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Prevalence of Hyperlipidemia in Newly Diagnosed and Uncontrolled Type-2 Diabetes Mellitus Patients Comparative to Non-diabetic Individuals

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ABSTRACT

Objective: Diabetes increases the risk of cardiovascular disease by two to four times, with 80% of related deaths and hospitalizations due to atherosclerosis. Dyslipidemia plays a crucial role in the development of atherosclerosis and heart diseases, making it a concern for newly diagnosed and uncontrolled type-2 diabetes mellitus patients in Bangladesh. To address this, a cross-sectional study in a south-western district of Bangladesh was conducted to assess the prevalence and pattern of hyperlipidemia.
Methods: In a study of 120 participants, 83 were included in the analysis. Basic information and medical history were collected, and diabetes was diagnosed based on blood glucose levels. Lipid profiles were evaluated, and hyperlipidemia was defined as specific levels, including total cholesterol over 200 mg/dL, triglycerides over 150 mg/dL, LDL-C over 100 mg/dL, and HDL-C less than 40 mg/dL.
Results: The uncontrolled diabetic and newly diagnosed type-2 diabetes mellitus groups had a higher frequency of hypertriglyceridemia, hypercholesterolemia, hyper LDL cholesterolemia, and hypo HDL-cholesterolemia compared to the diabetic controlled and non-diabetic groups. The prevalence of high triglyceride levels was higher in females (85%) than males (76%). Gender was significantly associated with LDL-c levels (p=0.04), while the age group of 40 years or older was significantly associated with TG levels (p=0.05).
Conclusion: Dyslipidemia, including hypercholesterolemia, hypertriglyceridemia, and elevated LDLc, is a growing concern in Bangladesh. The risk is higher in people with uncontrolled or newly diagnosed type-2 diabetes. Early detection and treatment are crucial to reduce the risk of related conditions, especially cardiovascular diseases, in Bangladesh.

Keywords: Type-2 diabetes mellitus, hypertriglyceridemia, LDL, physical activities, hypertension, cardiovascular diseases

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder that affects multiple organs in the body, including the pancreas, liver, eyes, kidneys, nerves, and blood vessels. One of the most severe complications associated with diabetes is atherosclerosis, a condition that hardens and narrows the arteries, leading to cardiovascular disease. People with diabetes are two to four times more likely to develop cardiovascular disease than those without diabetes, and around

80% of all diabetes-related deaths and hospital stays caused by complications are due to atherosclerosis. (1)

Hyperlipidemia, defined as elevated levels of low-density lipoprotein (LDL) cholesterol, total cholesterol, triglycerides, or lipoproteins, is a key risk factor for the development of atherosclerosis. (2) Recent research has implicated ceramides, sphingolipids that play a crucial role in cellular signaling pathways, in the development of atherosclerosis, heart failure, and ischemic heart disease. (3, 4) Ceramides promote inflammation, oxidative stress, and endothelial dysfunction, which are key factors in the development of cardiovascular disease. Elevated ceramide levels may also serve as a useful biomarker for predicting cardiovascular events in patients with diabetes and metabolic syndrome.(5) Therefore, the modulation of ceramide metabolism represents a potential target for the prevention and treatment of cardiovascular disease in patients with diabetes.

Several genes and their products, combined with environmental factors and lifestyle choices, have been found to play a significant role in the development of diabetes and cardiovascular diseases and their related adverse or deadly outcomes. Among these, the microRNA-34 family and Thioredoxin-interacting protein (TXNIP/TBP-2) have emerged as prominent contributors and essential regulators of diabetes, atherosclerosis, cardiovascular diseases, as well as cancerous and non-cancerous cellular proliferation and regeneration.

MicroRNA-34a (miRNA-34a) is a small non-coding RNA that has been implicated in various cellular processes, including apoptosis, proliferation, senescence, and metabolism. (6) miRNA-34a is upregulated in the pancreatic islets of diabetic individuals and animal models of diabetes. miRNA-34a overexpression has been shown to inhibit insulin secretion and impair insulin sensitivity, contributing to the development of diabetes. (7, 8, 9) In addition, miRNA-34a has been implicated in the pathogenesis of cardiovascular disease, including dyslipidemia, atherosclerosis, and myocardial infarction. (10, 11) Therefore, targeting miRNA 34a may represent a potential therapeutic strategy for preventing and treating both diabetes and cardiovascular disease. (12)

Thioredoxin-interacting protein (TXNIP), also known as thioredoxin-binding protein-2 (TBP 2), is a key mediator of cellular oxidative stress and is implicated in various pathological conditions, including dyslipidemia, diabetes, and cardiovascular complications. (13, 14) TXNIP has been shown to play a critical role in lipid metabolism, and its dysregulation has been linked to dyslipidemia. (15)

TXNIP plays a significant role in the development and progression of diabetes. TXNIP expression is upregulated in response to glucose, and its overexpression has been shown to impair glucose-stimulated insulin secretion, elevated level of glucagon, and promote beta-cell apoptosis, leading to the development of diabetes. (16) In addition, TXNIP is involved in the regulation of glucose metabolism and insulin signaling pathways. (17, 18, 19, 20) Furthermore, TXNIP has been implicated in the pathogenesis of cardiovascular complications associated with diabetes. It has been shown to promote vascular smooth muscle cell proliferation and migration, endothelial dysfunction, and inflammation, all of which contribute to the development of atherosclerosis and other cardiovascular complications. (21, 22) Therefore, understanding the role of TXNIP in dyslipidemia, diabetes, and cardiovascular complications may provide new insights into the pathophysiology of these diseases and may lead to the development of new therapeutic strategies. (23)

In our cross-sectional study hyperlipidemia was investigated and compared among newly diagnosed and uncontrolled type-2 diabetes mellitus patients with healthy individuals to get some insights for the

betterment of management and treatment of diabetes. The findings from the study suggest that hyperlipidemia treatment along with the treatment of hyperglycemia and insulin insensitivity may act beneficial for the patients with diabetes mellitus. As it is evident that hyperlipidemia and lipid profile among diabetes patients vary depending on the sex (male and female) and age, diabetes care should be directed targeting group specific needs

MATERIALS & METHODS

Study population

The present cross-sectional study protocol obtained approval from the ethics committee of the Gopalganj Diabetic Hospital located Gopalganj, Dhaka, Bangladesh. Blood samples were obtained between September 2022 and December 2022 from Gopalganj Diabetic Hospital, Gopalganj, Dhaka, Bangladesh. Among the 83 eligible individuals (38 men and 45 women), 20 subjects were newly diagnosed with type 2 diabetes mellitus, 32 subjects were diabetic and treated but uncontrolled type 2 diabetes mellitus, 11 subjects were diabetic and treated and controlled type 2 diabetes mellitus and 20 subjects were non-diabetic. The fasting glycemia was less than 6.9 mmol/L for the non-diabetic control group and were not being treated with glucose lowering drugs and did not have a history of diabetes, metabolic disease or metabolic syndrome.

