

Study of Lipoprotein (a) in Chronic Renal Failure

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ABSTRACT

To compare the Lipoprotein (a) levels between non-diabetics and diabetics and compare the Lipoprotein (a) levels between diabetics with normal kidney function and diabetic CRF patients. To compare the Lipoprotein (a) levels between non-diabetic and diabetic CRF patients. This study was undertaken to study the level of Lipoprotein (a) levels in Chronic renal failure patients and to compare the levels of Lipoprotein(a) in three study groups. The mean Lp (a) level was high in diabetics with normal renal function and even more in diabetic Chronic renal failure patients compared to the controls with normal FBS, HbA1c, Urea and Creatinine. The same was compared between the three study groups using One-way ANOV A test and Tukey's HSD test. The difference in Lp (a) levels among the three diabetic groups was significant ($P < 0.01$). This suggests that the Lp (a) levels.

Key words: Hyperglycaemia, Diabetes mellitus, Antioxidant, Lipoproteins

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INTRODUCTION

Diabetes mellitus is a systemic metabolic disorder caused by various reasons like impaired insulin secretion, insulin action, or both. The disease is characterized by the hyperglycaemic status and complications due to the same. Diabetes mellitus (DM) is associated with oxidative stress which occurs as a result of imbalance between pro-oxidants and antioxidants. Chronic hyperglycaemia and high fatty acid concentrations can cause damage in different types of cells by a variety of mechanisms collectively known as glucolipotoxicity, and oxidative stress is considered to be the common link [1,2]. Lipid peroxidation of the cellular structures, a consequence of increased oxygen free radicals, is thought to play an important role in atherosclerosis and micro vascular complications of DM [3].

Acute uncontrolled diabetes results in hyperglycaemia with ketoacidosis or the nonketotic hyperosmolar syndrome. The long-term complications of diabetes are micro-vascular (retinopathy, peripheral neuropathy) and macro-vascular (cardiovascular, peripheral arterial, and cerebra-vascular disease) complications. The two broad categories of diabetes are type 1 and type 2. In type 1 diabetes there is an absolute deficiency of insulin secretion. In type 2 diabetes, which is the more prevalent category there is a combination of resistance to insulin action and an inadequate compensatory insulin secretory response. Type 2 diabetes (accounting for 90-95% of

those with diabetes), previously referred to as non-insulin-dependent diabetes or adult onset diabetes, encompasses individuals from dominantly insulin resistance with relative insulin deficiency to predominantly an insulin secretory defect with insulin resistance [4,5].

Chronic renal failure (CRF) or chronic kidney disease (CKD) is a progressive loss in renal function over a period of months or years. It is differentiated from acute kidney disease in that the reduction in kidney function must be present for over 3 months. Often, chronic kidney disease is diagnosed as a result of screening of people known to be at risk of kidney problems, such as those with high blood pressure or diabetes. Chronic renal failure may also be identified when it leads to one of its recognized complications, such as cardiovascular disease, anemia. It is important to identify these risks early to reduce the development of diabetes and CRF, since CRF greatly amplifies the risk of cardiovascular events in the diabetic patient. The common causes of chronic renal failure are diabetes, hypertension and glomerulonephritis, among which diabetes is responsible for almost 30% of all CRF. Therefore, diabetes is the most common cause of CRF [6,7].

Chronic renal failure (CRF) is characterized by progressive loss of renal function. These patients are at risk for adverse cardiovascular outcomes. Cardiovascular disease is the leading cause for morbidity and mortality in these patients. Lipoprotein (a) (also called Lp (a)) is a lipoprotein subclass. Genetic studies and numerous epidemiologic studies have identified Lp (a) as a risk factor for atherosclerotic diseases such as coronary heart disease and stroke. Lipoprotein(a) (Lp (a)) is a

cholesterol-rich particle existing in human plasma, first described by Berg in 1963. Lp (a) is made up of a low-density lipoprotein (LDL) cholesterol particle attached to Apo lipoprotein (a), which is a plasminogen like glycoprotein 5. The prevalence of hyperlipidaemia or dyslipidaemia in CRF is much higher compared to the general population [6]. However, in patients with CRF, the impact of dyslipidemia on cardiovascular disease is uncertain [7]. Previous studies have shown that there was positive correlation between increased Lp (a) levels and CRF patients [8].

