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Original Research Article

Assessment of cardio-vascular disease risk in diabetic population of Northern India

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ABSTRACT

Background: Type 2 Diabetes mellitus (DM) is a chronic metabolic disorder. India has 72.9 million people living with diabetes (8.8%). The Cardio Vascular Disease (CVD) risk increases in patients with Type 2 diabetes. The Non-HDL-C level includes cholesterol carried in several atherogenic lipoproteins. The estimation of non-HDL-C may provide a better means to follow these patients toward their treatment goals. The study compares the level of non-HDL-C in non diabetic, pre-diabetic and diabetes patients and their occurrence of dyslipidemia.

Materials and Methods: The study group included 1418 patients and were grouped as – Non diabetic, pre-diabetic and Diabetic, having age group of 20 to 85 years. The Male:Female ratio was 1.9:1. Their blood samples were analysed in Clinical Biochemistry Laboratory on automated chemistry analyzer with quality checks.

Result: The Non Diabetic group (HbA1c<5.7%) had 564 patients having Non-HDL-C 127.85±1.79 mg/dl; the Pre-Diabetic group (HbA1c-5.7-6.4%) had 316 patients with Non-HDL-C 132.37±2.35 mg/dl and Diabetic group (HbA1c >6.4%) had 538 patients and its non HDL-C was 148±4.27 mg/dl.

Conclusion: This study showed the groups, pre-diabetic and diabetic, had Non-HDL-C >130mg/dl. An increase in Non-HDL-C levels is associated with increased risk of CVD according to Adult Treatment Panel (ATP) III guidelines.

1. Introduction

Diabetes mellitus (DM) type II is a fast growing on communicable disease in India with estimated 8.7% diabetic population in the age group of 20 and 70 years. The rising prevalence of diabetes is mainly driven by a combination of factors like rapid urbanization, sedentary lifestyles, unhealthy diets, tobacco use, and increasing life expectancy.[1] The diabetics cases are around 40 million in about 1000 million India's whole population. This denotes that India actually has the highest number of diabetics of any one country in the entire world.[2] Recent epidemiological evidence also indicates a rising DM incidence and prevalence in urban India's middle class and working poor.[3] Diabetes is also appeared to begin much earlier in life in India, meaning that chronic long-term complications will become more common in later stages of life. This denotes that Impaired Glucose Tolerance (IGT) is also becoming a mounting problem in India[2] DM patients have 2-3 times higher risk for cardiovascular disease(CVD) than adults without diabetes.[4] This is so because diabetes is highly associated with high blood pressure and cholesterol levels. These patients are characterised by elevated levels of triglycerides (TGs), apolipoprotein (apo) B and low levels of high density lipoprotein (HDL-C) with normal to elevated low density lipoprotein (LDL-C) levels.

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LDL- C is the primary target of lipid-lowering therapy and is used to classify patients into various CVD risk categories.[5] In spite of these, LDL-C levels does not encompass all cholesterol present in potentially atherogenic lipoprotein particles like very low density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), LDL-C, and lipoprotein(a). It has been suggested that Non-high density lipoprotein (Non-HDL-C) levels may reflect the risk of CVD better than LDL-C alone.[6,7] Hence, the study is to assess the association of HbA1c with Non-HDL-C and LDL-C level in non-diabetic, pre-diabetic and diabetic patients.

2. Materials and Methods

2.1. Study design

The cross-sectional study was conducted on patients attending Medicine Outdoor in Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna, Bihar, after approval by Institutional Ethics Committee. The study was conducted for the period of six months (January to June 2020).The patients were categorized into three groups according to the glycated haemoglobin (HbA1c) levels.

Non-diabetes group (Group – I) - The patients who attended the medicine outdoor with complains of illness with no personal or family history of diabetes and HbA1c level below 5.7%.

Pre-diabetes group (Group – II)- The suspected cases of diabetes mellitus with no personal or family history of diabetes and HbA1c level between 5.7% to 6.4%.

Diabetes group (Group – III) -The diagnosed cases of diabetes mellitus and on/off medication for diabetes and HbA1c level > 6.4%.

