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miRNA-146a as Biological Indicator in Type1 Diabetes Mellitus

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ABSTRACT:
Type1 diabetes mellitus (T1D) is a sickness that prompts the destruction of insulin-conveying pancreatic beta cells. Individuals with T1D require everyday insulin imbuements regular, insulin siphon treatment. Without insulin, diabetic ketoacidosis (DKA) creates and is dangerous. Been collected100 sample were remembered for this search, 50 of which were from individuals with T1D and the others from healthy individuals for examination. The glycated hemoglobin HbA1C percentage was measured in this study for both patient and healthy groups, where a higher percentage was observed in the patient group compared to the control group. Enzyme-Linked ImmunoSorbent Assay ELISA and polymerase chain reaction PCR techniques were used for the purpose of measuring the parameters used in this study, where interleukin-17a and interleukin-10 were measured using ELISA technology, and the outcomes got showed a perceptible increased level of interleukin-17a in patients contrasted with healthy group, while a recognizable diminishing in the level was noticed Interleukin-10 in the patient gathering contrasted with controls ($P<0.05$). MicroRNA-146a level was estimated utilizing PCR innovation and the outcomes got showed a critical expansion in the degree of miRNA-146a in the serum of patients with T1D contrasted with solid individuals ($P<0.05$).
KEYWORDS:-*Autoimmune diseases, Cytokines, Interleukin-10, Interleukin-17A, Polymerase chain reaction*

INTRODUCTION

MicroRNA (miRNA) is a small single-stranded RNA, 19–25 nucleotides in length. It is transcribed from DNA, rather than converted into protein, and handles various protein-element binding properties. Thus, miRNA shapes other protein coding qualities [1]. Mi-croRNA-146a is a small non-coding RNA, designated MIR146A in humans, located at Chr 5: 160.49–160.49 Mb. [2]. T1D results from an uncontrolled, prolonged, unresponsive benign β-cell response, and subsequent diabetes is induced by the persistent destruction of insulin-conducting cells [3]. In homo human, the quality locus LOC285628, positioned on the chromosome 5, encodes miR-146a in monocytes. This region of the genome is activated in response to lipopolysaccharide (LPS) activation and its function is reliant on the nuclear fragment of kappa B (NF-κB) [4]. This response is considered as one of the potential pathological hallmarks of the T1D [5]. By the participation of the receptor-activated NF-κB and AP-1, TRAF6 contributes to the destruction of endothelium produced by the elevated glucose levels in animal studies of T1D [6]. Cytokines are interesting, cell-hailed protein particles that previously showed up as a component of the safe response, at this point have been found to widely affect different pieces of physiology. Cytokines can take some structural variations, by which their classification might be within protein, peptide, or glycoprotein compounds; the statement of cytokines includes a huge and different gathering of regulators that are conveyed all through the body by grouped embryological early cells [7]. IL-17 is a key factor favorable to the fire cytokine produced by T cell co-drivers type 17 (Th17), a subset of CD4+-resistant scaffolding microorganisms. There are six important cytokines of IL-17; IL-17A to F with critical pro-inflammatory IL-17A [8]. Studies have shown that the IL-17A/IL-17 compound is unregulated in the pancreas and during lymphocyte depletion in patients with T1DM [9, 10]. Interleukin 10 (IL-10) is known as a vigorous anti-inflammatory cytokine that plays a pivotal, and often fundamental, role in limiting inflammation and autoimmune diseases such as diabetes mellitus disease [11]. In this study, we will discuss the behavior of miRNA146a in patients with type 1 diabetes, as by determining its level and its association with the cytokines used in the study, it could be a future therapeutic target to limit type1 diabetes.

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MATERIALS AND METHODS

1.1 Sample collection and Study design

100 samples were collected in this study, 50 of which were from patients with diabetes mellitus type 1 (T1D) (n = 50, F = 30, M = 20), with a mean age (57.1 ± 1.6 year) and 50 from healthy, (n = 50, F = 25, M = 25). The mean age for this group was (56.4 ± 2.34) Study has been between November 2022 to October 2023 where samples collected, At Al-Diwaniyah teaching hospital. Hemoglobin A1c (HbA1c), FBG was checked, all tests examination was acted in Al-Diwaniyah teaching hospital and the Essential sciences lab, college of Dentistry, university of Al-Qadisiyah. Weight (BMI) was deter-mined as body weight (kg) on length squared level (in meters). A blood test (5 ml) was taken from all groups, and then the serum was separated by 3000rpm-10-20 mints -4°C centrifugation. The isolated serum was fractionated using Ependroff tubes (0.3 ml), one portion of which was stored at (-20°C) for miRNA and cytokine assessment. FBG and hemoglobin are completely stabilized by routine systems using a robotic analyzer (Abbott, USA) in Al-Diwaniyah teaching hospital. ELISA was employed to test the amounts of serum IL-17A and IL-10. A qPCR method was recruited to infer serum miRNA146a levels. For miRNA extraction, 200 µl of serum was used using a serum miRNA disinfection unit (Bio world, USA). cDNA was generated from miRNAs using polypolymerase (A) after using the miRNAcDNA pooling package. (abm, Canada). Then, the PCR was led utilizing cDNAtaq man ace blend for miRNAqPCR (abm, Canada). Study design of this study show in (Fig.1).

