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Original Research Article

Determining Association of Apolipoprotein B and Dyslipidemia in Type 2 Diabetes Mellitus and its Relation with Albuminuria

Sunil Kumar[1], Krishna Prasad[2]

[1]Senior Resident, Department of Medicine, Government medical College and Hospital, Madhepura, Bihar, India

[2]Associate and HOD, Department of Medicine, Government medical College and Hospital, Madhepura, Bihar, India

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Corresponding Author: Dr. Sunil Kumar
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Abstract

Aim: The aim of the present study was to assess the correlation of Apo-lipoprotein B and dyslipidemia in Type 2 Diabetes mellitus and its relation with Albuminuria.

Methods: This Cross-Sectional Study was conducted in the Department of Medicine, Government medical College and Hospital, Madhepura, Bihar, India from July 2022 to June 2023 with 100 patients.

Results: Mean age of the study population was found to be 52.48±12.96 years with minimum and maximum age being 22 and 75 respectively. Among 100 patients, 55 (55%) and 45 (45%) patients were accordingly female and male. It was observed that 52 (52%), 14 (14%), 6 (6%), 6 (6%), 3 (3%), and 10 (10%) patients had HTN, IHD, CKD, CVA, Hypothyroidism and Other comorbidities correspondingly. Total of 9 (9%) patients had no comorbidities at all. Total of 20 (20%) and 80 (80%) patients belonged to HbA1c values <7 and >7 groups respectively. Distribution of ACR values with respect to different ranges of TC was not statistically significant (P value >0.05). Distribution of ACR with respect to HDL levels was fond to be suggestively significant at 91% level of confidence. Different level of triglyceride (0-10, 11-200 and >200) distribution of ACR (404(52.095-998.2), 713.6(81.5775-1158.8) and 350(144.5-770.5)) was not statistically significant. There was no significant difference was established in distribution of ACR with respect different levels of APO- A1, APO- B and APO B/APO A1. Significant positive correlation was found among TC, TG, LDL VLDL, and ApoB with correlation coefficient of 0.4, 0.34, 0.47, 0.24 and 0.32 respectively (P value<0.05).

Conclusion: In the present study, there was a significant positive correlation between Apolipoprotein B and albuminuria among patients with type 2 diabetes mellitus. There was also a positive correlation between Apolipoprotein B and dyslipidemia among these patients, who showed elevated total cholesterol, LDL cholesterol, and triglyceride levels.

Keywords: Apo-lipoprotein B, dyslipidemia, Type 2 Diabetes mellitus, Albuminuria

Introduction

Type 2 diabetes is associated with dyslipidemia comprising of multiple lipoprotein disorders. The most typical findings are high triglycerides and triglyceride rich lipoproteins, low levels of High Density Lipoprotein (HDL) cholesterol, normal or slightly increased Low Density Lipoprotein (LDL) cholesterol and presence of small dense LDL particles which are cholesterol depleted. [1] Apolipoprotein B and apolipoprotein A-1 are the main structural proteins of atherogenic lipoproteins and HDL particles, respectively. LDL comprises of a large buoyant LDL and a small dense LDL (sd-LDL). This small dense LDL is depleted in cholesterol and is considered to be more atherogenic than its normal counterpart because it is more easily oxidized, penetrates the arterial wall more freely and has higher affinity for proteoglycan. LDL cholesterol does not give the true picture because the small dense LDL is not measured, and it is this sub fraction of LDL which is particularly related to coronary artery risk and is frequently raised in diabetics. [1]

Coronary artery disease is the major cause of morbidity and mortality in industrialized countries. According to the Third Adult Treatment Panel (ATP III) guidelines of the US National Cholesterol Education Program (NCEP), increased LDL cholesterol is one of the primary risk factors for coronary artery disease. The guidelines recommend a full fasting lipid profile to include total cholesterol, LDL cholesterol, HDL cholesterol and triglyceride

levels. [2] However, recent studies have shown that apolipoprotein B provides better information regarding risk of coronary artery disease. [3-5] Apo B identifies high-risk dyslipidemia phenotypes that are not detected by standard lipid profile in type 2 diabetic patients. [6]

Apolipoproteins are amphipathic molecules which adjust the transportation and distribution of lipoproteins, encouraging binding of lipoproteins to the receptors with a subsequent activation of lipid enzymes. Apolipoproteins accompanied by several diseases, comprising of diabetic macro vasculopathy and micro vasculopathy and dysregulation of apolipoproteins A and B, are a concern in DR. [7] An important study was made to compare the correlation of DR with the values of apolipoproteins and with lipid profile in T2DM cases, which noticed that there is a potent correlation between serum apolipoproteins and the advancement and gravidity of DR in T2DM cases in comparison with traditional lipids. [8] In another important research aimed to evaluate the correlation between apo B and diabetic microvascular complication, the authors have displayed that apo B levels have a strong correlation with diabetic microvascular complications, and with the advancement of nephropathy grade, apo B level is significantly increased with the existence of at least one microvascular complication which associates positively with great values of apo B. [9]

The aim of the present study was to assess the correlation of Apo-lipoprotein B and dyslipidemia in Type 2 Diabetes mellitus and its relation with Albuminuria.

