ1-42, miR-155 levels between healthy group and diabetes group（$\bar{x}$±s）

Group	Health groups(n=20)	Diabetes group(n = 52)
PPARγ（pg/L）	1452.85±157.41	1234.96±131.08*
Aβ1-42（pg/mL）	50.16±29.07	67.34±23.75*
miR-155	1.02±0.42	0.52±0.35*

Note: Compared with the healthy group, *P<0.05.

Table 3. Comparison of PPARγ, Aβ1-42, miR-155 levels in patients with different degrees of diabetes（$\bar{x}$ ± s）

Group	Prophase(n=16)	Mild (n=25)	Medium(n=11)
PPARγ（pg/L）	1377.58±128.42	1235.48±106.32*	865.21±64.27*
Aβ1-42（pg/mL）	58.21±25.64	69.16±20.94*	94.65±17.49*
miR-155	0.67±0.29	0.38±0.21*	0.25±0.14*

Note: Compared with healthy group, *P<0.05.

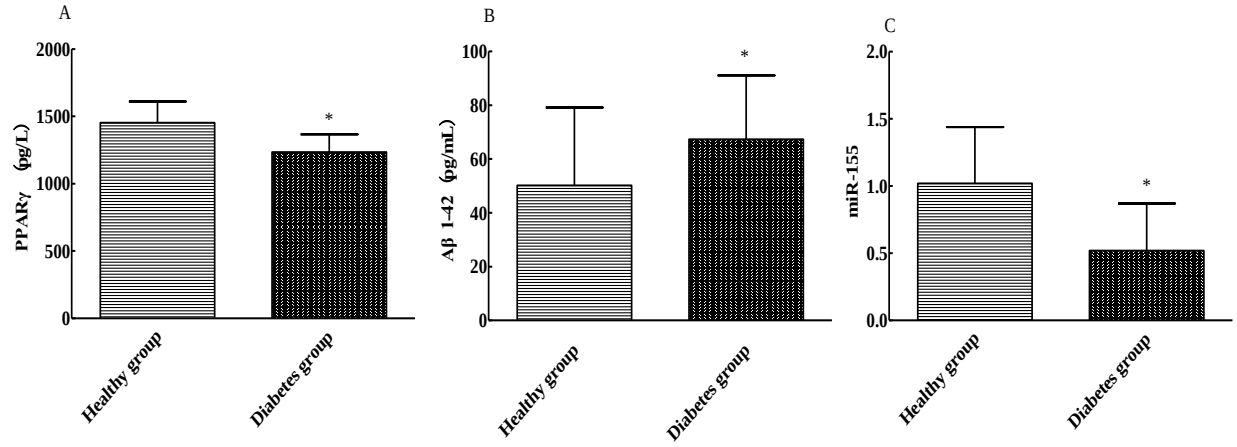

Figure 1. Comparison of PPARγ, Aβ1-42, miR-155 levels between healthy group and diabetes group(A: PPARγ;B: Aβ1-42;C: miR-155, Compared with the healthy group, *P<0.05

