

## A STUDY OF LIPID PROFILE IN PREDIABETES

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### ABSTRACT

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#### BACKGROUND

Lipid abnormalities are common in diabetes mellitus and play an important role in acceleration of atherosclerosis leading to increased cardiovascular diseases. Due to increasing burden of diabetes, it is becoming important to identify dyslipidaemia in high-risk state for diabetes especially prediabetes so that early intervention can reduce cardiovascular risk.

#### AIM

To study lipid profile in prediabetes individuals.

#### METHODS

This study was a cross-sectional case control study which included 107 prediabetes and 101 healthy controls. Lipid profile of prediabetes and controls were measured and statistically analysed.

#### RESULT

Total cholesterol, LDL, triglycerides, VLDL, TG/HDL ratio, and LDL/HDL ratio were significantly high whereas HDL was significantly low in prediabetes subjects as compared to controls.

#### CONCLUSION

This study showed significant lipid abnormalities in prediabetes subjects. Because of these they are at high risk of developing atherosclerotic cardiovascular diseases. Therefore, proper screening and appropriate therapy of these conditions becomes important.

#### KEYWORDS

Dyslipidaemia, Triglycerides, Lipoprotein, Cholesterol, Glycaemia, Normoglycaemic, Atherogenic.

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**INTRODUCTION:** Due to increasing burden of type 2 diabetes mellitus (T2DM) and its complications, much attention has been given to prevention, beginning with identifying at-risk individuals prior to diagnosis.<sup>1</sup> This has led to the designation of "prediabetes," which is typically defined as blood glucose levels above normal but below diabetes thresholds, is a risk state that defines a high chance of developing diabetes.<sup>2</sup> 347 million people worldwide have diabetes. Glycaemic levels are rapidly rising in developed and developing countries.<sup>3</sup> Increase in glycaemia has resulted in a rise in prediabetes prevalence. Prevalence of diabetes and pre-diabetes in India in 2011 was 62.4 and 77.2 million respectively.<sup>4</sup> Diagnostic criteria for prediabetes have changed over time.

According to the World Health Organization (WHO), high risk for developing diabetes relates to two distinct states, impaired fasting glucose (IFG) defined as fasting plasma glucose (FPG) of 110-125 mg/dL (in the absence of impaired glucose tolerance – IGT) and IGT defined as post-load plasma glucose of 140-199 mg/dL based on 2-hour oral glucose tolerance test (OGTT) or a combination of both.<sup>5</sup> The American Diabetes Association (ADA), although applying the same thresholds for IGT, uses a lower cut-off value for IFG (FPG 100-125 mg/dL) and has additionally introduced haemoglobin A1c levels of 5.7–6.4% as a new category of high diabetes risk.<sup>6</sup> Around 5–10% of people with prediabetes become diabetic annually.<sup>2</sup> Nearly 70% of prediabetes subjects can eventually develop diabetes if not managed in early stages.<sup>7</sup> Both IFG and IGT are associated with increased cardiovascular risk.<sup>8</sup> Dyslipidaemia, frequently occurring in T2DM patients, play a critical role in acceleration of macrovascular atherosclerosis and contribute to the excess risk of CVD.<sup>9</sup> Therefore, it is important to diagnose lipid abnormalities in prediabetes state itself. Many studies have been done on lipid profile in prediabetes subjects in developed countries. But there is paucity of such studies in India. Present study is aimed to study lipid profile in prediabetes individuals.

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**MATERIAL AND METHOD:** This study was a cross-sectional case control study carried out at U.P. Rural Institute of Medical Sciences and Research. 107 prediabetes

and 101 controls were recruited from OPD of the hospital. Study was conducted between January 2014 and December 2015(2 years).

Risk	LDLc	HDLc (Males)	HDLc (Females)	Triglycerides	Cholesterol
High	≥160	<40	< 50	≥200	≥240
Borderline	≥130-159	40-59	50-69	150-199	200-239
Desirable	100-129	>60	>70	<150	<200
Optimal	<100	-	-	-	-

**Table 1: NCEP (National Cholesterol Education Program) ATP III Classification of Lipid Levels**

Study was initiated after taking permission from Institutional Ethical Committee. Informed consent was taken from all participants before including in study.