Collection of participant data

Medical personnel gathered anthropometric and health related information like age, gender, body mass index (BMI), hypertension, history of cardiovascular disease or stroke, family history of diabetes, work stress, physical activity, smoking habits (current, ever or never), alcohol consumption (current, ever or never), history of major health issues (yes/no), pregnancy frequency. In order to compute the body mass index (BMI), weight (kg) divided by height squared (m2) (Yamazaki et al 2022). Professional nurses used automated sphygmomanometers to monitor each participant's blood pressure (BP) in the upper right arm after 10 minutes of rest in a seated position. The average of two blood pressure readings was noted. According to the American College of Cardiology (ACC)/American Heart Association (AHA) recommendations, blood pressure was classified as normal (less than 120/80 mmHg), raised (between 120 and 129/80 mmHg), prehypertension (above 130/80 mmHg), and hypertension (above 140/80 mmHg). (24)

Blood sample collection, transportation and preservation

Around 2 ml of blood sample was drawn by expert nurses from subject's peripheral venous both in fasting blood glucose (FBG) condition and two hours after the administration of 75 gram glucose in 250 ml water. After collection, the blood samples were immediately placed on ice. The level of blood glucose was measured in both conditions by Automatic blood glucose analyzer GA series (Yokohama, Kanagawa, Japan) from the Biochemistry lab of Gopalganj Diabetic Hospital, Gopalganj. The blood samples were transported to the lab in vacuum blood collection EDTA (anticoagulant) tube through a cooler box (Winner cooler box, Pran RFL Company, Bangladesh).The blood was then transferred to round bottom closed microcentrifuged tube (Interlab Limited, New Zealand). Plasma was obtained at 3000 rpm for 10 minutes by TC-SPINPLUS-8 (Topscien instrument company limited, Italy). Then both separated plasma and cellular part were stored separately in -86 °C FROILABO 340L Vertical Deep Freezer (Collégien, France).

Lipid Profiling

Total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), triglycerides (TG) and low-density lipoprotein cholesterol (LDL-c) in plasma (~300 µL) were quantitated using The Dimension® Xpand® Plus Integrated

Chemistry System (Siemens Healthineers, Erlangen, Germany) which is an automatic analyzer. Then dyslipidemia was categorized according to the guidelines of The American Diabetes Association. Dyslipidemia was defined as having at least one of the following: Elevated triglyceride (TG) >150 mg/dL, high total cholesterol (TC) >200 mg/dL, raised LDL-c >100 mg/dL, and lowered HDL-c 40 mg/dL in men and 50 mg/dL in women are all risk factors. (25)

STATISTICAL ANALYSIS

The data were processed and analyzed using Microsoft Excel 2013 and the Statistical Package for Social Science (SPSS) version 25.0, (IBM Corporation). Continuous variables were presented as mean ± SD while categorical variables were presented as percentages. Categorized variables were analyzed using the Chi-square test. When there was a single independent variable and a single dependent variable, the one-way Analysis of Variance (ANOVA) was employed to compare the mean values of more than two groups. All analyses were regarded statistically significant when the p-value was <0.05 otherwise not significant.

RESULT

A total of 83 participants were included in this study for lipidemic analysis, of which 63 had previously been diagnosed with type-2 diabetes and 20 served as a non-diabetic control group. The proportion of diabetic patients in the study was 75.9%, with the remaining 24.1% comprising non-diabetic participants. Among the diabetic individuals, 24.1% were newly diagnosed with type-2 diabetes mellitus, 38.55% had been previously treated but had uncontrolled diabetes, and 13.25% had been treated and had controlled diabetes. The study population included 38 (45.78%) male and 45 (54.22%) female participants, representing a male-to-female ratio of 1:1.2.

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Table 1. Newly diagnosed, uncontrolled, controlled, non-diabetic and sex-based sample distribution.

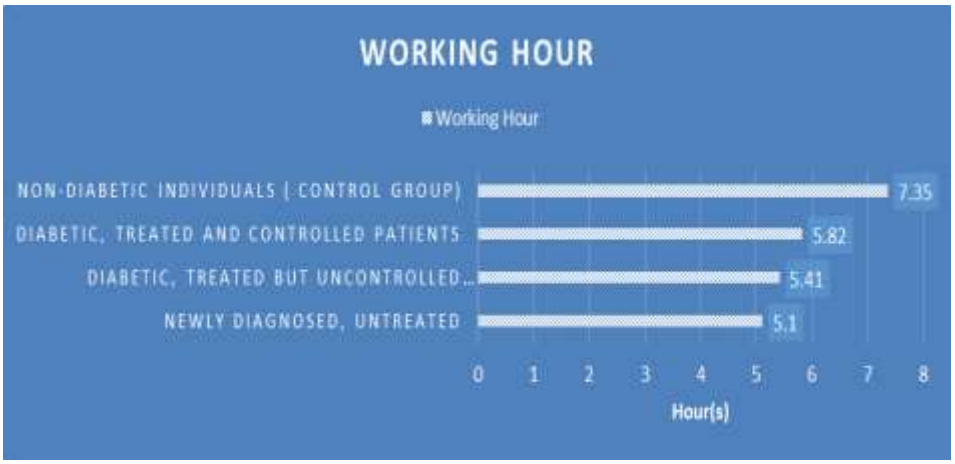
Category	Sample Number	Percentage (%)
Gross sample	83	100
Newly diagnosed type-2 diabetic patients	20	24.1
Diabetic, treated but uncontrolled patients	32	38.55
Diabetic, treated and controlled patients	11	13.25
Non-diabetic individuals (control group)	20	24.1
Male	38	45.78
Female	45	54.22

Table 2. Baseline characteristics of Diabetic participants

Characteristics	Frequency(n=63)	Percentage (%)
Age		
20-40	19	30.2
41-59	34	54
≥ 60	10	15.8
Marital status		
Married	59	93.7
single	4	6.3
Family History of Diabetes		
No one	34	54
Yes	29	46
Physical exercise		
No	24	38.1
Yes	39	61.9
Blurred Vision		
No	10	15.9
Little	22	34.9
Moderate	31	49.2
GI problem		
Little	23	36.5
Moderate	27	42.9
Severe	13	20.6

Allergic problem		
No	23	36.5
Yes	40	63.5
Teeth problem		
No	29	46
Little	21	33.3
Moderate	4	6.3
Severe	9	14.3
Nerve problem		
No	19	30.1
Little	17	27
Moderate	25	39.7
Severe	2	3.2
Smoking		
Never	50	79.4
Ever	5	7.9
Current	8	12.7
Alcohol		
Never	60	95.2
Occasionally	3	4.8
Appetite		
Low	8	12.7
Normal	20	31.7
High	35	55.6
Anxiety		
No	16	25.4
Yes	47	74.6
Regular checkup		
No	36	57.1
Yes	27	42.9

Figure 1. Comparison of working hours among several groups; diabetic and non-diabetic.



