Effects of lipid-lowering agents on plasma lipid profile and apolipoprotein B in patients with type 2 diabetes mellitus

Idowu, A.O.[1,2], Ebesunun, M.O.[3], Adekoya, A.O.[2,4], Taiwo, F.[1,2], Adesegun, O.A.[1], Idowu, A.A.[5], Uka, A.[1], Amusan, O.O.[1], Ehioghae, O.[1], Amballi, A.A.[3]

Abstract

Objectives: Type 2 Diabetes Mellitus (T2DM) accounts for about 90% of all cases of Diabetes Mellitus. Dyslipidaemia has been demonstrated to form a synergy with T2DM as risk factors for cardiovascular events. This study aimed to determine the plasma levels of Lipids and Apolipoprotein B-100 among Type 2 Diabetic patients, assess the effects of Lipid Lowering agents, and to study the relationship, if any, between these lipid parameters and glycemic control.

Methods: One hundred and fifty participants consisting of fifty T2DM patients on a lipid-lowering agent, fifty newly diagnosed T2DM patients who are drug naïve (not on any anti-diabetic agent) and fifty apparently healthy non-diabetic controls were recruited for this study. Fasting blood samples were collected from all study participants for determination of Total Cholesterol (TC), LDL-C, Triglycerides (TG), High-Density Lipoprotein (HDL-C) and Apo B-100.

Results: The results showed significant increases in plasma TC, LDL-C, TG and Apo B-100 with a remarkable reduction in plasma HDL-C level in the Type 2 Diabetic drug naïve group compared with the treatment and control groups. There was a significant positive correlation observed between serum Apo B-100 and level of glycaemia in the T2DM drug naïve group.

Conclusion: This study further confirms the therapeutic benefits of lipid-lowering agents in reducing Apo B-100 among T2DM patients. Furthermore, maintaining good glycaemic control reduces the risk for the development of dyslipidaemia.

Keywords: T2DM, Dyslipidaemia, Cardiovascular Diseases, Apolipoprotein B-100, Nigeria.

*Corresponding author
Idowu, A.O.
ORCID - ID: http://orcid.org/0000-0003-2902-958X
kolamed2002@yahoo.com

[1]Department of Internal Medicine, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria
[2]Benjamin S. Carson (Snr.) School of Medicine, Babcock University, Ilishan-Remo, Ogun State, Nigeria
[3]Department of Chemical Pathology & Immunology, Obafemi Awolowo College of Health Sciences, Olabisi Onabanjo University, Ogun State, Nigeria.
[4]Department of Paediatrics, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria
[5]Department of Pharmacy, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria

Effets des agents hypolipidémies sur le profil lipidique plasmatique et l'apolipoprotéine B chez les patients diabétiques de type 2

Idowu, A.O.[1,2], Ebesunun, M.O.[3], Adekoya, A.O.[2,4], Taiwo, F.[1,2], Adesegun, O.A.[1], Idowu, A.A.[5], Uka, A.[1], Amusan, O.O.[1], Ehioghae, O.[1], Amballi, A.A.[3]

Résumé

Contexte général de l'étude : Le diabète sucré de type 2 (T2DS) représente environ 90% de tous les cas de diabète sucré. Il a été démontré que la dyslipidémie forme une synergie avec le T2DS en tant que facteurs de risque d'événements cardiovasculaires. Cette étude visait à déterminer les taux plasmatiques de lipides et d'apolipoprotéine B-100 chez les patients diabétiques de type 2, à évaluer les effets des agents hypolipidémies et à étudier la relation, le cas échéant, entre ces paramètres lipidiques et le contrôle glycémique.

Méthode de l'étude : Cent cinquante participants comprenant cinquante patients T2DS sous hypolipidémies, cinquante patients T2DS nouvellement diagnostiqués qui sont naïfs de tout médicament (aucun agent antidiabétique) et cinquante témoins non diabétiques apparemment sains ont été recrutés pour cette étude. Des échantillons de sang à jeun ont été prélevés sur tous les participants à l'étude pour la détermination du cholestérol total (CT), du LDL-C, des triglycérides (TG), des lipoprotéines de haute densité (LHD-C) et de l'Apo B-100.

Résultat de l'étude : Les résultats ont montré des augmentations significatives du plasma CT, L-DL-C, TG et Apo B-100 avec une réduction remarquable du taux plasmatique de LHD-C dans le groupe diabétique de type 2 naïf par rapport aux groupes de traitement et de contrôle. Une corrélation positive significative a été observée entre le sérum Apo B-100 et le taux de glycémie dans le groupe naïf de Dt2.

Conclusion : Cette étude confirme en outre les avantages thérapeutiques des agents hypolipidémies dans la réduction de l'Apo B-100 chez les patients atteints de DT2. De plus, le maintien d'un bon contrôle glycémique réduit le risque de développement d'une dyslipidémie.