**Inclusion Criteria:**

- For cases:** Subjects who met following criteria for blood sugar level were included in case group (Prediabetes group).
  - Fasting plasma sugar level 110-125 mg/dL or,
  - Post prandial plasma sugar level (after 2 hours of 75 g oral glucose) 140-199 mg/dL or,
  - Combination of both of above.
- For Control:** Age and sex matched subject who has fasting plasma sugar level <110 mg/dL and post prandial plasma sugar level (after 2 hours of 75 g oral glucose) <140 mg/dL.

**Exclusion Criteria:** Subjects having conditions/disorders known to affect lipid profile like hypo or hyperthyroidism, nephrotic syndrome, renal failure, liver disorders, obesity (BMI>30 kg/m<sup>2</sup>), malnutrition (BMI<18.5 kg/m<sup>2</sup>), smoking, alcoholism, and diabetes were excluded from study.<sup>10,11</sup>

Biochemical measurements including fasting plasma sugar, postprandial plasma sugar (after 2 hours of 75 g oral glucose), thyroid stimulating hormone(TSH), 24-hour urinary protein, kidney function test (serum urea and creatinine), liver function test (serum bilirubin, albumin, SGOT, SGPT and alkaline phosphatase), fasting lipid profile (serum total cholesterol(TC), low density lipoprotein cholesterol(LDL), triglycerides(TG), high density lipoprotein cholesterol (HDL), very low density lipoprotein cholesterol (VLDL)), were done. Abnormal lipids were defined as per NCEP (National Cholesterol Education Program) ATP III classification as shown in Table 1.

Variables	Case(n=107)	Control(n=101)	Test statistics value	P value
Age	41.69±3.91	42.57±5.44	t= -1.337	0.183
Sex (M/F ratio)	61/46	57/44	χ <sup>2</sup> = 0.014	0.905
Sr. Total Cholesterol(mg/dL)	180.10±36.81	167.15±27.97	t= 2.865	0.005
Sr. LDL(mg/dL)	116.95±29.16	95.62±21.30	t= 6.047	<0.001
Sr. HDL(male) (mg/dL)	33.33±4.99	42.81±9.60	t= -6.662	<0.001
Sr. HDL(female) (mg/dL)	35.65±7.23	52.09±8.10	t= -10.165	<0.001
Sr. TG(mg/dL)	144.07±42.84	123.39±33.73	t= 3.881	<0.001
Sr. VLDL(mg/dL)	28.81±8.57	24.68±6.75	t= 3.881	<0.001
TG/HDL ratio(mg/dL)	4.30±1.40	2.77±1.00	t= 9.133	<0.001
LDL/HDL ratio(mg/dL)	3.50±1.03	2.15±0.70	t= 11.198	<0.001

**Table 2: Comparison of Baseline Variables and Lipid Profile of Cases (Prediabetes Subjects) and Controls**

**STATISTICAL ANALYSIS:** Statistical analysis was done using Microsoft Excel 2010 and IBM SPSS statistics version 23. Unpaired t test and chi-squared test were used for comparison. A 'p' value <0.05 was used for level of significance.

**RESULTS:** Mean lipid level including total cholesterol, LDL, HDL, TG, VLDL, triglycerides, high density lipoprotein-cholesterol concentration (TG/HDL) ratio and low density lipoprotein-high density lipoprotein cholesterol concentration (LDL/HDL) ratio of cases and controls with statistical significance are given in table 2. Comparison of dyslipidaemia between cases and control are given in Table 3 and Fig. 1.