Atherogenic lipid abnormalities are noticed in CRF patients. A study was done to show the impact of lipid abnormalities in patients with chronic renal failure, which revealed that there was increase in triglyceride, total cholesterol, and decrease in HDL-Cholesterol levels in chronic renal failure patients compared to controls [9].

MATERIALS AND METHODS

The study was conducted in 90 subjects attending Sree Balaji Medical College and Hospital totally.

Study individuals were divided into 3 groups

Group A-30 age, sex and Body mass index matched healthy controls.

Group B-Composes of 30 Type 2 diabetic patients with normal renal function, belonging to the age group between 40 and 50 years.

Group C-Composes of 30 diabetic Chronic renal failure patients, belonging to the age group between 40 and 50 years.

This study was conducted between December 2012 and May 2014. The Institutional Research and Ethical Committee approved the study protocol. Written informed consent was obtained from all the participants before enrolment in the study. Demographic data, age, gender, height, weight, DM duration, general history and medications, were recorded. (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL), serum urea and creatinine were measured.

Inclusion criteria

2 diabetics and diabetic CRF patients as Groups B and C respectively in the age group 40 - 50.

Exclusion criteria

Estrogen depletion.

Severe hypothyroidism.

Table 1: Master chart.

Group	Lp(a) mg/dl	Urea mg/dl	Creatinine mg/dl	FBS mg/dl	HbA1c %	TC mg/dl	HDL mg/dl	TG mg/dl	VLDL mg/dl	LDL mg/dl
A	9.6	18	0.9	108	5.2	180	34	172	34	112
A	10.2	27	1	98	4.4	165	42	145	29	94
A	8.9	35	0.3	81	4.8	146	33	128	26	87

Sample collection

The blood samples were collected by venepuncture under aseptic precautions.

RESULTS

The study population comprised of a total of 90 individuals and of these, Group-A were 30 healthy controls, Group-B were 30 Diabetic study individuals with normal renal functions and Group-C were 30 diabetics with Chronic renal failure. All the biochemical study parameters were analysed with the help of Statistical Product and Service Solutions (SPSS) 17 software (Table 1 and Table 2). Statistical tests used were Descriptives, ANOVA & TUKEY'S HSD test. The results of the various biochemical parameters for Group-A are as follows. Lp(a) concentration was 10.29 ± 1.2888 mg/dl (Mean and Standard deviation). The Mean and Standard of Urea, Creatinine, FBS, HbA1c, TC, HDL, TG, VLDL, LDL are 28.1 ± 8.31 mg/dl, 0.877 ± 0.339 mg/dl, 88.9 ± 11.598 mg/dl, $4.39 \pm 0.5592\%$, 159.1 ± 21.796 mg/dl, 44 ± 10.072 mg/dl, 155.43 ± 19.611 mg/dl, 31.07 ± 3.859 mg/dl and 84.03 ± 26.538 mg/dl respectively (Table 3).

The results of the various biochemical parameters for Group-B are as follows. Lp(a) concentration was 22.12 ± 4.32 mg/dl (Mean and Standard deviation). The Mean and Standard of Urea, Creatinine, FBS, HbA1c, TC, HDL, TG, VLDL, LDL are 28.8 ± 8.48 mg/dl, 0.897 ± 0.334 mg/dl, 150.27 ± 17.54 mg/dl, $7.94 \pm 0.59\%$, 242.77 ± 25.46 mg/dl, 35.03 ± 9.94 mg/dl, 209.63 ± 24.85 mg/dl, 41.93 ± 4.91 mg/dl and 165.8 ± 27.81 mg/dl respectively (Table 4). The results of the various biochemical parameters for Group-C are as follows. Lp(a) concentration was 51.1 ± 11.26 mg/dl (Mean and Standard deviation). The Mean and Standard of Urea, Creatinine, FBS, HbA1c, TC, HDL, TG, VLDL, LDL are 92.1 ± 19.695 mg/dl, 4.34 ± 1.49 mg/dl, 162.73 ± 28.29 mg/dl, $7.99 \pm 0.59\%$, 286.43 ± 41.16 mg/dl, 25.97 ± 5.23 mg/dl, 270.83 ± 48.63 mg/dl, 54.27 ± 9.61 mg/dl and 206.2 ± 43.16 mg/dl respectively (Table 5).