Mots-clés : DT2, dyslipidémie, maladies cardiovasculaires, apolipoprotéine B-100, Nigéria

*Corresponding author
Idowu, A.O.
ORCID - ID: http://orcid.org/0000-0003-2902-958X
kolamed2002@yahoo.com

[1]Department of Internal Medicine, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria
[2]Benjamin S. Carson (Snr.) School of Medicine, Babcock University, Ilishan-Remo, Ogun State, Nigeria
[3]Department of Chemical Pathology & Immunology, Obafemi Awolowo College of Health Sciences, Olabisi Onabanjo University, Ogun State, Nigeria.
[4]Department of Paediatrics, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria
[5]Department of Pharmacy, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria

INTRODUCTION

Diabetes mellitus, a metabolic disease of global concern, is associated with high risk of cardiovascular morbidity and mortality. The persistent hyperglycemia characteristic of diabetes mellitus results in vascular modifications contributing to atherosclerosis and other vascular pathologies (1). Cardiovascular Diseases (CVD) are the leading cause of mortality among patients with Type 2 Diabetes Mellitus (T2DM) (2). Dyslipidemia is a state that arises as a result of abnormalities in the plasma lipids. It is one of the key risk factors for cardiovascular disease among patients with T2DM. There is a synergistic relationship between T2DM and dyslipidaemia as risk factors for cardiovascular events (3,4).

In studies on the characterization of lipid parameters among patients with T2DM in Nigeria, extremely high prevalence rates of dyslipidaemia (up to 89.1%) were reported (5,6). The lipid pattern typically observed among people with T2DM comprised hypertriglyceridemia, reduced High-Density Lipoprotein Cholesterol (HDL-C) and elevated levels of Low-Density Lipoprotein Cholesterol (LDL-C) (7).

Owing to its poor solubility in water, virtually all cholesterol in the blood is carried in lipoprotein particles. Atherogenic lipoproteins, including Low Density Lipoprotein (LDL), Very Low-Density Lipoprotein (VLDL) and Intermediate-Density Lipoprotein (IDL), contain apo B-100. One molecule of apo B-100 is present in each atherogenic particle of LDL, VLDL and IDL, making apo B-100 a potential surrogate measure of the total number of atherogenic particles in blood (8,9). Apo B-100 can represent a more direct determinant of atherogenic properties of plasma lipids and is useful for the prediction of future cardiovascular events.

Few studies have been done evaluating plasma apoB-100 as a surrogate marker of atherogenesis amongst type 2 diabetics in Nigeria. Adaja et al reported positive correlations between apoB-100 and LDL, non-HDL cholesterol and total cholesterol, more so in poorly controlled diabetics (10). Sonuga et al also reported higher levels of atherogenic lipid biomarkers, including apoB-100, amongst young people with a family history of diabetes (11). Though, the use of biomarkers such as apoB-100 in clinical practice and research in Nigeria is gradually evolving, it is not yet considered as routine in the workup of type 2 diabetics.

This study aimed to determine the plasma levels of Lipids and apo B-100 among Type 2 Diabetic patients, assess the effects of Lipid Lowering agents, and study the relationship, if any, between these lipid parameters and glycemic control.

MATERIALS AND METHODS

Study Setting

The study was carried out at the Endocrinology, Diabetes and Metabolism division of the Department of Internal Medicine, Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, as well as the Diabetes Clinic of Babcock University Teaching Hospital (BUTH), Ilishan-Remo, Ogun-State, Nigeria. These facilities provide care to the patients from surrounding towns as well as neighboring states of Lagos, Oyo and Ondo.

Study Design and Sampling technique

This was a cross-sectional, comparative, hospital-based study. One hundred and fifty participants were recruited into the study - Fifty of them were T2DM patients who had been on a lipid lowering agent for a minimum period of 3 months, another fifty T2DM drug naïve patients matched for age and sex, and fifty apparently healthy non-diabetics who served as the control group. The sample size was calculated using the Cochran formula. All those above 30 years of age, who gave their informed consent, were included in the study. Individuals on medications that could affect the plasma lipid profile and apo B-100 including antipsychotics, anticonvulsants, immunosuppressants and thiazide diuretics, pregnant women and very ill diabetic patients were excluded from the study.

Data Collection

Demographic data and clinical history were obtained by interviewing the study participants and from information in their hospital case folders. Physical examination was performed on each participant to exclude those with physical findings in keeping with the exclusion criteria. Also, the peripheral stigmata of dyslipidemia were thoroughly looked out for in each study participants. Body weight, height, body mass index (BMI), waist circumference (WC), hip circumference (HC), waist-hip ratio (W/C) and blood pressure were measured in all study participants and recorded using standard methods. Laboratory assessment included collection of 10 mls of venous blood which was carefully drawn from each participant using the ante-cubital vein under aseptic procedure of

venipuncture between 8.00 – 8:30am after an overnight fast of at least 8 hours but not more than 12 hours.

The venous blood collected was divided appropriately as follows: 5mls into plain bottles for Fasting Lipid Profile (FLP) and Apo B-100 assays, while the remaining 5mls was equally distributed into Lithium heparin and fluoride oxalate bottles for the analysis of glycated hemoglobin (HbA1c) and fasting plasma glucose (FPG) respectively. These samples were kept in a cold chain box and transported to the laboratory for centrifugation and separation. The samples for FLP, apo B-100 and FPG were allowed to clot and thereafter centrifuged at 4000 revolutions per minute for 10 minutes, and separated within 30 minutes to extract serum and aliquoted into labelled Eppendorf bottles. Sera for FLP and apo B-100 were stored at -20^{0}C till ready for analysis. FLP was measured spectrophotometrically using enzymatic reagents while apo B-100 was assayed using ELISA method.

Glycated hemoglobin (HbA1c) was analyzed using the Clover A1c analyzer which utilizes the boronate affinity chromatography. The linearity range for HbA1c detection in this study ranged between 5.3% - 17%. All biochemical analyses were carried out in the chemical pathology laboratory of Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, using commercial kits, allowing the best performance of coefficient of variation (CV) and sensitivity.

