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Biofactors' impact on diabetes prognosis

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Abstract:

Background: Diabetes mellitus (DM) is a chronic disease with a high prevalence globally, leading to significant health complications, particularly cardiovascular diseases (CVDs). A prevalent complication in diabetes is dyslipidemia, which is defined by high lipid levels and raises the risk of atherosclerosis and associated cardiovascular problems. **Objective:** the investigation was to discover cardiovascular risk factors unique to a patient's gender with type 2 diabetes mellitus (T2DM). **Materials and Methods:** A cross-sectional study of 85 individuals (47 women and 38 males) in two age groups (40-59 and 60-80) was carried out. SPSS version 22 assessed health markers such as ASCVD risk percentages, lipid profiles, and BMI. **Results:** There were significant differences between both genders regarding BMI, HDL cholesterol, triglycerides, CRI, and Atherogenic Index (AI), with women having higher levels of these markers than males but lower levels of AI and ASCVD risk. **Conclusion:** In T2DM patients, gender-specific approaches are required to manage cardiovascular risk, highlighting the significance of customized therapies based on lipid profiles and other risk factors.

KEYWORDS: Biofactors, Diabetes Mellitus, Cardiovascular Risk, Gender Differences, atherosclerosis

LIST OF ABBREVIATIONS

T2DM	Type 2 Diabetes Mellitus
BMI	Body Mass Index
ASCVD	Atherosclerotic Cardiovascular Disease
CRI	Coronary Index
AI	Atherogenic Index
HDL	High-Density Lipoprotein
LDL	Low-Density Lipoprotein
GLU	Glucose
TC	Total Cholesterol
TG	Triglyceride

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INTRODUCTION

Long-term illness Worldwide, there is a notable prevalence of diabetes mellitus. Hyperglycemia, or abnormally high blood sugar, is brought on by problems with the production or utilization of insulin. Effective management of blood glucose levels and resolution of related problems are essential to reduce consequences that could jeopardize patients' overall health [1,2].

People with diabetes mellitus have a significantly higher chance of developing cardiovascular diseases (CVDs) than the general population, which poses a substantial threat to their health [3]. Dyslipidemia is a disorder that is frequently observed in individuals with diabetes and is one of the key factors that determines the higher risk of diabetes. Dyslipidemia is a medical disorder characterized by decreased levels of HDL cholesterol and elevated levels of LDL cholesterol and triglycerides [4,5]. There is a considerable correlation between cholesterol levels and cardiovascular health [6]. Reduced HDL cholesterol levels and increased triglyceride and LDL cholesterol levels contribute to the development of atherosclerosis, which is defined by the accumulation of plaque inside the arterial walls [7]. The risk of cardiovascular events such as myocardial infarctions and cerebrovascular accidents rises as arteries constrict or are blocked by plaque [8].

A study [9] found that diabetics whose cholesterol is well-controlled with medication and lifestyle modifications have a much lower risk of cardiovascular issues [10] It is important to take into account all lipoproteins that have the potential to cause atherosclerosis, also referred to as non-HDL cholesterol, when determining a diabetic's risk of cardiovascular problems [11]. The cholesterol level is what's left behind after subtracting HDL cholesterol from total cholesterol. The advancement of atherosclerosis is accelerated not only by low-density lipoprotein (LDL) cholesterol but also by VLDL and intermediate-density lipoprotein (IDL) cholesterol. Researchers have found that non-HDL cholesterol is a more accurate indicator of cardiovascular events than LDL cholesterol alone [4]. This will be particularly relevant for those who have diabetes. High non-HDL cholesterol levels are associated with an increased risk of cardiovascular issues in diabetics [12].

Diabetics are more likely to experience accelerated atherosclerosis due to metabolic problems brought on by inflammation and insulin resistance [13]. As non-HDL cholesterol is a highly reliable marker of cardiovascular disease risk, lowering its levels is the main objective of treatment [9]. Body mass index (BMI) is a major indicator of cardiovascular health. Insulin resistance is associated with an increased risk of hyperglycemia and dyslipidemia, which are defined by abnormal cholesterol levels; hyperglycemia and dyslipidemia are both worsened by a greater body mass index (BMI) [14,15]. Increased risk of cardiovascular disease and type 2 diabetes is associated with obesity, which in turn is associated with an elevated body mass index (BMI) [16,17].

