(RESEARCH ARTICLE)

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Extended lipid profile and urine albumin-creatinine ratio in type 2 diabetes mellitus

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Abstract

Background: Diabetes is a chronic metabolic disorder and has become the one of the most challenging global health problem of 21 st centuary. Diabetic nephropathy is a major complication of diabetes and an established risk factor for cardiovascular events. Lipid abnormalities occur in patients with diabetic nephropathy, which further increase their risk for cardiovascular events. We aimed to research association between extended lipid profile and urine albumin-creatinine ratio (UACR), hypothesizing that early detection and treatment of lipid abnormalities can minimize the risk for atherogenic cardiovascular disorder and cerebrovascular accident in patients with type 2 diabetes mellitus.

Methods: A hospital based cross- sectional study was conducted on 48 patients with type 2 diabetes mellitus. All patients fasting blood glucose (FBG), HbA1c, total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), triglyceride (TG), apolipoprotein-A (apo-A), apolipoprotein-B (apo-B), lipoprotein (a){Lp(a)} and urine-albumin creatinine ratio (UACR) evaluated. Patients taking steroids, any renal disease other than diabetic nephropathy and patients of uncontrolled hypertension were excluded from study. Based on UACR level patients were divided into three sub groups: normal (<30 mg/g), microalbumiuria (30-300 mg/g) and macroalbuminuria (>30 mg/g). Comparison between three subgroups of UACR and extended lipid profile was made using non parametric test (Kruskal Willis Test). Fisher's exact test was used to explore the association between UACR and extended lipid profile.

Result: 20.8% patients had UACR<30 mg/g, 54.2% patients had UACR:30-300 mg/g, 25.0% patients had UACR:≥300 mg/g; 62.5% patients had Lipoprotein(a): <30 mg/dl and 37.5% patients had Lipoprotein(a): > 30 mg/g. Significant association was found between UACR and Lipoprotein(a):

- 100.0% of the patients with [UACR: <30 mg/g] had [Lipoprotein-a: <30mg/dL].
- 57.7% of the patients with [UACR: 30-300 mg/g] had [Lipoprotein-a: <30 mg/dL].
- 42.3% of the patients with [UACR: 30-300 mg/g] had [Lipoprotein-a: ≥30 mg/dL].
- 41.7% of the patients with [UACR: >300 mg/g] had [Lipoprotein-a: <30 mg/dL].
- 58.3% of the patients with [UACR: >300 mg/g] had [Lipoprotein-a: ≥30 mg/dL].

Conclusion: The study showed that diabetic nephropathy resulting in raised UACR has significant association with increased lipoprotein (a) and consequently increased risk of atherosclerotic cardiovascular disease (ASCVD). Since Lipoprotein(a) investigation is not widely available, accessible and has varied estimation technique, UACR can be used as a marker of risk for ASCVD in place of Lipoprotein(a) in type 2 DM.

Keywords: Extended lipid profile; UACR; DM type 2; Diabetic nephropathy; Marker for ASCVD

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1. Introduction

Diabetes Mellitus is one of the most challenging health problem of 21 st century and has become global health problem now. The global diabetes prevalence in 2019 is estimated to be 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045. The prevalence is higher in urban (10.8%) than rural (7.2%) areas, and in high- income (10.4%) than low-income countries (4.0%) (1). Overall prevalence of Diabetes in India is 8.7% in the age group of 20 and 70 years (2).

Plasma lipid and lipoprotein abnormalities in diabetes, includes a significantly higher concentration of total cholesterol, triglycerides and low density lipoprotein (LDL) cholesterol and apolipoprotein-B (Apo-B), but a lower concentration of high density lipoprotein (HDL) cholesterol and apolipoprotein-A (Apo-A) (3). Progressive diabetic renal disease occurs in 20-40% of patients with diabetes and is the leading cause of end stage renal disease. Persistent increased albuminuria in the range of UACR 30-299 mg/g is an early indicator of diabetic kidney disease and is a marker for development of progressive diabetic kidney disease in type 2 diabetes.

Diabetic dyslipidemia is characterised by elevated fasting and post prandial triglycerides (TGL), low HDL-cholesterol, elevated LDL-cholesterol with predominance of lipoprotein (a).