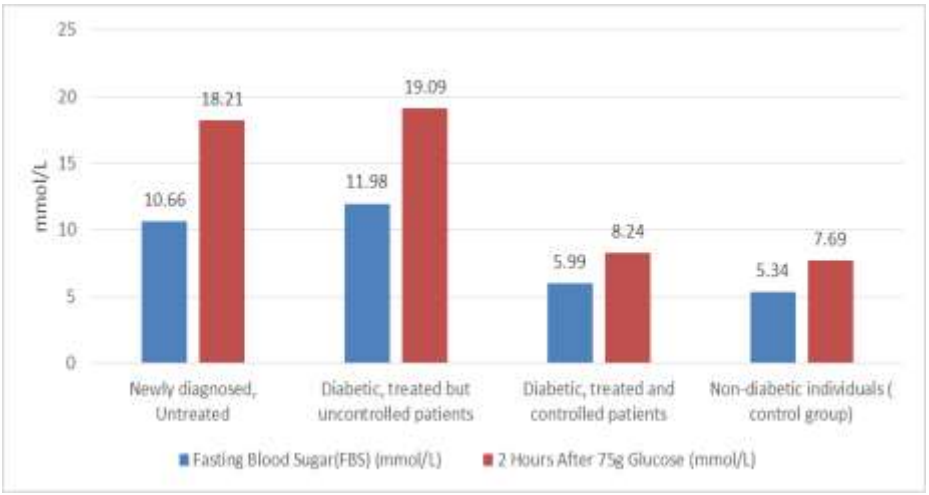


Figure 2. Comparison of blood glucose level in both fasting and 2 hours after 75g glucose administration conditions.

Table 3. Mean value of BMI, TC, TG, HDL-c, and LDL-c of Diabetic and Non-diabetic groups.

Category	BMI (kg/m^2)	TC (mg/dL)	TG (mg/dL)	HDL-c (mg/dL)	LDL-c (mg/dL)
Gross sample (N=83)	24.7±3.68	169.5±39.38	267.02±143.02	29.65±8.47	90.42±40.83
Newly diagnosed type-2 diabetic patients (N=20)	23.38 ±2.40	176.70±39.93	269.84±142.89	28.64±7.98	94.58±40.02
Diabetic, treated but uncontrolled patients (N=32)	24.80±3.51	171.63±37.42	304.47±166.07	29.11±7.98	82.39±40.35
Diabetic, treated and controlled patients (N=11)	24.67±5.39	149.91±25.69	255.10±139.25	27.24±7.65	72.16±35.17
Non-diabetic individuals (control group) (N=20)	25.89±3.74	169.71±47.79	210.83±83.01	32.84±9.76	109.13±39.98

Results are presented as mean (±SD) where appropriate. BMI-- Body Mass Index, TC--Total Cholesterol, TG-Triglycerides, HDL-c-- High-density Lipoprotein Cholesterol, LDL-c--Low-density Lipoprotein Cholesterol.

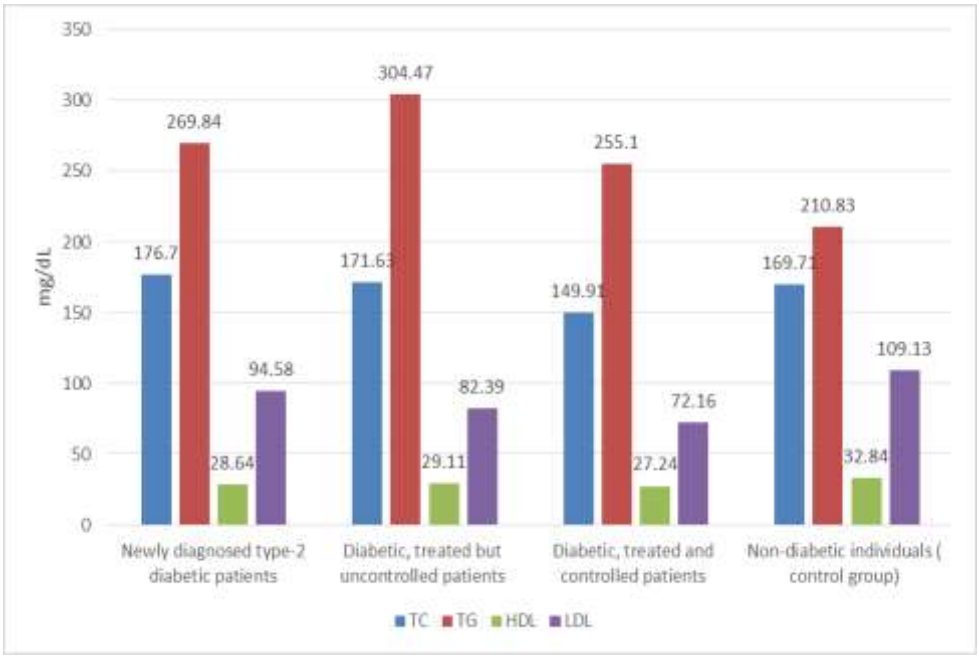


Figure 3. Lipid profile analysis of different groups of Diabetic patients and Non-diabetic control group.

Table 4. Prevalence of individual parameters of dyslipidemia and their association with gender, age, working hour, and BMI in non-diabetic individuals (As control)

Characteristics	TC		TG		LDL-c		HDL-c	
	High	Low	High	Low	High	Low	Low	High
Total Gender	2(10%)	18(90%)	16(80%)	4(20%)	13(65%)	7(35%)	15(75%)	5(25%)
Male	00(0%)	8(100%)	5(62.5%)	3(37.5)	4(50%)	4(50%)	5(62.5%)	3(37.5%)
Female	2(16.67)	10(83.33)	11(91.67)	1(8.33)	9(75%)	3(25%)	10(83.33%)	2(16.67%)
P value	.495(Chi-Square test)		.255 (Chi-Square test)		.356 (Chi-Square test)		.347 (Chi-Square test)	
Age (Years)								
< 40	0(0%)	8(100%)	7(87.5)	1(12.5)	5(71.43%)	2(28.57%)	6(85.71%)	1(14.28%)
≥40	2(16.67)	10(83.33)	9(75%)	3(25%)	8(61.54%)	5(38.46%)	9(69.23%)	4(30.77%)
P value	.495 (Chi-Square test)		.619 (Chi-Square test)		1.00 (Chi-Square test)		.613 (Chi-Square test)	
Working hour								
<6 hours	2(50%)	2(50%)	3(75%)	1(25%)	3(75%)	1(25%)	3(75%)	1(25%)
≥6 hours	0	16(100%)	13(81.25%)	3(18.75)	10(62.5%)	6(37.5%)	12(75%)	4(25%)
P value	.032 (Chi-Square test)		1.00 (Chi-Square test)		1.00 (Chi-Square test)		1.00 (Chi-Square test)	
BMI								
Underweight	00	00	00	00	00	00	00	00
Normal	00	8(100%)	5(62.5%)	3(37.5%)	5(62.5%)	3(37.5%)	49(50%)	4(50%)
Overweight	2(20%)	8(80%)	9(90%)	1(10%)	7(70%)	3(30%)	9(90%)	1(10%)
Obese	0	2(100%)	2(100)	0(00%)	1(50%)	1(50%)	2(100%)	0
P value	.329 (Chi-Square test)		.265 (Chi-Square test)		.848 (Chi-Square test)		.104 (Chi-Square test)	

Table 5. Prevalence of individual parameters of dyslipidemia and their association with gender, age, working hour, and BMI in type-2 diabetic (Newly diagnosed and uncontrolled) patient