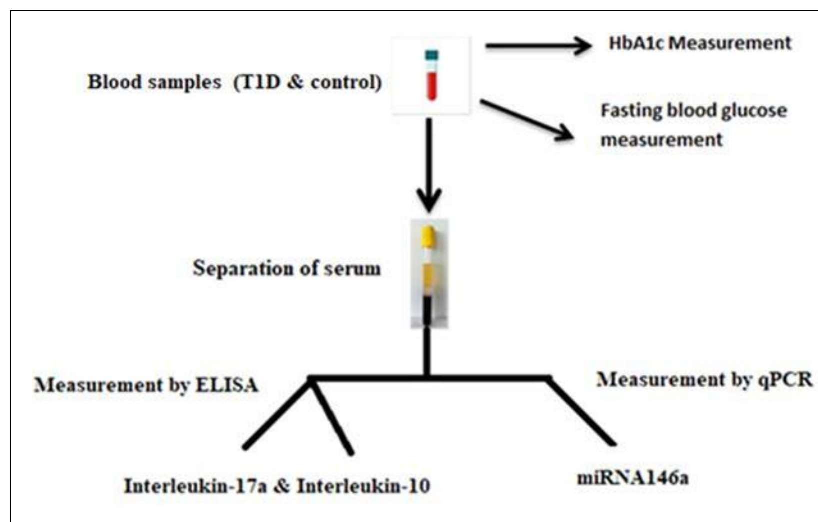

Figure 1 Study design.

1.2 Statistical Analysis

SPSS20 was used to analyze the data obtained in this study. It is conveyed as means ± SEM. One-way examination of variance and Tukey's post-hoc assessment or non-parametric portrayal (Kruskal Wallis) was continued as fitting to ponder a couple of Sets for normal and non-conventional scattering data independently ($P < 0.05$) was significant.

RESULTS

Characteristics and biochemical data of patients are displayed in (Table 1) In differentiated patients with T1D and controls, HbA1c levels mainly developed in T1D ($P<0.05$). Moreover, serum FBG was decrease in the T1D bundle looked as compared to the healthy subjects ($P< 0.05$). As shown in (Fig. 2), the level of IL-17a was increase in serum of T1D patients compared with healthy ($P< 0.05$). IL-10 levels declined ($P<0.05$) as compared to the healthy group (Fig. 3). As assessed by miRNA by qPCR, there was a huge increase in serum levels of miRNA-146a in the T1D group ($P<0.05$) as compared to the healthy group (Fig. 4).

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Table 1 the process yield and physical properties of the microcapsules

Measured Merits	Healthy subjects	Diabetic patients
Body mass index (Kg/m2)	25.98 (SE±5.3)	25.76 (SE±8.5)
HbA1c (Glycated hemoglobin)%	5.2 (SE±1.1)	8.3 (SE±2.4) *
Fasting blood glucose (mg/dl)	88.8 (SE±7.4)	240.1 (SE±64.4) *
Interleukin-17A	83.9 (SE±28.1)	380.3 (SE±93.1) *
Interleukin-10	76.3 (SE±21.5)	30.7 (SE±14.5) *
miRNA146a level	50.4 (SE±17.2)	83.6 (SE±39.9) *

*(P<0.05)

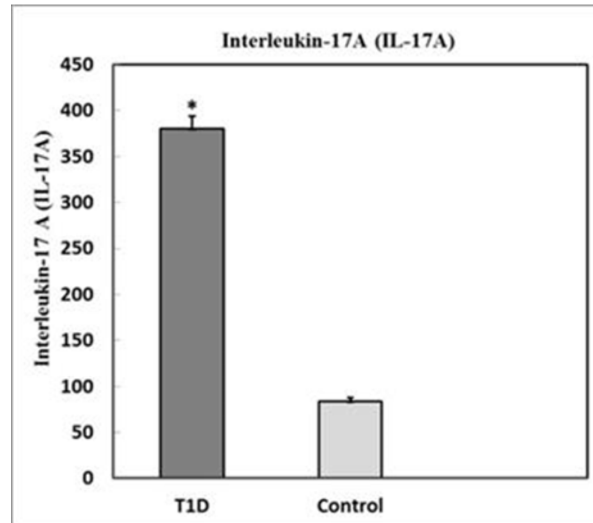

Figure 2 Interlukine-17A levels in serum patients with T1D, and control gatherings. Serum tests were disconnected from the blood of patients with T1D. Information are communicated as means ± SEM, for n =100, 50 patients and 50 control. * Shows massive contrasts contrasted with the healthy subjects (P < 0.05).

