

An Analytical Comparative Assessment of Serum Lipid Profile and Serum Lipo-Protein (A) in Type II Diabetes Mellitus Patients and Non-Diabetics

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Abstract

Aim: To evaluate the serum lipid profile and lipoprotein (a) levels in comparison to patients with type II diabetics with non-diabetics and to study the serum lipid profile and lipo-protein (a) levels in comparison to patients with type II diabetics on oral hypoglycemic agents and type II diabetics on insulin.

Methodology: This cross-sectional study was carried out in the Department of Medicine, Darbhanga Medical College and Hospital, Darbhanga, Bihar for 15 months. 100 diagnosed type 2 diabetic cases and 100 non-diabetic people with the age range of 31 to 60 years were selected by non-probability consecutive sampling. Informed consent from each subject were taken before the collection of samples. All the data were processed and analyzed using Microsoft excel and IBM-SPSSv22.0 for Windows. Statistical inference was based on 95% confidence interval and p value<0.05 was considered statistically significant. Variables were expressed as mean \pm standard error of means (SEM).

Results: The distribution of sex in diabetic cases, N=100 (male/female-46/54) and in non-diabetic people, N=100 (male/female-45/55). There were significant differences of FPG and HbA1c% in diabetics and non-diabetics. Serum Lp(a), total cholesterol, TG and LDL were significantly higher in diabetics than that of non-diabetics and serum HDL was significantly lower in diabetics than non-diabetics. Subjects with normal Lp(a) level were 15% in diabetics and 77% in non-diabetics and 19% patients had Lp(a) level in borderline risk group and in non-diabetics it was 23%, again in cases 66% patients were found in high-risk group. The comparison of type 2 diabetes mellitus patients with non-diabetic people with an χ^2 value=59.6 and odds ratio=21.65 for increased Lp(a). These were statistically significant i.e., there was association of increased Lp(a) with type 2 diabetes mellitus.

Conclusion: In conclusion, there was statistically significant difference in lipid profile level between diabetic patients and apparently healthy controls. From the present study we can conclude that type 2 diabetes mellitus is strongly associated with increased Lp(a) levels. Elevated Lp(a) levels promote atherosclerosis and thrombosis. So, Lp(a) may be a new metabolic syndrome risk factor and it may be useful as a cardiovascular risk biomarker in future clinical practice.

Keywords: Lipid, Diabetes mellitus, hyperglycemia, Cholesterol.

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Introduction

Diabetes mellitus is the most common endocrinal disease in the world today [1]. It is the major health problem affecting people all over the world. It is one of the most extensively investigated human diseases. The prevalence of disease has significantly increased worldwide and projected to increase in future. Amongst the various ethnic groups, Asian Indians seems to be at a particularly greater risk of developing diabetes [1]. Diabetes mellitus is a syndrome characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative deficiencies in insulin secretion and or insulin action. Dyslipidemia, one of the most common DM related comorbidities, refers to the increase of total cholesterol or/and triglycerides in the serum [2].

Lipid abnormalities are prevalent in DM patients because of insulin resistance (IR) which affects key enzymes and pathways in lipid metabolism: Apo protein production, regulation of lipoprotein lipase, action of cholesterol ester transfer proteins and hepatic and peripheral actions of insulin [3]. Hyperglycemia and the high level of IR associated with T2DM has multiple effects on fat metabolism which results in the production of atherogenic dyslipidemia characterized by lipoprotein abnormalities: elevated very low density lipoprotein cholesterol (VLDL) elevated low density lipoprotein cholesterol (LDL-c), elevated triacylglycerol (TAG) and decreased high density lipoprotein cholesterol (HDL-c) which are measured for cardiovascular risk prediction [4-8].