Characteristics	TC		TG		LDL-c		HDL-c	
	High	Low	High	Low	High	Low	Low	High
Total Gender	13(25%)	39(75%)	42(80.77%)	10(19.23%)	18(34.61%)	34(65.39%)	47(90.38%)	5(9.62%)
Male	4(16%)	21(84%)	19(76%)	6(24%)	5(20%)	20(80%)	24(96%)	1(4%)
Female	9(33.33%)	18(66.67%)	23(85.18%)	4(14.82%)	13(48.15%)	14(51.85%)	23(85.18%)	4(14.82%)
P value	.205 (Chi-Square test) .155 (ANOVA)		.492(Chi-Square test) .411(ANOVA)		0.04(Chi-Square test) 0.033 (ANOVA)		.352(Chi-Square test) .193 (ANOVA)	
Age (Years)								
< 40	4(30.77)	9(69.27%)	13(100%)	0	6(46.15%)	7(53.85%)	13(100%)	0
≥40	9(23.07)	30(76.92%)	29(74.36%)	10(25.64%)	12(30.76%)	27(69.24%)	34(87.18%)	5(12.82%)
P value	.714(Chi-Square test) .588 (ANOVA)		.050(Chi-Square test) .043(ANOVA)		.334(Chi-Square test) .322 (ANOVA)		.314(Chi-Square test) .181 (ANOVA)	
Working hour								
<6 hours	6(30%)	14(70%)	17(85%)	3(15%)	6(30%)	14(70%)	19(95%)	1(5%)
≥6 hours	7(21.87%)	25(78.13%)	25(78.12%)	7(21.88%)	12(37.5%)	20(62.5)	28(87.5%)	4(12.5%)
P value	.529(Chi-Square test) .520 (ANOVA)		.722(Chi-Square test) .550 (ANOVA)		.766(Chi-Square test) .589 (ANOVA)		.637(Chi-Square test) .382 (ANOVA)	
BMI								
Underweight	00	00	00	00	00	00	00	00
Normal	10(29.41%)	24(70.59%)	26(74.28%)	9(25.72%)	11(44%)	24(56%)	31(88.57%)	4(11.42%)
Overweight	3(20%)	12(80%)	14(93.33%)	1(6.67%)	7(46.67%)	8(53.33%)	14(93.33%)	1(6.67)
Obese	0	2(100%)	2(100%)	0	0	2(100%)	2(100%)	0
P value	.576(Chi-Square test) .323 (ANOVA)		.229(Chi-Square test) .096 (ANOVA)		.336(Chi-Square test) .829(ANOVA)		.781(Chi-Square test) .494 (ANOVA)	

The majority of diabetic participants (69.8%) were over the age of 40, with no significant difference in age distribution between genders. The mean age of non-diabetic control group was 42 years and the mean age of the diabetic group was 47.65 years. The mean age of diabetic patients in the male group was 50.6 years and the mean age of diabetic patients in the female group was 44.97 years. Approximately 46% of diabetic patients had a family history of diabetes.

Regarding lifestyle habits, healthcare providers recommended physical activity to maintain sound glucose metabolism and regulate blood glucose levels, and about 61.9% of diabetic patients engaged in activities such as walking, running, or yoga. The association between hyperglycemia and retinopathy is well-known, and 84.1% of diabetic patients in this study reported experiencing blurred vision. Among the participants, 63.5% reported gastrointestinal and allergic problems, 69.9% reported nerve problems, and 87.3% reported having appetite issues. Nearly three-quarters (74.6%) of diabetic patients reported experiencing anxiety. The frequency of smoking and alcohol consumption was not significantly different among diabetic individuals in this study. More than 50% of diabetic individuals in this study reported not regularly checking their body or blood glucose levels.

Figure 1 presents a comparison of working hours among four groups of study populations, with data showing that newly diagnosed untreated type-2 diabetic patients worked an average of 5.1 hours, while treated type-2 diabetic uncontrolled patients worked an average of 5.41 hours, and treated type-2 diabetic controlled patients worked an average of 5.82 hours. In contrast, the non-diabetic control group worked an average of 7.35 hours. Figure 2 presents the average fasting blood glucose level and glucose level after administering 75g glucose in four groups, with non-diabetic control group having lower blood glucose levels in both conditions than the other groups.

Table 3 displays the mean value of BMI, TC, TG, HDL-c, and LDL-c of diabetic and non-diabetic groups. The values of BMI, TC, and LDL-c among the groups were not significantly different, but the values of TG and HDL-c were significantly different in non-diabetic group than any others diabetic group. From the Figure 3, it is estimated that the TG level is higher in rest of the three groups rather than the non-diabetic control group. And only in the non-diabetic group

the HDL level is higher than the three other groups. Figure 2 showed that both in fasting blood sugar and 2 hours after 75g glucose administration condition, the blood glucose level was higher in newly diagnosed type-2 diabetic patients and Type-2 diabetic, treated uncontrolled patients than the Type-2 diabetic, treated controlled patients and non-diabetic individuals (control group).

Table 4 showed that females were more prevalent with high TC than males, and increased levels of TG and LDL in females were 91.67% and 75%, respectively. The level of lower HDL was 100% prevalent in males.

Table 5 presented the investigation of the prevalence of dyslipidemia in newly diagnosed and uncontrolled type-2 diabetic patients, stratified by gender, age, working hour, and BMI. The study found that high total cholesterol (TC) was more prevalent in females (33.33%) than males (16%). Elevated triglycerides were more prevalent in females (85.18%) than males (76%), and decreased high-density lipoprotein cholesterol (HDL-c) was more prevalent in females (85.18%) than males (96%). There was a significant association between gender and low-density lipoprotein cholesterol (LDL-c) level ($p=0.040$), and dyslipidemia was more prevalent in patients over 40 years old. The study did not find any significant association between dyslipidemia, working hour, and BMI ($p>0.050$ each). During the study, it was estimated that a significant percentage of patients with dyslipidemia worked more than 6 hours per day.

In conclusion, the results of this study showed that diabetic patients had higher levels of TG and lower levels of HDL-c compared to non-diabetic controls. Additionally, reduced physical activity and hyperglycemia were associated with worsening body conditions. The prevalence of dyslipidemia varied by gender in non-diabetic individuals. These findings suggest the need for increased physical activity and regular monitoring of lipid profiles in diabetic individuals, particularly those with dyslipidemia. Further studies are needed to confirm and expand upon these results.

DISCUSSION

The present study aimed to investigate the lipidemic analysis of diabetic and non-diabetic individuals. The results showed that the majority of the study population had type-2 diabetes, with 24.1% of participants newly diagnosed, 38.55% previously treated but uncontrolled, and 13.25% previously treated and controlled. In contrast, only 20 participants served as the non-diabetic control group. The high proportion of diabetic patients in the study highlights the importance of understanding the relationship between diabetes and lipid levels.

The study population included slightly more females than males, with a ratio of 1:1.2. The majority of participants were over the age of 40, and nearly all reported being married. About half of the diabetic patients had a family history of diabetes. Physical activity is recommended to regulate blood glucose levels, and nearly two-thirds of diabetic patients engaged in physical activity. However, more than 50% of diabetic individuals did not regularly check their body or blood glucose levels. The prevalence of dyslipidemia in non-diabetic individuals was also investigated, with females being more prevalent with high TC and lower HDL-c levels, and males having higher levels of TG and LDL-c.

The study also found a strong relationship between working hours and blood glucose levels, with reduced physical activity leading to worsened body conditions and promoting hyperglycemia. The non-diabetic control group worked longer hours and had lower blood glucose levels than the diabetic groups. Additionally, the values of TG and HDL-c were significantly different in the non-diabetic group compared to the diabetic groups, indicating the importance of monitoring lipid levels in diabetic patients.