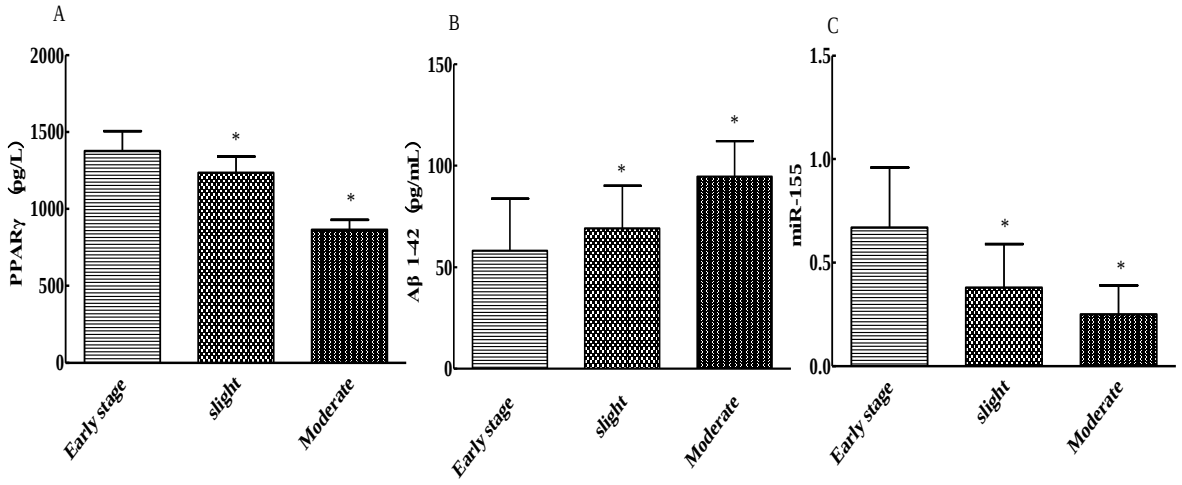

Figure 2. Comparison of PPARγ, Aβ1-42, miR-155 levels in patients with different degrees of diabetes(A: PPARγ;B: Aβ1-42;C: miR-155, Compared with pre-diabetes, *P<0.05.)

Table 4. Correlation analysis of PPARγ, Aβ1-42, miR-155 on the occurrence and development of diabetes

Group	Prophase (n=16)		Mild (n=25)		Medium (n=11)	
	r	*P*	r	*P*	r	*P*
PPARγ	-0.216	0.010	-0.168	0.034	-0.127	0.002
Aβ1-42	0.515	0.027	0.426	0.017	0.351	0.024
miR-155	-0.539	0.001	-0.312	0.031	-0.162	0.037

Table 5. Predictive efficacy of PPARγ, Aβ1-42, miR-155 levels on the occurrence and development of diabetes

Indicators	Sensitivity (%)	Specificity (%)	Accuracy (%)	Positive predictive value (%)	Negative predictive value (%)	AUC	95%*CI*
PPARγ	86.29	48.29	68.51	71.54	74.64	0.703	0.557~0.810
Aβ1-42	85.64	85.62	74.28	68.17	83.94	0.671	0.534~0.835
miR-155	76.42	83.12	72.94	74.28	72.66	0.859	0.691~0.857

Compared with the pre-diabetes group, the levels of mild and moderate PPARγ and Mir-155 were decreased, and the levels of Aβ1-42 were increased. It is basically consistent with the results of Chen and Akhbari's study, indicating that the occurrence and development of diabetes patients will cause the decrease of PPARγ and Mir-155, and the increase of Aβ1-42 level, and the larger the change range, the more significant the pathological change. When the body produces insulin to meet the needs, the metabolic channels cannot respond accordingly, resulting in the accumulation of insulin in the body due to blocked circulation, resulting in high blood sugar, which leads to the occurrence and development of diabetes. PPARγ, Aβ1-42 and Mir-155, as diabetes-related indicators, are involved in insulin metabolism and the occurrence and development of diabetes in vivo. PPARγ, as a transcription factor regulating target genes, changes conformation after activation with ligand to promote or inhibit the expression of target cells, and plays an important role in glucose and lipid metabolism, inflammation and atherosclerosis. PPARγ can promote PI3K gene expression, increase insulin sensitivity, improve glucose uptake and utilization, and regulate glucose and lipid metabolism. The decrease of blood glucose content in the body can also inhibit inflammation and reduce atherosclerosis. With the pathological changes caused by diabetes, the level of PPARγ in the body is significantly reduced, and the expression of the immune system is inhibited so that all tissues and organs are involved, and the development of diabetes is aggravated (19). Aβ1-42 is A substance deposited in the vascular wall and connective tissue, which is easy to accumulate and become the precipitation center. Excessive precipitation can lead to hyperphosphorylation of tubulin, neurotoxic effect and cognitive impairment, and its level is significantly expressed in diabetic patients, stimulating the nervous system and inhibiting antioxidant dismutase, leading to an increased risk of Alzheimer's disease (20). Mir-155 is an exon located in the non-coding gene cluster of B cells, which plays an important role in the body's inflammatory response and immune system. Related studies have found that Mir-155 inhibits the expression of cytokines and interleukins, controls the occurrence of inflammatory reactions and enhances the immune system function of the body. Moreover, it inhibits the expression of TIM-3 in peripheral blood monocytes or mediates the NE-κB pathway, thereby affecting the occurrence and development of diabetes mellitus (21). Therefore, when the progression of diabetes occurs, the levels of PPARγ and Mir-155 will decrease, and the levels of Aβ1-42 will increase.