Dyslipidemia concurrently with persistent increased albuminuria is considered as an alarming signal for both atherosclerotic cardiovascular disease (ASCVD) and end stage renal disease (ESRD). Detection of dyslipidemia with a corresponding increased UACR in the early setting of diabetes mellitus and its therapeutic intervention could control the resulting cardiovascular and renal complications (4,5). In this study we evaluate the individual fractions of Extended lipid profile and UACR in subjects with Type-2 Diabetes mellitus and try to find out any association between Extended lipid profile and UACR in patients of type2 DM.

2. Material and methods

Hospital based Cross Sectional study was conducted at a tertiary care hospital in India after obtaining necessary ethical clearance. After taking proper informed consent, 48 adult patients, aged18 years or older with T2DM were taken as study subject. Subjects with uncontrolled hypertension, taking steroids, urinary tract infection, hematuria, thyroid dysfunction and any renal disease other than diabetic nephropathy were excluded from study. CBC, LFT, KFT, fasting BS, 2 hours PPBS, HbA1c, URM, UACR, Lipid profile and Extended lipid profile was done. Extended lipid profile was done by ELISA based kits and reader. UACR was done in Beckman coulter AU 680 Machine using urine albumin and urine creatinine insert method. [Urine Albumin (mg/dl) / Urine Creatinine (g/dl) = UACR in mg/g = Albumin excretion in mg/day].Study subjects were divided according to UACR as normal (<30mg/g), microalbuminuria (30-300mg/g) and macroalbuminuria (>300mg/g).

2.1. Statistical analysis

The observations were compiled, tabulated and analysed statistically using MS EXCEL spreadsheet and SPSS. Continuous data was presented as mean and standard deviation. Proportion of deranged Extended lipid profile and UACR was calculated. Comparison between three subgroups of UACR and Extended lipid profile was made using non parametric test (Kruskal Willis Test). Fisher's exact test was used to explore the association between UACR and Extended lipid profile.

3. Results

In this study the mean age was 56 years and most of the patients (85.4 %) falling under the age group of 41 to 70 years. The female: male ratio was 1.4:1. Most of the patients (91.5%) have uncontrolled blood sugar with HbA1c >7. Majority of patients (54.2%) had microalbuminuria (UACR:30-300 mg/gm), 25.0% patients had macroalbuminuria (>300mg/gm) and 20.8% of the patients had normal UACR(<30 mg/gm). The mean (SD) of Total Cholesterol (mg/dl) was 159.96 (53.11) with 89.6% of the participants had Total Cholesterol: <200 mg/dl and 10.4% of the participants had Total Cholesterol: ≥200 mg/dl. The mean (SD) of Triglycerides (mg/dl) was 146.81(64.10) with 64.6% of the participants had Triglycerides: <150 mg/dl and 35.4% of the participants had Triglycerides: ≥150 mg/dl. The mean (SD) of HDL (mg/dl) was 38.08 (12.54) with 62.5% of the participants had HDL: <40 and 37.5% of the participants had HDL: ≥60. The mean (SD) of LDL (mg/dl) was 101.02 (50.74) with 85.4% of the participants had LDL: <130 mg/dl and 14.6% of the participants had LDL: ≥130 mg/dl. The mean (SD) of Apo-A (mg/dl) was 96.08 (33.91) with 70.8% of the participants had Apo-A: <110 mg/dl and 29.2% of the participants had Apo-A: ≥110 mg/dl. The mean (SD) of Apo-B (mg/dl) was 74.52 (31.00) with 68.8% of the participants had Apo-B: <80 mg/dl and 31.2% of the participants had Apo-

B: ≥80 mg/dl. The mean (SD) of Lipoprotein-a (mg/dl) was 42.61 (51.14) with 62.5% of the participants had Lipoprotein-a**:** <30 mg/dl and **37.5%** of the participants had Lipoprotein-a: ≥30 mg/dl.

There was a significant difference between the various groups of UACR in terms of distribution of Lipoprotein-a ($\chi 2$ = 8.479, p = 0.010) was found with strength of association between the two variables (Bias Corrected Cramer's V) = 0.37 (Moderate Association).