Bloodstream inflammation is induced by the release of inflammatory cytokines and free fatty acids by excess fat buildup, especially in the visceral area. As a result, atherosclerosis advances more rapidly [1]. Diabetics should modify their eating habits, increase their physical activity, and modify their behavioral patterns to maximize cardiovascular health and help with weight management [18]. According to research, reducing body mass index (BMI) is a straightforward way to improve cardiovascular health [19]. This is because decreasing body mass index has an impact on blood pressure, insulin sensitivity, and lipid profiles [20].

Reducing the risk of cardiovascular issues and managing diabetes both depend on reaching and maintaining a healthy weight [4]. The Atherosclerotic Cardiovascular Disease (ASCVD) risk percentage [21] can be used to estimate a patient's 10-year risk of cardiovascular events such as heart attacks or strokes. Because atherosclerotic cardiovascular disease (ASCVD) is more common in the diabetic community, this risk assessment should

be conducted more frequently in this demographic than in the general population [22]. The ASCVD risk score (4) takes into account factors like age, gender, race/ethnicity, blood pressure, cholesterol, diabetes, and smoking status. Due to their significantly increased risk of cardiovascular disease (CVD), people with diabetes should take steps to lower their risk factors [23,24].

This study aimed to determine which individuals with type 2 diabetes mellitus (T2DM) have cardiovascular risk factors particular to their gender and to underline the significance of customized therapies for improved risk management.

MATERIALS AND METHODS

The study is a cross-sectional analysis that was performed from December 2023 to June 2024 to investigate 85 individuals diagnosed with diabetic mellitus type 2 who experienced dyslipidemia and obesity during diseases. Biochemical biomarkers were evaluated in Rabie AL-Harythia Lab as part of the study after obtaining ethical approval from patients, categorized by sex: 38 male and 47 female participants; and age (46) individuals aged 40-59, (39) aged 60-80, The study gathered data on various demographic variables such as age and sex and BMI and measurement lipid profile.

Sampling technique

Patients with type 2 diabetes samples were tested using Cholestech LDX™ lipid profile test cassettes. Capillary whole blood specimens were obtained by finger stick using lithium heparin-coated capillary tubes. They were analyzed using the CHOLESTECH LDX™ analyzer from company Abbott. Additionally, various glucose testing methods exist. The glucose concentration is proportional to the amount of color formed. The Cholestech LDX glucose (GLU) test employs a glucose oxidase enzyme that catalyzes the oxidation of glucose to gluconolactone and hydrogen peroxide. A subsequent reaction produces a color that is detected by the photometer inside the Cholestech LDX analyzer.

Statistical Analysis

The study utilized SPSS version 22 to perform appropriate statistical tests, comparing the mean ± standard deviation of each parameter. Continuous variables were evaluated using independent t-tests. Categorical variables were analyzed using chi-square tests or Fisher's exact tests. A p-value of < 0.05 was judged statistically significant.

RESULTS

In this study, 85 individuals suffered from diabetic mellitus type 2, and the 38 male participants' mean age (of 58.1± 9.8), and 47 Females had a mean age (of 59.1±10.4).

According to the findings, males and females show significant differences in BMI, ASCVD risk percentage, HDL cholesterol, triglycerides, CRI, and Atherogenic Index (AI) levels, with p-values less than 0.05, indicating statistical significance. In particular, females demonstrated higher BMI, lower ASCVD risk percentage, higher HDL cholesterol, lower triglycerides, and lower AI compared to males. However, no significant differences were observed between males and females in terms of age, total cholesterol, LDL cholesterol, non-HDL cholesterol, TC/HDL ratio, glucose, and creatinine levels, with p-values greater than 0.05. Here are the detailed statistics for each parameter, with mean and standard deviation provided for both genders (Table 1).

In Table (2) significant differences are found across various cardiovascular risk parameters when stratified by TC/HDL ratio categories. Significant differences were observed in age, total cholesterol (TC), HDL cholesterol, triglycerides (TRG), LDL cholesterol, non-HDL cholesterol, creatinine (CRI), and Atherogenic Index (AI) across different TC/HDL ratio categories, all showing a p-value of 0.001, indicating high statistical significance.