Mahdavi et al. (22) investigated the expression levels of serum Mir-155 between the healthy control group and diabetes and obesity group of different degrees, and the results showed that there was no significant difference between diabetes and the healthy group. There was a negative correlation between Mir-155 levels and diabetes patients with different levels of obesity. Peng et al. (23) statistically compared the changes of Aβ1-42 levels in diabetic patients and the control group, and the results showed that the risk of diabetes increased with the increase of Aβ1-42 levels, and the two were positively correlated. The results of this study showed that PPARγ and Mir-155 levels were negatively correlated with

pre-diabetes, mild and moderate diabetes, while A β 1-42 was positively correlated with pre-diabetes, mild and moderate diabetes. It was basically consistent with the results of Peng and Mahdavi's study, suggesting that the levels of PPAR γ and Mir-155 were significantly decreased and the level of A β 1-42 was significantly increased during the development of diabetes patients, suggesting that the abnormal decrease of PPAR γ and Mir-155 in clinical examination and the abnormal decrease of A β 1-42 requires further diabetes progression. Intervention and improvement of patients' quality of life. The reasons why the results of this study were inconsistent with those of Akhbari and Mahdavi were analyzed as follows: The sample size of this study was small, which could not reflect the trend of THE levels of PPAR γ , A β 1-42 and Mir-155 during the occurrence of large-scale diabetes. This study is a horizontal study without a long-term follow-up investigation. Further longitudinal data analysis is required to avoid environmental and dietary factors affecting the disease process.

PPAR γ , A β 1-42 and Mir-155 all indirectly interfere with the occurrence and development of diabetes and are mostly used clinically in the diagnosis of cognitive impairment and inflammatory response, achieving significant effects, but rarely used in the diagnosis of diabetes occurrence and development (24-27). The results of this study showed that the levels of PPAR γ , A β 1-42 and Mir-155 can effectively predict the occurrence and progression of diabetes. The index detection of diabetes and sensitivity, specificity, accuracy, positive predictive value, negative predictive value were significantly higher, that PPAR gamma in patients with diabetes, A beta 1 to 42, abnormal levels of miR - 155, can reflect the blood sugar control situation, cognitive dysfunction and disease process, provide the basis for clinical diagnosis and control of diabetes patients.

In conclusion, decreased levels of PPAR γ and Mir-155 and increased levels of A β 1-42 in diabetic patients are closely correlated with their occurrence and development, which has positive reference significance for clinical diagnosis and treatment of diabetes.

References

1. Basu S, Yudkin JS, Kehlenbrink S, et al. Estimation of global insulin use for type 2 diabetes, 2018-30: a microsimulation analysis. Lancet Diabetes Endocrinol 2019, 7(1):25-33.

2. Holtrop J, Spiering W, Nathoe HM, et al. Apparent therapy-resistant hypertension as risk factor for the development of type 2 diabetes mellitus. J Hypertens 2020, 38(1):45-51

3. Piccinini CJ. Development of Type 2 Diabetes Mellitus in People With Intermediate Hyperglycemia. Clin Nurse Spec 2020, 34(2):48-49.

4. Kim MK, Han K, Koh ES, et al. Blood Pressure and Development of Cardiovascular Disease in Koreans With Type 2 Diabetes Mellitus. Hypertension 2019, 73(2):319-326.

5. Kotsis V, Jordan J, Stabouli S, et al. Cardiovascular, renal and liver protection with novel antidiabetic agents beyond blood glucose lowering in type 2 diabetes: consensus article from the European Society of Hypertension Working Group on Obesity, Diabetes and the High-risk Patient. J Hypertens 2020, 38(3):377-386.

6. Liu QQ, Wang P, He QJ, et al. PPARγ promotes diabetes-associated centrosome amplification via increasing the expression of SKA1 directly at the transcriptional level. J Cell Physiol 2019, 234(11):20694-20703.

7. Li H, Cao L, Ren Y, et al. GLP-1 receptor regulates cell growth through regulating IDE expression level in AB1-42-treated PC12 cells. Biosci Rep 2018, 38(4): 1284-1289.

8. Ye J, Kang Y, Sun X, et al. MicroRNA-155 Inhibition Promoted Wound Healing in Diabetic Rats. Int J Low Extrem Wounds 2017, 16(2):74-84.

