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Original article

Plasma Level of MiR- 200b in Type 2 Diabetic Retinopathy in Egyptian Patients

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Abstract:

Background: The incidence of diabetes mellitus is rapidly increasing, and it frequently causes considerable metabolic disorders and serious consequences. MicroRNA-200b (miR-200b) is a regulator of angiogenesis that has emerged as a diagnostic and predictive tool for certain disorders. **Aim:** to investigate the association of miR-200b with diabetic retinopathy (DR). **Methods:** The study included 100 subjects from Benha University Hospital: 40 patients with type 2 diabetes (T2D) without DR, 40 with T2D and DR, and 20 apparently healthy controls. MicroRNA-200b was assessed for all subjects using real time PCR with SYBR Green. **Results:** Diabetics had lower levels of miR-200b than healthy controls. While, those without DR had even lower miR-200b levels compared to those who did have DR. Additionally, lower miR-200b levels were associated with neuropathy but not with nephropathy. **Conclusion:** MiR-200b showed promise as a biomarker for both T2D and DR. It perfectly differentiated diabetic patients with and without retinopathy, while offering moderate accuracy for diagnosing diabetes in general. These findings suggest miR-200b may play a risky role in DR among diabetics, and further research is warranted to confirm these results.

Keywords: T2D, diabetic retinopathy, miR-200b, micro-RNA.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia. It may be due to impaired insulin secretion, resistance to peripheral actions of insulin, or both. According to the International Diabetes Federation (IDF), approximately 415 million adults between the ages of 20 to 79 years had diabetes mellitus in 2015 [1].

Diabetes is becoming a global public health burden, with an additional 200 million people expected by 2040. When combined with other metabolic abnormalities in diabetes mellitus patients, chronic hyperglycemia can cause damage to various organ systems, leading to the development of disabling and life-threatening health complications, the most prominent of which are microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular complications, which lead to a 2- to 4-fold increased risk of cardiovascular diseases [2].

Genetic and environmental factors can cause progressive decrease of β-cell bulk and function, leading to hyperglycemia. To develop personalized diabetic treatments, it's crucial to better understand the many causes of β-cell malfunction [3].

Diabetic retinopathy (DR) is a neurovascular condition that is the main cause of vision loss and blindness among working-age individuals. In addition to vision loss, DR is linked to chronic renal disease and mortality from cardiovascular disease in diabetes [4]. Although longer diabetes duration, poor glycemic management, and high blood pressure are the primary risk factors for DR, epidemiological data support the theory of variable genetic vulnerability to this chronic complication [5]. Epigenetic processes, including DNA methylation, histone posttranslational changes in chromatin, and noncoding RNAs, influence the interaction of genetic and environmental risk factors. The persistence of epigenetic modifications may contribute to the metabolic memory phenomenon, as well as oxidative stress, inflammation, and extracellular matrix accumulation, all of which lead to the development of DR [6].

Several studies have found aberrant MiR expression in retinal cells under hyperglycemic circumstances, as well as in DR mouse models. MiRs are tiny endogenous noncoding RNAs that, in general, mute gene expression at the posttranscriptional level by binding to specific sequences in the three untranslated regions of their target mRNAs, inhibiting protein synthesis [7]. MiRNAs influence cell formation and function by controlling the acquisition and maintenance of beta cell identity, cell growth, proliferation, differentiation, apoptosis, and metabolism. Because of their great stability in body fluids, multiple studies have revealed the potential of circulating miRNAs as indicators of diagnosis, prognosis, and therapy of type 2 diabetes and associated vascular consequences [8].

MiR-200b was discovered to be dysregulated in high glucose retinal cells and diabetic murine. It protects against vascular permeability and angiogenesis [9]. The MiR 200b 3p, a specific member of the MiR 200 family, has the ability to inhibit tumor growth. However, several studies have revealed that, in certain situations, this miRNA may potentially accelerate the development of particular tumors because of differences in the microenvironments and biological backgrounds of different cancers [10]. Downregulation of MiR-200b leads to increased inflammation. Diabetes can lead to increased angiogenesis and neovascularization in the retina, as MiR-200b levels decrease [11]. The aim of this work was to study plasma level of MiR-200b in T2D retinopathy in Egyptian patients.