Patient with Type I DM are generally not hyperlipidemic if they are under good glycemic control. But patient with Type II DM are usually dyslipidemic even if under relative good glycemic control [9]. They have several lipid abnormalities including

elevated plasma triglycerides, elevated Low Density Lipoprotein-Cholesterol (LDL-C) and decreased High Density Lipoprotein-Cholesterol (HDL-C). Insulin deficiency or insulin resistance diverts carbohydrate away from muscle glycogen storage into hepatic de novo lipogenesis, thus leading to the increase of plasma triglyceride concentration. The most common lipid abnormality noted in diabetics is hypertriglyceridemia [2]. Moreover oxidation of the LDL particles result in its increased incorporation in the arterial wall via a receptor independent pathway resulting in high incidence of cardiovascular and cerebrovascular disease in DM individuals [10]. The plasma cholesterol level is a strong predictor of the risk of cardiovascular events in patients with diabetes [11].

This study helps us in evaluating the present Indian scenario of lipid and diabetic portfolio, and advices about how aggressive a treatment should be for immediate control of blood sugars and lipids are to minimize the cardiovascular risks. The aim of the study was to evaluate the serum lipid profile and lipoprotein (a) levels in comparison to patients with type II diabetics with non-diabetics and to study the serum lipid profile and lipo-protein (a) levels in comparison to patients with type II diabetics on oral hypoglycemic agents and type II diabetics on insulin.

Materials and Methods

This cross-sectional study was carried out in the Department of Medicine, Darbhanga Medical College and Hospital, Darbhanga, Bihar for the period of 15 months

100 diagnosed type 2 diabetic cases and 100 non-diabetic people with the age range of 31 to 60 years were selected by non-probability consecutive sampling.

Informed consent from each subject were taken before the collection of samples. Patients with GDM, stroke, IHD, renal failure, liver failure, malignant diseases and acute infection were excluded from the study.

All the data were processed and analyzed using Microsoft excel and IBM-SPSSv22.0 for Windows. Statistical inference was based on 95% confidence

interval and p value<0.05 was considered statistically significant.

Results:

The distribution of sex in diabetic cases, N=100 (male/female-46/54) and in non-diabetic people, N=100 (male/female-45/55).

Table 1: Distribution of gender in diabetic cases and non-diabetic people.

Gender	Diabetic (100%)	Non-diabetic (100%)
Males	46%	45%
Females	54%	55%

There were significant differences of FPG and HbA1c% in diabetics and non-diabetics. Serum Lp(a), total cholesterol, TG and LDL were significantly higher in diabetics than that of non-diabetics and serum HDL was significantly lower in diabetics than non-diabetics.

Table 2: Comparison of fasting plasma glucose and HbA1c% amongst diabetics and non-diabetics by t-test significance.

Variables	Diabetics	Nondiabetics	P value	Significance
Fasting plasma glucose (mmol/l)	8.74±0.45	5.23±0.14	<0.05	Significant
HbA1c%	8.02±0.18	5.34±0.10	<0.05	Significant

Table 3: Comparison of Lipid parameters amongst diabetics (N=100) and non-diabetics (N=100) by t-test significance.

Variables	Diabetics	Nondiabetics	P value	Significance
Serum Lp (a) (mg/dl)	44.35±3.1	12.98±0.77	<0.05	Significant
T. Cholesterol (mg/dl) (Mean±SEM)	217.6±5.0	176.46±3.14	<0.05	Significant
Serum TG (mg/dl) (Mean±SEM)	190.9±6.88	122.9±2.04	<0.05	Significant
S. LDL (mg/dl) (Mean±SEM)	132.6±3.53	87.88±0.98	<0.05	Significant
S. HDL (mg/dl) (Mean±SEM)	37.7±0.8	50.34±0.78	<0.05	Significant

Subjects with normal Lp(a) level were 15% in diabetics and 77% in non-diabetics and 19% patients had Lp(a) level in borderline risk group and in non-diabetics it was 23%, again in cases 66% patients were found in high-risk group.

Table 4: Frequency distribution of serum Lp(a) level in diabetics (N=100) and non-diabetics (N=100).

Variables	Diabetics	Non-diabetics
Normal Lp(a) (<14 mg/dl)	15	77
≥14-≤30 mg/dl (Borderline high)	19	23
>30 mg/dl (High risk)	66	00

Total cholesterol, LDL-cholesterol were significantly higher in >30 mg/dl group compared to that of <30 mg/dl group in diabetic cases.