Laboratory Procedures

All laboratory procedures were carried out under strict and good laboratory practices. All blood samples drawn from study participants were transferred immediately into a dry-ice packed container and centrifuged within an hour after collection. Serum cholesterol and triglyceride levels were determined by enzymatic colorimetric methods using the method based on CHOD-PAP methodology. The principle is based on the methods described by Trinider and Teitz for total cholesterol and triglyceride respectively. HDL cholesterol was precipitated using the Dextran-sulphate-magnesium acetate precipitation method and analyzed as using method of Trinider. LDL cholesterol was calculated using the Friedwald formula: (LDL-C) = (Total Cholesterol) – (HDL – Cholesterol) – (TG/5). Apo B-100 was estimated using an enzyme immunoassay method.

Statistical Analysis

The data obtained were coded and entered into a computer for analysis. Data were analyzed using the Statistical Package for Social Science (SPSS) version 23 (SPSS, Chicago, IL, WA). Except otherwise stated, continuous variables were expressed as mean ± Standard Deviation (SD) and number counts (N), with proportions (%) for categorical data. Descriptive analyses were presented with frequency tables and graphs as appropriate. Analysis of Variance (ANOVA) was used to compare the means of continuous variables with more than two groups. Thereafter, post-hoc tests were carried out on the result of ANOVA tables generated to identify the two groups with a statistically significant difference. Students' t-test was used to compare continuous variables when two groups were involved. Correlation between Apo B-100 levels and glycaemic control was done using Spearman Rho's correlation coefficient. Other categorical variables were also compared using Chi-square test with the level of statistical significance set at p<0.05.

Ethical Consideration

Approval for the study was obtained from the Health Research and Ethics Committee of the Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State (OOUTH-HREC) with registration number OOUTH/HREC/221/2018AP. We obtained written informed consents from each participant. All relevant standards of Revised Declaration of Helsinki were followed.

RESULTS
Demographic and clinical parameters of the study participants

One hundred and fifty consecutive study participants were recruited for this study and were divided into three groups of fifty participants each. The mean age was 57.42 ± 11.72 years (see Table 1), with the age range being 31-85 years. All participants were Nigerian and predominantly Yoruba by tribe (96%). Over half of the study participants were women (57.3%); most (76.7%) were married with almost equal proportions of married participants in each of the three groups (see Table 2). The three groups were significantly different in the mean values of their height, weight, body mass index, waist circumference and hip circumference (p<0.05). The T2DM drug-naïve group had the highest values of anthropometric parameters. The mean systolic and diastolic blood pressures differed significantly among the three groups with the control group having the lowest mean blood

pressure values compared to the two diabetic groups (p<0.001) respectively, as shown in Table 3a (post hoc tests in Table 3b).

Class and duration of lipid-lowering agents used by study participants.

All T2DM patients in the lipid-lowering group were on statins, as shown in Table 4. All the study participants in this group had been on statins for a minimum period of 3 months, 34% had been on a statin for more than 2 - 5years, and 22% for more than 6 months – 1 year. Only 2% of those in this group had taken a statin for more than 5 years.

Relationship between duration of diabetes and use of lipid lowering agents

There was a significant association between duration of diabetes and use of lipid lowering agents, with majority (28%) of diabetics on lipid lowering agents having had diabetes for >2-5 years, and 66% of those not on lipid lowering agents having had diabetes for 0-6 months (see Table 4)

Lipid profile and Apo B-100 of study participants

Biochemical parameters among the three study groups are shown in Table 5a. The mean serum TC, LDL and TG were observed to be significantly higher in the T2DM drug-naive group than in the other two groups (p<0.05) (see Table 5a; post hoc tests in Table 5b). However, the mean serum HDL of the T2DM on lipid lowering agent group, T2DM drug naive group and non-diabetic control group were 50.31±20.60 mg/L, 33.78 ± 9.70 mg/L and 40.43 ± 16.31 mg/L respectively. Thus, HDL values were significantly lower in the T2DM drug naive group compared to the other two groups (p<0.05) (see Table 5a; post hoc tests in Table 5b). The mean apo B-100 was higher in the T2DM drug naive group compared to the other two groups, and this difference was statistically significant (p<0.05). The mean FPG & HbA1c (indices for glycaemic control) were also highest in the T2DM drug naive group (p<0.05) as shown in Table 5a (post hoc tests in Table 5b).

Relationship between serum Apo B-100 and glycemic control in the diabetic groups.

The correlation of the apo B-100 with the degree of glycaemic control using HbA1c between the two diabetic groups is shown in Table 6. There was a weak but positive correlation between Serum apo B-100 and level

of glycaemic control in the T2DM on lipid lowering agent group. However, serum apo B-100 was significantly correlated with the level of glycaemic control in T2DM drug naive group. Figures 1 and 2 further expressed the relationship between apo B-100 and the degree of glycaemic control using HbA1c. There is a linear relationship between apo B-100 and HbA1c with the regression line sloping upwards in the T2DM on lipid lowering agent group.

Relationship between degree of glycaemic control and lipid profile parameters

The correlation between the degree of glycaemic control using HBA_1C and the lipid parameters is depicted in Table 7. In the T2DM on lipid lowering agent group HbA1c, was weakly but positively correlated with the TC and HDL. There was a negative correlation between HbA1c, LDL and TG. In the T2DM drug naive group, HBA_1C was positively correlated with LDL and TG while it was negatively correlated with TC and HDL. None of the correlation coefficients were statistically significant.

