

## Non High Density Lipoproteins (Non-HDL-C) and the degree of glycemic control of type 2 diabetes mellitus

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### ABSTRACT

**Objective:** To evaluate the level of non high density lipoprotein among dyslipidemic type 2 diabetic patients and its correlation to the degree of glycemic control according to HbA1c.

**Patients and methods:** The study was conducted prospectively on 113 patients with type 2 diabetes mellitus. 62 (54.9%) patients were females and 51(45.1%) patients were males. Their ages ranged from 34 to 67 with a mean age  $50.37 \pm 8.76$  years. All consulted endocrine and diabetic center in Al-Mawani General Hospital in Basrah Southern Iraq during the period from April 2010 to February 2012. Fasting blood was taken for each patient and send for sugar, lipid profile and HbA1c. Height, weight were taken to calculate body mass index (BMI). Non-HDL-C were calculated by subtracting HDL-C from total cholesterol.

**Result:** The level of non-HDL-C was significantly elevated in patients with poorly controlled type 2 DM (P-value  $< 0.01$ ) in spite of absent of increments of their HDL-C levels that shows a mean value of  $(43.19 \pm 12.68)$  in patients with poorly controlled as compared to fairly controlled diabetes  $(40.25 \pm 14.18)$ .

**Conclusions:** Non-high density lipoprotein level can be calculated easily from total cholesterol and high density lipoproteins, it provides an index of atherogenic lipid other than low density lipoprotein and its level below 130 mg/dl directly correlated with the glycemic control as measured by HbA1c.

الدهون الغير كثافة عالية ودرجة السيطرة على مستوى السكري عند مرضى داء السكري من النوع الثاني.

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الهدف؛ لتقييم مستوى البروتين الشحمي الغير العالي الكثافة بين نوع مريض السكري وواعثلال البروتينات الشحميه عند المرضى من النوع الثاني وارتباطه إلى درجة السيطرة على السكري طبقاً ل HbA 1 c.

المرضى والطرق: الدراسة أجرت مستقبلياً في ١١٣ مريض بنوع داء السكري. ٦٢ (٥٤.٩%) مرضى كانوا إناث و ٥١ (٤٥.١%) مرضى كانوا ذكور. أعمارهم تراوحت من ٣٤ إلى ٦٧ مع متوسط عمر  $50.37 \pm 8.76$  سنوات. كُلت المرضى راجعوا المركز الإفرزي والسكري في مستشفى الموالي العام في البصرة جنوب العراق أثناء الفترة من أبريل/نيسان ٢٠١٠ إلى فبراير/شباط ٢٠١٢. أخذت عينة دم في حالة صوم لمدة ثمانية ساعات من كل مريض وأرسلت إلى فحص نسبة السكري، بروتينات الشحميه و HbA 1 c. الطول، والوزن أُخذ لحساب دليل كتلة الجسم. تم حساب البروتين الشحمي غير عالي الكثافة بواسطة طرح البروتين الشحمي عالي الكثافة من الكوليسترول الكلي.

النتائج: مستوى البروتين الشحمي غير عالي الكثافة مرتفع بشكل ملحوظ في المرضى داء السكري بالنوع ٢ المسيطر عليه أظهرت مستوى دلالة (P > ٠.٠١) بالرغم من عدم وجود زيادات في البروتين عالي الكثافة. والقيمة المتوسطة  $(43.19 \pm 12.68)$  في المرضى المسيطر عليه مقارنة بمرضى السكري إلى مرض السكر المسيطر عليه جداً  $(40.25 \pm 14.18)$ .

الاستنتاجات: مستوى البروتين الشحمي الغير عالي كثافة يُمكن أن يُحسب بسهولة من الكوليستيرول الكلي والبروتينات الشحميه العاليه الكثافة، يُؤدّد دليل atherogenic lipid غير البروتين الشحمي المنخفض الكثافة (LDL -C). ومستواه تحت (130 mg \ dl) ربطاً مباشرة بالسيطرة على مستوى كما هو مدروسة من قبل HbA 1 c.