Table 5: Comparison of fasting serum lipid profile between Lp(a)≤30 mg/dl group and >30 mg/dl group in diabetics cases (n=100) by t-test significance.

Variables	Lp(a)≤30 mg/dl	Lp(a)>30 mg/dl	P value	Significance
Total cholesterol (mg/dl) (Mean±SEM)	196.89±5.46	230.32±6.22	<0.05	Significant
Serum TG (mg/dl) (Mean±SEM)	191.88±15.12	191.34±8.12	>0.05	Not significant
Serum LDL (mg/dl) (Mean±SEM)	114.10±5.42	141.8±4.24	<0.05	Significant
Serum HDL (mg/dl) (Mean±SEM)	38.6±1.32	36.9±0.82	>0.05	Not significant

There was significant differences of serum Lp(a) level between good and poor glycaemic control in diabetics cases.

Table 6: Distribution of serum Lp(a) level according to glycaemic status in diabetics cases.

Glycemic status	HbA1c>7%	HbA1c≤7%	P value	Significance
HbA1c%	52.34±2.98	45.34±3.83	<0.05	Significant

The comparison of type 2 diabetes mellitus patients with non-diabetic people with an χ^2 value=59.6 and odds ratio=21.65 for increased Lp(a). These were statistically significant i.e., there was association of increased Lp(a) with type 2 diabetes mellitus.

Table 7: Association between type 2 diabetes mellitus and serum Lp(a) levels.

Groups	Category of Lp(a)			χ^2 value and Odds ratio	P value (significance)
	Lp(a)≥14 mg/dl	Lp(a)<14 mg/dl	Total		
Type 2 diabetic cases	85	15	100	$\chi^2=59.6$	<0.05 (significant)
Nondiabetic People	23	77	100	Odds ratio=21.65	<0.05 (significant)

Discussion:

Diabetes mellitus is the most common metabolic degenerating disease affecting mainly carbohydrate, lipid and protein metabolism. Diabetes mellitus is mainly due to insulin deficiency or insulin resistance. Insulin being an anabolic hormone its deficiency causes hyperglycemia due to increased gluconeogenesis and glycogenolysis and it affects lipid and protein metabolism by causing increased lipolysis which leads to ketosis and ketoacidosis and it affects overall protein biosynthesis which causes increased circulating amino acid pool. Insulin plays a central role in regulating blood glucose. Deficiency of insulin or resistance to the action of insulin as seen in the diabetes mellitus is characterized by

hyperglycemia. According to WHO criteria FPG \geq 126 mg/dl on 2 occasions is diagnostic of diabetes mellitus.2 Random blood glucose \geq 200 mg/dl on 2 occasions is also diagnostic of diabetes mellitus [2].

Previous study reported that lipid compositions of various tissues altered in diabetes [12]. Hence, it is postulated that circulatory lipids play a vital role in progression of T2DM, not only by way of lipid abnormalities but also by modifying the composition, structure and firmness of cellular membranes [12]. Several studies reported high levels of TAG, TC and LDL-c among diabetic patients, a finding observed in the present study too. However, another study in Nigeria reported a different finding [13] which is higher TAG in controls. The main cause

for lipid abnormalities in T2DM patients is impaired secretion of insulin that affects the liver apolipoprotein production and regulates the enzymatic activity of lipoprotein lipase (LpL) and cholesterol ester transport protein (CETP). Moreover, its deficiency reduces the activity of hepatic lipase; therefore, several steps involved in the production of biologically active LpL might be altered in T2DM compared to controls.