DISCUSSION

Statins have been revealed to have potential therapeutic benefits in reducing atherogenic lipoproteins which include LDL-C, VLDL, IDL and apo B-100 (12-14). Affordability and availability are factors that possibly would have contributed to statins being widely used for the treatment of dyslipidemia among Type 2 Diabetics as found in this present study. Also, it is presumed that most clinicians are not updated on the novel lipid-lowering agents, indications for their initiation and their side effect profiles, thus contributing to the common use of statins over other agents in most centers.

Mean values of anthropometric indices (Wt, BMI, WC, HC and W/H) were most elevated in the T2DM statin-naive group compared to the other two groups studied. This finding is in accordance with previous studies which showed that BMI, WC, W/H ratio are positive indicators of development of Type 2 Diabetes (15,16). Mean values of these anthropometric indices were lower in the Type 2 Diabetics on lipid lowering agents. This can be credited to the quality of care rendered to Type 2 Diabetics which comprise counseling on dietary adjustments, lifestyle interventions targeted at reduction of central adiposity and optimizing care to improve quality of life.

Mean serum LDL-C value was highest in the T2DM statin-naïve group compared to the

treatment and control groups. This correlates with earlier studies which reported mean LDL-C values to be elevated in statin naive participants relative to diabetic participants on statin therapy (17-19). Diabetic dyslipidaemia encompasses both quantitative and qualitative lipoprotein abnormalities that together culminate in a shift toward a more atherogenic lipid profile that includes elevated LDL-C especially in patients who are not on lipid-lowering medications (19). Probable explanations for this increase in LDL-C in the lipid lowering naive group include a significant decrease in the catabolism of LDL (20,21). This may ultimately precipitate lipid deposition within arterial walls increasing the risk of cardiovascular morbidity. Also, the increase in LDL-C levels in the statin-naive group can be attributed to the reduction of LDL cell-surface receptors compared to the group on statins (21). It is worthy of note that statins have been reported to increase cell surface LDL receptor expression resulting in facilitation of increased clearance of LDL-C from the bloodstream and a subsequent reduction in circulating LDL-C levels by 20 to 55%, hence the reduced LDL-C in the Type 2 Diabetic on lipid lowering agent group in this study (22). Previous studies have also suggested increased glycation of LDL secondary to chronic hyperglycaemia as a cause of elevated LDL-C (23,24). This present study also found elevated mean glycated hemoglobin in the drug naïve group which further supports a possible increase in non-enzymatic glycation of proteins including LDL-C.

As had been reported elsewhere and confirmed in this study, statins have the capacity to increase the concentration of HDL-C (25). In this study, the mean serum HDL-C level was higher in the T2DM on lipid-lowering agent group compared to the drug naïve group. In this study, the statin-mediated elevation of HDL-C level in the T2DM on lipid-lowering agents is in consonance with previous studies with similar findings. With statins, there are elevations in HDL-C range between 3% and 15% (26).

Mean Triglyceride levels were significantly higher in the T2DM not on lipid lowering agent. This may be somewhat attributed to an increased number of VLDL. The production rate of VLDL in patients with Diabetic dyslipidemia yet to initiate lipid lowering agent has a positive correlation with the insulin resistance in these patients (27). Statins decrease TG levels by endocytosing TG-rich Apo B-100 particles (28), hence, the reduction in mean TG concentration among the T2DM on statin in this study.

Mean apo B-100 level which is considered to be an approximation of the total number of atherogenic particles is highest in the T2DM not on statins compared to the two other groups. Apo B-100 is the goal of therapy of the ADA/ACC consensus statement on lipoprotein management in patients with Cardio-metabolic risk. Statins lower LDL-C and VLDL both of which are atherogenic lipids containing apo B-100. A management consideration for the high-risk patient is to assay apo-B during statin therapy to make sure that the total number of atherogenic particles is decreased (28). Biochemical indicators for glycaemia including HbA_{1c} and FPG are also significantly elevated in the drug-naïve group compared to the treatment group. This indicates the therapeutic benefit of glucose lowering agent and also exemplify compliance with medications, routine clinic visits and possibly regular lifestyle interventions as recommended by their managing Physicians/Endocrinologists. Apo B-100 had a linear relationship with HbA_{1c} as a measure of glycaemic control in both diabetic groups. There was a significant positive correlation observed in the T2DM drug naive group. The findings from this study consistently suggested that elevated apo B-100 levels was associated with poor glycaemic control which is in accordance with previous studies (29-31).

Hwang et al indicated that Apo B-100 is an effective predictor of T_2DM (32). In patients with diabetic dyslipidemia who are drug naive, apo B-100 containing lipoprotein particles undergo compositional changes, including the increased formation of LDL and TG particles as also seen in this present study (33). The poorer the glycaemic control is, the higher the level of apo B-100 is, especially in the drug naive group.

Limitations of the Study

The choice of lipid lowering agent used in this study was limited to statins. This study was not able to compare the effect of statins with the other lipid lowering agents and did not categorize individual type of statin used. Also, the study was performed using a cross-sectional design and did not control for potential biases from diet, physical activity, smoking and alcohol history, and duration of statin use. A longitudinal study would have served this purpose better, however limitations in funding and other logistics prevented this from being implemented in the current study.

CONCLUSION

This study further confirms the therapeutic benefits of statins in reducing atherogenic lipids and Apo B-100 among T2DM patients as previously reported. Also, the study corroborates earlier studies regarding the positive correlation between poor glycemic control and the risk of developing dyslipidemia.

