THE RISK FACTORS ASSOCIATED WITH DIABETIC DYSLIPIDEMIA AND ANTHROPOMETRIC PARAMETERS LINKED WITH AND WITHOUT DYSLIPIDEMIA IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

Objective: To ascertain and identify risk determinants linked with and without dyslipidemia in type 2 diabetic patients.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Fauji Foundation Hospital and Military Hospital, Rawalpindi, Pakistan, from Jan 2018 to Jan 2019.

Methodology: Total 90 subjects were divided into three groups; diabetes with dyslipidemia, diabetes without dyslipidemia and controls. Their blood sugar, lipid profile, HbA1c, hepatitis screening and anthropometric data were considered.

Results: Out of 90 patients, females and males were 73 (80.2%) and 17 (18.7%) respectively. Dyslipidemic females displayed higher LDL-C (3.29 ± 0.95) and lower HDL-C (0.74 ± 0.25) values, while males showed high total cholesterol (5.60 ± 1.30) and triglyceride (2.88 ± 1.40) levels. Female dyslipidemics and non-dyslipidemics exhibited highest HbA1c values (8.90 ± 2.25 and 7.81 ± 1.41). Female and male dyslipidemics displayed highest BMI measures (25.27 ± 3.44).

Conclusion: Significant associations were seen among type-2 diabetes mellitus subjects (with and without dyslipidemia) and age, gender, HbA1c, lipid profile, BMI and obesity.

Keywords: Body mass index, Dyslipidemia, HbA1c, HDL-C, LDL-C, Pakistan, Total cholesterol, Triglycerides, Type 2 diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) among prime four non communicable diseases is one of the 21st century most rapidly spreading illness[1]. International Diabetes Federation (IDF) has recorded death rate of five million due to hazards of diabetes each year[2]. Diabetes is loftily prevalent in Pakistan, ranking it worldwide at position number seven with multiple risk factors association. World Health Organization (WHO) showed the prevalence rate of DM among total population of Pakistan around 13% (7.1 million people of the country)[3]. The aberration of one or more blood lipoprotein levels i.e. low density lipoprotein cholesterol (LDL-C), triglycerides (TAGs), high density lipoprotein cholesterol (HDL-C) and total cholesterol (TC) is defined as dyslipidemia[4]. The major risk factor for development of cardiovascular disease encompasses atherosclerosis sprouted due to dyslipidemia, one of main hazards of T2DM. It is also achieving epitome of prevalence in Pakistan due to its major contribution in onset of related complications[5].

The heterogeneous picture of linking multiple parameters of lipid profile with T2DM has been evident in varied studies. Some studies have found low HDL-C levels followed by raised TAGs to trigger cardiovascular risks in T2DM[6]. Other researches have focused more on HDL-C levels primarily, inducing insulin resistance and making it the influential factor for diabetic dyslipidemia stimulation. A cross-sectional study displayed high LDL-C, TAGs, TC and low HDL-C serum levels in T2DM patients[7]. Serum lipid levels alter in conformity with certain factors e.g. age, gender, HbA1c, lipid profile, BMI, sedentary

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life style, obesity and genetics, contributing major roles in increasing DM global prevalence[8].

Age is one of the most predominant determinants for T2DM risk, showing prevalence between 40 to 60 years, in younger adults. Associated dyslipidemias vulnerability can prevail with earliest hyperglycemia exposure. According to IDF 2013, out of 382 million carriers, most subjects were found to be between 40 to 59 years, while out of global 5.1 million T2DM related mortality cases, half of the people were <60 years. Few studies emphasized more on the older age for onset of T2DM macrovascular complications[9]. Whereas, other cases demonstrated significance of alarming risks in younger age groups[10].

Gender is another important demographic parameter in identification and prevalence of T2DM. Type 2 diabetic females have been given higher prevalence than diabetic males across globe according to reported data collections. A gender based study conducted for determination of linked coronary heart diseases (CHD) in T2DM revealed that T2DM affected females with recent and long standing diabetes history carried higher rates of CHD risks than the diagnosed diabetic males.

HbA1c is an important biochemical determinant for DM diagnosis and its control rate. A T2DM analysis was conducted across the world to see HbA1c test probability ≥6.5% in subjects undergoing oral glucose tolerance tests (OGTT). Shift of diagnostic criteria from OGTT to HbA1c in diabetic subjects was concluded, with enhanced diagnostic differences in both tests at a greater dimension. Evaluation based on HbA1c levels in T2DM participants with 10 years vascular complications, accounted marked reductions in risk outcomes[11-13].