## INTRODUCTION

**D**iabetes is associated with greatly increased cardiovascular disease (CVD).<sup>[1]</sup> Many factors have a role in the accelerated atherosclerosis in diabetic patient. dyslipidemia is a key contributors. LDL (low density lipoprotein) is a major determinant of atherosclerosis. Other lipoprotein abnormalities including VLDL (very low density lipoprotein), IDL (intermediate density lipoprotein) and apoprotein B accumulate as a result of altered lipoprotein metabolism.<sup>[2]</sup> These types of lipoproteins have been shown to be highly atherogenic. Several guidelines using LDL-C as primary target of therapy for cardiovascular diseases however, several findings have shown that lowering LDL-C to the goal with statins is not enough to prevent primary and secondary CVD. Several lipid parameters are used to monitor dyslipidemia like TC/HDL-C, Non-HDL-C/HDL-C, LDL-C/HDL-C.<sup>[3]</sup> The Adult Treatment Panel III (ATPIII) of the US National Cholesterol Education Program advised recently that Non-HDL cholesterol can be used as a secondary target of therapy in people with triglyceride levels >200 mg/dl, especially those with diabetes or the metabolic syndrome. Friedwarld equation generally less accurate to determine lipid abnormalities when triglyceride level is high and became inapplicable if triglycerides level more than 400 mg/dl.<sup>[4]</sup> The advantages of using Non-HDL cholesterol as a screening tool include the fact that it requires measurement of only total cholesterol and HDL cholesterol both of which can be measured reasonably accurately in a non fasting sample, as opposed the LDL cholesterol measurement, which requires a fasting sample. Serum Non-HDL-C, indicating the cholesterol contents of all atherogenic lipoprotein in blood other than LDL like VLDL, IDL and apoprotein B. It represents as risk factor for cardiovascular disease and as secondary prevention after a control of LDL. It can be calculated simply by subtraction HDL

from total cholesterol (total cholesterol-HDL).<sup>[5]</sup> The (ATP-III) of the National Cholesterol Education Program recommended a therapeutic goal for Non-HDL cholesterol of 30 mg/dl higher than the goal for LDL cholesterol. This means that Non-HDL-C should be less than 130 mg/dl in patients with diabetes who are a risk equivalent to ischemic heart disease.<sup>[6]</sup> The aim of the study is to know whether the use of Non-HDL-C is strongly correlated with diabetic control and dyslipidemia in type 2 diabetes mellitus (D M).

## PATIENTS AND METHODS

The study was performed at the endocrine and diabetic center in Al-Mawani General Hospital Basrah Southern Iraq and approved by the department of medicine, Basrah College of Medicine. A total of 113 patients were studied prospectively, 62 patients were females and 51 patients were males during the period from April 2010 to February 2012. Their ages ranged from 34 to 67 years and a mean age  $50.37 \pm 8.76$  year. All with type 2 diabetes mellitus and were managed by oral anti diabetics agents, Insulin or with both combination therapy. Height and weight were measured for all patients and body mass index was calculated from weight in kilogram over height in sequarmeter. World health organization classification was used for grouping of patients, The morbid obese patients with BMI above  $40 \text{ kg/m}^2$  were excluded from study owing to its effect on result of study. Blood sample was taken from each patients after twelve hours over night and send for fasting plasma sugar, lipid profile including (total cholesterol triglycerides, low density lipoprotein, very low density lipoprotein, high density lipoprotein) and HbA1c. Non-HDL-C was calculated from subtracting HDL from total cholesterol (Non-HDL= total cholesterol-HDL).

*To simplify the study, patients were grouped as follow:*

Group A: Diabetic patients with good control (HbA1c level < 7%).

Group B: Diabetic patients with fair control (HbA1c > 7% - 8%).

Group C: Diabetic patients with poor control (HbA1c > 8%).