Subjects and Methods

This case-control study was conducted between September 2022 and June 2023 at Benha University Hospital. The study

included a total of 100 subjects, comprising 40 T2D patients without DR, 40 T2D patients with DR, and 20 healthy volunteers matched for age and sex. Ethical approval was obtained from Faculty of Medicine, Benha University(Internal Medicine Department and outpatient clinic in Benha University Hospital and Ophthalmology clinic in Benha University Hospital) , and informed consents were obtained from all participants. The inclusion criteria for T2D diagnosis is fasting blood sugar of greater than or equal to 126 mg/dl , hemoglobin A1c (HBA1c) of greater than or equal to 6.5% , and /or random blood sugar of greater than or equal to 200mg/dl, and age at diagnosis of diabetes ≥30 years. While Exclusion criteria: Included any clinical condition that impairs fundus examination, such as severe cataract, subjects with type1 diabetes, if they were taking: steroid, anti-inflammatory drugs, type 2 diabetes mellitus patients of less than 5 years duration

Physical and clinical examinations were conducted on the participants. This included measuring blood pressure, conducting local examinations to identify signs of diabetic retinopathy through fundus examination using indirect ophthalmoscope and slit lamp with auxiliary lenses. The severity of diabetic retinopathy was graded based on the International Clinical Diabetic Retinopathy Disease Severity Scale. The presence and severity of macular edema were also assessed. Fundus Fluorescein Angiography was performed on all participants, and laboratory investigation were: Blood glucose (fasting and postprandial, HbA1c and MiR-200b using RT-q PCR using SYBR®Green method.

Blood sample:

Seven milliliters of venous blood were drawn after fasting 6 hours under complete aseptic conditions and then divided into sterile vacutainers from each participant and distributed as following:

- three ml of blood was put in plain tube for serum separation to measure fasting blood sugar FBS .
- two ml of blood was put in EDTA tube for HBA1c.
- two ml of blood was put in EDTA tube for plasma separation for molecular assessment.

Fasting Blood Glucose principle was determined by means of coupled reaction (Glucose oxidase and Peroxidase), a colored complex measured spectrophotometrically [12].

HbA1c level was measured by an enzymatic method in which whole blood samples lysed by protease. This process releases glycosylated N-terminal dipeptide from the hemoglobin beta chains. It serves as substrates for specific fructosyl peptide oxidase enzyme. The HbA1c concentration was measured by determining the resultant hydrogen. [13]

Clinical chemistry tests were done using (Dialab auto-analyzer, S/N:47142109, Austria). Using Dialab reagent kit provided by DIALAB Production and Vertib, IZ NOE-Sued, Hondastrasse, Objekt M55,2351 Wr. Neudorf (Austria). HBA1c was measured by (Architect c4000 chemical analyzer, S/N:C462233, Japan).

MicroRNA typing

1. MicroRNA was extracted by using MiReasy Mini Kit (cat. No. 217004) according to the manufacturer's instructions (QIAGEN, Germany, lot N 169023580) .

Principle :

The miRNeasy Mini Kit combines phenol/guanidine-based lysis of samples and silica membrane–based purification of total RNA. QIAzol Lysis Reagent, included in the kit, is a monophasic solution of phenol and guanidine thiocyanate, designed to facilitate lysis of tissues, to inhibit RNases, and also to remove most of the cellular DNA and proteins from the lysate by organic extraction.

Plasma samples are homogenized in QIAzol Lysis Reagent. After addition of

chloroform the homogenate is separated into aqueous and organic phases by centrifugation.

RNA partitions to the upper, aqueous phase, while DNA partitions to the interphase and protein

to the lower, organic phase or the interphase.

2. RNA Reverse Transcription was done using EasyScript ®First Strand cDNA Synthesis SuperMix kit (transGenBiotech,Beijing China) Cat no AE301. provides all necessary components for cDNAsynthesis fromtotal RNA or mRNA.

Principle:

Multiple copy gene detection. Deficient RNase H activity to reduce RNA template degradation during the first-strand cDNA synthesis.