Body mass index (BMI) also known as Quetelet index, is a measure of body fat, universally expressed in units of kg/m^2. A study in two large US prospective cohorts showed the link between BMI in both genders and T2DM risks[14]. A T2DM mendelian randomization analysis in 14 prospective studies highlighted central and general obesity as risk factors for CVDs in T2DM. Another work in 4 cohorts focused on over-weightness and metabolic syndrome onset in childhood to trigger T2DM from 14 years of their lives onwards.

METHODOLOGY

This was cross-sectional comparative study, conducted from January 2018 to January 2019, using non probability purposive sampling technique. Sampling was done at Fauji Foundation Hospital and Pak Emirates Military Hospital, Rawalpindi, Pakistan. The ethical approval was taken from the institutional Ethical Review Committee of Army Medical College, NUMS. Sample size was calculated using standardized WHO calculator with following statistical assumptions; confidence level = 95%, alpha error = 5%, study power = 80%, anticipated standard deviation of LDL-C = 1.1mmol/L and relative precision of 0.33[11-15]. The calculated sample size was 90 subjects. We divided it equally into three groups; diagnosed T2DM patients with dyslipidemias (n=30), diagnosed T2DM without dyslipidemias (n=30) and normal healthy controls (n=30). Study began with an informed written consent, detailed history, general physical and systemic examination and proformas (personal, lifestyle and health related laboratory tests details). The non-T2DM patients having dyslipidemias, patients on lipid lowering drug therapy and those possessing comorbids /chronic illnesses were excluded from study. Whole venous blood sample (5ml) of each patient was drawn in fasting periods. Fasting blood sugar (FBS): ≥7.0 mmol/L and random blood sugar (RBS): >11.1 mmol/L was considered as the cut off values, as per American Diabetes Association (ADA). Fasting lipid profile encompassed serum TC <5.20 mmol/L, TAGs <1.70 mmol/L, LDL-C <2.50 mmol/L and HDL-C >1.0 mmol/L. Hepatitis screening included hepatitis B surface antigen (HBsAg) and hepatitis C antibody (Anti-HCV) tests. Anthropometric parameters were considered too; age, gender, HbA1c, lipid profile, BMI and obesity. Age groups between 23 and 72 years, inclusive of males and females were selected. HbA1c <6.5% and BMI (according to

Inter-national criteria-based) between 18.5 to 24.9 were considered as the normal ranges. Weight and height were measured using electronic digital scale and wall-mounted stadiometer. Data analysis was carried out using SPSS 21 software.

Table-I: The data of anthropometric parameters of study subjects (n=30).

Parameters	Group I Diabetics With Dyslipidemia	Group II Diabetics Without Dyslipidemia	Group III Controls	*p*-value
Age	50.17 ± 10.81	53.50 ± 10.79	34.57 ± 8.70	<0.001
HbA1c	8.90 ± 2.25	7.81 ± 1.41	5.22 ± 0.58	<0.001
BMI	25.27 ± 3.44	24.95 ± 3.61	23.28 ± 4.26	0.097
TC	5.60 ± 1.30	4.38 ± 0.78	4.46 ± 0.65	<0.001
TAGs	2.88 ± 1.40	1.28 ± 0.30	1.27 ± 0.35	<0.001
HDL-C	0.74 ± 0.25	1.28 ± 0.33	1.29 ± 0.30	<0.001
LDL-C	3.29 ± 0.95	2.04 ± 0.50	1.83 ± 0.50	<0.001

p≤0.05 (ANOVA- Analysis of variance), HbA1c: Glycosylated hemoglobin, BMI: Body mass index, TC: Total serum cholesterol, TAGs: Triglycerides, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol.

Differences between three groups were analyzed using one-way analysis of variance (ANOVA) with post hoc test. The expression of data was executed as mean ± standard deviation (SD), with consideration of a significant *p*-value of ≤0.05, using Tukey's HSD (Honestly Significant Difference) as the method to show the associations.