9. Tu H, Zhang D, Li YL. Cellular and Molecular Mechanisms Underlying Arterial Baroreceptor Remodeling in Cardiovascular Diseases and Diabetes. Neurosci Bull 2019, 35(1):98-112.

10. Pham NM, Do VV, Lee AH. Polyphenol-rich foods and risk of gestational diabetes: a systematic review and meta-analysis. Eur J Clin Nutr 2019, 73(5):647-656.

11. American Diabetes Association. 5. Prevention or Delay of Type 2 Diabetes: Standards of Medical Care in Diabetes-2018. Diabetes Care 2018, 41(1):51-54.

12. Fathi A., Barak M, Damandan M, Amani F, Moradpour R, Khalilova I., Valizadeh M. Neonatal

Screening for Glucose-6-phosphate dehydrogenase Deficiency in Ardabil Province, Iran, 2018-2019. Cell Mol Biomed Rep 2021, 1(1): 1-6.

13. Meigs JB. The Genetic Epidemiology of Type 2 Diabetes: Opportunities for Health Translation. Curr Diab Rep 2019, 19(8):62-67.

14. Inayat H, Azim MK, Baloch AA. Analysis of Inflammatory Gene Expression Profile of Peripheral Blood Leukocytes in Type 2 Diabetes. Immunol Invest 2019, 48(6):618-631.

15. Guo H, Zhang Q, Yuan H, et al. Nitric Oxide Mediates Inflammation in Type II Diabetes Mellitus through the PPARγ/eNOS Signaling Pathway. PPAR Res 2020, 26(8):89612-89615.

16. Latini A, Spallone V, D'Amato C, et al. A common polymorphism in MIR155 gene promoter region is associated with a lower risk to develop type 2 diabetes. Acta Diabetol 2019, 56(6):717-718.

17. Chen HC, Cao JX, Cai YT, et al. Interaction of human IAPP and Aβ1-42 aggravated the AD-related pathology and impaired the cognition in mice. Exp Neurol 2020, 334(10):113490-113495.

18. Akhbari M, Khalili M, Shahrabi-Farahani M, et al. Expression Level of Circulating Cell Free miR-155 Gene in Serum of Patients with Diabetic Nephropathy. Clin Lab 2019, 65(8):169-174.

19. Bendaya I, Riahi A, Kharat M, et al. STAT1 and STAT6 Act as Antagonistic Regulators of PPARγ in Diabetic Patients with and without Cardiovascular Diseases. Clin Lab 2018, 1;64(3):287-294.

20. Meakin PJ, Coull BM, Tuharska Z, et al. Elevated circulating amyloid concentrations in obesity and diabetes promote vascular dysfunction. J Clin Invest 2020, 130(8):4104-4117.

21. Gao J, Zhao G, Li W, et al. MiR-155 targets PTCH1 to mediate endothelial progenitor cell dysfunction caused by high glucose. Exp Cell Res 2018, 366(1):55-62.

22. Mahdavi R, Ghorbani S, Alipoor B, et al. Decreased Serum Level of miR-155 is Associated with Obesity and its Related Metabolic Traits. Clin Lab 2018, 64(1):77-84.

23. Peng X, Xu Z, Mo X, et al. Association of plasma β-amyloid 40 and 42 concentration with type 2 diabetes among Chinese adults. Diabetologia 2020, 63(5):954-963.

24. De Riva V, Galloni E, Lealini B, et al. Ratio Aβ1-42:p-Tau: a Possible Diagnostic Tool in Differentiating Dementias. Clin Lab 2019; 1, 65(5):1922-1927.

25. Azeez S, Jafar, S., Aziziaram, Z., Fang, L., Mawlood, A., Ercisli, M. Insulin-producing cells from bone marrow stem cells versus injectable insulin for the treatment of rats with type I diabetes. Cell Mol Biomed Rep 2021, 1(1): 42-51.

26. Kazemi E, Zargooshi J, Kaboudi M, Izadi F, Motlagh HR, Kahrizi D, Khazaie H, Mahaki B, Mohammadian Y. Investigation of gene expression and genetic simultaneous control associated with erectile dysfunction and diabetes. Cell Mol Biol 2021, 67(3):195-200.

27. Mahami-Oskouei M, Norouzi B, Ahmadpour E, et al. Expression analysis of circulating miR-146a and miR-155 as novel biomarkers related to effective immune responses in human cystic echinococcosis. Microb Pathog 2021 157(3):104962-104965.