Materials and Methods

This Cross-Sectional Study was conducted in the Department of Medicine, Government medical College and Hospital, Madhepura, Bihar, India from July 2022 to June 2023 with 100 patients.

Inclusion criteria: Age of the patient more than 18 years less than 70 years. All patients with Type 2diabetes mellitus were diagnosed with fasting glucose of more than 126mg/dl, postprandial more than 200mg/dl with symptoms, and HbA1c more than or equal to 6.5gm%.

Exclusion criteria: Patients who are taking lipid-lowering drugs within 6 weeks and weight-reducing diet. Patients with hypothyroidism, familial dyslipidemia, familial hypercholesterolemia, and alcoholics to avoid a false increase in apolipoproteins.

Written informed consent was taken from the patients with Type 2 Diabetes mellitus who fulfill the inclusion and exclusion criteria will be enrolled in the study.

Clinical examination and investigations will be done and data will be collected using a proforma (Annexure- 2). After detailed history taking, thorough clinical examination, the following investigations are done.

- Complete hemogram
- fasting lipid profile
- HBA1C
- Fasting Blood sugar , Postprandial blood sugar level.
- Urine routine, Spot PCR
- Serum ApoB levels using immunoturbidimetric method.
- RFT

Results

Table 1: Demographic characteristics of study population

Characteristic		values
AGE (years), mean ±SD		52.48±12.96
Sex, n(%)	Female	55 (55%)
	Male	45 (45%)
Comorbidities, n(%)	HTN	52 (52%)
	IHD	14 (14%)
	CKD	6 (6%)
	CVA	6 (6%)
	Hypothyroidism	3 (3%)
	Other	10 (10%)
	None	9 (9%)

Mean age of the study population was found to be 52.48±12.96 years with minimum and maximum age being 22 and 75 respectively. Among 100 patients, 55 (55%) and 45 (45%) patients were accordingly female and male. It was observed that 52 (52%), 14 (14%), 6 (6%), 6 (6%), 3 (3%), and 10 (10%) patients had HTN, IHD, CKD, CVA, Hypothyroidism and Other comorbidities correspondingly. Total of 9 (9%) patients had no comorbidities at all.

Table 2: Association of HbA1c with urine ACR and retinopathy

Variables		HbA1C			p- value
		<7	>7	total	
Fundoscopy	Normal	12	30	52 (52%)	0.163
	NPDR	8	24	32 (32%)	
	PDR	0	16	16 (16%)	
ACR, median(IQR)		284(146.05-931.10)	404(88.20-980.00)	371.5(88.00-960.5)	0.975

Total of 20 (20%) and 80 (80%) patients belonged to HbA1c values <7 and >7 groups respectively.

Table 3: Fasting Lipid Profile and its association with proteinuria (urine ACR)

Lipid		ACR, median (IQR)	P value
TC	0-200	283.80(68.03-946.00)	0.220
	201-220	434.00(272.00-960.1)	
	>220	778.1(624-1008)	
LDL	≤115	281(74.36-907.5)	0.120
	116-145	667.05(275.00-984.55)	
	>145	849.00(735-1089)	
VLDL	≤30	404(54.76-1103)	0.634
	>30	350(107.90-871)	
HDL	<40	234(44.025-845.2)	0.092
	40-50	954(202-1409.64)	
	>50	548(113.025-1122.65)	
Triglyceride	0-10	404(52.095-998.2)	0.803
	11-200	713.6(81.5775-1158.8)	
	>200	350(144.5-770.5)	

Distribution of ACR values with respect to different ranges of TC was not statistically significant (P value >0.05). Distribution of ACR with respect to HDL levels was fond to be suggestively significant at 91% level of confidence. Different level of triglyceride (0-10, 11-200 and >200) distribution of ACR (404(52.095-998.2), 713.6(81.5775-1158.8) and 350(144.5-770.5)) was not statistically significant.