- Participants with UACR: <30 mg/g had the largest proportion of Lipoprotein-a: <30 mg/dl.
- Participants with UACR: >300 mg/g had the largest proportion of Lipoprotein-a: ≥30 mg/dl.

Table 1 Association between UACR and Lipoprotein-a (n = 48)

Lipoprotein-a	UACR				Fisher's Exact Test	
	<30 mg/g	**30-300 mg/g**	**>300 mg/g**	**Total**	**χ2**	**P Value**
<30 mg/dl	10 (100.0%)	15 (57.7%)	5 (41.7%)	30 (62.5%)	8.479	0.010
≥30 mg/dl	0 (0.0%)	11 (42.3%)	7 (58.3%)	18 (37.5%)		
Total	10 (100.0%)	26 (100.0%)	12 (100.0%)	48 (100.0%)		

- 100.0% of the participants with [UACR: <30 mg/g] had [Lipoprotein-a**:** <30 mg/dl].
- 57.7% of the participants with [UACR: 30-300 mg/g] had [Lipoprotein-a: <30 mg/dl].
- 42.3% of the participants with [UACR: 30-300 mg/g] had [Lipoprotein-a: ≥30 mg/dl].
- 41.7% of the participants with [UACR: >300 mg/g] had [Lipoprotein-a: <30 mg/dl].
- 58.3% of the participants with [UACR: >300 mg/g] had [Lipoprotein-a: ≥30 mg/dl].
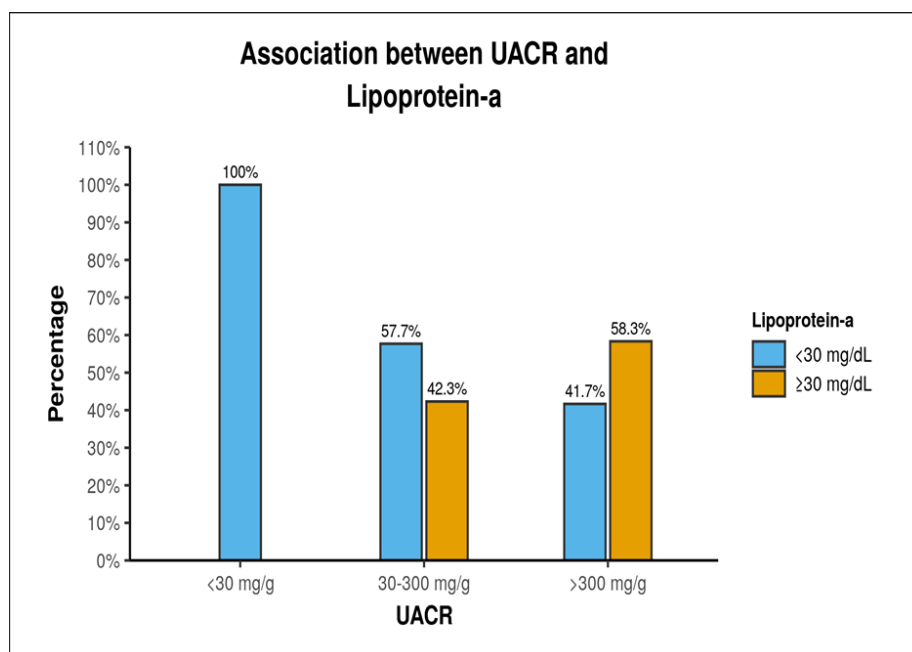
Figure 1 Association between UACR and Lipoprotein-a

There was no significant association was found between various groups of UACR with Apo-A and Apo-B was found among Extended lipid profile.

4. Discussion

In our study mean age of patients was 55.77 years. The youngest patients enrolled in the study was age 31 and the oldest was of 81 years. Majority of the patients (85.4%) were in the 41- 70 age group, with maximum (33.3%) patients were fall in the age group of 61 - 70 years.

In a study conducted by Sana M, Chaudhry M, Malik A, et al. on prevalence of microalbuminuria in type 2 DM it was found that the mean age of the participants was 54.5 ± 10.3 years (49). In our present study females were predominantly affected, 58.3% (28) were females and 41.7% (20) were males; the female to male ratio being 1.4:1.