This study showed the significant difference of FBS, HbA1c% and serum cholesterol, LDL, HDL and TG between diabetic cases and non-diabetic people. It has been established that patients with type 2 DM have increased morbidity and mortality due to coronary risk events. This increased risk has been shown to be independent from conventional risk factors [14]. Different factors have been found to be responsible for an increased prevalence of CAD in DM. One of these are the elevated levels of serum Lp(a) [15]. Our study has revealed that Lp(a) levels were significantly elevated in diabetic patients than non-diabetic people. In this study, increased serum Lp(a) was also significantly associated with type 2 diabetes mellitus patients ($\chi^2=59.6$, $p<0.05$). The current data of increased serum Lp(a) level in type 2 diabetes mellitus patient was similar to the studies done by other authors like Singla, Ogbera, Joseph, Ziaee [16-19].

In another studies the researchers failed to demonstrate the association of serum Lp(a) with type 2 diabetes mellitus [20, 21]. The possible reason could be the large size of apo(a) isoforms leading to lower Lp(a) levels [22]. This study showed that 86% type 2 diabetic patients had increased serum Lp(a) level. Again, in diabetic cases 19 patients had serum Lp(a) level in borderline risk group (>14 to 30 mg/dl) and in non-diabetics, 23 subjects were found to be in this group. On the other hand, 66 patients had Lp(a) level in high-risk group (>30 mg/dl). Total cholesterol,

LDL-cholesterol were significantly higher in Lp(a)>30 mg/dl group compared to that of Lp(a) 30mg/dl) has been considered as an important predictor of vascular disease in type 2 diabetes mellitus patients [23-25]. The author also suggested that gaining metabolic control have a positive effect on serum Lp(a) level. The mechanism of elevated Lp(a) in diabetes mellitus is glycation of its apolipoproteins, which causes decreased metabolism of Lp(a). Glycation also prolongs the half-life of Lp(a), which may leads the higher plasma concentration of Lp(a) in diabetes mellitus [26,27].

Conclusion:

In conclusion, there was statistically significant difference in lipid profile level between diabetic patients and apparently healthy controls. From the present study we can conclude that type 2 diabetes mellitus is strongly associated with increased Lp(a) levels. Elevated Lp(a) levels promote atherosclerosis and thrombosis. So, Lp(a) may be a new metabolic syndrome risk factor and it may be useful as a cardiovascular risk biomarker in future clinical practice.

References:

1. Enas.A. "Prevalence of coronary artery disease in Asian Indians". American journal of cardiology, 1992; 70:945-950.
2. Burtis C.A, Ash wood E.R. Tietze Text book of Clinical Chemistry. 3 end: W.B. Saunders Company; 1999: 512 and 790-791.
3. Frank B, Stampfer J, Steven M. Elevated risk of cardiovascular disease prior to clinical diagnosis of type 2 diabetes. Diabetes Care. 2002;25:1129-1134.
4. Shahid SH. Frequency distribution of atherogenic dyslipidemia in Saudi type 2 diabetic patients. Pak J physiol. 2006; 2(2):20-23.
5. Grundy SM, Cleeman JI, Merz CN, Brewer HB, Jr, Clark LT,