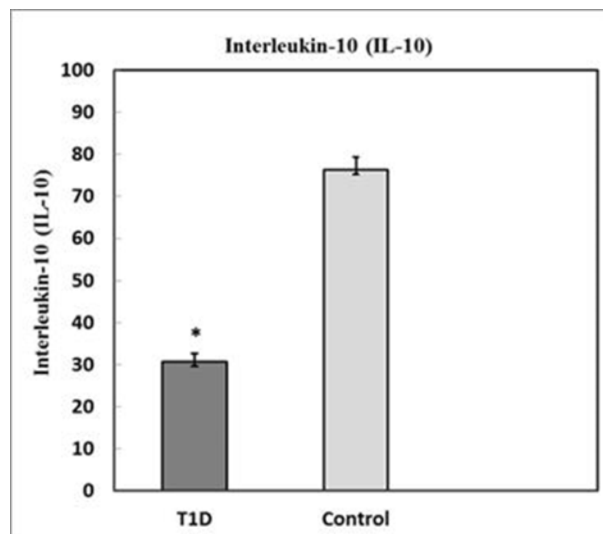

Figure 3 Interlukine-10 levels in serum patients with T1D, and control gatherings. Serum tests were disconnected from the blood of patients with T1D. Information are communicated as means ± SEM, for n =100, 50 patients and 50 control. * Shows massive contrasts contrasted with the healthy subjects (P < 0.05).

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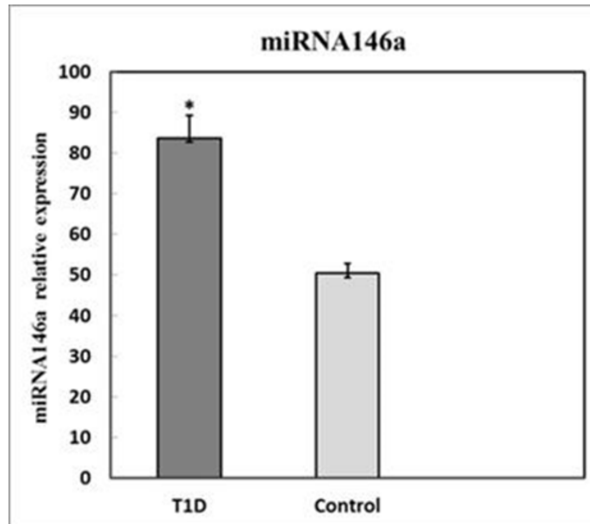

Figure 4 (A) Levels of microRNA-146a gene in Type 1 diabetes mellitus compared to healthy subjects. *= Significant differences ($p \leq 0.05$).

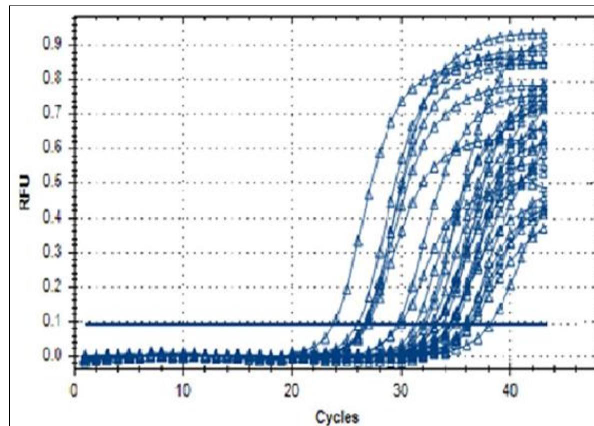

Figure 4 (B) Amplification curve of microRNA-146a of T1D patient group.

DISCUSSION

An exceptionally labile HbA1c/HbA1c ratio was linked to increased blood glucose, weakness, a prolonged hepatitis, and renal illness, according to a different study [12]. Lately, the labile HbA1c number has been recognized as a sign of fast fluctuations in blood sugar concentrations [13]. IL-17A-F, which is primarily supplied by Th17 cells, appears to be one of the pathogenesis components of the immune system disorders, such as diabetes [14]. The reduction in IL-10 levels in patients was consistent over a long period of time due to decreased oxidative pressure in patients with stable glycemic control. Therefore, an additional opportunity may be created for a useful immunogenic treatment methodology for diabetic patients, as has been proposed in various studies [15]. It is advisable to employ miR-146a as a prediction factor for the development of clinical diabetes, since the joint control of miR-146a may open windows within undeniable levels for the diabetes and concurrent com-plication managing treatment and its related complications [16]. In addition, we hypothesize that mixed treatment of miR-146a with standard and novel ant diabetic medicines may have the potential to achieve success in combating T1D and their associated disadvantages.