Table 4: Serum Apo-lipoprotein association with urine MCR

Apo-lipoprotein		ACR, median (IQR)	P value
APOA1	≤120	356 (87.2-931.1)	0.515
	>120	438 (145-1089)	
APOB	<99	273.7 (62.82-885.25)	0.184
	100-119	468 (75.755-1018.5)	
	120-139	473.5 (147-1029.4)	
	≥140	813.57 (590-1016.425)	
ApoB/Apo A ratio	<0.6	496 (294.32-818.675)	0.981
	0.6-0.8	318.2 (144.75-921)	
	>0.8	339.6 (80.6775-965.05)	

There was no significant difference was established in distribution of ACR with respect different levels of APO-A1, APO- B and APO B/APO A1.

Table 5: Correlation between ACR and some biochemical parameters

Variables	Pearson correlation coefficient	P- Value
TC	0.4	0.00028
TG	0.34	0.0012
LDL	0.47	<0.0001

VLDL	0.24	0.032
HDL	-0.038	0.64
ApoA1	0.1	0.32
ApoB	0.32	0.0048
Apo B/Apo A Ratio	0.078	0.36

Significant positive correlation was found among TC, TG, LDL VLDL, and ApoB with correlation coefficient of 0.4, 0.34, 0.47, 0.24 and 0.32 respectively (P value<0.05).

Discussion

The burden of diabetes is mainly due to macrovascular and microvascular complications, including coronary heart disease, stroke, peripheral vascular disease, retinopathy, neuropathy, nephropathy, and lower-extremity amputations. [10] Dyslipidemia inT2DM is a major risk factor of CVD. Dyslipidemia is characterized by low high-density lipoprotein (HDL) and high triglyceride (TG) and small density low- density lipoprotein (SDLDL). [11] Total plasma Apo B is a reliable surrogate for true low-density lipoprotein particle number, regardless of size, because it is an accurate measure of the total number of very low-density lipoprotein and low-density lipoprotein particles. [12]

Mean age of the study population was found to be 52.48±12.96 years with minimum and maximum age being 22 and 75 respectively. Among 100 patients, 55 (55%) and 45 (45%) patients were accordingly female and male. It was observed that 52 (52%), 14 (14%), 6 (6%), 6 (6%), 3 (3%), and 10 (10%) patients had HTN, IHD, CKD, CVA, Hypothyroidism and Other comorbidities correspondingly. Total of 9 (9%) patients had no comorbidities at all. The considerable sex-ratio differences are observed across countries and this may be due to the influence of differences in biology, culture, lifestyle, environment, and socioeconomic level. [13] There are also reports which claim that gender had no significance role in the prevalence of disease. [14] Total of 20 (20%) and 80 (80%) patients belonged to HbA1c values <7 and >7 groups respectively. It has been reported that microalbumin levels in urine is predictive of elevated HbA1c levels and the spot urine albumin-creatinine ratio is a stronger indicator of microalbuminuria (urinary ACR). [15]

Distribution of ACR values with respect to different ranges of TC was not statistically significant (P value >0.05). Distribution of ACR with respect to HDL levels was fond to be suggestively significant at 91% level of confidence. Different level of triglyceride (0-10, 11-200 and >200) distribution of ACR (404(52.095-998.2), 713.6(81.5775-1158.8) and 350(144.5-770.5)) was not statistically significant. Elevated TG, LDL and reduced HDL are linked to T2DM. [16] The abnormal levels of TG, LDL and HDL are associated with increased risk of cardiovascular complications. [17] Abnormal lipid profile in type 2 diabetes is due to increased fatty acid flow due to insulin resistance. In our study, the increasing trend of TC, TG, LDL and VLDL with increasing severity of proteinuria was observed. Distribution of patients with respect to lipid profiles and severity of proteinuria did not show any significant difference.

There was no significant difference was established in distribution of ACR with respect different levels of APO- A1, APO- B and APO B/APO A1. Significant positive correlation was found among TC, TG, LDL VLDL, and ApoB with correlation coefficient of 0.4, 0.34, 0.47, 0.24 and 0.32 respectively (P value<0.05). Positive linear correlation of TG and LDL as well as negative correlation of HDL with ApoB was reported by Kumar et al, (2019). [18,19] Similar result was also reported by Wambugu and Beatrice (2014) but they did not report the association with HDL. [20]

Conclusion

In the present study, there was a significant positive correlation between Apolipoprotein B and albuminuria among patients with type 2 diabetes mellitus. There was also a positive correlation between Apolipoprotein B and dyslipidemia among these patients, who showed elevated total cholesterol, LDL cholesterol, and triglyceride levels. However, the present study did not find any significant correlation between HbA1c levels and urinary ACR values among these patients.