Then Real time –PCR was done using HERA plus SYBR®Green q-PCR kit (WF1030800X) (Willowfort ,Birmingham). Genotyping of dsDNA samples was done using SYBR®dye. A standard curve using specific miRNA mimics (miRNA mimics, Qiagen) and melting curve analysis were included in all reactions.

Principle:

HERAplus SYBR®Green qPCR provide a convenient and powerful method for DNA detection on and quantitation , allowing for gene expression analysis and population genotyping .

In addition to the highly sensitive SYBR®Green dye, HERA is formulated with a unique ROX passive reference dye that is compatible across a variety of instrument platforms.

Stages:

1- HERA plus Enzyme Activation.

2- Cycle denaturation.

3- Primer annealing and extension.

Primer used

MiR -200b F

CTCAACTGGTGTCGTGGAGTCGGCA ATTCAGTTGAGTCATCATT

MiR-200b R

ACACTCCAGCTGGGTAATACTGCCT GGTAA

Statistical Analysis

The acquired data were updated, processed, and tabulated using IBM Corp.'s Statistical Package for Social Science (released in 2017). IBM SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp.). The Student T Test determined the statistical significance of mean differences between two study groups for parametric data. The Mann Whitney Test assessed the statistical significance of differences in non-parametric variables between two study groups. A one-way ANOVA test was used to examine the statistical significance of differences between more than two study group parametric variables. The Chi-Square test investigated the association between two qualitative variables. Correlation analysis measured the strength of correlation between two quantitative variables. The receiver operating characteristic curve was used to assess sensitivity and specificity for quantitative diagnostic tests. When the dependent variable is categorical, logistic regression can be used to predict risk variables. A p-value <0.05 at a 95% confidence range indicates statistical significance.

Approval code: MS 19.7.2022

Results

The sex distribution was similar across all groups. The mean age varied slightly, with DM with retinopathy having the highest mean age (51.03 years) and DM without retinopathy the lowest (45.93 years). No significant difference was found regarding sex and age among the groups. There was no significant difference in smoking prevalence among the groups. However, the DM without retinopathy group had a significantly higher proportion of subjects with a family history of diabetes compared to the control group and the DM with retinopathy group. No significant difference was observed in hypertension prevalence among the three groups. The

mean fasting blood sugar (FBS) levels were statistically significant higher in both DM groups than in the control group (p1<0.001,p2<0.001,p3<0.001). Regarding HbA1c, patients with diabetes and retinopathy had the statistically significant highest mean, followed by patients with diabetes and without retinopathy, and the lowest level in the healthy group (p1<0.001, p2<0.001, p3<0.001) Table 1.
The duration of diabetes was slightly higher in the group with DR compared to the group without retinopathy, but this difference was not statistically significant. All subjects in the DM with retinopathy group had abnormal findings. While, 25% of subjects in the DM without retinopathy group also had abnormal findings. Neuropathy was more prevalent among those with DR than T2D without DR. Among T2D patients, 40% of those with no DR had nephropathy, while, 45% of those with DR had nephropathy. There was no significant difference in nephropathy prevalence between the two diabetes groups. There was no significant difference in insulin use between the T2D groups Table 2.

There was statistically significant decrease in MiR-200b expression in D.M patients without retinopathy when compared to control group and D.M patients with retinopathy (p2<0.001,p4<0.001) sequentially But there is no statistically significant difference in MiR-200b expression between D.M patients with retinopathy and control group (p3=0707) Table 3.

Table 1: Comparison of the studied groups regarding baseline data.