2.2. Sample size and data collection

The study included 1418 patients. After the patient's consent, 5 ml overnight fasting blood sample was drawn with aseptic precautions. Lipid parameters (total cholesterol, HDL-C, LDL-C and Non-HDL-C), glycated haemoglobin, fasting plasma glucose and post-prandial plasma glucose was estimated by auto analyzer Beckman Coulter AU5800. The method of analysis was as follows:

The total cholesterol, HDL-C and LDL-C was estimated by direct oxidase/peroxidise method. The Non-HDL-C was calculated by-

Non-HDL-C= Total Cholesterol – HDL-C[8,9]

The glycated haemoglobin was estimated by turbidimetric immune-inhibition method. Third party quality control was used to have independent, unbiased performance evaluation of the parameters analyzed. The quality checks were performed daily at specified intervals as lab protocol. The patients with history of pregnancy, chronic kidney disease, malignancy, hormonal treatment, drug addiction, alcoholism and/or smoking and with complication of diabetes/ hypertension/drug were excluded.

2.3. Statistical analysis

Microsoft Excel was used for correlation. All p-values less than 0.05 were considered statistically significant.

3. Results

The study group had the mean age of 45.14 ± 12.23 years. While the male and female ratio was 1.9:1. Treatment goal for non-HDL-C was 30mg/dl above the LDL target i.e. 130mg/dl.[10] Thus, in the study, the patients were divided on Non-HDL-C levels into <130mg/dl & >130 mg/dl in all three groups (non diabetic, pre diabetic and diabetic).

3.1. Relation of non-HDL-C and HbA1c in non diabetic group

The (361) males and (203) females were included in this group. The mean of LDL-C was 100.8±1.7 mg/dl and HDL-C was 47.59±0.79. The mean and standard deviation of different parameters in males and females are given in Table 2. The p value does not show significant relationship between Non-HDL-C and HbA1c in male and female groups in Table 1.

3.2. Relation of non-HDL-C and HbA1c in pre diabetic group

The (217) males and (99) females were included in this group. The mean of LDL-C was 103.58 ±1.87 mg/dl and HDL-C was 47.39±0.76. The mean and standard deviation of different parameters in males and females are given in Table 3. The p value does not show significant relationship between Non-HDL-C and HbA1c in male and female groups in Table 1.

3.3. Relation of non HDL-C and HbA1c in diabetic group

The (358) males and (180) females were included in this group. The mean of LDL-C was 105.08 ± 3.73 mg/dl and HDL-C was 48.15 ± 1.03. The mean and standard deviation of different parameters are given in Table 4. The p-value shows some significance relationship between Non-HDL-C and HbA1c in male and female groups in Table 1.

4. Discussion

DM is a chronic disorder that occurs when pancreas is unable to produce insulin as per requirement or tissues are unable to utilize the produced insulin. Ineffective function of insulin or improper control of raised glucose levels leads to serious complications affecting heart and kidney. These may be mainly attributed by lipid abnormalities. Thus, HbA1c and dyslipidemia are independent risk factors

Table 1: Relation between HbA1c to non-HDL-C and LDL-C

Group based on HbA1c Levels	Grouped as per Non-HDL-C Levels (mg/dl)		Non HDL-C		LDL-C		n
			p value	r value	p value	r value	
Non-diabetes	Male	<130	0.777	0.020	0.975	0.002	191
		>130	0.515	0.050	0.928	.007	169
	Female	<130	0.296	0.099	0.098	.156	112
		>130	0.434	0.082	0.024	.236	91
Pre-diabetes	Male	<130	0.486	0.068	0.317	.090	106
		>130	0.037	0.198	0.212	.119	111
	Female	<130	0.273	0.153	0.574	.078	53
		>130	0.512	0.09	0.011	.370	46
Diabetes	Male	<130	0.166	0.121	0.630	.042	132
		>130	0.000	0.387	0.278	.072	226
	Female	<130	0.296	0.119	0.913	.012	78
		>130	0.057	0.189	0.477	.071	107

Table 2: Mean and Standard Deviation of different parameters in non-diabetic group