The Means of different groups of patients, namely A, B & C are unequal. The ONE-WAY ANOVA test was used to calculate the Means of each and every independent variable of the group. The Means of individual variable was compared between and within the groups. It also indicates that the P value is significant ($P < 0.01$) between the groups and insignificant within the same group (Table 6).

A	11.8	21	0.6	105	5.4	167	56	155	31	80
A	10.6	17	1.3	93	4.7	189	32	134	27	130
A	12.1	26	0.4	83	3.5	133	30	162	32	71
A	9.8	38	0.6	72	4.3	146	48	118	24	74
A	10.9	20	0.9	101	3.9	129	51	155	31	47
A	8.1	28	1.4	95	4.6	186	34	177	35	117
A	10.5	16	0.5	73	5.2	157	56	132	26	75
A	12.4	25	1.3	84	3.6	154	39	166	33	82
A	9.3	37	0.4	109	4.9	130	36	146	29	65
A	11.4	23	1.1	74	4.1	176	59	155	31	86
A	-8.7	19	0.9	97	4.6	190	34	148	30	126
A	10.3	29	0.7	86	5.1	153	60	174	35	58
A	9.4	15	1.2	93	3.7	161	44	179	36	81
A	8.8	30	0.8	79	4.1	127	57	167	33	37
A	10.4	24	0.5	99	5.4	146	33	188	38	75
A	9.9	33	1.1	75	4.2	173	45	154	31	97
A	12.3	40	1.3	87	3.8	188	45	165	33	110
A	11.9	22	1	100	4.5	139	32	116	23	84
A	8.4	36	0.7	76	3.9	122	60	177	35	27
A	10.7	32	1.3	89	4.3	190	54	149	30	106
A	12.6	25	1.4	103	4.7	168	56	157	31	81
A	9.5	41	0.8	71	4.2	173	40	165	33	100
A	8.5	34	0.6	89	3.7	168	41	143	29	98
A	10.1	39	1.2	77	4	133	56	178	36	41
A	11.5	18	0.6	101	4.4	172	36	177	35	101
A	9.3	31	1.1	78	4.9	130	42	162	32	56
A	10.8	44	0.4	91	3.6	182	35	119	24	123
B	16.8	41	1.2	189	7.9	210	30	184	37	143
B	22.1	20	0.8	142	8.4	208	55	230	46	107
B	27.CJ	27	1.4	129	7.4	247	33	243	49	165
B	15.5	31	1.2	169	8.6	238	50	223	45	143
B	18.3	42	0.7	139	7.5	233	31	184	37	165
B	20.7	36	1.1	150	8.7	226	49	190	38	139
B	19.2	16	0.4	144	7.3	283	51	194	39	193
B	26.9	28	0.6	174	8.1	249	32	211	42	175
B	21.5	35	1.4	125	7.7	209	54	186	37	118
B	16.7	21	0.9	154	8.1	271	48	251	50	173
B	28.6	30	0.5	140	7.6	283	33	234	47	203
B	19.2	18	0.8	132	7.1	213	44	180	36	133
B	27.3	44	1	171	8.5	215	40	188	38	137
B	19.4	29	0.9	152	7.2	243	36	194	39	168
B	26.5	22	0.4	137	7.5	223	31	222	44	148