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CONCLUSION

It is clear that a high level of miRNA146a in the serum of T1D patients is associated with a high concentration of IL-17A and a low concentration of IL-10. An increase in the level of miRNA146a likely contributes indirectly to development of T1D.which might act as potential biomarker and remedial objective for T1D.

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REFERENCES

[1] *R. Kannan, and S.Vaishnavi, "MicroRNAs" – Biology and clinical applications, Journal of Oral and Maxillofacial Pathology, 18, 2014, 224-234.*
[2] *M. Ghaffari, S. Razi, H. Zalpoor, M. Nabi-Afjadi, F. Mohebichamkhorami, and H.Zali, Association of MicroRNA-146a with Type1and 2 Diabetes and their Related Complications, Journal of Diabetes Research. 2023, 13.*
[3] *Q. Zhang, C. Gonelle-Gispert, Y. Li , Z. Geng, S. Gerber-Lemaire, Y. Wang, and L. Buhler, Islet Encapsulation: New Developments for the Treatment of Type 1 Diabetes. Frontiers in Immunology. 2022, 13, 869984.*
[4] *D. Taganov, P. Boldin, K. Chang, and D.Baltimore, "NF-κB"-dependent induction of microRNA miR-146, an inhibitor targeted to signaling proteins of innate immune responses, Proceedings of the National Academy of Sciences, 2006,103,12481–12486.*
[5] *A. Mollah, S. Pai, C. Moore, J. O'Sullivan, J. Harrison, J Peng, B. Prins, et al, Abnormal NF-kappa B function characterizes human type 1 diabetes dendritic cells and monocytes, Journal of Immunology, 2008,180, 316675.*
[6] *C. Xing, D. Xiang, L. Caiying, Effects of troxerutin on vascular inflammatory mediators and expression of microRNA-146a/NF-κB signaling pathway in aorta of healthy and diabetic rats, Journal of Pharmacy Practice, 24, 2022, 395-402.*
[7] *A. Mousa, M. Bakhiet, Role of Cytokine Signaling during Nervous System Development. International Journal of Molecular Sciences, 14(2013), 2013,13931-13957.*
[8] *J. McGeachy, J. Cua, L. Gaffen, The IL-17 family of cytokines in health and disease, Immunity,50(2019), 2019, 892–906.*
[9] *S. Arif, F. Moore, K. Marks,T. Bouckenooghe, M. Dayan, R. Planas, et al, Peripheral and Islet Interleukin-17 Pathway Activation Characterizes Human Autoimmune Diabetes and Promotes Cytokine-Mediated β- CellDeath, Diabetes,60(2011), 2011, 2112–2119.*
[10] *V. Meehan, K.Wang, Interleukin-17 Family Cytokines in Metabolic Disorders and Cancer, Genes, 13(9), 2022, 1643.*
[11] *S. Iyer, G. Cheng, Role of Interleukin 10 Transcriptional Regulation in Inflammation and Autoimmune Disease, Critical Reviews in Immunology, 32(1), 2012, 23–63.*
[12] *P. Loh, K. Peng, L. Chen, K. Sethi, Application of smoothed continuous labile hemoglobin A1c reference intervals for identification of potentially spurious HbA1c results, Journal of Clinical Pathology, 67, 2014, 712-6.*
[13] *S. Kato, I. Otaka, H. Toyama, R. Kusumi, K. Takahashi, M. Nara, et al, Cases of fulminant type 1 and type 2 diabetes mellitus whose HbA1c levels were unmeasurable due to increased labile HbA1c, Diabetol International, 13, 2022, 698-703.*
[14] *B. Linhartova, J. Kastovsky, S. Lucanova, J. Bartova, H. Poskerova , J. Vokurka, et al, Interleukin-17A Gene Variability in Patients with Type 1Diabetes Mellitus and Chronic Periodontitis: Its Correlation with IL-17 Levels and the Occurrence of Periodontopathic Bacteria,2and LydieIzakovicovaHolla, Med of Inflammation, (2016), 2016, 9.*
[15] *F. Haber, M. Barbalho, A. Sgarbi, S. Haber, W. Labio, F. Laurindo, et al, The Relationship between Type 1 Diabetes Mellitus, TNF-α, and IL-10GeneExpression, Biomedicines,11(2023), 2023, 1120.*
[16] *M. Ghaffari, S. Razi, H. Zalpoor, M. Nabi-Afjadi, F. Mohebichamkhorami, H. Zali, Association of MicroRNA-146a with Type1and 2 Diabetes and their Related Complications, Journal of Diabetes Research, (2023), 2023,13.*

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