# Relationship between Glycemic Control and Cardio-Metabolic Risk Factors among Patients with Type 2 Diabetes Mellitus in Sana'a City-Yemen Relationship between Glycemic Control and Cardio-Metabolic Risk Factors among Patients with Type 2 Diabetes Mellitus in Sana'a City-Yemen

Faisal Ali, Lotfy Maktary, Lotfy Maktary, Nora Al-khaldid

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Faisal Ali[1]; Lotfy Maktary[2]; Lotfy Maktary[2]; Nora Al-khaldid[2]

[1]Sanaa University Sana'a YE
[2]Sanaa University Faculty of Medicine Sana'a YE

**Corresponding Author:**
Faisal Ali
Sanaa University
Sana'a-Yemen
Sana'a
YE

## *Abstract*

**Background:** Impaired lipid metabolism in diabetic patients can lead to cardiometabolic complications.. So far, no data regarding such association are being available among Yemeni diabetic patients.

**Objective:** This laboratory based cross-sectional study was conducted in National Center of Public Health Laboratories, ,Yemen from January 2022 to March 2022 over a period of 3 months to determine the correlation of glycemic control and lipid profile in patients with type 2 diabetes mellitus (T2 DM).

**Methods:** A sample of 145 T2DM patients of both sexes recruited for this study. Anthropometric measures, fasting blood glucose (FBS) and fasting serum lipids (total cholesterol, TC; triglycerides, TG, low-density lipoprotein cholesterol, LDL-C and high-density lipoprotein cholesterol, HDL-C) measured. Data analyzed via descriptive statistics, Pearson's correlation and Multiple Logistic Regression test.

**Results:** The age of respondents ranged from 20 to 80 years with the mean age of 54.35±8.02 years. Among the patients male were 82 (56.6%) and female were 63 (43.4%). 105 (72.4%) were at no risk while 40 (27.6%) were at risk of having diabetic dyslipidemia. Mean body mass index (BMI), FBS and HbA1c were 25.02±5.22 kg/m2, 1.37±.489 and 1.67±0.474 respectively. Significant positive correlation of HbA1c and FBS with BMI, TC, TG, LDL-C and negative correlation with HDL-C was found. Significantly, higher TC, TG, LDL-C and HDL-C were found in poor glycemic control (HbA1c ? 6.0) group than good glycemic control (HbA1c < 6.0) group.

**Conclusions:** The findings of this study showed that, higher levels of glycemic parameters are significantly associated with dyslipidemia. These findings also indicate that HbA1c can be utilized for screening of high risk diabetic patients for early diagnosis of dyslipidemia and timely intervention with lipid lowering drugs. Clinical Trial: non

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# Relationship between Glycemic Control and Cardio-Metabolic Risk Factors among Patients with Type 2 Diabetes Mellitus in Sana'a City-Yemen

Faisal Ali[a,b,c,d,*], Lutfi Al_Maqtari[e], Gamil Othman[c], Mariam shakeeb[d], Nora Al-khaldi[d]

[a] Clinical Nutrition and Dietetics Department, University Hospital, Faculty of Medicine and Health Sciences, Sana'a University, Sana'a, Yemen.

[b]Adjunct Research Advisor in Nan Yang Academy of Sciences (NAS), Singapore.

[c] Department of Clinical Pharmacy and Pharmacy Practice, University of Science and Technology, Sana'a, Yemen.

[d] Clinical Biochemistry Department, Faculty of Medicine, Al-Hikma University, Sana'a,-Yemen.

[e]Department of Haematology, Faculty of Medicine and Health Sciences, Sana'a University, Sana'a, Yemen.

*Corresponding author: Clinical Associate Professor. Director of Diabesity & MNT Program.

sshrmany@yahoo.co.uk



## Abstract

**Background**: Impaired lipid metabolism in diabetic patients can lead to cardiometabolic complications.. So far, no data regarding such association are being available among Yemeni diabetic patients.

**Objective:** This laboratory based cross-sectional study was conducted in National Center of Public

Health Laboratories, ,Yemen from January 2022 to March 2022 over a period of 3 months to determine the correlation of glycemic control and lipid profile in patients with type 2 diabetes mellitus (T2 DM).

**Methods:** A sample of 145 T2DM patients of both sexes recruited for this study. Anthropometric measures, fasting blood glucose (FBS) and fasting serum lipids (total cholesterol, TC; triglycerides, TG, low-density lipoprotein cholesterol, LDL-C and high-density lipoprotein cholesterol, HDL-C) measured. Data analyzed via descriptive statistics, Pearson's correlation and Multiple Logistic Regression test.

**Results**: The age of respondents ranged from 20 to 80 years with the mean age of 54.35±8.02 years. Among the patients male were 82 (56.6%) and female were 63 (43.4%). 105 (72.4%) were at no risk while 40 (27.6%) were at risk of having diabetic dyslipidemia. Mean body mass index (BMI), FBS and HbA1c were 25.02±5.22 kg/m2, 1.37±.489 and 1.67±0.474 respectively. Significant positive correlation of HbA1c and FBS with BMI, TC, TG, LDL-C and negative correlation with HDL-C was found. Significantly, higher TC, TG, LDL-C and HDL-C were found in poor glycemic control (HbA1c ≥ 6.0) group than good glycemic control (HbA1c < 6.0) group.