Some recent study carried out in Bangladesh, India and Pakistan also reported a similar prevalence of

dyslipidemia among individuals with type-2 diabetes. Like ours, an increase in TG level in majority of the diabetic patients was common finding for all of them. But none of the study in this region reported a significant difference in TG level increase in diabetes patients. Our study found a significant difference in TG level in the age group ≥40 years of diabetic patients when compared with the healthy control. Gender was also significantly associated with LDL-c level in our study. Increased levels of TG and LDL in females were 91.67% and 75% respectively. The level of lower HDL-c in females was 83.33%. On the other hand, high level of TG and LDL-C in males were 62.5% and 50%, respectively. The amount of lower HDL-c in males was 62.5%.

Several studies have investigated the prevalence of dyslipidemia in individuals with diabetes mellitus in South Asia. Bhuiyan AS et al. conducted a study in Bangladesh, which included 120 diabetic patients admitted to the Department of Cardiology at Mymensingh Medical College Hospital from April 2012 to March 2013. The study found a high prevalence of dyslipidemia among the patients, with 86% of patients affected. Gender, age, BMI, and duration of diabetes mellitus were not found to be significantly associated with dyslipidemia. The study also reported that most patients had serum triglyceride levels above the normal range, while about half of the participants had high serum total cholesterol levels. (26)

Similarly, Chowdhury JA et al. conducted an observational study in Bangladesh in 2016, which included 100 diabetic individuals and 100 healthy controls. The study found that both male and female participants with diabetes had significantly higher blood pressure and serum total cholesterol levels than healthy controls. (27)

Another cross-sectional study conducted by Das H and Banik S in Noakhali, a southern district of Bangladesh, evaluated the prevalence of dyslipidemia among 1008 diabetic patients. The study reported that 71% of female and 73% of male patients had dyslipidemia, with high LDL and low HDL levels. High TG, high TC, high LDL, and low HDL were also frequently observed, affecting 41.96%, 35.42%, 71.33%, and 49.70% of patients, respectively. (28)

Ahmmed MdS et al. also conducted a cross-sectional study in Bangladesh to evaluate the prevalence of dyslipidemia and associated risk factors in newly diagnosed type-2 diabetes patients. The study reported a high prevalence of dyslipidemia among both male and female participants, with most patients having high TG, high TC, high LDL, and low HDL levels. (29)

Karim MN et al. conducted a cross-sectional study in Bangladesh involving 366 consecutive eligible T2DM patients aged over 30 years. The study found that low HDL cholesterol was the most frequent form of dyslipidemia observed, affecting 59.3% of patients. The study also reported that poor glycemic control and comorbid hypertension were predictors of dyslipidemia. Both the TC-HDL ratio and LDL-HDL ratio were identified as good predictors of all four parameters of dyslipidemia. (30)

Finally, Basit A et al. conducted a National Diabetes Survey in Pakistan, which included 10,834 subjects aged 20 years or above. The study found a high prevalence of dyslipidemia, affecting a significant proportion of participants. The study identified diabetes, obesity, and hypertension as significant determinants of dyslipidemia. (31)

Overall, these studies highlighted the high prevalence of dyslipidemia among individuals with diabetes in South Asia and underscore the need for effective strategies to manage dyslipidemia and prevent its associated complications.

Several genes and their corresponding products are critically linked with diabetes and cardiovascular diseases and with their detrimental or fatal consequences. Based on the very current understanding, MicroRNA-34a and TXNIP (TBP-2) are the two major players among them. The following

discussions may account a significant part of our findings with diabetic dyslipidemia linking the some of the present understanding of the pathophysiology of type-2 diabetes mellitus and related complications specially microvascular and macrovascular complications including the diabetic cardiovascular pathologies.

MiRNA-34a is upregulated in the pancreatic islets of diabetic individuals and animal models of diabetes. (32) miR-34a overexpression has been shown to inhibit insulin secretion in response to glucose by downregulating the expression of SIRT1, a key regulator of insulin secretion, and the insulinotropic transcription factor, MafA. (33) Moreover, miR-34a can also impair insulin sensitivity by targeting the insulin receptor substrate (IRS) 1 and 2, leading to decreased activation of the PI3K-Akt signaling pathway. (34)

MiRNA-34a has also been shown to be involved in the pathogenesis of cardiovascular diseases (CVDs), including dyslipidemia, atherosclerosis, and myocardial infarction (MI). (35) Dyslipidemia is a major risk factor for the development of CVDs, and studies have shown that miRNA-34a regulates cholesterol metabolism by targeting several key genes involved in cholesterol homeostasis, such as ATP-binding cassette transporter A1 (ABCA1), liver X receptor alpha (LXRα), and sirtuin 1 (SIRT1). (36, 37, 38) In addition to its role in regulating cholesterol metabolism, miRNA-34a also plays a crucial role in the development of atherosclerosis. Studies have shown that miRNA-34a promotes the formation of foam cells by suppressing ABCA1 and LXRα, which are essential for cholesterol efflux from macrophages. (36, 37) Moreover, miRNA-34a can activate the nuclear factor-kappa B (NF-κB) pathway and promote inflammation by targeting SIRT1 and other anti-inflammatory genes, leading to the acceleration of atherosclerosis progression. (38)

MiRNA-34a also modulates ceramide levels in cells by regulating the expression of enzymes involved in the biosynthesis of ceramide, such as serine palmitoyltransferase (SPT) and ceramide synthase 6 (CerS6). (39, 40, 41)

Additionally, miRNA-34a can target genes involved in the regulation of ceramide metabolism and signaling, such as sphingosine-1-phosphate receptor 1 (S1PR1) and peroxisome proliferator-activated receptor delta (PPARδ). (42, 43) MiRNA-34a expression is upregulated in the myocardium after MI, and it promotes myocardial apoptosis and fibrosis by targeting several anti-apoptotic and pro-fibrotic genes, including SIRT1, B-cell lymphoma 2 (Bcl-2), and Smad4. (44, 45) Therefore, inhibition of miRNA-34a could be a potential therapeutic approach for treating CVDs. Preclinical studies have investigated the use of various miRNA-34a inhibitors, such as antagomirs, locked nucleic acids (LNAs), and small molecule inhibitors, to target miRNA-34a in CVDs, with promising results. (46, 47) However, further studies are needed to investigate the safety and efficacy of miRNA-34a inhibition in human clinical trials.