Recommendations: Physicians should be trained at all levels of care about the other lipid lowering agents, indications for use and side effect profile so as to provide holistic care for T2DM patients. With the already available direct measures to establish the severity of dyslipidemia by assaying the conventional lipoproteins, apo B-100 can be added as a surrogate/potential biomarker as this correlate better with progression of the disease. Finally, further studies should pay more attention to Apo B/ Apo A1 ratio which reflects the balance of atherogenic and athero-protective particles and provides a unique assessment of cardiovascular risk.

Competing Interests: Authors have declared no conflict of interest.

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Table 1: Mean Age of Study Participants

AGE	DM-L Mean±SD	DM-L^0 Mean±SD	CN Mean±SD	Test statistics value (ANOVA)	p-value
AGE	57.86±11.48	56.62±12.48	57.78±11.37	0.173	0.841

Mean age of all participants = 57.42±11.72 years

DM-L – Diabetics on lipid lowering agent, DM-L^0 – Diabetics not on lipid lowering agent, CN – Control, N – Total Number, *p value <0.05 is statistically significant.

Table 2: Socio-Demographic characteristics of the study population

CHARACTERISTICS	DM-L (%) N=50	DM-L^0 (%) N=50	CN (%) N=50	Total (%)	Test Statistics Value (X^2)	p-Value
TRIBE						
Yoruba	47(94.0)	47(94.0)	50(100.0)	144(96.0)	6.577	0.160
Hausa	0(0.0)	1(2.0)	0(0.0)	1(0.7)		
Igbo	3(6.0)	2(4.0)	0(0.0)	5(3.3)		
GENDER						
Male	16(32.0)	27(54.0)	21(42.0)	64(42.7)	4.960	0.084
Female	34(68.0)	23(46.0)	29(58.0)	86(57.3)		
OCCUPATION						
Civil Service	11(22.0)	13(26.0)	13(26.0)	37(24.7)	22.239	0.035*
Self-employed	21(42.0)	24(48.0)	27(54.0)	72(48.0)		
Unemployed	0(0.0)	1(2.0)	3(6.0)	4(2.7)		
Apprentice	0(0.0)	0(0.0)	2(4.0)	2(1.3)		
Retired	16(32.0)	11(22.0)	3(6.0)	30(20.0)		
Student	1(2.0)	1(2.0)	2(4.0)	4(2.7)		
Others	1(2.0)	0(0.0)	0(0.0)	1(0.7)		
MARITAL STATUS						
Single	1(2.0)	2(4.0)	7(14.0)	10(6.7)	20.618	0.002*
Married	39(78.0)	38(76.0)	38(76.0)	115(76.7)		
Separated	0(0.0)	6(12.0)	3(6.0)	9(6.0)		
Widow/Widower	10(20.0)	4(8.0)	2(4.0)	16(10.7)		
EDUCATIONAL STATUS						
None	7(14.0)	2(4.0)	0(0.0)	9(6.0)	29.073	0.001*
Primary	9(18.0)	3(6.0)	1(2.0)	13(8.7)		
Secondary	9(18.0)	7(14.0)	17(34.0)	33(22.0)		
Tertiary	22(44.0)	37(74.0)	30(60.0)	89(59.3)		
Technical	2(4.0)	1(2.0)	1(2.0)	4(2.7)		
Vocational Training	1(2.0)	0(0.0)	1(2.0)	2(1.3)		
RELIGION						
Christianity	30(60.0)	43(86.0)	46(92.0)	119(79.3)	17.647	0.001*
Islam	20(40.0)	7(14.0)	4(8.0)	31(20.7)		

DM-L – Diabetics on lipid lowering agent, DM-L^0 – Diabetics not on lipid lowering agent, CN – Control, N – Total Number, *p value <0.05 is statistically significant.

Table 3a: Comparative Values of Anthropometric Indices and Blood Pressure in Study Participants

VARIABLES	DM-L Mean±SD	DM-L^0 Mean±SD	CN Mean±SD	Test statistics value (ANOVA)	p-value
Ht(m)	1.64±0.09	1.66±0.09	1.70±0.09	5.889	0.003[*]
Wt (kg)	75.18±16.96	84.42±12.95	72.51±10.77	10.256	0.001[*]
BMI (kg/m^2)	27.53±5.20	30.46±4.00	26.03±4.22	12.483	0.001[*]
WC (cm)	90.54±14.04	97.07±8.56	79.05±8.10	37.158	0.001[*]
HC (cm)	99.32±10.60	104.37±8.25	97.00±8.20	8.597	0.001[*]
W/H	0.90±0.15	0.91±0.13	0.76±0.22	12.213	0.001[*]
SBP (mmHg)	132.42±13.73	138.16±14.48	122.42±11.08	18.276	0.001[*]
DBP (mmHg)	76.96±15.27	86.44±8.51	76.92±8.14	12.141	0.001[*]

DM-L – Diabetics on lipid lowering agent, DM-L^0 – Diabetics not on lipid lowering agent, CN – Control, Ht: Height, Wt: Weight, BMI: Body Mass Index, WC: Waist Circumference, HC: Hip Circumference, W/H: Waist/Hip ratio, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, [*]P value <0.05 is statistically significant.