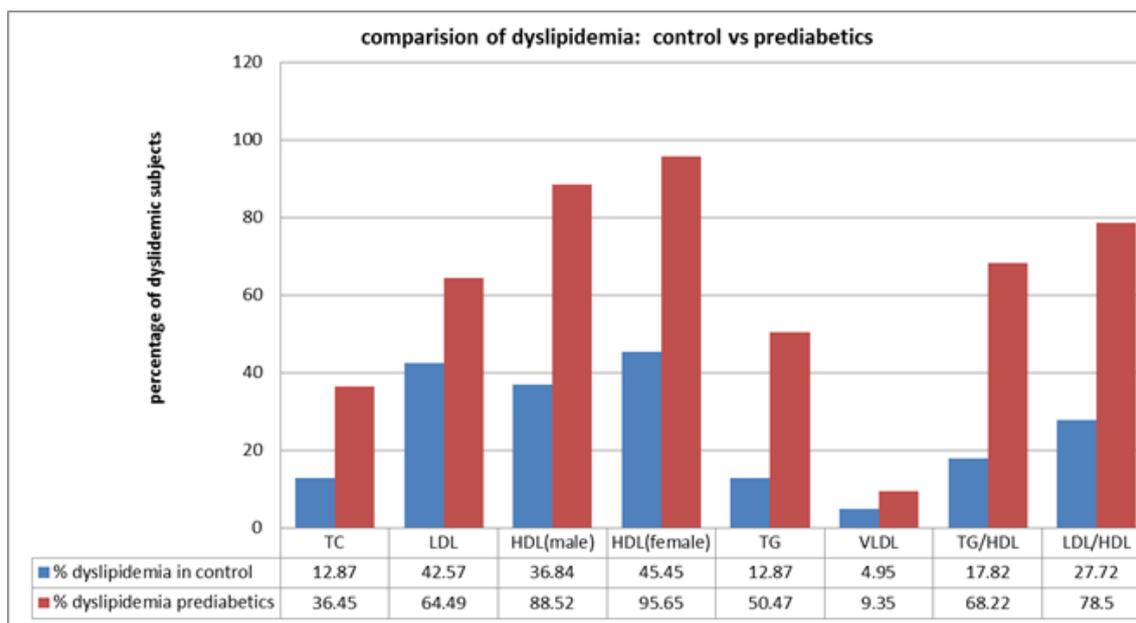
Serum Lipids	Case Group	Control Group	Test Statistic Value	P Value
Total Cholesterol(mg/dL)				
<200	68(63.55%)	88(87.13%)		
≥200	39(36.45%)	13(12.87%)	χ <sup>2</sup> =53.055	<0.001
LDL Cholesterol(mg/dL)				
<100	38(35.51%)	58(57.43%)		
≥100	69(64.49%)	43(42.57%)	χ <sup>2</sup> =21.021	<0.001

HDL Cholesterol(Male) (mg/dL)				
<40	54(88.52%)	21(36.84%)		
≥40	7(11.48%)	36(63.16%)	$\chi^2 = 70.045$	<0.001
HDL Cholesterol(Female) (mg/dL)				
<50	44(95.65%)	20(45.45%)		
≥50	2(4.35%)	24(54.55%)	$\chi^2 = 46.747$	<0.001
Triglycerides(mg/dL)				
<150	53(49.53%)	88(87.13%)		
≥150	54(50.47%)	13(12.87%)	$\chi^2 = 134.894$	<0.001
VLDL(mg/dL)				
<38	97(90.65%)	96(95.05%)		
≥38	10(9.35%)	5(4.95%)	$\chi^2 = 4.385$	0.036
TG/HDL Ratio				
<3.5	34(31.78%)	83(82.18%)		
≥3.5	73(68.22%)	18(17.82%)	$\chi^2 = 185.591$	<0.001
LDL/HDL Ratio				
<2.5	23(21.50%)	73(72.28%)		
≥2.5	84(78.50%)	28(27.72%)	$\chi^2 = 137.736$	<0.001

**Table 3: Lipid Abnormalities in Cases vs. Control**

**DISCUSSION:** In our study, total cholesterol in prediabetes subjects was significantly higher than controls (180.10 mg/dL of case vs. 167.15 mg/dL of control). This observation

was similar to previous studies. Williams et al observed that mean cholesterol was higher in prediabetes subject (174.2 mg/dL) than control (157.5 mg/dL).<sup>12</sup>