**Conclusion:** The findings of this study showed that, higher levels of glycemic parameters are significantly associated with dyslipidemia. These findings also indicate that HbA1c can be utilized for screening of high risk diabetic patients for early diagnosis of dyslipidemia and timely intervention with lipid lowering drugs.

**Keywords:** Type2 DM, Lipid profile, Dyslipidemia, Cardiometabolic diseases, glycosylated hemoglobin.

## Introduction

With the increase of diabesity, there has been a parallel escalation in the incidence and prevalence of cardiometabolic complications [1, 2]. Type 2 Diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by hyperglycemia due to increased insulin resistance or impaired insulin secretio [ 3,4 ] affecting about 347 million people worldwide .More than 80% of death from diabetes occur in low and middle-income countries. About 50% of people with diabetes die of cardiovascular diseases including stroke [ 5,6 ].The chronic hyperglycemia of T2DM is associated with long-term

damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels [ 7 ].. Elevated fasting and postprandial triglycerides, low HDL-cholesterol, elevated LDL-cholesterol and the predominance of small dense LDL particles characterize diabetic Dyslipidemia. These lipid changes represent the major link between diabetes and the increased cardiovascular risk of diabetic patients [ 8 ]. In addition to genetic disorder, there are environmental factors such as diet, exercise and smoking habits play important role in manifestation and progression of dyslipidemia.. [ 9 ]..The dyslipidemia is a major risk factor for coronary heart disease (CHD) [ 10 ].Patients with T2DM have increased risk of cardiovascular disease associated with atherogenic dyslipidemia. Coronary artery disease, especially myocardial infraction is the leading cause of morbidity and mortality worldwide because of disturbance in lipoproteins [11,9]..Persistent hyperglycemia causes glycosylation of all proteins, especially collagen cross-linking and matrix proteins of arterial wall. This eventually causes endothelial cell dysfunction, contributing further to atherosclerosis [ 12]. Previous studies in people with (T2DM) have found an increased association between vascular diseases and high TG and low HDL-C - [ 13 ]. Although many studies have confirmed the relationship between glycemic control and lipid profiles variables in patients with T2DM, the result are quite inconsistent [ 14 ]..Previous studies have shown that good control of glycemic levels and lipid profiles variables can effectively prevent complications such as cardiovascular disease, diabetic nephropathy and diabetic retinopathy [ 15 ].

Glycated hemoglobin or glycosylated hemoglobin (HbA1c) is a form of hemoglobin formed by the condensation of glucose with the N-terminal Valine residue of each B- chain of HbA1c to formed an unstable Schiff-base, is measured primary to identify the average plasma glucose concentration over prolonged periods of time (2-3 months). Normal level of glucose produce a normal amount of glycosylated hemoglobin. HbA1c serves as marker for average blood glucose levels prior to measurement [ 15, 13].

HbA1c predicts the risk for development of microvascular and macrovascular complication ion

diabetic patients. The World Health Organization (WHO), and American Diabetic Association guideline introduced the use of HbA1c for diagnosis and assessment of glycemic control of DM [16, 17 ]. Numerous studies were conducted to establish positive correlation between HbA1c and other glycemic parameters. But very few studies have been conducted so far, not only our community but also in the world, to explore the interplay between HbA1c biomarker along with serum lipid profiling alterations in type 2 diabetic patients and cardiovascular disease. Findings of those studies conducted previously were not studied this relationship clearly. Therefore, there is a need to investigate further to discover the relationship between glycemic control, HbA1c marker, and lipid profiles abnormality as independent cardiovascular disease risk factors. Is strong impact of long-term glycemic control on lipid profile parameters could have been established HbA1c as dual biomarker? This will help clinicians to assess glycemic and lipid profiles status and to predict long-term complications by measuring HbA1c alone in type 2 diabetes subjects. Therefore, this study was conducted to see the correlation between glycemic control and serum lipid profile in type 2 diabetic patients and to evaluate the utility of HbA1c as an indirect biomarker of cardiometabolic diseases.

## Methods

### Study location:

The study was conducted at National Center of Public Health Laboratories in Sana'a City, Yemen, which is considered an main reference laboratory diagnostic services in the field of public health to all citizens in Yemen by scientific methods. It was conducted from January 2022 to March 2022.

### Study design and period:

An laboratory-based, quantitative cross-sectional study was conducted between January 2022 and March2022. The Laboratories had about 207 patients per month with diabetes mellitus on routine follow-up in biochemistry department. From these, 200 cases were type-2 diabetes mellitus and the rest 7 cases were type-1 diabetes mellitus. Those patients had regular follow-up at least once per

month.

**Study Participants and Sample Size**

The targeted population was type-2 DM patients who came for routine follow up and willing to participate in the study during the study period. Of a total population of 622 patients, a sample size of 145 T2DM patients was needed. The required sample size was calculated based on a margin of error of 5%, a 95% confidence level, and an 80% response distribution. Raosoft® [ 18]. was used to perform this calculation. 145 T2DM patients were recruited based on convenience sampling.