		Control N = 20	**DM without retinopathy n = 40**	**DM with retinopathy n = 40**	***p***
Sex	**Male**	12(60%)	26(65%)	24(60%)	P1=0.880
	Female	8(40%)	14(35%)	16(40%)	
Age (years)	**Mean ± SD.**	48.80 ± 9.93	45.93 ± 9.70	51.03 ± 9.93	P1=0.073
	Min. – Max.	35.0 – 64.0	32.0 – 64.0	30.0 – 65.0	
Smoking		9(45%)	18(45%)	20(50%)	P1=0.887
Family history					P1=0.006*
		10(50%)	32(80%)	19(47.5%)	p2=0.017* p3=0.855
					p4=0.002*
Hypertension		11(55%)	19(47.5%)	18(45%)	P1=0.763
SBP (mmHg)	**Mean ± SD.**	139.0 ± 26.93	143.4 ± 34.33	152.5 ± 39.14	P1=0.307
DBP (mmHg)	**Mean ± SD.**	87.25 ± 13.91	85.88 ± 14.0	90.63 ± 16.18	P1=0.353
Fundus examination	**Normal**	20(100%)	30(75%)	0(0%)	P1<0.001* p2=0.023*
	Abnormal	0(0%)	10(25%)	40(100%)	p3<0.001* p4<0.001*
FBS (mg/dl)					P1<0.001*
	Mean ± SD.	87.15 ± 7.16	185.2 ± 51.72	205.4 ± 29.86	p2<0.001* p3<0.001* p4=0.051
HBA1c (%)					P1<0.001*
	Mean ± SD.	5.04 ± 0.32	8.52 ± 1.33	9.38 ± 1.12	p2<0.001* p3<0.001* p4=0.002*

SD.: Standard deviation, Min.: Minimum, Max.: Maximum, P1: Comparing the control and DM groups, p2: Comparing control and DM without retinopathy, p3: Comparing control and DM with retinopathy, p4: Comparing DM without and with retinopathy, *: P value Significant <0.05.

Table 2: Comparison of diabetics with and without retinopathy groups.

		DM without retinopathy n = 40	DM with retinopathy n = 40	*p*
Duration of DM (years)	**Median (min-max)**	10 (5-30)	13 (6-30)	0.136
Fundus examination	**Normal**	30(75%)	0(0%)	<0.001*
	Abnormal	10(25%)	40(100%)	
	Tegroid	10(25%)	0(0%)	
	Hard exudate	0(0%)	5(12.5%)	
	Dot, blot he	0(0%)	1(2.5%)	
	Microaneurysms	0(0%)	10(25%)	
	Hge and exudate	0(0%)	1(2.5%)	
	Macular ischemia	0(0%)	1(2.5%)	
	Retinal detachment	0(0%)	1(2.5%)	
	Neovascularization	0(0%)	5(12.5%)	
	Cotton wool spots	0(0%)	7(17.5%)	
	Irma	0(0%)	8(20%)	
	Abnormal foveal reflex	0(0%)	1(2.5%)	
Neuropathy		32(80%)	39(97.5%)	0.029*
Nephropathy		16(40%)	18(45%)	0.651
Treatment	**Oral hypoglycemic**	32(80%)	40(100%)	0.005*
	Insulin	13(32.5%)	13(32.5%)	1.000

SD.: Standard deviation, Min.: Minimum, Max.: Maximum.

Table 3: Comparison of the studied groups regarding plasma level of MiR-200b.

	Control N = 20	DM n = 80	DM without retinopathy n = 40	DM with retinopathy n = 40	Pairwise
MiR-200b					
Mean ± SD.	0.998 ± 0.076	0.760 ± 0.233	0.537 ± 0.046	0.984 ± 0.073	P1<0.001*
Min. – Max.	0.872 – 1.123	0.482 – 1.085	0.482 – 0.614	0.833 – 1.085	p2<0.001*
					p3=0.707
					p4<0.001*

SD.: Standard deviation, Min.: Minimum, Max.: Maximum, P1: Comparing the control and DM groups, p2: Comparing control and DM without retinopathy, p3: Comparing control and DM with retinopathy, p4: Comparing DM without and with retinopathy, *: P value Significant <0.05.