TXNIP (Thioredoxin-interacting protein) is a key regulatory protein involved in glucose and lipid metabolism. Dysregulation of TXNIP has been associated with both onset and progression of type 2 diabetes, dyslipidemia, and cardiovascular diseases. Bodnar JS et al. identified TXNIP as the gene responsible for combined hyperlipidemia in 2002, using positional cloning. (48) Xie X et al. conducted two studies, one in 2021 and the other in 2022, to evaluate the association of TXNIP with prediabetes and T2D. In the 2021 study, the authors found that TXNIP was a predictor for PD. In the 2022 study, the authors identified TXNIP and IRAK-M as potential diagnostic factors for prediabetes. (49, 50) Zhang D et al. conducted a case-control study in 2020 and found that TXNIP methylation was associated with T2DM incidence in a Chinese population, with interactions between TXNIP methylation, obesity, and hypertriglyceridemia that may

influence T2DM risk. (50) Van Greevenbroek MM et al. investigated the frequency distribution of a SNP in the TXNIP gene and its effect on metabolic parameters. The authors found that carriers of the TXNIP-T variant had higher triglyceride concentrations and higher diastolic blood pressure in diabetic subjects, while non-diabetic carriers had lower fasting glucose concentrations. (51, 52) Zhao YC et al. studied the plasma levels of TXNIP in patients with IGR and hypertriglyceridemia and found that increased levels of TXNIP may contribute to islet β-cell dysfunction in these patients. (53) Szpigel A et al. found that TXNIP expression was increased in individuals with type 2 diabetes, and there was a correlation between TXNIP expression and plasma fasting glucose and triacylglycerol concentrations. The study also found an association between TXNIP expression and inflammatory markers and markers of the UPR. (54) Guo H et al. investigated the relationship between TXNIP and hepatic fat levels in patients with T2DM and found that TXNIP expression was positively correlated with HFF. (55) Roberta Scrimieri et al. in 2021 reported high level of glucose induced TXNIP increased lipogenesis and reduced fatty acid oxidation resulting increased accumulation of triglycerides and lipid droplets. (56)

Cardiac dysfunction is a condition that affects the heart's ability to pump blood effectively and can be caused by a variety of factors, including hypertension, myocardial infarction, and cardiomyopathy. Studies have indicated that TXNIP, a protein that is upregulated in the heart under stress conditions such as ischemia-reperfusion injury and pressure overload-induced hypertrophy, plays a role in the development of cardiac dysfunction. (57, 58)

Inhibition of TXNIP has been identified as a potential therapeutic strategy for the treatment of cardiac dysfunction. In animal models, both pharmacological inhibition and genetic deletion of TXNIP have been shown to improve cardiac function and decrease myocardial damage following ischemia-reperfusion injury and pressure overload-induced hypertrophy. (59, 60) Additionally, TXNIP inhibition has been found to decrease oxidative stress and inflammation in the heart, which are major contributors to the development of cardiac dysfunction. (61) Byon CH et al. investigated the role of Thioredoxin interacting protein (Txnip) in the inflammatory response of vascular smooth muscle cells (VSMC) and atherosclerosis development. Results showed that Txnip ablation reduced oxidative stress and inflammation in VSMC and macrophages, leading to a decrease in NF-κB nuclear translocation and macrophage adhesion to VSMC. In Txnip-ApoE double knockout mice, atherosclerotic lesions were significantly reduced in the aortic root and abdominal aorta compared to control ApoE knockout mice. These findings suggest that targeting Txnip expression could be a potential intervention for atherosclerosis and vascular inflammatory disease. (62) Li, Y et al. explored the regulatory effects of long non-coding RNA GAS5 on the miR-194-3p/TXNIP axis in coronary atherosclerosis (AS). Using AS rat models, GAS5, miR-194-3p, and TXNIP expression levels were tested in coronary vascular tissues and endothelial cells (ECs). Results showed that GAS5 was upregulated while miR-194-3p and TXNIP were downregulated in AS. GAS5 bound to miR-194-3p while miR-194-3p targeted TXNIP. Inhibiting GAS5 or overexpressing miR-194-3p promoted EC proliferation and suppressed apoptosis in AS. The study suggests that inhibiting GAS5 could enhance EC growth through the miR-194-3p/TXNIP axis, providing a potential therapeutic strategy for AS. (63)

Several specific and non-specific inhibitors of TXNIP, including SRI-37330 (substituted quinazoline sulfonamide), verapamil (U.S. FDA approved antihypertensive drug), W2476 [9- ((1-(4-acetyl-phenyloxy)-ethyl)-2-)adenine], and quinazolin-4(3H)-one derivatives have shown potential in

improving diabetes. SRI-37330 is an orally bioavailable, non-toxic small molecule that has effectively rescued mice from streptozotocin- and obesity-induced diabetes. (64) Verapamil has also shown promising results in improving lipid metabolism, with a significant decrease in total cholesterol, triglycerides, and LDL cholesterol observed in type 2 diabetes patients after 12 weeks of treatment. (65) Similarly W2476 has been shown to have a significant effect on lipid metabolism and glycemic control, with the potential to reduce the risk of cardiovascular disease in patients with diabetes. (66) Quinazolin-4(3H)-one derivatives have also been evaluated for their inhibitory effects on TXNIP and have shown potential as α-glucosidase inhibitors, which could improve the metabolic status of diabetic patients by modulating lipid metabolism. (67, 68, 69)

However, there were some limitations in our study which should be taken into consideration. The study only included 83 participants, which may not be representative of the entire population of patients with type-2 diabetes mellitus in this district of Bangladesh. This may limit the generalizability of the study's findings to other populations. The dietary habits of the participants were not considered in the study. The study used a cross-sectional design, which can only establish a correlation between hyperlipidemia and diabetes but cannot determine causality or the temporal sequence of events. Longitudinal studies are needed to better understand the relationship between diabetes and hyperlipidemia over time.

CONCLUSION

In conclusion, this study highlighted the high prevalence of hyperlipidemia in newly diagnosed type-2 diabetes mellitus patients and uncontrolled diabetic patients in Gopalganj, a district of Bangladesh. The results indicate that hypertriglyceridemia, hypercholesterolemia, and elevated low-density lipoprotein cholesterol are common and serious conditions in this population, especially among females and individuals with uncontrolled diabetes. Furthermore, this study found a significant association between age and triglyceride levels and gender and LDL-c levels. These findings suggested the importance of early identification and management of hyperlipidemia in diabetes individuals to reduce the risk of related illnesses, especially cardiovascular problems. Healthcare providers should consider regular lipid profiling as part of routine diabetes management in addition to hyperglycemic control, especially for those with uncontrolled diabetes and newly diagnosed individuals. Further research is needed to investigate the effectiveness of lipid-lowering therapies in reducing cardiovascular risk in this population