Table 3b – Tukey HSD Post Hoc Test for Anthropometric Indices and Blood Pressure in Study Participants

Variables			Mean Difference	p value	95% Confidence Interval Lower Bound	Upper Bound
Height (m)	DM-L	DM-L0	-.02240	0.410	-.0639	.0191
		Control	-.05958*	**0.003**	-.1011	-.0181
	DM-L0	DM-L	.02240	0.410	-.0191	.0639
		Control	-.03718	0.089	-.0787	.0043
	Control	DM-L	.05958*	**0.003**	.0181	.1011
		DM-L0	.03718	0.089	-.0043	.0787
Weight (Kg)	DM-L	DM-L0	-9.2400*	**0.003**	-15.775	-2.705
		Control	2.6700	0.599	-3.865	9.205
	DM-L0	DM-L	9.2400*	**0.003**	2.705	15.775
		Control	11.9100*	**0.000**	5.375	18.445
	Control	DM-L	-2.6700	0.599	-9.205	3.865
		DM-L0	-11.9100*	**0.000**	-18.445	-5.375
Body Mass Index (Kg/m2)	DM-L	DM-L0	-2.93040*	**0.004**	-5.0642	-.7966
		Control	1.49560	0.224	-.6382	3.6294
	DM-L0	DM-L	2.93040*	**0.004**	.7966	5.0642
		Control	4.42600*	**0.000**	2.2922	6.5598
	Control	DM-L	-1.49560	0.224	-3.6294	.6382
		DM-L0	-4.42600*	**0.000**	-6.5598	-2.2922
Waist Circumference (cm)	DM-L	DM-L0	-6.5300*	**0.007**	-11.541	-1.519
		Control	11.4900*	**0.000**	6.479	16.501
	DM-L0	DM-L	6.5300*	**0.007**	1.519	11.541
		Control	18.0200*	**0.000**	13.009	23.031
	Control	DM-L	-11.4900*	**0.000**	-16.501	-6.479
		DM-L0	-18.0200*	**0.000**	-23.031	-13.009
Hip Circumference	DM-L	DM-L0	-5.0500*	**0.017**	-9.353	-.747
		Control	2.3200	0.411	-1.983	6.623
	DM-L0	DM-L	5.0500*	**0.017**	.747	9.353
		Control	7.3700*	**0.000**	3.067	11.673
	Control	DM-L	-2.3200	0.411	-6.623	1.983
		DM-L0	-7.3700*	**0.000**	-11.673	-3.067
Waist/Hip Ratio	DM-L	DM-L0	-.01684	0.871	-.0964	.0627
		Control	.13470*	**0.000**	.0551	.2143
	DM-L0	DM-L	.01684	0.871	-.0627	.0964
		Control	.15154*	**0.000**	.0720	.2311
	Control	DM-L	-.13470*	**0.000**	-.2143	-.0551
		DM-L0	-.15154*	**0.000**	-.2311	-.0720
Systolic Blood Pressure (mmHg)	DM-L	DM-L0	-5.740	0.078	-11.98	.50
		Control	10.000*	**0.001**	3.76	16.24
	DM-L0	DM-L	5.740	0.078	-.50	11.98
		Control	15.740*	**0.000**	9.50	21.98
	Control	DM-L	-10.000*	**0.001**	-16.24	-3.76
		DM-L0	-15.740*	**0.000**	-21.98	-9.50
Diastolic Blood Pressure (mmHg)	DM-L	DM-L0	-9.482*	**0.000**	-14.75	-4.21
		Control	.038	1.000	-5.23	5.31
	DM-L0	DM-L	9.482*	**0.000**	4.21	14.75
		Control	9.520*	**0.000**	4.25	14.79
	Control	DM-L	-.038	1.000	-5.31	5.23
		DM-L0	-9.520*	**0.000**	-14.79	-4.25

The mean difference is significant at the 0.05 level

Table 4 Comparison between duration of diabetes and use of lipid lowering agents

VARIABLES	DM-L (%) N=50	DM-L^0 (%) N=50	Total (%)	Test Statistics Value (X^2)	p-Value
Duration of diagnosis					
0 – 6months	6(12.0)	33(66.0)	39(39.0)	85.126	0.001*
6months – 1year	4(8.0)	16(32.0)	20(20.0)		
>1year – 2years	0(0.0)	1(2.0)	1(1.0)		
>2 – 5years	14(28.0)	0(0.0)	14(14.0)		
>5 – 10years	10(20.0)	0(0.0)	10(10.0)		
>10years	16(32.0)	0(0.0)	16(16.0)		

DM-L – Diabetics on lipid lowering agent, DM-L^0 – Diabetics not on lipid lowering
agent, OAD – Oral Anti-diabetic Drugs,

Table 5a: Biochemical parameters of study participants

PARAMETERS	DM-L Mean±SD	DM-L^0 Mean±SD	CN Mean±SD	Test statistics value (ANOVA)	p-value
TC (mg/dl)	172.15±47.95	215.28±38.70	181.49±33.45	15.709	0.001*
LDL (mg/dl)	99.02±48.24	144.66±39.27	125.01±36.86	15.035	0.001*
HDL (mg/dl)	50.31±20.60	33.78±9.70	40.43±16.31	13.230	0.001*
TG (mg/dl)	114.12±54.99	169.58±69.13	80.26±31.03	34.797	0.001*
Apo B (mg/ml)	0.0237±0.014	0.0244±0.0265	0.0163±0.0008	3.206	0.043*
FPG (mg/dl)	139.14±51.43	182.10±57.91	84.02±8.72	59.694	0.001*
HBA1c (%)	8.26±1.94	9.08±1.81	4.54±0.31	18.382	0.001*

