

# Cross-sectional study of pattern of Dyslipidemia and Prevalence of Atherogenic Diabetic Dyslipidemia in newly detected Diabetic patients



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## ABSTRACT

**Background:** India has seen an ever increasing number of diabetic patients and in turn rise in cardiovascular diseases. Many studies have shown diabetic patients to have dyslipidemia, with certain common patterns early in the disease. **Aims and Objective:** The current study was done to identify pattern of dyslipidemia and prevalence of ADD in treatment naïve diabetic patients. **Material and Methods:** Fasting lipid profile was analysed in treatment naïve diabetic patients at a tertiary care teaching hospital. Various factors influencing the results were analysed statistically. **Results:** Prevalence of dyslipidemia was 89.2%, whereas atherogenic diabetic dyslipidemia was seen in 34.2% and raised non-HDL cholesterol in 73.3%. **Conclusion:** Our study showed a high prevalence of dyslipidemia in newly diagnosed diabetics indicating the importance of screening for dyslipidemia in newly diagnosed cases and implementation of timely lipid lowering therapy to prevent CVD. It also highlights the importance of pattern of dyslipidemia called Atherogenic diabetic dyslipidemia and raised Non-HDL cholesterol in diabetic patients.

**Key words:** Atherogenic diabetic dyslipidemia; Dyslipidemia; Newly detected diabetes mellitus; Non HDL cholesterol; LDL; Triglycerides

## INTRODUCTION

It is currently estimated that diabetes prevalence by 2030 will include 439 million adults worldwide.<sup>1</sup> Cardiovascular disease (CVD) is the leading cause of death worldwide, and mortality due to CVD is higher in low- and middle-income countries.<sup>2,3</sup> In India, there has been an alarming increase in the prevalence of CVD over the past two decades so much so that accounts for 24% of all deaths among adults aged 25–69 years.<sup>4</sup> The risk for coronary artery disease (CAD) is 2-4 times higher in diabetic subjects, and in Indians, CAD occurs prematurely, i.e. one to two decades earlier than in the West.<sup>5</sup> Dyslipidemia is an abnormally increased amount of lipids (e.g. cholesterol and/or triglycerides) and is one of the major risk factors for CVDs in Diabetes. Diabetic dyslipidemia consists of

specifically mild to marked elevation of triglyceride rich lipoproteins- very low density lipoprotein-cholesterol (VLDL-C) and VLDL-C remnants, and low levels of high density lipoprotein-cholesterol (HDL-C). Raised serum triglycerides (TG) and low HDL-C often precede the onset of T2DM. In addition, low density lipoprotein cholesterol (LDL-C) particles are converted to smaller, perhaps more atherogenic, lipoproteins termed 'small dense LDL-C' (sd-LDL-C).<sup>6</sup> This combination of hypertriglyceridemia, low HDL-C and high levels of LDL-C, termed as 'Atherogenic Dyslipidemia' – better addressed as Atherogenic Diabetic Dyslipidemia (ADD), is particularly seen in Asian Indians. Although precise reason for such dyslipidemia is unknown, genetic predisposition and characteristic body composition (excess intra-abdominal fat) may be important contributors. A common

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outcome of such a body composition and dyslipidemia in Asian Indians is the tendency to develop insulin resistance.<sup>7</sup>

A study by Parikh R M et al<sup>8</sup> found that the majority of Indian type 2 diabetics are dyslipidemic at baseline. Majority of these diabetic patients failed to achieve all standard goals of dyslipidemia management. In a substantial number of patients this was attributable to the fact that the HDL-C target was not met.<sup>8</sup> Hence this study was done to identify pattern of dyslipidemia and prevalence of ADD in treatment naïve diabetic patients.