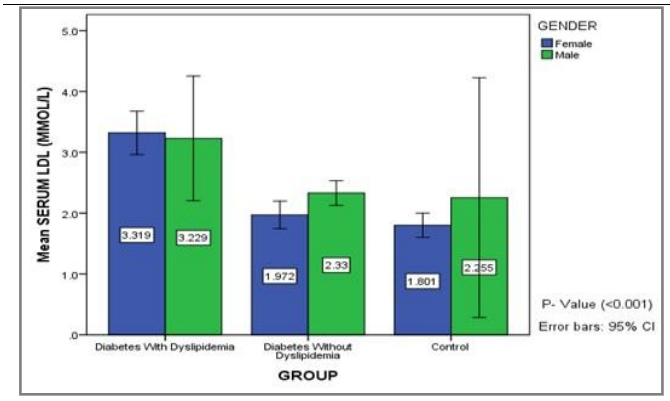

Figure-1: Graphical representation of distribution and correlation of lipid profile parameter [LDL-C] of study subjects with three groups (T2DM with dyslipidemia, T2DM without dyslipidemia and normal healthy controls).

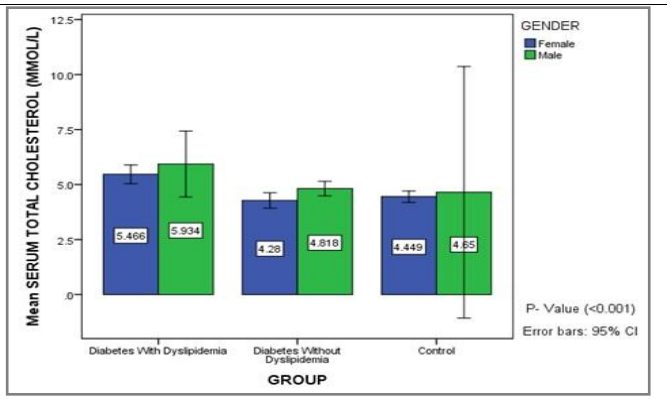

Figure-2: Graphical representation of distribution and correlation of lipid profile parameter [total cholesterol] of study subjects with three groups (T2DM with dyslipidemia, T2DM without dyslipidemia and normal healthy controls).

RESULTS

Total females and males included in the study were 73 (80.2%) and 17 (18.7%) out of 90 subjects. Females and males with T2DM dyslipidemia included 21 (70%) and 9 (30%), respectively. The T2DM without dyslipidemia comprised of 24 females (80%) and 6 males (20%). The control group included number of females as 28 (93.33%) and males as 2 (6.70%). The results of anthropometric parameters assessment are described in table-I. Mean age of patients in dyslipidemia group was 50.17 ± 10.81 with range seen between 45 to 55 years of life. And in group without dyslipidemia, the mean age recorded was 53.50 ± 10.79 with range seen between 25 to 72 years, affecting young females and old males in both groups, respectively (fig-5c). Total cholesterol and triglyceride levels were seen with higher values in males of dyslipidemic group, having a mean value of 5.60 ± 1.30 and 2.88 ±

1.40, respectively (fig-2 & fig-3). Females carried higher values of LDL-C, with mean value of 3.29 ± 0.95, respectively (fig-1). HDL-C levels showed lower values in females, with a mean of 0.74 ± 0.25, respectively (fig-4). The HbA1c was observed highest in females of dyslipidemic and non-dyslipidemic groups, with mean values of 8.90 ± 2.25 and 7.81 ± 1.41, respectively (fig-5a). The BMI was highest in dyslipidemic group, with a mean value of 25.27 ± 3.44, respectively (fig-5b).

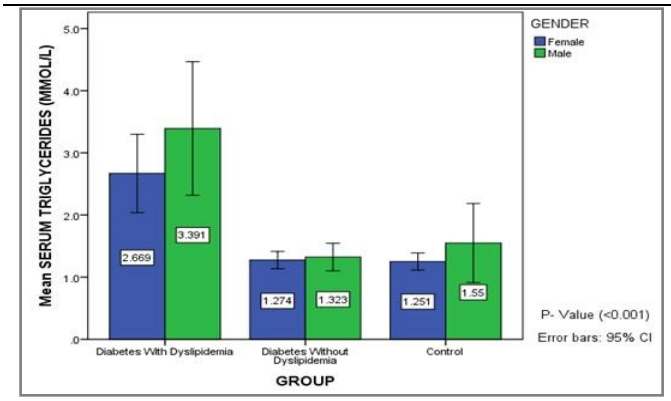

Figure-3: Graphical representation of distribution and correlation of lipid profile parameter [triglycerides] of study subjects with three groups (T2DM with dyslipidemia, T2DM without dyslipidemia and normal healthy controls).