**Fig.1: Bar Diagram Showing Comparative Dyslipidaemia: Prediabetes vs. Control**

In our study, mean LDL cholesterol was significantly higher in prediabetes subjects than controls (116.95 mg/dL of cases vs. 95.62 mg/dL of control). Magge et al observed that obese prediabetes adolescents have significantly more atherogenic lipoprotein profile compared with obese normoglycaemic peers.<sup>13</sup> Shin et al also found LDL cholesterol significantly higher in prediabetes subject (150.5±38 mg/dL) than non-diabetic controls (134±34.6 mg/dL). They also proved that there was correlation between raised blood glucose level and low density

lipoprotein.<sup>14</sup> Miyazaki et al also found higher LDL cholesterol level in prediabetes subjects. They also stated that lipid profile in IGT/IFG appears to be very similar to diabetic dyslipidaemia.<sup>15</sup> Similarly, Rahbar et al reported that prediabetics are at higher risk of having increased level of LDL cholesterol (LDL-c).<sup>16</sup> In our study, HDL cholesterol was significantly lower in both male as well as female as compared with male and female controls respectively. This observation was similar to earlier observations in prediabetes subjects. Shin et al also found significantly lower

HDL in prediabetes subject ( $49.9 \pm 11.6$  mg/dL) as compared to non-diabetic controls ( $54.7 \pm 13.3$  mg/dL).<sup>14</sup>

Miyazaki et al observed low HDL level in prediabetes subject compared to controls.<sup>15</sup> Similarly Rabhar et al also observed higher risk of having low HDL cholesterol in prediabetes subjects.<sup>16</sup> In our study, serum triglycerides were significantly higher in prediabetes than controls (144.07 mg/dL of cases vs. 123.39 mg/dL of controls). This observation was again similar to observations in previous studies on prediabetes. Miyazaki et al observed raised triglycerides in prediabetes subjects.<sup>15</sup> Rahbar et al also observed prediabetes subjects are at high risk of having high triglycerides.<sup>16</sup> Similarly Barzi et al, Gaziano et al and Boizel et al observed significantly higher serum triglycerides levels in IFG/IGT subjects compared to normal fasting glucose/normal glucose tolerance (NFG/NGT) subjects.<sup>17-19</sup> Similarly, VLDL was higher in prediabetes subjects than controls in our study. In our study, triglycerides-high density lipoprotein cholesterol concentration (TG/HDL) ratio was higher in prediabetes subject than in controls (4.30 of cases vs. 2.77 of controls). Miyazaki et al observed that IGT/IFG subjects had higher TG/HDL ratio than controls ( $4.0 \pm 2.5$  for cases and  $2.7 \pm 1.9$  for controls).<sup>15</sup> Barzi et al, Gaziano et al and Boizel et al also reported higher TG/HDL ratio in IFG/IGT subjects compared to NFG/NGT subjects.<sup>17-19</sup> McLaughlin et al concluded that TG/HDL ratio  $>3.5$  predicts insulin resistance. They found that this cut-off had high sensitivity (79%) and specificity (85%) in their study population and concluded that a plasma TG/HDL cholesterol concentration ratio might provide a simple means of identifying insulin resistance.<sup>20</sup> In our study, LDL/HDL ratio was significantly higher in prediabetes subjects as compared with controls. However, Miyazaki et al showed no statistical difference in LDL/HDL ratio between case group and control group.<sup>15</sup>

**CONCLUSION:** This study showed significant lipid abnormalities in prediabetes subjects. Total cholesterol, LDL, triglycerides, VLDL, TG/HDL ratio, and LDL/HDL ratio were significantly higher whereas HDL was significantly lower in prediabetes subjects. Dyslipidaemia in these individuals put them in high risk category for cardiovascular diseases. Therefore, proper screening of prediabetes and associated dyslipidaemia is necessary as life style modification and pharmacotherapy can control these conditions and thereby reduce cardiovascular risk.

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