4.1. Glycemic control of patients

In present study 8.5% (4) of patients had HbA1c level ≤7 % and 91.5% (43) patients had HbA1c level >7%. It was observed that patient having uncontrolled blood glucose with HbA1c >7% are associated with more prevalence of albuminuria, the same was also observed in a study conducted by Sana M, Chaudhry M, Malik A, et al.[7]

4.2. Diabetic nephropathy and UACR of patients

Chronic kidney disease (CKD) in patients with type 2 diabetes is associated with increased risk of end-stage renal disease (ESRD) and cardiovascular disease (CVD). Urine albumin-to-creatinine ratio (UACR) is a sensitive and early indicator of progressive diabetic kidney damage, which should be used routinely to accurately assess CKD stage and to monitor kidney damage.

In our study majority of patients (54.2%) had microalbuminuria (UACR=30-300 mg/gm), 25% patients had macroalbuminuria (UACR > 300mg/g) and only 20.8% of patients had normal UACR (<30mg/g).

In a study conducted by Sana M, Chaudhry M, Malik A, et al. on prevalence of microalbuminuria in type 2 DM it was found that the mean age of the participants was 54.5 ± 10.3 years which included 60.9% males and 39.1% females. The overall incidence of diabetic nephropathy was 30.1%, with 25.6% having microalbuminuria and 4.5% having macroalbuminuria (7).

4.3. Lipid profile of patients

In our study result of serum lipid profile showed that the mean (SD) values for TC, TG, HDL and LDL was 159.96 (53.11) mg/dl; 146.81(64.10) mg/dl; 38.08(12.54) mg/dl and 101.02(50.74) mg/dl respectively, with 89.6% of the participants had TC: <200 mg/dl; 10.4% of the participants had TC: ≥200 mg/dl; 64.6% of the participants had TG: <150 mg/dl; 35.4% of the participants had TG: ≥150 mg/dl; 62.5% of the participants had HDL: <40; 37.5% of the participants had HDL: ≥60; 85.4% of the participants had LDL: <130 mg/dl and 14.6% of the participants had LDL:≥130 mg/dl.

In a study conducted by Chellamma Jayakumari, Puthiyaveetil et al on Lipid Profile in Indian Patients with Type 2 Diabetes, the lipid profiles of patients not taking statins (*n* = 708) was assessed and pattern of dyslipidemia showed that High LDL cholesterol was present in 119 of these patients (16.8%). Four hundred patients (56.5%) and 817 patients (84.1%) had an LDL cholesterol level ≥100 and ≥70 mg/dl, respectively. A TG level ≥250 mg/dl was found in 53 patients (7.49%), whereas 207 patients (29.4%) had a TG level ≥150 mg/dl. Low HDL cholesterol (<40 mg/dl in males and <50 mg/dl in females) was seen in 303 patients (42.7%) (8)

4.4. Extended lipid profile of patients

In our study evaluation of extended lipid profile results showed that the mean (SD) of Apo-A (mg/dl) was 96.08 (33.91); the mean (SD) of Apo-B (mg/dl) was 74.52 (31.00) and the mean (SD) of Lipoprotein(a) (mg/dl) was 42.61 (51.14) respectively; with 70.8% of the participants had Apo-A: <110 mg/dl; 29.2% of the participants had Apo-A: ≥110 mg/dl; 68.8% of the participants had Apo-B: <80 mg/dl, 31.2% of the participants had Apo-B: ≥80 mg/dl; 62.5% of the participants had Lipoprotein-a: <30 mg/dl, 37.5% of the participants had Lipoprotein-a: ≥30 mg/dl.

In Indian context no any study was conducted in the past on each component of Extended lipid profile {Apo-A, Apo-B, Lp(a)}.

4.5. Association between extended lipid profile and UACR

A significant association between the patients with various subgroups of UACR in terms of distribution of Lipoprotein-a ($\chi 2$ = 8.479, p = 0.010) was found in our present study with the strength of association between the two variables (Bias Corrected Cramer's V) = 0.37 (Moderate Association).