**Eligibility:**

**Inclusion Criteria:**

All type-2 diabetes mellitus patients who came for routine follow up at biochemistry department during the study period at National Center of Public Health Laboratories.

**Exclusion Criteria:**

Patients with hyperlipidemia due to other causes such as a history of nephrotic syndrome, thyroid dysfunction, heart disease, liver disease,patient taking lipid lowering drugs, T1DM, pregnancy, children and age less than 20.

**Definition of Variables**

Obesity for both sexes was defined as BMI of ≥ 25 kg/$m^2$ . T2DM was defined as FPG ≥ 7.0 mmol/L or 2hPG ≥ 11.1 mmol/L. [19]. Cut-off values for serum lipid profiles were: high T-Chol ≥ 5.0 mmol/L, high Tg ≥ 1.7 mmol/L, high LDL-C ≥ 3.4 mmol/L, and low HDL-C <1.04 mmol/L (for men) and <1.3 mmol/L (for women) [20]. Using the above-mentioned cut points of Tg and HDL-C. .

**Ethical Approval:**

Ethical clearance was obtained from Ethical Review Committee of Al-Hikma University and the

Department of Clinical Biochemistry at National Center of Public Health Laboratories. Verbal agreement was first taken after the data collectors explained the objectives and nature of the study to the participants. Blood samples were drawn by trained health professional. researchers did physical measurements for each diabetic patient. Study participants did not suffer major discomfort and there were no need of extra blood sample other than that was taken for diagnostic purpose. The amount of blood taken from each patient throughout the study period was 5ml that did not affect their health. . Researchers under health professionals supervision following the standard good clinical practice carried out the whole procedure. Research participation, confidentiality and consent were followed as per Helsinki declaration which local adaptation to allow both verbal and written instructions.

**Sample Procedure:**

The sample was selected by convenient sampling from type-2 DM patients who came for routine follow up and willing to participate in the study during the study period.

**Data Collection and Measurement Procedure:**

Data on demographic and behavioral characteristics were collected through a face-to-face interview by using a structured questionnaire (sex, age, diabetic duration, drugs for diabetes, physical activity, chronic disease, and restricted carbohydrate diet of each patient).

**Physical measurements**

Physical measurements of height and weight needed to calculate body mass index (BMI). Height and weight was measured after the participants had removed their shoes, heavy clothing, and belts.

Body mass index (BMI) was calculated as weight (kg)/height2(m).

**Biochemical measurements**

Five milliliters (5ml) of venous blood was collected from each study participants by trained health professional after overnight fasting. Then, the blood specimen was allowed to stay for 20-30 minutes for clot formation. The specimen was then centrifuged at 3000 revolutions per minute (rpm) and the serum was separated from the whole blood. Glucose and lipid profile Laboratory tests included Triglycerides and cholesterol, Low Density lipid-C, High density level were measured by automated clinical chemistry analyzer ( Cobas 6000 analyzer) according to manufacturer's instructions.

**Quality Assurance:**

The data quality assessment was started with socio-demographic data collection and continued throughout blood sample collection and statistical analysis. The blood sample was taken under aseptic techniques with standard operational procedure. The machine for biochemical analysis was checked for its consistency. Results were checked for completeness on daily basis by the immediate supervision.

**Data Processing and Analysis:**

The collected data were analyzed using SPSS software version 21 (IBM, USA). Descriptive statistics such as means, standard deviation, frequencies, and percentages was used to present socio-demographic characteristics. Pearson's correlations were used to test the correlation of glycosylated hemoglobin (HbA1c) with BMI, FBS and lipid profiles. Unpaired t test was performed to compare between dependent and independent variables. Odds ratio (OR) was computed by using multiple

logistic regression test to measure the strength of association between all risk factors ( independent variables) and outcomes ( dependent variables). P-value < 0.05 at 95% confidence level was considered statistically significant.

## Results

### Socio Demographic Characteristics of Study Patient's:-

The characteristics of the subjects were summarized in Tables 1, 2 &3. Table No. (1) shows that the sample consisted of two age groups, Majority of the patients incorporated in this study belongs to age group 40-80-years (80.6%), followed by 19.3% in age group 20-40 years. Among the patients' male were 82 (56.6%) and female were 63 (43.4%) in close proportions. It is found that the mean value is a median value between (1, 2) as it was equivalent to 1.43 and with a standard deviation of 0.497, which indicates homogeneity in the distribution of the sample according to gender. In addition, Majority of the patients incorporated in this study belongs to underweight 52 (35.9%), followed by (31.7.%) in obese group based on the mathematical calculation of BMI of patients.

Also, the sample consisted in terms of healthy diet to patients who are fully committed to the diet and they were at 22.1% and those who are committed sometimes and they were by 26.2% of the sample but the non-adherents to the diet were 51.7%. In terms of physical activity, those who exercised for 30 minutes per day were the most with 47.6% followed by those who did not engage in physical activity at a rate of 29.7%.