The results showed that there was a statistically significant positive correlation between MiR-200b levels and HbA1c. However, there was no statistically significant correlation between MiR-200b levels and duration of DM, SBP, DBP, FBS among patients with diabetes. Figure 1

The receiver operating characteristic curve of plasma level of MiR-200b was conducted for discrimination between patients with DM and control group. MiR-200b showed a moderate accuracy AUC (0.771) as a diagnostic ability for patients with DM. At bests cut-off value (≤0.983), sensitivity was 75%, specificity was 70%, PPV was 90.91%, NPV was 41.18%, and accuracy was 74%. In addition, the ROC curve of MiR-200b was conducted for discrimination between DM patients with retinopathy and DM patients without retinopathy. MiR-200b showed a perfect accuracy AUC (1.000) as a diagnostic ability for DM patients with retinopathy. At bests cut-off value (>0.614), sensitivity was 100%, specificity was 100%, PPV

was 100%, NPV was 100%, and accuracy was 100%. Figure 2

Logistic regression analysis was statistically conducted for the prediction of susceptibility to DM. Only low MiR-200b was significantly associated with susceptibility to DM. Table 4

Moreover, logistic regression analysis was conducted for the prediction of retinopathy among patients with DM. In the multivariate analysis, only the negative family history and high MiR-200b were still statistically significant associated with retinopathy. Table 4.

Table 4. Logistic Regression Analysis for Prediction of DM Susceptibility and Retinopathy.

Predictor	DM Susceptibility (OR, 95% CI, p-value)	Retinopathy Prediction (Univariate and Multivariate OR, 95% CI, p-value)
Gender	1.062 (0.598–1.887, p=0.837)	Univariate: 1.143 (0.648–2.017, p=0.644)
Age	0.998 (0.970–1.027, p=0.896)	Univariate: 1.033 (1.004–1.063, p=0.023*) Multivariate: 1.001 (0.998–1.004, p=0.490)
Smoking	1.059 (0.604–1.858, p=0.841)	Univariate: 1.134 (0.654–1.966, p=0.654)
Family History	1.383 (0.784–2.439, p=0.263)	Univariate: 0.398 (0.219–0.726, p=0.003*) Multivariate: 0.937 (0.883–0.995, p=0.034*)
Hypertension	0.818 (0.467–1.435, p=0.484)	Univariate: 0.939 (0.541–1.629, p=0.823)
SBP	1.005 (0.996–1.013, p=0.293)	Univariate: 1.004 (0.997–1.012, p=0.266)
DBP	1.003 (0.984–1.022, p=0.785)	Univariate: 1.013 (0.995–1.032, p=0.161)
MiR-200b	0.015 (0.001–0.181, p=0.001*)	Univariate: 8.068 (7.134–9.125, p<0.001*) Multivariate: 7.448 (6.442–8.610, p<0.001*)

OR: Odd Ratio; CI, confidence interval. *: Significant when p value <0.05.

OR: Odd Ratio; CI, confidence interval. *: Significant when p value <0.05.

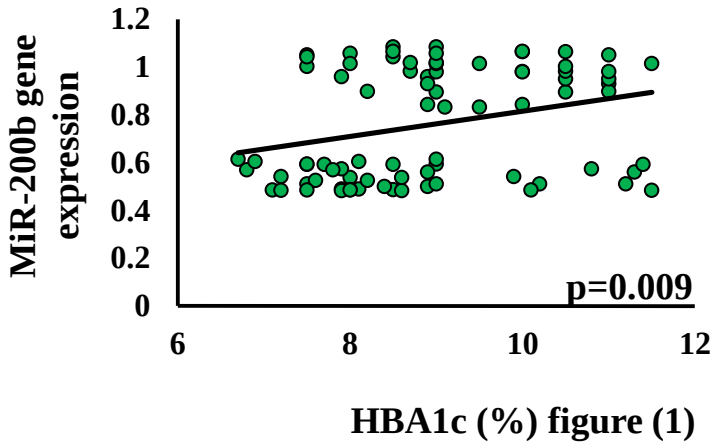
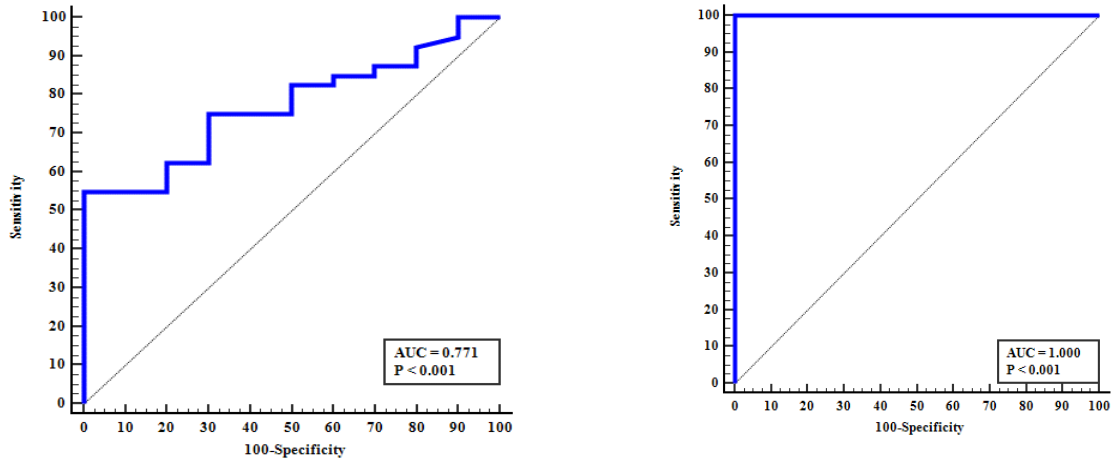