100.0% of the participants with [UACR: <30 mg/g] had [Lipoprotein-a: <30 mg/dl]; 57.7% of the participants with [UACR: 30-300 mg/g] had [Lipoprotein-a: <30 mg/dl]; 42.3% of the participants with [UACR: 30-300 mg/g] had [Lipoprotein-a: ≥30 mg/dl]; 41.7% of the participants with [UACR: >300 mg/g] had [Lipoprotein-a: <30 mg/dl] and 58.3% of the participants with [UACR: >300 mg/g] had [Lipoprotein-a: ≥30 mg/dl].

- Participants with UACR: <30 mg/g had the largest proportion of participants with Lipoprotein (a): <30 mg/dl.
- Participants with UACR: >300 mg/g had the largest proportion of participants with Lipoprotein (a): ≥30 mg/dl.

There was no significant association between the patients with various subgroups of UACR in terms of distribution of Apo-A was found ($\chi 2$ = 2.253, p = 0.362) with the strength of association between the two variables (Cramer's V) = 0.22 (Low Association). Similarly there was no significant association between the patients with various subgroups of UACR in terms of distribution of Apo-B ($\chi 2$ = 0.577, p = 0.840) was found with the strength of association between the two variables was (Cramer's V) = 0.11 (Low Association)

No any such study was conducted in past on association between Extended lipid profile and UACR.

In our study mean(SD) value of the of total cholesterol (mg/dl) was 159.96 (53.11) with most of study subject(89.6%) had total cholesterol <200 mg/dl and rest of the study subjects had total cholesterol >200 mg/dl; the mean(SD) of triglycerides (mg/dl) was found to be 146.81(64.10) with most of the study subjects (64.6%) have triglyceride <150mg/dl and 35.4% of study subjects had triglycerides level >150 mg/dl; the mean(SD) of HDL was 38.08 (12.54) mg/dl with 62.5% of participants had HDL <40 mg/dl and rest of the participants had HDL >40 mg/dl and the mean (SD) of LDL (mg/dl) was 101.02 (50.74) with 85.4% of the participants had LDL <130 mg/dl and 14.6% of the participants had LDL ≥130 mg/dl.

In a study conducted by Funmilayo Esther Omotoye et al found that the mean total cholesterol was (167.24 ± 53.3 mg/dl), triglycerides (95.84 ± 39.9 mg/dl), HDL (50.16 ± 19.1 mg/dl), LDL (110.50 ± 41.9mg/dl) & LDL / HDL ratio (2.24 ± 7.2). A total of 50 participants; 20 (40%) males and 30 (60%) females were recruited for the study. The mean age of the participants was 57.82 ± 3.3 years (60.85 ± 8.0 and 55.80 ± 8.6 male and female respectively) while their age ranges between 40 and 72 years. Mean of the lipid profiles was not significant between male and female ([9]).

This difference in lipid profile can be due to smaller sample size, geographical and demographical variation in the study population, and not taking into account other confounders such as hypothyroidism, liver disease, use of drugs or toxins (alcohol, herbal preparation, etc) which can alter lipid profile.

Many previous study showed that increased lipoprotein (a) [Lp(a)] concentrations are predictive of atherosclerotic cardiovascular disease (ASCVD). In our current study significant positive association found between increased Lp(a) and UACR was found. Since Lp(a) investigation is not widely available, accessible and had varied estimation technique hence UACR can be used as a surrogate marker of risk for ASCVD.

5. Conclusion

- Microalbuminuria were present in most of the patients which is an early indicator of progressive diabetic kidney disease.
- Albuminuria measured in the form of raised UACR had statistically significant association with increased Lipoprotein (a) level and consequently there is increased risk of atherosclerotic cardiovascular disease (ASCVD) as proved in many independent studies.
- Since lipoprotein (a) investigation is not widely available, accessible and has varied estimation techniques hence UACR can be used as a surrogate marker for raised lipoprotein (a) and an increased risk of ASCVD.

Compliance with ethical standards

Disclosure of conflict of interest

We declare that there is no financial and personal conflict of interest.

Statement of ethical approval

An ethical committee approval has been obtained for the study.

Statement of informed consent

We declare that an Informed consent was obtained from all individual participants included in the study.

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