B	20.9	34	1	160	8.4	273	29	193	39	205
B	28.1	19	1.3	127	7.2	219	23	205	41	155
B	23.1	38	0.6	156	8.8	230	38	231	46	146
B	19.7	25	0.4	143	7.9	220	27	192	38	155
B	16.1	32	1.1	178	8.3	263	39	255	51	173
B	21.3	40	0.9	135	7.6	288	25	200	40	223
B	14.9	23	1.1	129	8.8	240	22	195	39	179
B	25.7	17	0.3	163	8	222	26	206	41	155
B	27.4	37	1.3	176	7.3	256	18	205	41	197
B	23.6	26	0.9	131	7.8	268	28	199	40	200
B	19.5	19	0.8	157	8.9	287	33	282	56	198
B	18.9	24	1.2	146	7.4	265	31	203	41	193
B	22.8	39	0.4	168	8.2	244	27	186	37	180
B	8.3	33	0.9	133	9	236	30	222	44	162
B	6.7	18	1.4	159	7.1	221	38	201	40	143
C	19.5	92	3.4	214	7.9	289	22	289	58	209
C	15.8	110	4.1	135	8.9	290	19	303	61	210
C	2.3	67	3.2	189	8.3	302	33	189	38	231
C	17.6	125	5.3	139	7	322	30	289	58	234
C	4.8	78	2.7	145	7.5	319	28	321	64	227
C	9.3	94	4.9	194	7.8	249	23	209	42	184
C	8.7	108	4.1	127	8.2	302	22	287	57	223
C	7.4	62	2.7	150	7.4	344	27	193	39	278
C	16.8	90	2.4	127	7.6	340	30	321	64	246
C	8.5	76	3.8	204	8.7	311	33	198	40	238
C	9.4	97	5.2	155	8.1	372	25	276	55	292
C	1.6	114	6.5	210	7.9	342	23	253	51	268
C	3.8	88	5.9	125	7.7	302	28	298	60	214
C	8.9	65	3.6	175	8.5	293	30	254	51	212
C	1.5	105	6	129	8	255	26	336	67	162
C	5.7	75	2.7	140	7.2	290	24	300	60	206
C	5.1	99	4.3	201	8.4	302	17	274	55	230
C	39.8	116	7.1	130	7.5	250	22	260	52	176
C	44.6	68	2	150	8.7	283	28	312	62	193
C	36.9	86	4.8	168	8.6	321	30	219	44	247
C	65.4	101	5.4	194	7.1	202	18	204	41	143
C	43.9	72	3.6	165	7.9	235	29	288	58	148
C	69.2	118	6.4	139	8.8	301	20	198	40	241
C	45.1	127	7.3	135	8.5	283	22	200	40	221
C	52.3	81	2.9	197	7.1	244	38	273	55	151
C	61.2	103	4.1	160	7.3	239	33	300	60	146
C	56.3	69	3.2	149	8.9	220	18	304	61	141

C	47.5	123	6	179	8.6	306	31	291	58	217
C	35.4	85	3.7	187	7.4	221	27	322	64	130
C	65.6	70	2.8	170	8.1	264	23	364	73	168

Table 2: Groups.

Group	Frequency	Percent	Valid Percent	Cumulative Percent
Group A	30	33.3	33.3	33.3
Group B	30	33.3	33.3	66.7
Group C	30	33.3	33.3	100
Total	90	100	100	

Table 3: Descriptive statistics-Group A.

	N	Minimum	Maximum	Mean	Std. Deviation
Lipoprotein (a)	30	8.1	12.6	10.29	1.2888
Urea 111g/dl	30	15	44	28.1	8.31
Creatinine mg/dl	30	0.3	1.4	0.877	0.339
FBSmg/dl	30	71	109	88.9	11.598
HbAl c%	30	3.5	5.4	4.39	0.5592
TC mg /dl	30	122	190	159.1	21.796
HDLm g/dl	30	30	60	44	10.072
TG mf /dl	30	116	188	155.43	19.611
VLDLn1g/dl	30	23	38	31.07	3.859
LDLm g/dl Valid N (listwise)	30	27	130	84.03	26.538

Table 4: Descriptive statistics-Group B.

	N	Minimum	Maximum	Mean	Std.Deviation
Lipoprotein (a) mg/di	30	14.9	28.6	22.12	4.3154
Urea mg/di	30	16	44	28.8	8.475
Creatinine mg/dl	30	0.3	1.4	0.897	0.3347
FBS mg/dl	30	125	189	150.27	17.544
HbAlc %	30	7.1	9	7.943	0.5911
TCmg/dl	30	208	288	242.77	25.461
HDL mg/di	30	18	55	35.03	9.936
TG mg/dl	30	180	282	209.63	24.848
VLDL mg/di	30	36	56	41.93	4.913
LDL mg/di	30	107	223	165.8	27.805
Valid N (listwise)	30				

Table 5: Descriptive Statistics-Group C

	N	Minimum	Maximum	Mean	Std.Deviation
Lp(a) mg/dl	30	31.6	69.3	51.097	11.2604

Urea mg/dl	30	62	127	92.13	19.695
Creatinine mg/dl	30	2	7.3	4.337	1.4827
FBS mg/dl	30	125	214	162.73	28.285
HbA1c %	30	7	8.9	7.987	0.5888
TC mg/dl	30	202	372	286.43	41.155
HDL mg/dl	30	17	38	25.97	5.229
TG mg/dl	30	189	364	270.83	48.632
VLDL mg/dl	30	38	73	54.27	9.609
LDL mg/dl	30	130	292	206.2	43.164
Valid N (listwise)	30				

Table 6: One-way analysis of variance (One-way anova).