Figure 1: Correlation between MiR-200b with HbA1C among DM patients.



A B

Figure 2: ROC Curve for plasma level of MiR-200b for discrimination between (A) patients with DM and the control group; (B) DM patients with retinopathy and DM patients without retinopathy.

Discussion

Diabetic retinopathy (DR) is one of the most prevalent microvascular consequences of diabetes mellitus and the leading cause of visual impairment in diabetic patients. The pathogenesis of DR is yet uncertain [10].

MiR-200b was discovered to be dysregulated in high glucose-exposed retinal cells and diabetic murine, indicating its role in the development of DR. Additionally, miR-200b protects against vascular permeability and angiogenesis. Downregulation of miR-200b leads to increased inflammation, angiogenesis, and neovascularization in the retina [14].

The current study revealed a statistically significant decrease in MiR-200b expression in DM patients without retinopathy when compared to control group and D.M patients with retinopathy sequentially. But there is no statistically significant difference in MiR-200b expression between D.M patients with retinopathy and control group. The difference in MiR-200b expression between the two groups (Diabetic and control) was highly significant. Lower levels of MiR-200b were consistently observed in individuals with diabetes, regardless of retinopathy status. The mean MiR-200b in the diabetes group was 0.760, and in the control group it was 0.998.

The association of the plasma levels of miR-miR-200b with DR in type 2 diabetic outpatients was assessed and revealed that miR-200b was undetectable in seven of 186 (3.8%) type 2 diabetic patients. Patients with type 2 diabetes without DR had approximately two fold lower levels of miR-200b in comparison to controls. With regard to retinopathy, the mean levels of miR-200b were 40% lower in patients with DR as compared to those without DR, but the difference between the groups of diabetic patients did not reach formal statistical significance [14].

The current study showed that patients with normal fundus examinations had lower mean MiR-200b expression levels (0.534) compared to those with abnormal fundus examinations (0.896). In addition, the patients without retinopathy had statistically significant lower mean MiR-200b levels (0.537) compared to those with retinopathy (0.984). Also, patients without neuropathy had statistically significant lower mean MiR-200b

expression levels (0.593) compared to those with neuropathy (0.781). However, there was no significant association between MiR-200b expression levels and nephropathy among patients with diabetes.

In a previous study in Germany, plasma levels of miR-200b were decreased at least threefold in type 2 diabetic inpatients in comparison to healthy controls [15], patients with DR had about 60% lower plasma levels of miR-200b than subjects without diabetes [16].

The present study revealed that there was no statistically significant association between MiR-200b expression levels and smoking, sex or hypertension among patients with diabetes. However, there was a statistically significant difference in MiR-200b expression levels between patients with and without a family history of DM. Patients with a family history had lower mean MiR-200b expression levels compared to those without a family history.

It was found that miR-200b expression increased in cigarette smoke-exposed cell lines [17].