## MATERIALS AND METHODS

This was cross sectional study carried on the patients attending the Medicine OPD of East Point College of Medical Sciences and Hospital, Bangalore during 6 months period of October 2018 to March 2019. Patients with type 2 diabetes mellitus visiting consecutively in the Medicine OPD were enrolled for this study. The patients enrolled in the study were newly detected Diabetes patients. The patients of type 1 diabetes mellitus were not considered for this study. The patients who were also suffering from coronary artery disease (CAD) or had history of cerebrovascular accident (CVA) or were diagnosed as having CAD or CVA after enrolment and those patients already taking statins or other drugs for lipid lowering were excluded from this study. Diabetic patients suffering from metabolic disorders or chronic systemic diseases were also excluded from the study. In those patients included in the study, detailed history was taken and clinical examination was done. The demographic parameters of the patients were recorded and their weight, height and BMI were recorded using standard methods. Fasting blood sample of the patients after at least 8 hours overnight fast was taken to measure serum lipid profile parameters of total cholesterol (TC), triglycerides (TG), low density lipid cholesterol (LDL-C) and high density lipid cholesterol (HDL-C). The cut-off normal values for individual lipid levels were taken as per guidelines of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III).<sup>9</sup> The body mass index (BMI) was calculated by the Quetelet Index,  $BMI = \text{Weight (Kg)}/\text{Height (m}^2\text{)}$  from weight and height measurements. The data of the individual patients was entered in the Microsoft Excel sheet and was analysed statistically using SPSS software. Prevalence and pattern of dyslipidemia was analysed in the study population. Various sociodemographic characters associated with dyslipidemia, atherogenic diabetic dyslipidemia and high Non-HDL cholesterol were analysed using appropriate statistical tests.

## RESULTS

We studied a total of 120 patients, out of which 63 (52%) of them were males and 57 (48%) were females. Mean age of the patients was 47.8 yrs. 64 (53.3%) patients were urban dwellers and 56 (46.6%) were from rural areas. Prevalence of dyslipidemia was 89.2% with 107 patients having abnormalities in lipid profile either alone or in combination. Out of 107 patients, 60 were male and 47 were female with significant p-value of 0.024. Dyslipidemia was highest in age group of 51-60 years (n=39). It was higher among urban population with 55.1% (n=59) prevalence. Prevalence of dyslipidemia was analysed with various variables as depicted in Table 1.

Atherogenic diabetic dyslipidemia defined as a combination of high TG, high LDL, low HDL, was seen in 34.2% (n=41) of patients out of which 58.5% (n=24) were males and 41.5% (n=17) were females. 56.1% (n=23) were urban population and 43.9% (n=18) were from rural areas. Atherogenic diabetic dyslipidemia had significant association (p value=0.036) with Hypertension when compared with the other variables as depicted in Table 2.

Non-HDL-C was elevated in 73.3% (n=88) of the patients, out of which 53.3% (n=46) were males and 47.7% (n=42) were females. Among the total 88 patients 56.8% (n=50) were urban population and 43.2% (n=38) were rural population. Among patients having elevated non-HDL-C, increasing BMI and higher waist circumference showed significant association with p-values of <0.001 and 0.027 respectively as depicted in Table 3.

The various sociodemographic details associated with dyslipidemia are detailed below in Table 4.

Prevalence of Atherogenic Diabetic Dyslipidemia (ADD) was 34.2% in our study. On comparing different lipid parameters with the diabetic control status, only ADD had significant correlation with poor glycemic control (HbA1c >8) with a significant p-value as depicted in Table 5.

## DISCUSSION

According to IDF Diabetes Atlas Update 2017, 425 million people have diabetes worldwide and half of the people with diabetes remain undiagnosed and two-thirds i.e. 279 million live in the urban areas.<sup>10</sup> Patients with DM have a 2- to 4-fold increased risk of cardiovascular, peripheral vascular and cerebrovascular disease, which are the leading causes of morbidity and mortality in this population. Many Western epidemiological studies have shown an association between diabetic dyslipidemia, which is characterized

**Table 1: Factors associated with dyslipidemia**

Variable	No. of patients	Dyslipidemia				P value
		Absent		Present		
		n	%	n	%	
BMI						0.291
Normal	19	3	15.8	16	84.2	
Over Weight	52	3	5.8	49	94.2	
Obese	49	7	14.3	42	85.7	
Waist circumference						0.502
Normal	28	4	14.3	24	85.7	
Abnormal	92	9	9.8	83	90.2	
Smoking habit						0.114
Absent	89	12	13.5	77	86.5	
Present	31	1	3.2	30	96.8	
Alcohol consumption						0.223
Absent	84	11	13.1	73	86.9	
Present	36	2	5.6	34	94.4	
Hypertension						0.552
Absent	74	9	12.2	65	87.8	
Present	46	4	8.7	42	91.3	