**Table (1) – Socio Demographic characteristics of study patient's (n = 145).**

| Variable | Label | N | % | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Age | 20 - 40 year | 28 | 19.3 | 1.81 | 0.396 |
| | 41 - 80 year | 117 | 80.7 | | |
| Sex | Male | 82 | 56.6 | 1.43 | 0.497 |
| | Female | 63 | 43.4 | | |
| BMI | Healthy weight | 10 | 6.9 | 2.82 | 0.962 |
| | Underweight | 52 | 35.9 | | |
| | Overweight | 37 | 25.5 | | |
| | Obese | 46 | 31.7 | | |

| | | | | | |
|---|---|---|---|---|---|
| Healthy Diet | Always Restricted | 32 | 22.1 | 1.38 | 0.809 |
| | Sometime Restricted | 38 | 26.2 | | |
| | Not Restricted | 75 | 51.7 | | |
| Physical activity | Active > 60 min / day | 5 | 3.4 | 2.03 | 0.794 |
| | Active 60 min / day | 28 | 19.3 | | |
| | Active 30 min / day | 69 | 47.6 | | |
| | Sedentary patient | 43 | 29.7 | | |

Data expressed as Mean ± Std.Deviation; std , Standard; n ,Frequency; %, Percentage

**Clinical Characteristics Of Study Patient's**

Table No. (2) has shown that patients who suffer from the disease for more than a year, were the majority 80% followed by patients who suffer from diabetes less than one year were 13.8%, and finally the patients of the year with 6.2%. In terms of taking medicines, they fall into two categories: a category that takes medicines, at a rate of 76.6%, and a category that does not take medicines, at a rate of 23.4%, with an average of 0.77 and a standard deviation of 0.425. Also in terms of suffering from chronic diseases, there were 128 patients without chronic diseases, with a rate of 88.3%, and 17 subjects, with a rate of 11.7%, suffering from chronic diseases.

| Variable | Label | N | % | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Diabetes duration | One year | 9 | 6.2 | 2.21 | 0.756 |
| | > than one year | 116 | 80.0 | | |
| | < One year | 20 | 13.8 | | |
| Drugs use | Yes | 111 | 76.6 | 0.77 | 0.425 |
| | No | 34 | 23.4 | | |
| Chronic disease | No | 128 | 88.3 | 0.12 | 0.323 |
| | Yes | 17 | 11.7 | | |

**Table (2) – Clinical characteristics of study patient's (n = 145).**

Data expressed as Mean ± Std.Deviation; std, Standard; n, Frequency; %, Percentage.

**Characteristics Analysis Of Blood Glucose, Lipid Profile In Typ2 DM Patients**

Table No. (3) has shown the biochemical parameters of blood glucose, glycated hemoglobin (HbA1c) , lipid profile and to evaluate the utility of LDL/HDL ratio as an independent marker of

dyslipidemia and CVD risk.. The proportion of patients with normal blood sugar was higher 88% compared with those with abnormal blood sugar 57%. In contrast, the proportion of type2DM with poor glycemic control was higher 66.9% than those with good glycemic control 33% based on HbA1C findings. It was also observed that the Table 3 shows that the metabolic control percentage of TC, TG, HDL-C, and LDL-C for all T2D patients was 57.2%, 71.7%, 66.9%, and 97.2% respectively. According to the results of LDL/HDL ratio its noted that the majority of type2 DM was at no diabetic dyslipidemia and CVD risk 72.4% compared with those at high risk of getting dyslipidemia and thus CVD.



**Table (3). Characteristics analysis of blood glucose, lipid profile in Typ2 DM patients (n=145).**

| Variable | Label | N | % | Mean | Std. Deviation |
|---|---|---|---|---|---|
| FBS | 3.5 - 6.4 mmol/l | 88 | 60.68 | 1.37 | 0.4885 |
| | > 6.5 mmol/l | 57 | 39.31 | | |
| HbA1c | 4.8-6% | 48 | 33.1 | 1.67 | 0.474 |
| | >6% | 97 | 66.9 | | |

| | | | | | |
|---|---|---|---|---|---|
| TC | Less than 200 | 83 | 57.2 | 1.4276 | 0.48324 |
| | More than 200 | 62 | 42.8 | | |
| TG | Less than 200 | 104 | 71.7 | 1.2828 | 0.43099 |
| | More than 200 | 41 | 28.3 | | |
| LDL | 50-150mg/dl | 97 | 66.9 | 1.3310 | 0.47222 |
| | >150mg/dl | 48 | 33.1 | | |
| HDL | 35 - 65 mg/dl | 141 | 97.2 | 1.0241 | 0.14827 |
| | > 65 mg/dl | 4 | 2.8 | | |
| Risk Factor | 0.0 - 3.3 | 105 | 72.4 | 1.2759 | 0.45086 |
| | > 3.3 | 40 | 27.6 | | |

Data expressed as Mean ± Std.Deviation; std, Standard; n, Frequency; %, Percentage

**Correlation Of Glycosylated Hemoglobin (Hba1c) With BMI, FBS And Lipid Profiles.**

To assess the impact of HbA1c with parameters of serum lipid profile values in type 2 diabetic subjects and discover the relationship between glycemic control and lipid profile parameters. Pearson's correlation test was done to find out correlation of glycosylated Hemoglobin (HbA1c) with BMI, FBS and lipid profiles. Significant .positive correlation of HbA1c was found with BMI, FBS, TC, TG, LDL-C, (r=0.237& p= 0.004, r=0.506 & P=001, r=0.415 & p 0.001, r=0.202& p= 0.014, r= 0.191& p 0.021) respectively and negative correlation with HLD-C ( r=.-0.274 , & p =0.001)