- Hunninghake DB. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation*. 2004;110(2):227–239.
6. Nigam PK. Serum Lipid Profile: Fasting/Non-fasting? *Ind J Clin Biochem*. 2011;26(1):96–97.
 7. Mullugeta Y, Chawla R, Kebede T, Worku Y. Dyslipidemia Associated with Poor Glycemic Control in Type 2 Diabetes Mellitus and the Protective Effect of Metformin Supplementation. *Ind J Clin Biochem*. 2012;27(4):363–369.
 8. Maitra A. The Endocrine System. In: Kumar V, Abbas AK, Fausto N, Aster JC, editors. *Robbins and Cotran Pathologic Basis of Disease*. 8th ed. New Delhi: Elsevier. 2010:1097–1164.
 9. Study of Lipid Profile and Glycated Hemoglobin in Diabetes Mellitus S.W. Masram, M.V. Bimanpalli, Suresh Ghangle, *Indian Medical Gazette*. 2012; 257-265
 10. Gopalan C. Raising incidence of obesity and diabetes, *Nutrition Foundation of India*; 2006.
 11. Rosengren A, Welin L, Tsipogianni A, Wilhelmsen L. Impact of cardiovascular risk factors on coronary heart disease and mortality among middle aged diabetic men: a general population study. *BMJ*. 1989;299:1127–1131.
 12. Leticia AS, Deoliveira MS, Paula Salles AMF, Das Graças MC. Hemostatic changes in patients with type 2 diabetes mellitus. *Rev Bras Hematol Hemoter*. 2010;32(6):482–488.
 13. Oluyomia EOB, Fisayo AM, Bayodea FJ, Kehindea FM, Adedayo Ademigbuji E. Lipid profile of a group of Nigerian diabetic patients. *Archives of Appli Sci Research*. 2010;2(4):302–306.
 14. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors and 12-yr cardiovascular mortality for men screened in the multiple risk factor intervention trial. *Diab Care*. 1993;16(2):434–44.
 15. Kostner KM, Kostner GM. Lipoprotein (a): a historical appraisal. *J Lipid Res*. 2017;58(1):1–14.
 16. Singla S, Kaur K, Kaur G, Kaur H, Kaur J, Jaswal S. Lipoprotein (a) in type 2 diabetes mellitus: Relation to LDL:HDL ratio and glycemic control. *Int J Diabetes Dev Ctries*. 2009; 29(2): 80–4.
 17. Ogbera AO, Azenabor AO. Lipoprotein(a), C-reactive protein and some metabolic cardiovascular risk factors in type 2 DM. *Diabetol Metab Syndr*. 2010; 2:51.
 18. Joseph J, Ganjifrockwala F, George G. Serum Lipoprotein(a) Levels in Black South African type 2 diabetes mellitus patients. South Africa: Hindawi Publishing. 2016.
 19. Ziaee A, Sarreshtedari M, Abrishamchian N, Karimzadeh T, Oveisi S, Ghorbani A. Lipoprotein(a) in patients with type 2 diabetes compared with nondiabetic patients. *IJDO*. 2011;3(1):19–24.
 20. Månsson M, Kalies I, Bergström G, Schmidt C, Legnehed A, Hultén LM, et al. Lp(a) is not associated with diabetes but affects fibrinolysis and clot structure ex vivo. *Sci Rep*. 2014; 4:5318.
 21. Liu C, Xu MX, He YM, Zhao X, Du XJ, Yang XJ. Lipoprotein(a) is not significantly associated with type 2 diabetes mellitus: cross-sectional study of 1604 cases and 7983 controls. *Acta Diabetol*. 2017;54(5):443–53.
 22. Structure and reference value of Lp(a). Available at: <https://Wikipedia.org/wiki/Lipoprotein>. Accessed on 06 February 2018.
 23. Tsimikas S. Lp(a) as a new target for reduction of risk of cardiovascular disease and emergence of novel therapies to lower Lp(a). *Curr Opin Endocrinol Diabetes Obes*. 2016;23(2): 157–64.

24. Nicholls SJ, Tang WH, Scoffone H, Brennan DM, Hartiala J, Allayee H, et al. Lipoprotein(a) levels and long-term cardiovascular risk in the contemporary era of statin therapy. *J Lipid Res.* 2010;51(10):3055-61.
25. Morita Y, Himeno H, Yakuwa H, Usui T. Serum lipoprotein(a) level and clinical coronary stenosis progression in patients with myocardial infarction: revascularization rate is high in patients with highLp (a). *Circ J.* 2006; 70(2):156-62.
26. Ramirez LC, Arauz-Pacheco C, Lackner C, Albright G, Adams BV, Raskin P. Lipoprotein(a) levels in diabetes mellitus: relationship to metabolic control. *Ann Intern Med.* 1992;117(1):42-7.
27. Acendra A. H. Y., Sampayo F. H., Robles A. C. W., Ariza M. A. V., León J. S. T., & Badillo L. Y. E. Association between Guillain-Barré Syndrome and Application of the Janssen Vaccine. *Journal of Medical Research and Health Sciences*, 2022; 5(4): 1950–1954.