	Non diabetic male				Non diabetic female			
	Mean±Standard Deviation	Minimum	Maximum	Standard Error	Mean±Standard Deviation	Minimum	Maximum	Standard Error
Age	45.81±12.82	18	85	0.6751	43.28±12.63	20	70	0.8888
HbA1c	5.08±0.34	4	5.65	0.0180	5.03±0.420	4	5.65	0.0295
T. Cholesterol	173.44±44.98	70	344	2.3675	176.82±43.51	66.9	335	3.0544
HDL-C	47.25±21.67	14.1	376	1.1405	48.19±12.69	25	85	0.8907
non HDL-C	127.36±42.96	24.9	272	2.2610	128.71±42.29	31.4	272	2.9681
LDL-C	100.38±43.99	18.1	422.5	2.3157	101.58±33.42	29.3	229	2.3458
FBS	97.21±42.01	56	504	2.2141	95.17±27.71	52	253	1.9451
BSPP	175.53±89.95	76	595	4.7347	172.88±84.55	75	601	5.9345

Table 3: Mean and Standard Deviation of different parameters in pre-diabetic group

	Pre diabetic male				Pre diabetic female			
	Mean±Standard Deviation	Minimum	Maximum	Standard Error	Mean±Standard Deviation	Minimum	Maximum	Standard Error
Age	45.77±11.43	20	76	0.7761	41.85±11.36	21	75	1.1424
HbA1c	6.03±0.16	5.7	6.4	0.0114	6.02±0.18	5.7	6.4	0.0182
T. Cholesterol	178.52±39.68	77	282	2.6942	181.03±45.71	88	340	4.5943
HDL-C	46.78±13.00	10.6	105	0.8830	48.73±14.73	6.5	85.1	1.4808
non HDL-C	131.95±39.26	24	242.8	2.6656	132.30±47.21	50.8	305.4	4.7449
LDL-C	102.76±33.79	37	204	2.2944	105.38±32.52	20.3	182	3.2686
FBS	92.88±24.51	60	241	1.6643	90.43±17.16	64	168	1.7254
BSPP	180.89±77.15	72.5	569	5.2377	187.14±110.17	80	606	11.0733

for CVD. In clinical practice, lipid profile along with history of diabetes is used for treatment and calculation of CVD risk. Although LDL has always been regarded as the most atherogenic lipoproteins but it lacks TGs and VLDLs levels.[11] In laboratories, LDL evaluation is either estimated directly or using Freidwald's equation. Using the Friedewald equation for LDL, ignores the important atherogenic VLDL remnants as targets for therapy and also fails to calculate accurate levels when triglycerides is >400 mg/dl. To remove the inaccuracy of the Friedwald equation in calculating LDL, measurement of Non-HDL-C can provide a better biochemical picture of these patient and helps in their treatment goals. The ATP III of National Cholesterol Education Program (NCEP) emphasizes the need of for optimization of LDL-C levels and it has been recently recommended that non-HDL cholesterol may be a better predictor of atherosclerosis in DM.[12,13] Non-HDL-C incorporates all cholesterol in potentially atherogenic lipoprotein particles, VLDL, IDL, LDL and lipoprotein(a). Recently, non-HDL was shown to be a better predictor of

Table 4: Mean and Standard Deviation of different parameters in diabetic group

	Diabetic male				Diabetic female			
	Mean±Standard Deviation	Minimum	Maximum	Standard Error	Mean± Standard Deviation	Minimum	Maximum	Standard Error
Age	46.21±12.65	20	80	0.6690	43.60±11.53	20	70	0.8600
HbA1c	7.97±1.36	6.5	13	0.0719	8.06±1.45	6.5	13	0.1083
T. Cholesterol	198.58±57.78	80	357	3.0541	196.16±55.09	87	359	4.1065
HDL-C	46.17±13.28	8.4	86.2	0.7022	48.15±13.82	12.6	111	1.0304
non HDL-C	152.41±56.59	31.4	310.9	2.9909	148.00±57.36	21	314.4	4.2760
LDL-C	104.67±41.109	20.4	293.5	2.1723	105.06±3.73	26	396.5	5.1024
FBS	108.29±46.63	59	461	2.4647	109.59±3.31	58	397	44.5049
BSPP	218.67±97.96	80	685	5.1777	223.26±100.85	77	549	7.5174