Table (4). Correlation of glycosylated Hemoglobin (HbA1c) with BMI, FBS and lipid profiles.

| Variables | R | P. Value | Result |
|---|---|---|---|
| BMI | 0.237 | 0.004 | Sig |

| | | | |
|---|---|---|---|
| FBS | 0.506 | 0.001 | Sig |
| TC | 0.415 | 0.000 | Sig |
| TG | 0.204 | 0.014 | Sig |
| LDL | 0.191 | 0.021 | Sig |
| HDL | - 0.274 | 0.001 | Sig |

**Comparison Of Lipid Profiles Between Good And Poor Glycemic Control**

Unpaired t test was done to compare the lipid profiles between good glycemic control and poor glycemic control. TC, TG and LDL-C were found significantly higher in poor glycemic control and surprisingly HDL-C was also significantly higher in poor glycemic control .

**Table (5). Comparison of lipid profiles between good and poor glycemic control**

| Variables | Sex | N | Mean | Std. Deviation | T | p. value | Result |
|---|---|---|---|---|---|---|---|
| TC | Male | 82 | 1.6585 | .47712 | 0.097 | 0.923 | Non sig |
| | female | 63 | 1.6508 | .48055 | | | |
| TG | Male | 82 | 1.4390 | .49932 | 0.700 | 0.485 | Non sig |
| | female | 63 | 1.3810 | .48952 | | | |
| HDL | Male | 82 | 1.1585 | .36749 | -0.256 | 0.798 | Non sig |
| | female | 63 | 1.1746 | .38268 | | | |
| LDL | Male | 82 | 1.4512 | .50068 | -0.486 | 0.628 | Non sig |
| | female | 63 | 1.4921 | .50395 | | | |
| HbA1C | Male | 82 | 1.6463 | .48105 | -0.657 | 0.512 | Non sig |
| | femal | 63 | 1.698 | .46263 | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | e | | 4 | | | | |
| FBS | Male | 33 | 1.3939 | .49620 | 0.345 | 0.732 | Non sig |
| | female | 23 | 1.3478 | .48698 | | | |

Data expressed as Mean + Std.Deviation; std, Standard; n, Frequency; T, t-test

**The results of sugar and lipid parameters of Male and Female type 2 Diabetic patients**

Table No ( 6) .was shown slight difference between females and males in FBS, HbA1C and lipid profiles but did not show any statistical significance (p. value > 0.05).

**Table (6). The results of sugar and lipid parameters of Male and Female type 2 Diabetic patients**

| Variables | Sex | N | Mean | Std. Deviation | T | p. value | Result |
|---|---|---|---|---|---|---|---|
| TC | Male | 82 | 1.6585 | .47712 | 0.097 | 0.923 | Non sig |
| | female | 63 | 1.6508 | .48055 | | | |
| TG | Male | 82 | 1.4390 | .49932 | 0.700 | 0.485 | Non sig |
| | female | 63 | 1.3810 | .48952 | | | |
| HDL | Male | 82 | 1.1585 | .36749 | -0.256 | 0.798 | Non sig |
| | female | 63 | 1.1746 | .38268 | | | |
| LDL | Male | 82 | 1.4512 | .50068 | -0.486 | 0.628 | Non sig |
| | female | 63 | 1.4921 | .50395 | | | |
| HbA1C | Male | 82 | 1.6463 | .48105 | -0.657 | 0.512 | Non sig |
| | female | 63 | 1.6984 | .46263 | | | |
| FBS | Male | 33 | 1.3939 | .49620 | 0.345 | 0.732 | Non sig |
| | female | 23 | 1.3478 | .48698 | | | |

Odds ratio (OR) by using multiple logistic regression test was computed to measure the strength of association between all risk factors (i.e., independent variables) which includes sociodemographic, clinical and biochemical parameters with outcomes (i.e., dependent variables) which includes lipid profile adjusted for normal and high levels of blood concentration (See tables in appendix). Most of risk factors have shown no significant association with lipid profiles except for older age (41-80) showed a significant association with TC (OR): 2.250, $p < 0.05$); TG (OR: 4.08,$p < 0.005$); and

diabetic patients who didn't use any drugs showed strong significant association with TC OR: 2.4, $p < 0.05$); LDL (OR: 2.59,$p < 0.017$).