DM-L – Diabetics on lipid lowering agent, DM-L^0 – Diabetics not on lipid lowering agent, CN – Control, TC – Total Cholesterol, LDL – Low Density Lipoprotein, HDL – High Density Lipoprotein, TG – Triglycerides, Apo B – Apo lipoprotein B, FPG – Fasting Plasma Glucose, HBA1c – Glycosylated Hemoglobin, *P value <0.05 is statistically significant

Table 5b: Tukey HSD Post Hoc Test for Biochemical parameters of study participants

Variables			Mean Difference	p value	95% Confidence Interval Lower Bound	Upper Bound
Total Cholesterol (mg/dl)	DM-L	DM-L^0	-30.944	**0.001**	-50.437	-11.452
		Control	6.322	0.723	-13.170	25.814
	DM-L^0	DM-L	30.944	**0.001**	11.452	50.437
		Control	37.266	0.000	17.774	56.759
	Control	DM-L	-6.322	0.723	-25.814	13.170
		DM-L^0	-37.266	**0.000**	-56.759	-17.774
LDL Cholesterol (mg/dl)	DM-L	DM-L^0	-45.638	**0.000**	-65.406	-25.870
		Control	-25.986	**0.006**	-45.755	-6.218
	DM-L^0	DM-L	45.638	**0.000**	25.870	65.406
		Control	19.651	0.052	-0.117	39.420
	Control	DM-L	25.986	**0.006**	6.218	45.755
		DM-L^0	-19.652	0.052	-39.420	0.117
HDL Cholesterol (mg/dl)	DM-L	DM-L^0	16.534	**0.000**	8.875	24.193
		Control	9.884	**0.007**	2.225	17.543
	DM-L^0	DM-L	-16.534	**0.000**	-24.193	-8.875
		Control	-6.6500	0.103	-14.309	1.009
	Control	DM-L	-9.884	**0.007**	-17.543	-2.225
		DM-L^0	6.650	0.103	-1.009	14.309
Triglycerides (mg/dl)	DM-L	DM-L^0	-55.464	**0.000**	-81.060	-29.868
		Control	33.854	**0.006**	8.258	59.450
	DM-L^0	DM-L	55.464	**0.000**	29.868	81.060
		Control	89.318	**0.000**	63.722	114.914
	Control	DM-L	-33.854	**0.006**	-59.450	-8.258
		DM-L^0	-89.318	**0.000**	-114.914	-63.722
Apolipoprotein B (mg/ml)	DM-L	DM-L^0	-0.0006	0.979	-.008936	0.007556
		Control	0.0074860	0.084	-.000760	0.015732
	DM-L^0	DM-L	0.0006900	0.979	-.007556	0.008936
		Control	0.0081760	0.053	-.000070	0.016422
	Control	DM-L	-0.0074860	0.084	-.015732	0.000760
		DM-L^0	-0.0081760	0.053	-.016422	0.000070
Fasting Plasma Glucose (mg/dl)	DM-L	DM-L^0	-42.964	**0.000**	-64.27	-21.66
		Control	55.120	**0.000**	33.81	76.43
	DM-L^0	DM-L	42.964	**0.000**	21.66	64.27
		Control	98.084	**0.000**	76.78	119.39
	Control	DM-L	-55.120	**0.000**	-76.43	-33.81
		DM-L^0	-98.084	**0.000**	-119.39	-76.78
HBA1C (%)	DM-L	DM-L^0	-0.822	**0.023**	-1.5534	-0.0914
		Control	3.718	**0.000**	2.9876	4.4496
	DM-L^0	DM-L	0.822	**0.023**	0.0914	1.5534
		Control	4.541	**0.000**	3.8100	5.2720
	Control	DM-L	-3.718	**0.000**	-4.4496	-2.9876
		DM-L^0	-4.541	**0.000**	-5.2720	-3.8100

The mean difference is significant at the 0.05 level

Table 6: Correlation of glycemic control and Apolipoprotein B in the diabetic groups

	r	p
HbA1c & Apo B in DML	0.277	0.052
HbA1c & Apo B in DML^0	0.422	0.002

DM-L – Diabetics on lipid lowering agent,
DM-L^0 – Diabetics not on lipid lowering agent,
Apo B – Apolipoprotein B.

Table 7: Relationship between degree of glycaemic control and lipid profile parameters

		DM-L n=50		DM-L^0 n=50	
Independent Variable	**Dependent Variables**	r	p	r	P
HBA1c	TC (mg/dl)	0.119	0.410	-0.013	0.927
	LDL-C (mg/dl)	-0.024	0.870	0.166	0.250
	HDL-C (mg/dl)	0.103	0.478	-0.174	0.228
	TG (mg/dl)	-0.015	0.919	0.022	0.880