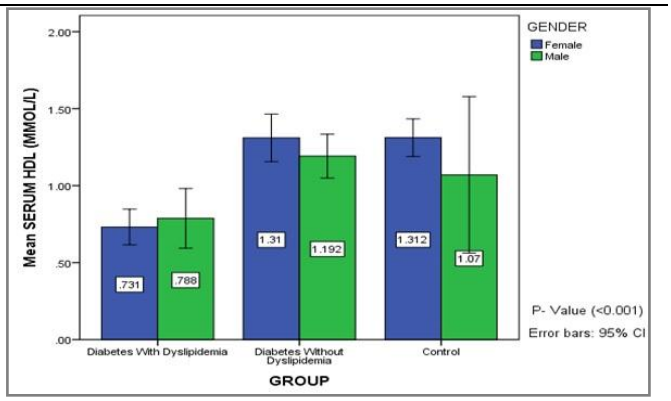

Figure-4: Graphical representation of distribution and correlation of lipid profile parameter [HDL-C] of study subjects with the three groups (T2DM with dyslipidemia, T2DM without dyslipidemia and normal healthy controls).

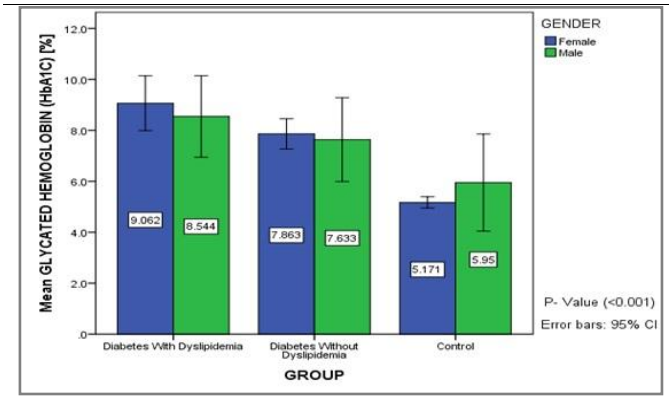

Figure-5(a): Graphical representation of the distribution and correlation of glycosylated hemoglobin [HbA1c] of the study subjects with the three groups (T2DM with dyslipidemia, T2DM without dyslipidemia and normal healthy controls).

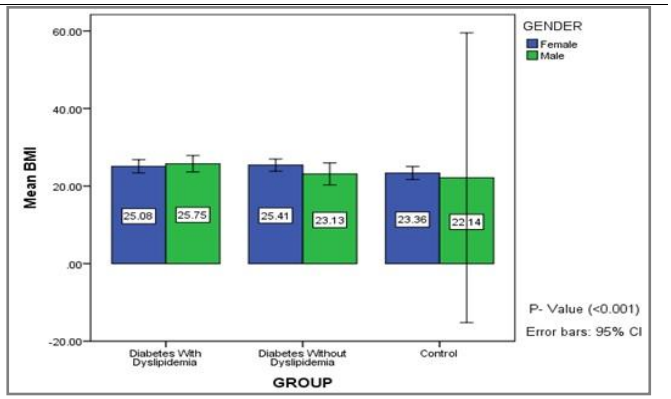

Figure-5(b): Graphical representation of distribution and correlation of body mass index [BMI] of the study subjects with three groups (T2DM with dyslipidemia, T2DM without dyslipidemia and normal healthy controls).

DISCUSSION

Among the various types of DM, T2DM is the most broadly occurring form that has affected communities globally at rate doubled to that of victims of last three decades. Dyslipidemia in T2DM contributes as a part of metabolic syndrome, triggering onset of CVDs[15-18]. Elevated TAGs causes transfer of cholesteryl esters to very low density lipoprotein cholesterol (VLDL-C) from HDL-C and LDL-C, forming LDL-C particles, engulfed by arterial wall macrophages, stimulating atherosclerosis[18]. The preceding surveys have a mixed picture of lipoprotein levels de-rangement in T2DM. Few goaled on TAGs and HDL-C with focused alterations in raised TAGs, followed by low HDL-C levels. Few

have empha-sized solely on reduced HDL-C levels. In our study, also raised TAGs were seen significant, followed by lower HDL-C levels. Some studies have proved TAGs alone to be more significant for dyslipidemia, followed by TC levels. Rests of the literatures have shown TC to be linked with individual's life style habits and sedentary life style modifications for the onset of dyslipidemia. However, in our results, TC levels