Table (3) analyzes the impact of coronary index (CRI) risk on various cardiovascular and metabolic parameters, finding significant variations in HDL cholesterol, triglycerides (TRG), TC/HDL ratio, creatinine (CRI), and Atherogenic Index (AI), with p-values of 0.001, indicating high statistical significance.

Table 1. Sociodemographic and laboratory parameters

Demographic and Para -clinical characteristics	Male (n=38) Mean±Std.D	Female (n=47) Mean±Std.D	P-value
Age (yr)	58.1± 9.8	59.1±10.4	0.667
BMI (kg/m2)	30.1±4.5	33.7 ± 6.8	0.017*
ASCVD%	21.9 ± 12.8	16.1±13.6	0.006**
TC	155.8 ± 43.4	172.9±41.5	0.067
HDL	30.7.9±8.9	43.1±12.7	0.001*
TRG	173.8 ± 103.8	165.4 ±80.2	0.043*
LDL	87.8.±37.7	102.9±62.3	0.678
Non-HDL	124.9±44.9	132.1±48	0.191
TC/HDL	5.5±2.3	4.4±2	0.02*
GLU	135.3±61.2	139.2±64.5	0.780
CRI	6.1±4.5	4.3±3.5	0.043*
AI	0.68 ±0.32	0.54±0.29	0.04*
*The p-value ≤ 0.05 is statistically significant ** The p-value ≤ 0.01 is highly significant			

Table 2. Mean comparison of assessed parameters depending on TC/HDL ratio subgroups

Parameters	TC/HDL ratio	Mean±Std.D	P-value
Age (yr)	less than 3.5	60.3±10.9	0.045*
	3.5-5	61.4±10.3	
	more than 5	55.4±8.5	
BMI (kg/m2)	less than 3.5	32.9±7.6	0.519
	3.5-5	31.1±5.7	
	more than 5	32.4±4.9	
ASCVD%	less than 3.5	14.5±14.9	0.634
	3.5-5	18.3±18.2	
	more than 5	17.7±13.6	
TC (mg/dl)	less than 3.5	142.5±26	0.001**
	3.5-5	148. ±39.6	
	more than 5	195.3±38.4	
HDL (mg/dl)	less than 3.5	49.8±11.2	0.001**
	3.5-5	35.8±9.8	
	more than 5	29.6±7.5	
TRG (mg/dl)	less than 3.5	127.9±56.7	0.001**
	3.5-5	51.7± 10.3	
	more than 5	229.4±102.4	
LDL(mg/dl)	less than 3.5	67.3±20.4	0.001**
	3.5-5	86.4±28.9	
	more than 5	125.4±68	
Non-HDL	less than 3.5	92.5±20	0.001**
	3.5-5	112.1±30.8	
	more than 5	169.1±39.9	
TC/HDL	less than 3.5	2.9±0.39	0.001**
	3.5-5	4.2±0.43	
	more than 5	7.0±1.9	
GLU (mg/dl)	less than 3.5	135.3±70.4	0.795
	3.5-5	132.2±40.0	
	more than 5	142.9±70.9	
	Total	137.5±62.7	
CRI	less than 3.5	2.7±1.3	0.001**
	3.5-5	3.8±1.8	
	more than 5	7.8±4.9	
AI	less than 3.5	0.39±0.2	0.001**
	3.5-5	0.54±0.22	
	more than 5	0.8±.0.32	

Table 3. Mean comparison of assessed parameters depending on CRI risk subgroups:

Parameters	CRI risk	Mean	P-value
Age	less than 2	58±12.5	0.619
	2-4	60.2±11.1	
	more than 4	57.9 ±8.5	
BMI	less than 2	34.3±7.3	0.253
	2-4	31.2±7.3	
	more than 4	31.9±	
ASCVD	less than 2	14.3±	0.623
	2-4	18.9±	
	more than 4	16.6±12.8	
TC	less than 2	162.3±41.2	0.435
	2-4	157.8±45	
	more than 4	171.2±42.4	
HDL	less than 2	47.8±15.3	0.001**
	2-4	42.8±10.9	
	more than 4	30.3±7.5	
TRG	less than 2	93.9±42.1	0.001**
	2-4	120.2±34.1	
	more than 4	229.3±90.1	
LDL	less than 2	115.9±94.2	0.257
	2-4	90.6±38.7	
	more than 4	92.3±37.1	
Non-HDL	less than 2	117.1±50.4	0.067
	2-4	117.6±49.3	
	more than 4	140.7±40.9	
TC/HDL	less than 2	4.3±3.3	0.001**
	2-4	3.8±0.97	
	more than 4	5.9±1.8	
GLU	less than 2	122.3±	0.556
	2-4	139 ±1.8	
	more than 4	142.3±57.9	
CRI	less than 2	1.4±0.61	0.001**
	2-4	2.8±	
	more than 4	7.9±3.94	
AI	less than 2	0.17±0.11	0.001**
	2-4	0.44±0.09	
	more than 4	0.86±0.18	

Table (4) shows a concise summary of the Pearson correlation findings from the study, focusing on significant relationships between various cardiovascular and metabolic parameters.

Table 4. Pearson Correlations among Assessed Parameters

	Pearson Correlations r-value	P-value
Age * ASCVD	0.649**	0.001
Age * TC	-0.405**	0.001
Age * non-HDL	-0.352**	0.001
Age * Glu	0.300**	0.005
ASCVD * HDL	-0.260*	0.016
ASCVD * Glu	0.281**	0.009
TC * TRG	0.408**	0.001
TC * LDL	0.598**	0.001
TC * non-HDL	0.940**	0.001
TC * TC/HDL	0.511**	0.001
TC * CRI	0.247*	.023
HDL * TRG	-0.34**	0.001
HDL * TC/HDL	-0.668**	0.001
HDL * Glu	-0.246*	.023
HDL * CRI	-0.537**	0.001
HDL * AI	-0.594**	0.001
TRG * Non-HDL	0.473**	0.001
TRG * TC/HDL	0.537**	0.001
TRG * CRI	0.869**	0.001
TRG * AI	0.818**	0.001
LDL * Non-HDL	0.685**	0.001
LDL * TC/HDL	0.562**	0.001
Non-HDL * TC/HDL	0.705**	0.001
Non-HDL * CRI	0.354**	0.001
Non-HDL * AI	0.317**	0.003
TC/HDL * CRI	0.555**	0.001
TC/HDL * AI	0.463**	0.001
CRI * AI	0.924**	0.001
***. Correlation is significant at the 0.01 level (2-tailed).*		
**. Correlation is significant at the 0.05 level (2-tailed).*		

Table 5. According to the CRI highly risk group in Figure (A)

Parameters	AUC	Sensitivity	Specificity	Cutoff value	Asymptotic significance
TRG	0.924	0.857	0.884	154.5000	0.001
TC/HDL	0.839	0.857	0.767	4.2000	0.001
CRI	1.000	1.000	1.000	4.0144	0.001
AI	1.000	1.000	1.000	.6027	0.001
Null hypothesis: true area = 0.5					

Table 6. According to the TC/HDL highly high-risk group in figure (c)

Parameters	AUC	Sensitivity	Specificity	Cutoff value	Asymptotic significance
TC	0.847	0.882	0.706	159.5000	0.001
TRG	0.814	0.706	0.804	173.0000	0.001
LDL	0.814	0.765	0.784	93.0000	0.001
Non-HDL	0.929	0.882	0.863	130.0000	0.001
TC/HDL	1.000	1.000	1.000	5.0000	0.001
CRI	0.821	0.853	0.725	3.7465	0.001
AI	.821	0.853	0.725	.5736	0.001
Null hypothesis: true area = 0.5					

For the CRI moderate risk group in Figure (**1**), the parameter HDL showed an area under the curve (AUC) of 0.704, with a sensitivity of 0.852 and a specificity of 0.5. The cutoff value was 32.5, with an asymptotic significance of 0.003.