References

1. Jiang R, Schulze MB, Li T, Rifai N, Stampfer MJ, Rimm EB, Hu FB. Non-HDL cholesterol and apolipoprotein B predict cardiovascular disease events among men with type 2 diabetes. Diabetes care. 2004 Aug 1;27(8): 199 1-7.
2. Expert Panel on Detection E. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). Jama. 2001 May 16;285 (19):2486-97.
3. Snehalatha C, Ramachandran A, Sivasankari S, Satyavani K, Viswanathan V, Misra J, Girinath MR, Sathyamurthy I. Is increased apolipoprotein BA major factor enhancing the risk of coronary artery disease in type 2

diabetes?. The Journal of the Association of Physicians of India. 2002 Aug 1;50:1036-8.
4. Walldius G, Jungner I. The apoB/apoA-I ratio: a strong, new risk factor for cardiovascular disease and a target for lipid-lowering therapy–a review of the evidence. Journal of internal medicine. 2006 May;259(5):493-519.
5. Kim BJ, Hwang ST, Sung KC, Kim BS, Kang JH, Lee MH, Park JR. Comparison of the relationships between serum apolipoprotein B and serum lipid distributions. Clinical chemistry. 2005 Dec 1;51(12):2257-63.
6. Wägner AM, Pérez A, Calvo F, Bonet R, Castellvi A, Ordóñez J. Apolipoprotein (B) identifies dyslipidemic phenotypes associated with cardiovascular risk in normocho lesterolemic type 2 diabetic patients. Diabetes Care. 1999 May 1;22(5):812-7.
7. Zhang X, Nie Y, Gong Z, Zhu M, Qiu B, Wang Q. Plasma apolipoproteins predicting the occurrence and severity of diabetic retinopathy in patients with type 2 diabetes mellitus. Frontiers in Endocrinology. 2022 Jul 22;13:915575.
8. Krishnamoorthy R, Kaliaperumal R, Venkatachalam R, Poovitha R, RAJAGOPALAN G. Apolipoproteins an Early and Better Diagnostic Marker for Diabetic Retinopathy. Journal of Clinical & Diagnostic Research. 2017 Oct 1;11(10).
9. Rizk MN, Aly H, Samir P, Mofty HE, Allah OK. Apolipoprotein B level and diabetic microvascular complications: is there a correlation?. The Egyptian Journal of Internal Medicine. 2013 Sep;25:137-42.
10. Harding JL, Pavkov ME, Magliano DJ, Shaw JE, Gregg EW. Global trends in diabetes complications: a review of current evidence. Diabetologia. 2019;62(1):3-16.
11. Shulman GI. Ectopic fat in insulin resistance, dyslipidemia, and cardiometabolic disease. N Engl J Med. 2014 Sep 18;371(12):1131-41.
12. Rizk MN, Aly H, Samir P, el Mofty H, Allah OK. Apolipoprotein B level and diabetic microvascular complications: is there a correlation?. Egypt J Intern Med 2013;25:137–142.
13. Kautzky-Willer A, Harreiter J, Pacini G. Sex and Gender Differences in Risk, Pathophy siology and Complications of Type 2 Diabetes Mellitus. Endocr Rev. 2016;37(3): 278-316.
14. Pramayudha R., Achmad C., Erwinanto et al. 2018. Correlation between HbA1c Levels with Carotid Intima Media Thickness in Newly Diagnosed Type 2 Diabetes Mellitus Patients. ACI (ActaCardiologiaIndonesiana) 5 (2): 111-118.
15. US Renal Data System. USRDS 2013 annual data report: atlas of chronic kidney disease and end-stage renal disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Digestive and Kidney Diseases, Vol. 2014. 2013.
16. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2011 Jan;34 Suppl 1(Suppl 1):S62-9.
17. Krauss RM. Lipids and Lipoproteins in Patients With Type 2 Diabetes. Diabetes Care. 2004; 27 (6): 1496–1504.
18. World Health Organization . Abbreviated Report of a WHO Consultation. Geneva: WHO; 2011. Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus.
19. Yau JW, Rogers SL, Kawasaki R, et al; Meta-Analysis for Eye Disease (META-EYE) Study Group. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012 Mar;35(3):556-64.
20. Waeber B, Feihl F, Ruilope L. Diabetes and hypertension. Blood Press. 2001;10(5-6):311-2 1.