		Sum of Squares	Df	Mean Square	F	Significance
Lp(a)	Between Groups	26447.802	2	13223.901	269.73	0
	Within Groups	4265.305	87	49.026		
	Total	30713.106	89			
Urea	Between Groups	81118.689	2	40559.344	230.106	0
	Within Groups	15334.967	87	176.264		
	Total	96453.656	89			
lLe	Between Groups	238.056	2	119.028	147.234	0
	Within Groups	70.333	87	0.808		
	Total	308.389	89			
FBS	Between Groups	93726.467	2	46863.233	113.163	0
	Within Groups	36028.433	87	414.12		
	Total	129754.900	89			
HbA1	Between Groups	255.641	2	127.82	380.114	0
	Within Groups	29.255	87	0.336		
	Total	284.896	89			
Total Choles	Between Groups	251206.667	2	125603.333	133.759	0
	Within Groups	81695.433	87	939.028		
	Total	332902.1	89			

DISCUSSION

The study was done on Type 2 Diabetic patients with normal renal function and Diabetic Chronic renal failure patients. Age, Sex and BMI matched healthy individuals were taken as controls. Between the two study groups and the control group, the routine biochemical parameters, fasting blood sugar (FBS), glycated haemoglobin (HbA1C), serum urea, serum creatinine and lipid profile differed significantly [10].

Serum Lipoprotein (a) was also estimated in patients under, all the three groups to show the significance of the atherosclerotic pathogenic effect of the same. The fasting plasma sugar was done to assess the short term

glycaemic control. The difference in short term glycaemic control (FBS) values between the two study groups was statistically significant ($P < .001$). To assess the long term glycaemic control HbA1C levels were measured. The difference in mean values between two study groups was also statistically significant ($P < 0.001$). This shows that long term glycaemic control was significantly proportional to the Lp(a) levels in controls of Group A, Group B-diabetics with normal renal function and Group C-diabetics with CRF [11]. This suggests that long term glycaemic control is directly related to the complications of diabetes. This study also observed that there is significant elevation of total cholesterol, LDL, VLDL, triglycerides and significant lowering of HDL in diabetics

with normal renal function when compared to healthy controls. The levels of Lp (a) were significantly increased in Group C Diabetic CRF patients which is evident from the Mean and Standard Deviation of 51.097 ± 11.26 . The Lp (a) levels were 10.29 ± 1.29 and 22.12 ± 4.32 among Group A and B respectively. The significance is also shown by the One- way ANOVA test and TUKEY'S HSD test with $P < 0.001$ [12-15].

The studies conducted shows the genetically importance of apoA isoforms and the level of Lp(a) depending on the apoA isoform. There are also other studies based on the genetic relationship between apoA and Lp (a), the isoforms and the gene polymorphism [16-21]. These studies suggest that despite significant correlation between APOA kringle 4 size polymorphism and Lp (a) levels, there sequence variations either in the APOA gene or closely linked genes may account for relatively higher Lp (a) levels. Various other studies conducted showed the decreased levels of Lp (a) among the patients using atorvastatin [22,23]. There are also other studies based on the treatment modalities for increased Lp (a). Unlike the above mentioned studies, our study shows significantly increased levels among the patients on statin therapy. These unique features of Lp (a) justifies the elevation in the level of Lp (a) in Diabetics and Diabetic CRF causing generation of clots and atherosclerosis [24-27].

CONCLUSION

The results of this study and previous studies provide ample evidence that the levels of Lp (a) are increased in patients with type 2 diabetes mellitus and also in patients with diabetic CRF. The present study observed that there is positive correlation of Lp (a) levels with the duration of diabetes and is progressive with the diabetic complications. As in the general population, Lp (a) is a risk factor for cardiovascular events in CRF patients.

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ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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