DM-L – Diabetics on lipid lowering agent, DM-L^0 – Diabetics not on lipid lowering agent,
TC – Total Cholesterol, LDL – Low Density Lipoprotein, HDL – High Density Lipoprotein,
TG – Triglycerides, HBA1c – Glycosylated Hemoglobin
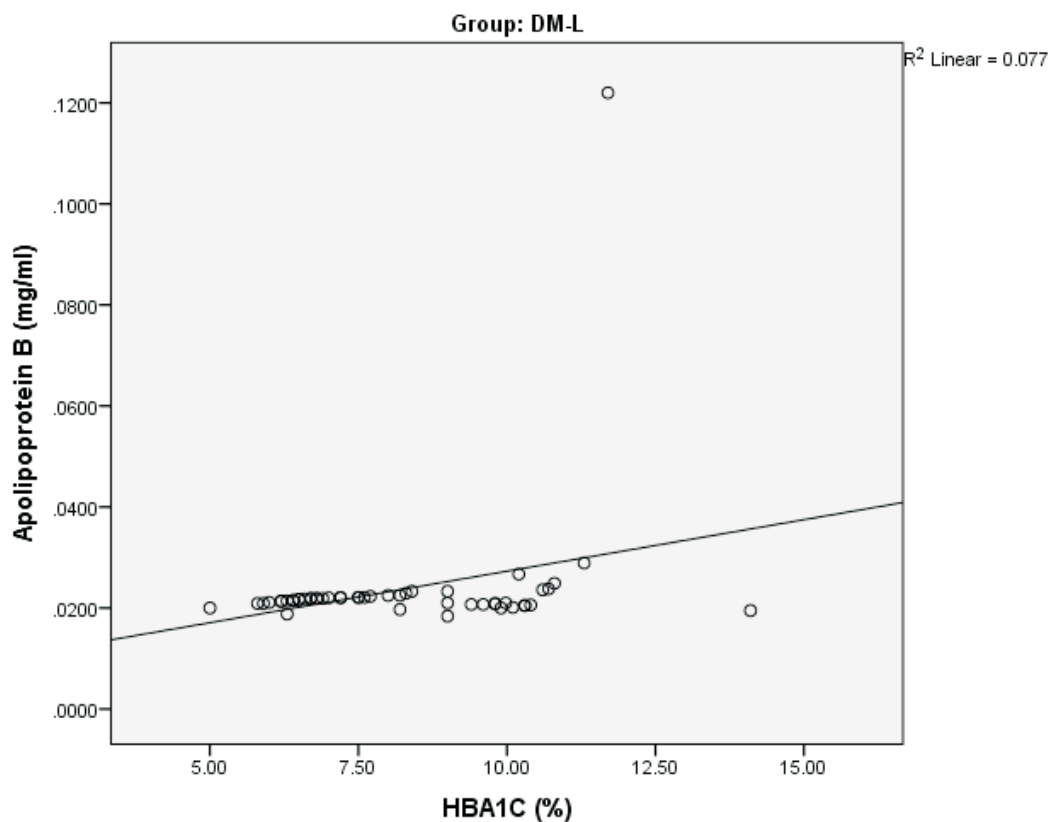
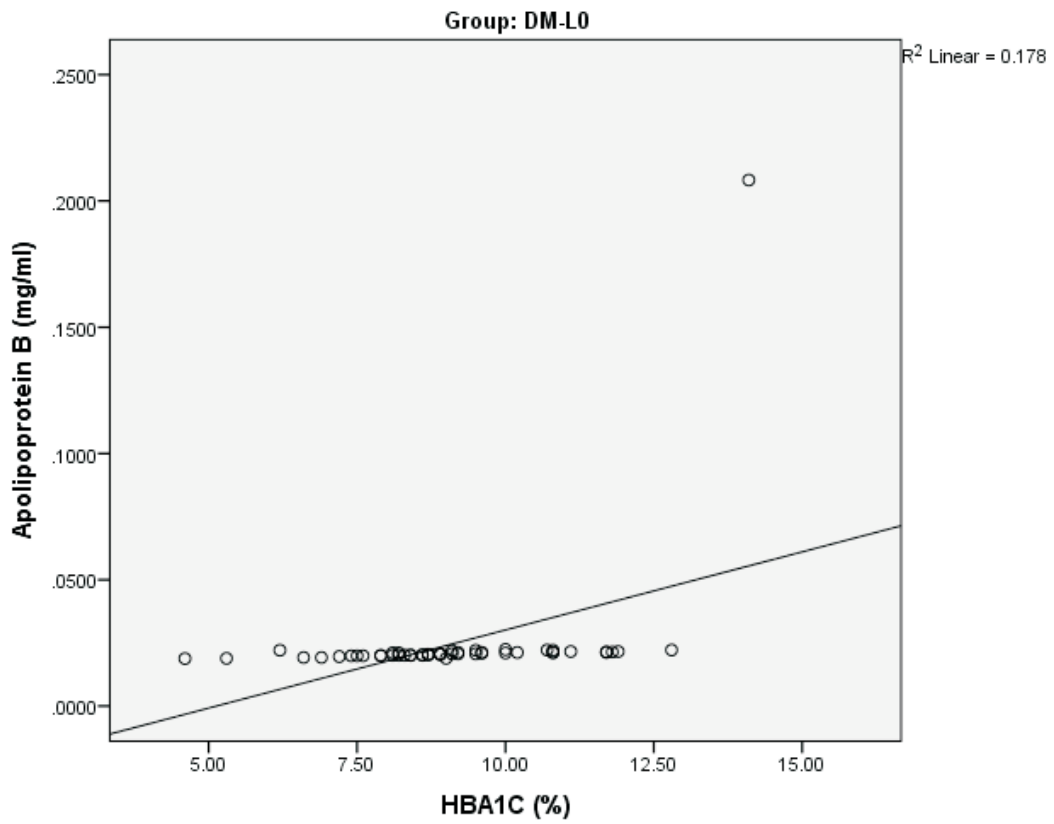**Figure 1: Scatter plot of Apolipoprotein B and HBA1c in Diabetics on lipid lowering agents**

Figure 2: Scatter plot of Apolipoprotein B and HBA1c in Diabetics not on lipid lowering agents