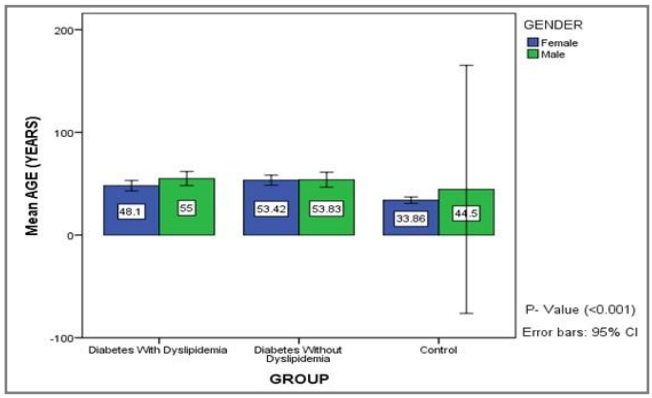

Figure-5(c): Graphical representation of distribution and correlation of age of the study subjects with the three groups (T2DM with dyslipidemia, T2DM without dyslipidemia and normal healthy controls).

are highly raised, followed by raised TAGs. Other authors have combined all the four parameters of low HDL-C and raised LDL-C, TAGs and TC to label dyslipidemia. Our study corresponded to the latter, descending order of readings showed raised LDL-C, followed by elevated TC, TAGs and lastly reduced HDL-C levels.

Previous studies reported a direct relationship between age and T2DM (with and without dyslipidemias). According to few researches, age for T2DM complications onset is recorded at early adulthood, between 30 to 45 years. Some others reported on late adulthood to be more diagnostically significant for onset of T2DM dyslipidemias i.e. <60 years age. In our study, we found dyslipidemia to be more prevalent between 45 to 55 years and T2DM non-dyslipidemia between 25 to 72 years. Previous work reported that T2DM with and without dyslipidemia has different age onsets, also evident from our findings too. This showed that age is not the only factor affecting T2DM dyslipidemics and non-dyslipidemics, but many other parameters impart important roles. The prior data regarding affiliation of gender with T2DM (with and without dyslipidemias) showed positive correlation in males as well as females, but it was seen to be highly prevalent in females as compared to males in multiple studies. According to our findings, females of both diabetic groups were also found more prevalent than males. Also correlation was seen between the age and gender in both T2DM groups. Onset of T2DM was seen late in dyslipidemic and non-dyslipidemic males as compared to dyslipidemic and non-dyslipidemic females that displayed earlier onsets. Similar association for the onset of T2DM in young females and older males has been reported in former literatures too. It may be so, because glycemic control is poor in females due to lipoprotein and hormone-sensitive lipases higher activities as compared to males.

Various past studies have targeted HbA1c as the world-wide diagnostic tool for diabetes. In our study, positive association was concluded as well between T2DM and HbA1c levels. The HbA1c levels were highly raised in diabetic dyslipidemia group, mildly elevated in diabetic non-dyslipidemia group and normal values were observed in the controls. Preceding researches have also focused on HbA1c levels that aimed for diminutions in T2DM prevalence and its risk outcomes, particularly the vascular complications. In our result, HbA1c levels were remarkably increased in diabetic dyslipidemic females, when equated to subjects of diabetic non-dyslipidemia and control groups. Hence, significant relationship of HbA1c with diabetic dyslipidemia was found in our study, also proving the role of HbA1c in the onset of T2DM linked CVD risks. Moreover, squat HbA1c levels in non-dyslipidemic diabetics and controls showed inter-linkages with diminished T2DM related complications. Previous literatures have been reported on the beneficial correlation of BMI and obesity with T2DM and its linked CVD risks. However, one of the prior survey focused on the association of T2DM linked macrovascular complications with overweightness. In our study, positive commu-

nion has been noted between BMI and T2DM associated risks, chiefly prevalent in diabetic dyslipidemic males that had BMI >25. Whereas, overweight diabetic dyslipidemic females were seen less prevalent that may encounter CVD endangerments in the near future. Weight loss regimes must be introduced for the glycemic controls in affiliated subjects[18].

Thus, age, gender, lipid profile, HbA1C, BMI and obesity have been documented to contribute major roles in the onset of T2DM with and without dyslipidemias. Also, our results correlated with numerous past studies conclusions, proving significance for the medical importance of risk factors determination in T2DM with dyslipidemia.

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We are thankful to our participants.

CONCLUSION

Significant associations were seen among type-2 diabetes mellitus subjects (with and without dyslipidemia) and age, gender, HbA1c, lipid profile, BMI and obesity.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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