**Table 2: Factors associated with Atherogenic Diabetic Dyslipidemia (ADD)**

	Atherogenic diabetic dyslipidemia				P value
	No		Yes		
	N	n	n	%	
BMI					0.422
Normal	19	15	4	21.1	
Over Weight	52	33	19	36.5	
Obese	49	31	18	36.7	
Waist circumference					0.105
Normal	28	22	6	21.4	
Abnormal	92	57	35	38.0	
Smoking habit					0.290
Absent	89	61	28	31.5	
Present	31	18	13	41.9	
Alcohol consumption					0.120
Absent	84	59	25	29.8	
Present	36	20	16	44.4	
Hypertension					0.036
Absent	74	54	20	27.0	
Present	46	25	21	45.7	

**Table 3: Factors associated with raised non HDL-C**

	Raised Non HDL-C				P value
	Absent		Present		
	N	n	n	%	
BMI					<0.001
Normal	19	12	7	36.8	
Over weight	52	10	42	80.8	
Obese	49	10	39	79.6	
Waist circumference					0.027
Normal	28	12	16	57.1	
Abnormal	92	20	72	78.3	
Smoking habit					0.285
Absent	89	26	63	70.8	
Present	31	6	25	80.6	
Alcohol consumption					0.105
Absent	84	26	58	69.0	
Present	36	6	30	83.3	
Hypertension					0.165
Absent	74	23	51	68.9	
Present	46	9	37	80.4	

by hypertriglyceridemia; low levels of HDL cholesterol; postprandial lipemia and small, dense LDL cholesterol particles and the occurrence of cardiovascular disease.<sup>11-13</sup>

The ‘Chennai Urban Population Study’ showed 11% prevalence of CAD, which is 10 times more than what it was in 1970. Clustering of risk factors for CAD such as hyperglycemia, central obesity, dyslipidemia, and hypertension (HTN) tend to occur, and, interplay of these risk factors could explain the enhanced CAD risk in Indians. Additionally, low-grade inflammation and a possible inherent genetic susceptibility are other contributing factors.<sup>14</sup>

Our study showed a high prevalence of dyslipidemia of 89.2% among the 120 patients enrolled of which 56.1% were males and 43.9% were females which were statistically significant. In our study prevalence was higher in urban population with 92% of newly detected diabetics being dyslipidemic compared to 85% in the rural diabetics. According to ICMR INDIAB study, prevalence of dyslipidemia was 79% and there was no urban rural difference observed in the four regions studied in ICMR study.<sup>15</sup>

Most of subjects of our study had mixed pattern of dyslipidemia. On analysis of Individual parameters, total cholesterol was elevated in 43.3%(n=52) of patients,

**Table 4: Sociodemographic details associated with dyslipidemia**

Serum Lipid	Gender	Age (yrs)			DM		Obesity		Hypertension	
		<45 (N=43)	45-60 (N=68)	>60 (N=9)	Controlled (N=46)	Uncontrolled (N=74)	Overweight (N=52)	Obese (N=49)	No (N=74)	Yes (N=46)
TC>=200 mg/dL	Male	11	17	1	5	24	14	13	19	10
	Female	5	15	3	5	18	10	10	14	9
	Total	16	32	4	10	42	24	23	33	19
	%	37.2%	47.1%	44.4%	21.7%	56.8%	46.2%	46.9%	44.6%	41.3%
TG>=150 mg/dL	Male	17	28	2	17	30	22	21	28	19
	Female	11	22	3	15	21	17	14	17	19
	Total	28	50	5	32	51	39	35	45	38
	%	65.1%	73.5%	55.6%	69.6%	68.9%	75.0%	71.4%	60.8%	82.6%
HDL<40 mg/dL	Male	12	26	2	14	26	19	15	24	16
	Female	8	17	1	8	18	13	8	13	13
	Total	20	43	3	22	44	32	23	37	29
	%	46.5%	63.2%	33.3%	47.8%	59.5%	61.5%	46.9%	50.0%	63.0%
LDL>=100 mg/dL	Male	13	27	3	13	30	22	19	25	18
	Female	8	19	4	9	22	14	12	20	11
	Total	21	46	7	22	52	36	31	45	29
	%	48.8%	67.6%	77.8%	47.8%	70.3%	69.2%	63.3%	60.8%	63.0%