**Discussion**

To the best of our knowledge, the present study is the first study in Yemen and among the few studies of a west Asian population attempting to investigate the correlation between serum lipids (T-Chol, Tg, LDL-C, and HDL-C) and degrees of glycemic control. Furthermore, this research revealed the preventive impact of good T2DM management against diabetic dyslipidemia development. We found that early detection and treatment of hyperlipidemia in T2DM can minimize the risk for atherogenic cardiovascular disorder. . In this current study, it was observed that the mean age was 1.81 ± 0.396 with range from 41 to 80 years. The majority of population were > 40 years. Probably aged populations were more prone to develop diabetes mellitus. Out of these 145 subjects 82 (56.6%) were males and 63 (43.4%) were females (Table-I). There were more males than females with T2DM in this study. The high proportion of males than females in this study may be due to the nature of emotional life stress and pressure that are more common in men than women in eastern population. These findings are consistent with Khan study, showed that the mean age was 58.69±10.21 years, males were 51.7%, and females were 49.3% [21].. Mean BMI of the respondents was 2.82 + 0.962 with a Range of 18.5-24.9 kg/m 2. Most of the diabetic patients (35.9%) in this study was in the BMI range of ≤18.5 $kg/m^2$ .Western pacific region of world health organization (WHO) states BMI >23 $kg/m^2$ in Asian population is associated with adverse metabolic outcomes. [22].

High prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-C and low HDL-C was found in type 2 diabetics in this study which are well known risk factors for cardiovascular diseases. Goldberg reported that the cause of dyslipidemia in type 2 diabetes mellitus might be that insulin is not working properly which affects the liver apolipoprotein production. [ 23 ].The apolipoprotein regulates the enzymatic activity of lipoprotein lipase (LPL) and Cholesterol ester transport protein. Insulin impacts the liver apolipoprotein production which regulates the enzymatic activity of lipoprotein lipase and Cholesterol ester transport protein. [ 23,24].

These could be the likely causes of dyslipidemia in diabetes mellitus as reported by Goldberg. The

mean values of FBS, TC, TG, were higher in males as compared to female type 2 diabetic patients, while. HbA1c, LDL-C, HDL-C were higher in female as compared to males. This observation is in conformity with a study conducted by [ 26 ].Gender wise evaluation of the data shows that there is no statistically significant difference in glycemic parameters as well as lipid profile between males and females. Statistically significant correlation was found between HbA1c and FBS. A significant correlation between glycemic parameters (HbA1c and FBS) and lipid profile parameters was found in this study. Strong direct correlation of HbA1c and FBS with TG, LDL, TC, and inverse correlation was found with HDL in both male and female. This correlation was statistically significant in both sexes except for HDL in female. Though HDL in female is also inversely correlated with glycemic parameters, it was not statistically significant. These Observations are in agreement with earlier studies [ 27, 28 ]. HbA1c predicts the risk for development of microvascular and macrovascular complications in diabetic patients.

The World Health Organization (WHO) and American Diabetic Association guidelines introduced the use of HbA1c for diagnosis and assessment of glycemic control of DM [ 29,30 ]. In the present study, diabetic patients were divided into 2 groups as per the HbA1c cut off value of 6.0%. The diabetic patients with HbA1c value ≥ 6.0% exhibited a significant increase in TC, LDL-C, TG, with significant decrease in HDL-C in comparison to patients with HbA1c value ≤6.0%..Statistically significant differences of mean values of lipid profile parameters between subjects of good glycemic control and poor glycemic control were found. This finding are also similar to the study done by [16,21].showed the impact of glycemic control on various lipid parameters in which severity of dyslipidemia increases in patients with higher HbA1c value.

As elevated HbA1c and dyslipidemia are independent risk factors of CVD, diabetic patients with elevated HbA1c and dyslipidemia can be considered as a very high risk group for CVD. Improving glycemic control can substantially reduce the risk of cardiovascular events in diabetics [ 31,32]. It has been estimated that reducing the HbA1c level by 0.2% could lower the mortality by 10% .[ 33]. The Diabetes complications and control trial (DCCT) established HbA1c as the gold standard of glycemic control. The level of HbA1c value <7.0% was said to be appropriate for reducing the risk of cardiovascular complications. Several studies have reported significant

correlations between HbA1c and lipid profiles and suggested the importance of glycemic control in normalizing dyslipidemia. The results of the present study suggest the importance of glycemic control in order to manage dyslipidemia and risk for cardiovascular disease. The correlation between HbA1c and BMI as well as lipid profile was statically significant, these finding was similar to finding made by [ 34 ]. In contrast the correlation between FBS and BMI and lipid profile has shown no significant correlation, this could be attributed to the participants' diet and level of physical activity. (2017) [24, 25].

**Conclusions**

Elevated total serum cholesterol, Triglyceride, LDL-C and low HDL-C were observed in type 2 diabetics with poor glycemic control compared to patients with good glycemic control. This indicates that HbA1c can be used as a potential biomarker for predicting dyslipidemia in type 2 diabetic patients in addition to glycemic control. So, HbA1c may be utilized for screening of risks of cardiovascular events of diabetic patients and also for timely intervention with lipid lowering drugs.

**Limitations of the Study**

The method of recruitment of the diabetic patients from one diagnostic center was the major limitation. Moreover, the sample size was lower than expected. As a result, the conclusion of study is not often generalized to all diabetic patients. More medical centers need to be involved in the future to better represent diabetic patients in the country. Lastly,, lack of more information on diet, medication, and comorbidities in patients with T2DM may also have an impact on the results. . However, a more detailed record of diet and level of physical activity would be useful. Despite these limitations, our study had provided valuable findings, which warrant for further investigation in the future.