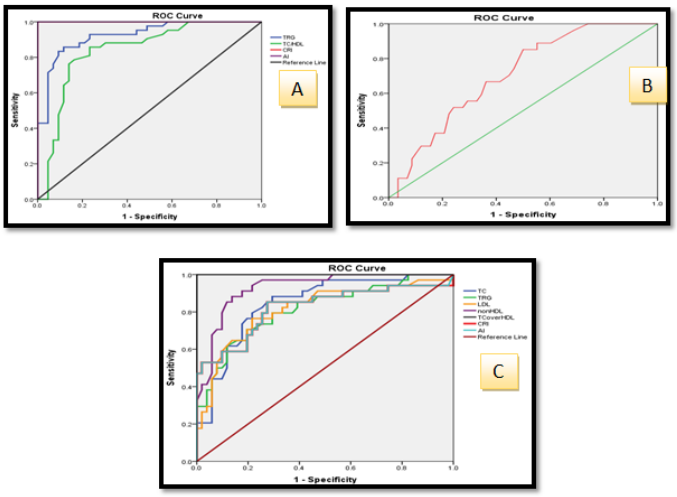

Figure 1. Receiver operating characteristic (ROC) curve, A- According to AI highly risk group; B- According to AI medium risk group; C- According to CRI highly risk group

DISCUSSION

The study presents a comprehensive analysis of the biochemical and demographic parameters in a cohort of type 2 diabetes mellitus (T2DM) patients, highlighting significant gender differences in cardiovascular risk factors. Females exhibited a significantly higher BMI compared to males (33.7 ± 6.8 vs. 30.1 ± 4.5, p=0.017), which aligns with previous studies indicating that women with T2DM often have higher BMI, increasing insulin resistance and cardiovascular risk (10). This higher BMI in females suggests a greater need for targeted weight management interventions to mitigate associated risks. On the other hand, males had a higher ASCVD risk percentage (21.9 ± 12.8 vs. 16.1 ± 13.6, p=0.006), possibly due to higher levels of atherogenic lipids and CRI, emphasizing the need for more aggressive cardiovascular risk management in male patients [12].

Interestingly, females had higher HDL cholesterol levels than males (43.1 ± 12.7 vs. 30.7 ± 8.9, p=0.001), which is known to protect against

cardiovascular diseases. This protective lipid profile could explain the lower ASCVD risk percentage in females despite their higher BMI [9]. However, males showed higher levels of triglycerides (173.8 ± 103.8 vs. 165.4 ± 80.2, p=0.043) and Atherogenic Index (AI) (0.68 ± 0.32 vs. 0.54 ± 0.29, p=0.04), indicating a higher risk of atherogenesis and cardiovascular events [12].

The study also delves into the relationship between the TC/HDL ratio and cardiovascular risk. Participants with higher TC/HDL ratios had significantly higher total cholesterol (TC) and lower HDL levels, indicating increased cardiovascular risk. This finding is consistent with studies linking higher TC/HDL ratios with greater atherosclerotic burden and cardiovascular events [11]. The higher TC/HDL ratios were also associated with elevated triglycerides and non-HDL cholesterol, further supporting the increased atherogenic risk in these individuals. Another significant aspect of the study is the impact of the coronary index (CRI) risk on various cardiovascular parameters. Higher CRI risk was associated with lower HDL and higher triglycerides, indicating poor lipid control and increased cardiovascular risk. This correlation is well-documented, where low HDL and high triglycerides are critical components of dyslipidemia in T2DM [9].

Pearson correlations among assessed parameters highlighted significant relationships, particularly the strong positive correlation between age and ASCVD (r=0.649, p=0.001). This suggests that older age is associated with higher ASCVD risk, underscoring age as a non-modifiable risk factor for cardiovascular diseases [8]. Additionally, strong correlations between total cholesterol and atherogenic lipids, such as triglycerides (r=0.408, p=0.001), LDL (r=0.598, p=0.001), and non-HDL (r=0.940, p=0.001), emphasize the interconnectedness of these lipid parameters in contributing to cardiovascular risk [9].

CONCLUSIONS

The study's findings underscore significant gender differences in cardiovascular risk factors among T2DM patients. Despite higher BMI, females had protective lipid profiles with higher HDL levels, while males exhibited higher ASCVD risk percentages and inflammatory markers. These results highlight the need for gender-specific approaches in managing cardiovascular risk in diabetic patients. The robust correlations and predictive power of lipid and inflammatory markers further validate their critical role in cardiovascular risk assessment and management. Future research and clinical practice should continue exploring tailored interventions addressing these gender-specific risk profiles to optimize cardiovascular outcomes for all T2DM patients.

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