**Table 5: Comparison of ADD with HbA1c**

Atherogenic diabetic dyslipidemia	HbA1c		Total
	<=8	>8	
NO	35	44	79
YES	11	30	41
Total	46	74	120
	38.3%	61.7%	100.0%

P-value = 0.0062

triglycerides was elevated in 67.5% (n=81), LDL was elevated in 60% (n=72), elevated non-HDL was found in 73.3% (n=88) and low HDL was found in 55% (n=66) of the patients. Hence the most frequent lipid abnormality was elevated non-HDL levels suggesting importance of non-HDL cholesterol to be used as co-primary target for therapeutic interventions along with primary LDL targets especially in patients with TGs in range of 200-500 as suggested by Lipid association of India guidelines.<sup>16</sup> The result of the study done by Dixit et al indicates that the most common recognized abnormality was hypertriglyceridemia.<sup>17</sup> Abbate and Brunzell reported that the increase in triglycerides in poorly controlled patients was related to the decrease of activities of adipose tissue and muscle lipoprotein lipase activity.<sup>18</sup>

According to ICMR-INDIAB increased TC was 13.9%, increased TG in 29.5%, low HDL was the most common abnormality with 72.3% and high LDL in 11.8%, 4.8% of patients had all four lipid abnormalities in form of high TC, high TG, high LDL and low HDL.<sup>15</sup> Our study showed much higher prevalence of 28% for the four lipid

abnormalities mentioned above. In our study, most of the diabetic patients had mixed dyslipidemia i.e. more than one lipid abnormality. The most common mixed abnormality detected was hypertriglyceridemia and low HDL levels (41.6%) which was in similarity with the western studies where similar pattern was observed,<sup>19</sup> whereas study done by Pandya et al among the Gujarati population showed that the most common mixed lipid abnormality was high TG and high LDL.<sup>20</sup>

Prevalence of Atherogenic Diabetic Dyslipidemia(ADD) was 34.2% in our study which was comparable to study done by Parikh et al where the prevalence of ADD was 36.1%. On comparing different lipid parameters with the diabetic control status, only ADD had significant correlation with poor glycemic control (HbA1c >8) with a significant p-value. Hence control of diabetes is of prime importance, as it can lead to reduced incidence of Atherogenic Diabetic dyslipidemia.

In recent times the focus is shifting on reducing the non-HDL-C (all the atherogenic lipoproteins), as many trials have demonstrated non-HDL-C levels as a better predictor of CVD risk than is LDL-C. LDL-C may actually be underestimating the burden of atherogenic, cholesterol-carrying lipoproteins. Our study had significant correlation of non-HDL cholesterol with BMI and waist circumference.

## CONCLUSION

Our study showed a high prevalence of dyslipidemia at 89.2% in newly diagnosed diabetics indicating the importance of screening for dyslipidemia in newly diagnosed cases and institution of timely lipid lowering

therapy to prevent ASCVDs. Our study also highlights the importance of pattern of dyslipidemia called Atherogenic diabetic dyslipidemia and raised Non-HDL cholesterol which is shown to have higher prevalence in our study. Non HDL-C is now being set as co-primary target especially in patients with triglyceride levels of more than 200mg/dl, indicating the role of newer combined PPAR- $\alpha/\gamma$  agonists which are effective in managing lipids and insulin sensitization that control hyperglycemia simultaneously, when the LDL and Non-HDL targets are not reached even after optimum dose of statins. Hence it is of paramount importance to aim for strict goals, specific thresholds, early and regular screening for dyslipidemia in Indian diabetics so that early, prompt and appropriate preventive measures can be instituted to reduce the occurrence of Atherosclerotic cardiovascular diseases.

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**VK**-Concept and design of the study, collected data, prepared first draft of manuscript; **ARK**- Concept and design of the study, collected data, statistically analyzed and interpreted, prepared first draft of manuscript; **PB**- Concept and design of the study, critical revision of the manuscript

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