**Clinical Implications**

Lipid abnormality monitoring and management in patients with T2DM is not critical issue in Yemen. T-Chol, Tg, HDL-C, and LDL-C are globally routine biomarkers available for investigating lipid abnormalities. However, as in many developing countries the charge of these tests are mostly high and the access to clinical laboratory measurements along with degree of health awareness is limited. A previous systematic review and meta-analysis of randomized controlled trials (RCTs) have obviously found that patients with T2DM benefit more from treatment with lipid lowering medications than non-diabetic patients [35]. Therefore, early screening and correction of lipid

disorders are highly recommended for the primary and secondary care prevention of T2DM. Up to date, there is no evidence-based criteria for screening lipid related diseases in most developing countries including Yemen, Despite cardiovascular complications is mainly related to lipid metabolism alterations and largely associated with the significant contributors directly or indirectly to the diabetes care system cost [36]. Much still has to be done. For example, studies, which unveil novel mechanisms implicated in cardiometabolic diseases, may open new therapeutic horizons. Altogether, controlling hyperglycemia condition via adherence to effective antidiabetic drugs, healthy diet and regular physical activity along with lipid particles frequent checkup is crucial to prevent cardio-metabolic complications in T2DM.

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**References**

1. Kuklina EV, Tong X, George MG, Bansil P. Epidemiology and prevention of stroke: a worldwide perspective. Expert Review of Neurotherapeutics. 2012;12(2):199–208. doi: 10.1586/ern.11.99.

2. Joseph Fomusi Ndisang and Sharad Rastogi Cardiometabolic Diseases and Related Complications: Current Status and Future Perspective. Biomed Res Int. 2013; 467682, 2013: 1-3. doi: 10.1155/2013/467682 .

3. DeFronzo, R. A. Pathogenesis of type 2 diabetes mellitus. The Medical clinics of North America. United States, 2004; 88(4):787–835, ix. doi: 10.1016/j.mcna.2004.04.013.

4. Yanling Wu, Yanping Ding, Yoshimasa Tanaka,[3]and Wen Zhang Risk Factors Contributing to Type 2 Diabetes and Recent Advances in the Treatment and Prevention..2014; 11(11): 1185–1200.. doi: 10.7150/ijms.10001

,

5. Balakumar, P., Maung -U, K. and Jagadeesh, G. (2016). Prevalence and prevention of cardiovascular disease and diabetes mellitus. Pharmacological research. Netherlands, 2016; 113: 600–609. doi:10.1016/j.phrs.2016.09.040.

6. Mooradian AD. Dyslipidemia in type 2 diabetes mellitus. Nature Clinical Practice Endocrinology and Metabolism. 2009; 31:50-159. doi: 10.1038/ncpendmet1066

7. Chan, J.C.; Malik, V.; Jia, W.; Kadowaki, T.; Yajnik, C.S.; Yoon, K.H.; Hu, F.B. Diabetes in Asia: Epidemiology, risk factors, and pathophysiology. JAMA 2009, 301, 2129–2140. doi: 10.1001/jama.2009.726..

8. Miller M, Stone NJ, Ballantyne C, et al. Triglycerides and cardiovascular disease: a scientific statement from the American Heart Association. Circulation. 2011; 123 (20):2292–333. 21502576

9. Wu, L.; Parhofer, K.G. Diabetic dyslipidemia. Metabolism 2014, 63, 1469–1479. 10. Krishna,P., Roopakala and KM. Prasanna KM Kumar.. Dyslipidemia in type 1 diabetes mellitus in the young. Int. J. Diab. Dev. Ctries, 2005, 25(4): 110-12. doi. 10.4103/0973-3930.27015.

11. Roberto, T., A.R. Dodesini, Lepore G. Lipid and Renal disease, J. Am. Soc.Nephrol.. 2006; 17:S145-7. doi: 10.1681/ASN.2005121320

12. Taskinen, M.R.; Borén, J. New insights into the pathophysiology of dyslipidemia in type 2 diabetes.Atherosclerosis. 2015; 239: 483–495. ;239(2):483-95. doi: 10.1016/j.atherosclerosis.2015.01.039. .

13. Lee, J.S.; Chang, P.Y.; Zhang, Y.; Kizer,J.R.; Best, L.G.; Howard, B.V.Triglyceride and HDL-C Dyslipidemia and Risks of Coronary Heart Disease and Ischemic Stroke by Glycemic Dysregulation Status: The Strong Heart Study. Diabetes Care. 2017,40:: (4) 529–537. doi: 10.2337/dc16-1958.

14. Laverdy, O.G.; Hueb, W.A.; Sprandel, M.C.; Kalil-Filho, R.; Maranhão, R.C. Eects of glycemic control upon serum lipids and lipid transfers to HDL in patients with type 2 diabetes mellitus: Novel findings in unesterified cholesterol status.Exp. Clin. Endocrinol. Diabetes. 2015. 123(4): 232–239.. doi: 10.1055/s-0034-1396863

15. Jaiswal, M.; Schinske, A.; Busui, R.P. Lipids and lipid management in diabetes. Best Pract Res Clin Endocrinol Metab. 2014, 28(3):325-38 doi: 10.1016/j.beem.2013.12.001

16. Ramona G. Relationship between glycosylated hemoglobin and lipid metabolism in patients with type 2 diabetes. Studia Universitatis. “Vasile Goldi”, Seria tiinele Vieii. 2011,;21(2)::

313-318.