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REFERENCES

1. American Diabetes Association. (2019). Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes-2019. Diabetes care, 42(Supplement 1), S103-S123.
2. Goldberg, I. J., & Eckel, R. H. (2017). Mc-Graw Hill. Dyslipidemia and atherosclerosis.
3. Haus, J. M., Kashyap, S. R., Kasumov, T. et al. Plasma ceramides are elevated in obese subjects with type 2 diabetes and correlate with the severity of insulin resistance. Diabetes. 2009; 58(2): 337-343.
4. Holland, W. L., Brozinick, J. T., Wang, L. P. et al. Inhibition of ceramide synthesis ameliorates glucocorticoid-, saturated-fat-, and obesity-induced insulin resistance. Cell metabolism. 2007; 5(3): 167-179.
5. Hulsmans, M., & Holvoet, P. The vicious circle between oxidative stress and inflammation in atherosclerosis. Journal of cellular and molecular medicine. 2010; 14(1-2), 70-78.
6. Hermeking H. The miR-34 family in cancer and apoptosis. Cell Death Differ. 2010: 17: 193-199.
7. Wei R, Yang J, Liu GQ, et al. Dynamic expression of microRNAs during the differentiation of human embryonic stem cells into insulin-producing cells. Gene. 2013; 518(2):246-55.
8. Chakraborty C, Doss CG, Bandyopadhyay S, et al.. Influence of miRNA in insulin signaling pathway and insulin resistance: micro-molecules with a major role in type-2 diabetes. Wiley Interdiscip Rev RNA. 2014; 5(5):697-712.
9. García Jacobo R, Uresti-Rivera E, Portales-Pérez D, et al. Circulating miR-146a, miR-34a and miR-375 in type 2 diabetes patients, pre-diabetic and normal glycaemic individuals in relation to β-cell function, insulin resistance and metabolic parameters. Clin Exp Pharmacol P 2019; 46(12):1092-1100.
10. Li X, Khanna A, Li N, et al. Regulation of miR-34a/SIRT1 axis in angiotensin II-induced hypertension and associated cardiac hypertrophy. Am J Hypertens. 2016; 29(6):756-764
11. Wu Y, Xiao Y, Ding X, et al. MicroRNA-34a regulates cardiac fibrosis after myocardial infarction by targeting Smad4. Expert Opin Ther Targets. 2018; 22(11): 897-906.
12. Hua CC, Liu XM, Liang LR, Wang LF, Zhong JC. Targeting the microRNA-34a as a Novel Therapeutic Strategy for Cardiovascular Diseases. Front Cardiovasc Med. 2022; 8:784044.
13. Shao W, Yu Z, Chiang Y, et al. TXNIP regulates peripheral glucose metabolism in humans. PLoS Med. 2013;10(6):e1001562.
14. Zhou Y, Wang Y, Wang J, et al. Thioredoxin-interacting protein (TXNIP) in cancer and diabetes mellitus. J Cell Physiol. 2018; 233(12): 9169-9180.
15. Yao X, Panichpisal K, Kurtzman N, Nugent K. TXNIP overexpression suppresses proliferation and induces apoptosis in SMMC7721 cells. Int J Med Sci. 2010; 7(6):336-343.
16. Chen J, Fontes G, Saxena G, et al. Insulin resistance and metabolic derangements in obese mice are ameliorated by a novel peroxisome proliferator-activated receptor γ-sparing thiazolidinedione. J Biol Chem. 2012; 287(27): 23537-23548.
17. Parikh H, Carlsson E, Chutkow WA, et al. TXNIP regulates peripheral glucose metabolism in humans. PLoS Med. 2007; 4(5):e158.
18. Shao D, Han J, Hou X, et al. TXNIP regulates hepatic glucose production via the PERK signaling pathway. Int J Mol Med. 2018; 41(2):715-722.
19. Wu N, Zheng B, Shaywitz A, et al. AMPK-dependent degradation of TXNIP upon energy stress leads to enhanced glucose uptake via GLUT1. Mol Cell. 2013; 49(6): 1167-1175.
20. Wu Y, Song P, Xu J, et al. Activation of AMPKα2 in adipocytes is essential for nicotine-induced insulin resistance in vivo. Nat Med. 2015; 21(4):373-382.

21. Shah MS, Brownlee M. Molecular and cellular mechanisms of cardiovascular disorders in diabetes. Circ Res. 2016; 118(11): 1808-1829.
22. Wang Y, De Keulenaer GW, Lee RT. Vitamin D(3)-up-regulated protein-1 is a stress-responsive gene that regulates cardiomyocyte viability through interaction with thioredoxin. J Biol Chem. 2002; 277(28): 26496-26500.
23. Shao M, Zhou H, Wu Y, et al. Thioredoxin-interacting protein (TXNIP) in metabolic and cardiovascular diseases. J Diabetes. 2020; 12(3):186-197.
24. Carey, R.M., Whelton, P.K. and 2017 ACC/AHA Hypertension Guideline Writing Committee*. Prevention, detection, evaluation, and management of high blood pressure in adults: synopsis of the 2017 American College of Cardiology/American Heart Association Hypertension Guideline. *Annals of internal medicine*, 2018; *168*(5): pp.351-358.
25. American Diabetes Association, 2009. Diagnosis and classification of diabetes mellitus. Diabetes care, 32(Suppl 1), p.S62.
26. Bhuiyan AS, Bari MA, Aditya G. et al. Prevalence and Pattern of Dyslipidemia in Diabetes Mellitus Patients Admitted in the Department of Cardiology, Mymensingh Medical College Hospital, Mymensingh, Bangladesh. Mymensingh Med J. 2021; 30(1):21-27.
27. Chowdhury JA, Nessa A, Nessa W. et al. Association of Hypertension and Hypercholesterolemia in Patients with Type-2 Diabetes Mellitus. Mymensingh Med J. 2021; 30(3): 651-656.
28. Das H, Banik S. Prevalence of dyslipidemia among the diabetic patients in southern Bangladesh: A cross-sectional study. Diabetes Metab Syndr Clin Res Rev. 2019; 13: 252–257.
29. Ahmmed MdS, Shuvo SD, Paul DK, et al. Prevalence of dyslipidemia and associated risk factors among newly diagnosed Type-2 Diabetes Mellitus (T2DM) patients in Kushtia, Bangladesh. Gyasi RM, editor. PLOS Glob Public Health. 2021; 1: e0000003.
30. Karim MN, Ahmed KR, Bukht MS, Akter J. et al. Pattern and predictors of dyslipidemia in patients with type 2 diabetes mellitus. Diabetes Metab Syndr. 2013 ;7(2): 95-100.
31. Basit A, Sabir S, Riaz M, Fawwad A, et al. NDSP 05: Prevalence and pattern of dyslipidemia in urban and rural areas of Pakistan; a sub analysis from second National Diabetes Survey of Pakistan (NDSP) 2016–2017. J Diabetes Metab Disord. 2020; 19: 1215–1225.
32. Ferreira, A. F., Rezende, L. F., & Santos, R. S. The Role of MicroRNA in Diabetes-Related Pathophysiological Pathways. Frontiers in endocrinology. 2021; 12: 647343.
33. Pullen, T. J., da Silva Xavier, G., Kelsey, G. et al. miR-29a and miR-29b contribute to pancreatic beta-cell-specific silencing of monocarboxylate transporter 1 (MCT1). Molecular and cellular biology. 2011; 31(15):3182-3194.
34. Daval, M., Foufelle, F., & Ferré, P. Functions of AMP-activated protein kinase in adipose tissue. Journal of physiology and biochemistry. 2006; 62(1): 41-51.
35. He X, Wang Y, Zhu J, et al. MiR-34a in age and tissue related cardiovascular diseases. Aging Dis. 2020; 11(1):153-163.
36. Li, Y., Song, Y. H., Li, Y. et al. MicroRNA-34a/microRNA-93 regulate cholesterol efflux from endothelial cells through targeting ABCA1. International journal of molecular medicine. 2011; 27(4): 481-487.
37. Ouimet, M., Ediriweera, H. N., Gundra, U. M. et al. MicroRNA-33-dependent regulation of macrophage metabolism directs immune cell polarization in atherosclerosis. The Journal of clinical investigation, 2016; 126(12): 4330-4342.
38. Zeng, Y., Zhang, L., Zhu, Y. et al. MicroRNA-34a regulates cholesterol efflux and inflammation by targeting ATP-binding cassette transporter A1. FEBS letters. 2016; 590(6): 856-867.
39. Wei, Y., Nazari-Jahantigh, M., Chan, L. et al. The microRNA-342-5p fosters inflammatory macrophage activation through an Akt1-and microRNA-155-dependent pathway during atherosclerosis. Circulation. 2013; 127(15): 1609-1619.
40. Li, Z., Hassan, M. Q., Jafferji, M. et al. Biological functions of miR-29b contribute to positive regulation of osteoblast differentiation. Journal of Biological Chemistry. 2015; 290(28): 15676-15694.
41. Li, C., Wang, Y., Cao, X., Sun, R. et al. MicroRNA-34a regulates ceramide synthase 6 in an Akt-dependent manner in ovarian