In the retinas of non-diabetic patients and diabetic patients, miR-200b was found to be located in the vascular endothelium and in neuronal and glial elements. Studies in vitro showed that miR-200b is highly expressed in normal human retinal endothelial cells, while it was down-regulated under hypoglycemic environment [18].

The current study showed a statistically significant positive correlation between MiR-200b expression levels and age, HbA1c. However, there was no statistically significant correlation between MiR-200b expression levels and duration of DM, SBP, DBP, FBS among patients with diabetes. However another study found that the results indicated that miR-200b expression levels did not correlate with patient gender or age [19].

The current study revealed statistically significant difference in retinopathy, neuropathy and nephropathy in DM patients with retinopathy when compared to control group. p increase and there is statistically significant difference in neuropathy and nephropathy in DM without retinopathy when compared to control group ($p2<0.001$, $p2=0.001$) sequentially. Also there is statistically significance difference in retinopathy and neuropathy in DM patients with retinopathy when compared to DM patients without retinopathy ($p4<0.001$, $p4=0.029$, $p4=0.651$) sequentially

It was showed that all cases with T2DM patients with retinopathy had neuropathy and macrovascular complications who were significantly older, with a longer diabetes duration, than the control group. The gender and mean BMI were not significantly different between cases and control, across all complications. Interestingly, the median glycated hemoglobin levels were significantly higher in the retinopathy cases compared to controls, possibly due to the formation of thrombus, a pathophysiological basis of early diabetic retinopathy [20].

Regarding fundus examination, all subjects in the DM with retinopathy group had abnormal findings including, hard exudate, dot, blot, micro aneurysms, hemorrhage and exudate. In addition, 25% of subjects in the DM without retinopathy group also had abnormal findings.

While the initial findings in a previous study showed that 141 (56.4%) patients with diabetes had normal eye conditions, whereas patients who had mild DR, moderate DR, maculopathy, cataract, and refractive errors were 24 (9.6%), 10 (4.0%), 4 (1.6%), 3 (1.2%), and 68 (27.2%), respectively [21].

Logistic regression analysis was conducted for the prediction of susceptibility to DM, using sex, age, smoking, family history, hypertension, SBP, DBP, and MiR-200b as covariates. Only low MiR-200b expression was significantly associated with susceptibility to DM.

Logistic regression analysis was conducted for the prediction of retinopathy among

patients with DM, using sex, age, smoking, family history, duration of DM, hypertension, SBP, DBP, FBS, HBA1c, neuropathy, nephropathy, insulin, anti-hypertensive, and MiR-200b as covariates. The older age, negative family history, high FBS, high HBA1c, presence of neuropathy, and high MiR-200b were significantly associated with retinopathy in the univariate analysis. In the multivariate analysis, only the negative family history and high MiR-200b were still significantly associated with retinopathy.

The receiver operating characteristic (ROC) curve of plasma expression level of MiR-200b was conducted in the present study for discrimination between patients with DM and control group. MiR-200b showed a moderate accuracy AUC (0.771) as a diagnostic ability for patients with DM. At bests cut-off value (≤0.983), sensitivity was 75%, specificity was 70%, PPV was 90.91%, NPV was 41.18%, and accuracy was 74%. Figure 2 (A)

The ROC curve of MiR-200b was conducted for discrimination between DM patients with retinopathy and DM patients without retinopathy. MiR-200b showed a perfect accuracy AUC (1.000) as a diagnostic ability for DM patients with retinopathy. At bests cut-off value (>0.614), sensitivity was 100%, specificity was 100%, PPV was 100%, NPV was 100%, and accuracy was 100%. Figure 2 (B).

Conclusion

In conclusion, the current investigation demonstrated that persons with T2D had consistently reduced levels of MiR-200b, independent of retinopathy status. Patients without DR had significantly lower average MiR-200b levels than those with DR. Additionally, those without neuropathy exhibited a statistically significant lower MiR-200b expression level than those with neuropathy. However, there was no significant link between MiR-200b expression levels and nephropathy in T2D patients.

Down-regulating miR-200b in T2D may cause apoptosis, inflammation, and cell disruption, resulting in retinal degeneration, and angiogenesis.

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