17. Aryal, N.; Weatherall, M.; Bhatta, Y.K.D.; Mann, S. Lipid Profiles, Glycated Hemoglobin, and Diabetes in People Living at High Altitude in Nepal. Int. J. Environ. Res. Public Health. 2017, 14(9):1041...doi: 10.3390/ijerph14091041

18. Raosoft, Inc. Sample Size Calculator. [cited January 18, 2019]. http://www. raosoft.com/samplesize.html (Accessed June 12, 2022).

19. World Health Organization. Definition, Diagnosis and Classification of Diabetes Mellitus and Its Complications;Report of a WHO Consultation; World Health Organization: Geneva, Switzerland, 1999.

20. Guidelines Subcommittee. 1999 World Health Organization-International Society of Hypertension guidelinesfor the management of hypertension. J. Hypertens. 1999, 17, 151–183.

21. Khan HA. Clinical significance of HbA1c as a marker of circulating lipids in male and female type 2 diabetic patients. Acta Diabetol.. 2007;44(4):193=200. doi: 10.1007/s00592.

22. Bilen, O.; Kamal, A.; Virani, S.S. Lipoprotein abnormalities in South Asians and its association with cardiovascular disease: Current state and future directions. World J. Cardiol. 2016; 8 (3), 247–257.. doi: 10.4330/wjc.v8.i3.247

23. Goldberg I J. Lipoprotein lipase and lipolysis: central roles in lipoprotein metabolism and atherogenesis. J Lipid Res. 1996; 37:693-707. 8732771.

24. Yazici, D. and Sezer, H. Insulin Resistance, Obesity and Lipotoxicity.", Advances in experimental medicine and biology Adv Exp Med Biol..2017;960:277-304. DOI: 10.1007/978-3-319-48382-5_12

25. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Powe NR, Golden SH. Meta analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med. 2004; 27(12): 421- 431. 15381515.

26. Hamidreza Samimagham , Mariana Bargak , Mehran Ghasemzadeh , Mitra Kazemi Jahromi. The Association of Glycated Hemoglobin With Lipid Profile Indices in Type 2 Diabetic Patients. Acta Medica Iranica, 2020, 58, 8: 376-382. DOI10.18502/acta.v58i8.4587
.

27. Rosediani M, Azidah AK, Mafauzy M. Correlation between fasting plasma glucose, post prandial glucose and glycated haemoglobin and fructose amine. Med J Malaysia. 2006; 61:67–71. 16708736.

28. Ito C, Maeda R, Ishida S, Sasaki H, Harada H. Correlation among fasting plasma glucose, two hour plasma glucose levels in OGTT and HbA1c. Diabetes Res Clin Pract. 2000; 50(3):225-30.. doi: 10.1016/s0168-8227(00)00187-x

29. American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care 2013, 36, 1033–1046.

30. Balakumar, P., Maung -U, K. and Jagadeesh, G. Prevalence and prevention of cardiovascular disease and diabetes mellitus.", Pharmacological research. Netherlands, 2016. 113:. 600–609. doi: 10.1016/j.phrs.2016.09.040.

31. Sarkar S, Meshram, A. (2017). HbA1c and lipid profile levels in the known type 2 diabetic group in the rural region of Vidarbha, Maharashtra, India.J Evid Based Med Health,2017. 4: 1915-1920. doi: 10.18410/jebmh/2017/374.

32.

33. Samdani TS, Mitra P, Rahim MA. Relationship of glycated haemoglobin with lipid profile among patients with type 2 diabetes mellitus. Birdem Medical Journal, 2017. 7(1), 43-47. **doi:** https://doi.org/10.3329/birdem.v7i1.31271.

34. Khaw KT, Wareham N, Bingham S, Luben R,Welch A, Day N. Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European Prospective Investigation into Cancer in Norfolk. Ann Intern Med. 2004; 141,6:: 413-20. doi: 10.7326/0003-4819-141-6-200409210-00006

35. Ozder A. Lipid profile abnormalities seen in T2DM patients in primary healthcare in Turkey: a cross-sectional study. Lipids in health and disease, 2014 13(1), 183. doi: 10.1186/1476-511X-13-183.

36. Ren, X.; Chen, Z.A.; Zheng, S.; Han, T.; Li, Y.; Liu, W.; Hu, Y. Association between triglyceride to HDL-C ratio (TG/HDL-C) and insulin resistance in Chinese patients with newly diagnosed type 2 diabetes mellitus. PLoS ONE 2016, 11, e0154345. doi: 10.1371/journal.pone.0154345.

37. Safari S, Amini M, Aminorroaya A, Feizi A. Patterns of changes in serum lipid profiles in prediabetic subjects: results from a 16-year prospective cohort study among first-degree relatives of type 2 diabetic patients. Lipids Health Dis..2020;;19(1):193. doi: 10.1186/s12944-020-01371-

# Supplementary Files