cancer cells. Cancer Management and Research. 2020; 12: 2213.
42. Liu, C., Tang, D. G., & Chen, K. MicroRNA-34a: a potent tumor suppressor that regulates multiple cellular pathways. Journal of cellular physiology. 2018; 233(12): 9269-9280.
43. Li, C., Cheng, X., Wang, Y. et al. MiR-34a targets sirtuin 1 and regulates the apoptosis of ovarian granulosa cells. Apoptosis. 2015; 20(8): 1071-1078.
44. Chen, L., Zhu, X., Qiu, J.et al. MiR-34a regulates apoptosis of H9c2 cardiac muscle cells induced by hypoxia through Bcl-2. International journal of clinical and experimental medicine. 2014; 7(12): 5493.
45. Yan, L., Hu, F., Yan, X. et al. MiRNA-34a affects myocardial apoptosis after myocardial infarction in rats. Journal of Cellular Biochemistry. 2019; 120(5): 8176-8184.
46. He, X., Liang, X., Zhu, Y et al. Advances in research on miRNA-34a and its application prospects in cardiovascular diseases. Life Sciences. 2020; 246, 117393.
47. Boon, R. A., Iekushi, K., Lechner, S. et al. MicroRNA-34a regulates cardiac ageing and function. Nature. 2013; 495(7439), 107-110.
48. Bodnar JS, Chatterjee A, Castellani LW. Positional cloning of the combined hyperlipidemia gene Hyplip1. Nat Genet. 2002; 30(1):110-6.
49. Xie X, Bai G, Liu H. et al. Early Predictors in the Onset of Type 2 Diabetes at Different Fasting Blood Glucose Levels. Diabetes Metab Syndr Obes. 2021; 14:1485-1492.
50. Xie X, Bai G, Zhang L. et al. Changes in plasma IRAK-M in patients with prediabetes and its relationship with related metabolic indexes: a cross-sectional study. *Journal of International Medical Research*. 2022; 50(8).
51. Zhang D, Cheng C, Cao M. et al. TXNIP hypomethylation and its interaction with obesity and hypertriglyceridemia increase type 2 diabetes mellitus risk: A nested case-control study. J Diabetes. 2020; 12(7):512-520.
52. van Greevenbroek MM, Vermeulen VM, Feskens EJ. et al. Genetic variation in thioredoxin interacting protein (TXNIP) is associated with hypertriglyceridaemia and blood pressure in diabetes mellitus. Diabet Med. 2007; 24(5):498-504.
53. Zhao YC, Zhu J, Song GY. Relationship between thioredoxin-interacting protein (TXNIP) and islet β-cell dysfunction in patients with impaired glucose tolerance and hypertriglyceridemia. Int J Clin Exp Med. 2015; 8(3):4363-8.
54. Szpigel, A., Hainault, I., Carlier, A. et al. Lipid environment induces ER stress, TXNIP expression and inflammation in immune cells of individuals with type 2 diabetes. Diabetologia. 2018; 61:399-412.
55. Guo, H., Zhang, Y., Liao, L, et al. Circulating TXNIP levels and risk of non-alcoholic fatty liver disease in type 2 diabetes patients. Journal of Diabetes Investigation. 2022; 13(1):97-105.
56. Scrimieri R, Cazzaniga A, Castiglioni S, et al. Vitamin D Prevents High Glucose-Induced Lipid Droplets Accumulation in Cultured Endothelial Cells: The Role of Thioredoxin Interacting Protein. Biomedicines. 2021; 10; 9(12):1874.
57. Hwang H, Lee JW, Kang ES, et al. Thioredoxin-interacting protein regulates cardiac hypertrophy through mTORC2-Akt-FoxO1 signaling pathway. Chem Biol Interact. 2013; 206(1):100-108.
58. Zhou X, Chen J, Zhang L, et al. The emerging roles of thioredoxin-interacting protein (TXNIP) in pathological injury and inflammatory reactions. Cell Signal. 2018; 42:169-177.
59. Nishida K, Nomura M, Mishima T, et al. Thioredoxin-interacting protein promotes oxidative stress and renal inflammation in obesity-related chronic kidney disease. Clin Sci (Lond). 2018; 132(8):839-859.
60. Ansari HR, Raghava GPS. Identification of Thioredoxin-interacting protein (TXNIP) inhibitors using structure-based drug designing approach. Sci Rep. 2017; 7(1):4910.
61. Chen Y, Guo H, Xu D, Jiang H. Thioredoxin-interacting protein mediates NLRP3 inflammasome activation involved in the regulation of oxidative stress and inflammation in paraquat-induced acute kidney injury. Chem Biol Interact. 2018; 279:109-117.
62. Byon CH, Han T, Wu J, Hui ST. Txnip ablation reduces vascular smooth muscle cell inflammation and ameliorates atherosclerosis in apolipoprotein E knockout mice. Atherosclerosis. 2015; 241(2):313-21.

63. Li, Y., Geng, Y., Zhou, B. et al. Long Non-coding RNA GAS5 Worsens Coronary Atherosclerosis Through MicroRNA-194-3p/TXNIP Axis. Mol Neurobiol. 2021; 58:3198-3207.
64. Xiao X, Zhu H, Yang B, et al. Oleanolic acid ameliorates isoproterenol-induced myocardial injury in rats via modulation of oxidative stress and apoptosis. Sci Rep. 2017; 7:41789.
65. Thielen, L. A., Chen, J., Jing, G., et al. (2020). Identification of an anti-diabetic, orally available small molecule that regulates TXNIP expression and glucagon action. Cell Metabolism, 32(3), 353-365.
66. Carnovale C, Dassano A, Mosini G, et al. The β-cell effect of verapamil-based treatment in patients with type 2 diabetes: a systematic review. Acta Diabetologica. 2020; 57(1):117-131.
67. Gonzalez-Monjal E, Fernandez-Rodriguez E, Perez-Pevida B, et al. W2476, a new selective PPARα modulator, improves lipid metabolism and reduces inflammation in type 2 diabetic rats. Scientific Reports. 2020; 10(1):11675.
68. Moheb SM, Ghanadian M, Sharifzadeh M, et al. Synthesis and biological evaluation of quinazolin-4(3H)-one derivatives as potential inhibitors of thioredoxin-interacting protein and α-glucosidase for the treatment of type 2 diabetes. Eur J Med Chem. 2022; 226:114716.
69. Li X, Yu Y, Li W, et al. Discovery of novel quinazolin-4(3H)-one derivatives as potent thioredoxin-interacting protein inhibitors for the treatment of type 2 diabetes. Bioorg Chem. 2023; 118:105173.

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