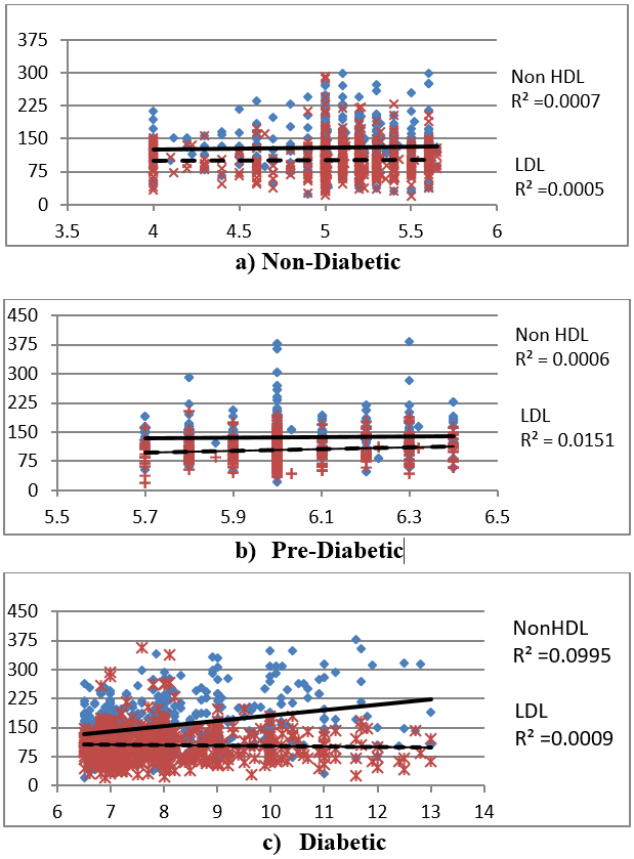

Fig. 1: a, b, c): Comparison of LDL and non HDL in Non-diabetic, Pre-diabetic and Diabetic group

CVD than LDL-C, even in patients with triglyceride levels below 200 mg/dl. Some studies reports that the risk of CVD may also be due to low HDL-C cholesterol level. Therefore, Non-HDL-C values not only indicate about bad cholesterol but also show compromised state of HDL-C values. The treatment goal for Non-HDL-C is 30 mg/dl above the LDL-C target. For diabetic patients without CVD, treatment target for LDL-C and Non HDL-C is < 100 mg/dl and <130mg/dl respectively. For diabetic patients with CVD, treatment target for LDL-C is <70 and Non-HDL-C is < 100mg/dl. [10]

In this study, the diabetic group show higher Non-HDL-C levels (150.2 ± 56.97 mg/dl). Infact LDL-C also does not show good relation to glycated haemoglobin (Figure 1). Some study suggest that in diabetic patients, with increased TGs, Non–HDL-C has been superior to LDL-C in predicting CVD risk. [14–16] In the Framingham Heart study, Non–HDL-C was found to be superior to LDL-C in individuals who had TGs that were either increased or within the reference interval. [17–19] A study also reported that 64.6%, 71.5% patients with diabetes not achieving targeted goals i.e. LDL-C<100mg/dl and Non-HDL-C<130mg/dl respectively. [20] So, more aggressive lipid-lowering therapy should be implemented for better control of complications.

Interestingly, pre-diabetic group also show the higher levels of Non-HDL-C than the treatment goal of diabetic group (>130mg/dl). This impaired diabetic group increases our consciousness toward the presentation of disease in future. The approx. 50% of pre-diabetes male patients have >130 mg/dl of Non-HDL-C values.

These patients show highly significant relation of glycated haemoglobin to Non-HDL-C (p= 0.037) in its 20% population approximately. It is expected that around 35 per cent of IGT sufferers are going to develop DM. [2] Non-HDL-C could be an important indicator in monitoring CVD with impaired fasting glucose. [20] The lifestyle induced changes are making its impression in disease iceberg. These populations need keep an eye on the preventive measures and adaptation of healthy lifestyle. So, it has been suggested that direct reporting of Non-HDL-C along with standard lipid profile result would improve goal achievement. The advantages of using non-HDL-C as risk evaluating tool include that it requires random serum sample. It is simple, convenient, cost-effective and most importantly it is calculated by simple equation using values of total cholesterol and HDL. Several studies also said that high proportion of patients unable to achieve

targeted goals of non-HDL-C, so need more aggressive lipid lowering therapy and improvement of lifestyle. This helps in prevention of future complications.

5. Source of Funding

None.

6. Conflicts of Interest

No conflict of interest was disclosed in this study.

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