Data were fed on a computer and statistical analysis was done by using Statistical Package for Social Sciences (SPSS version 15). Data expressed as mean ± standard deviation of variable computered for comparison of the results were done by one way ANOVA test. The difference of distribution was represented by their percentages which was compared by statistic test with chi-square test. P-value of less than 0.05 was regarded as significant.

**RESULTS**

Table-1, shows the demographic distributions of participants regarding age, gender and type of treatment used. This study was done on 113 patients, 51(45.1%) males and 62(54.9%) females. The majority of patients were using oral hypoglycemia drugs 76(67.3%) while minority of patients were using insulin 14(12.4%). Combined treatment were used by 23(20.2%) Patients. It also demonstrated that the majority of patients (77%) and (72.5%) had Non-HDL above 130 and LDL above 100 respectively, while the minority (23%) had Non-HDL below 130 and (27.4%) had LDL below 100 respectively. Only minority of the studied (23.9%) patients had HbA1c below 7,

while the majority of patients their HbA1c above 8%.

**Table 1. General characteristics of the Study subjects.**

Variable	Patients NO. %
gender female	62(54.9)
gender male	51(45.1)
Oral anti diabetic treatments	76(67.3)
insulin treatments	14(12.4)
Combined treatment	23(20.2)
NHDL >130	87 (77.0)
NHDL <130	26 (23.0)
LDL >100	82 (72.5)
LDL <100	31(27.4)
HbA1c <7	27 ( 23.9)
HbA1c >7- <8	29 (25.7)
HbA1c >8	57 (50.4)
BMI ( kg/M <sup>2</sup> ),in group A	21.81±2.41
BMI ( kg/M <sup>2</sup> ),in group B	25.86±1.12
BMI ( kg/M <sup>2</sup> ),in group C	32.24±4.13

Table-2, Demonstrates the comparison of lipids type between groups of patients according to level of HbA1c, It clearly shows evidence of significant relation of Non-HDL-C with the degree of glycemic control in comparison with other types of lipids except for LDL-C. (P-value 0.000 for Non-HDL and 0.000 for LDL-C lipid type respectively. There is inverse relations with VLDL-C and triglycerides levels i.e. it is higher in control group in comparison to other non control group. however it was insignificantly correlated with Non- HDL-C.

**Table 2. Comparison of LDL, NHDL, TC, HDL, TG, VLDL Levels between groups.**

Variable	Group a(n.27 )	Group B ( n.29)	Group C n.57	P-value
LDL -C (mg/dl)	72.55±20.06	110.72±9.34	156.03±31.57	0.000
Non-HDL (mg/dl)	119.66±30.75	145.24±20.84	191.91±33.72	0.000
T C (mg/dl)	159.92±39.39	187.86±19.61	235.10±37.44	0.000
HDL (mg/dl)	40.25 ± 14.18	42.62± 10.14	43.19±12.68	0.589
TRIGLYCERID(mg/dl)	236.67±134.37	177.31±101.25	176.74±96.84	0.047
VLDL (mg/dl)	47.11±26.93	34.51±17.10	35.94±19.77	0.046
Ratio of Total/HDL cholesterol	4.59	4.65	5.87	0.003

The values are expressed as a mean ± SD

Table-3, Shows the target of Non-HDL and LDL and the degree of control of diabetes mellitus. When HbA1C was above 8 Non of these patient had target of LDL below 100 mg/dl or Non-HDL below 130, while the majority of them 57(50.4%) had both LDL above 100 mg/dl and Non-HDL above 130 (P-

value<0.05). When HbA1c was below 7, 18(15.9%) patients had Non-HDL below 130 and 27(23.9%) Patients had LDL below 100. These figures seem to be more when we compared to 10 patients with Non-HDL above 130 and 0(0%) patients with LDL above 100 for the same level of HbA1c.

**Table 3. level of NHDL and LDL with degree of diabetic control.**

HBA1C level	NHDL<130 NO. %	NHDL>130 NO. %	LDL<100 NO. %	LDL>100 NO. %
<7%	18 (15.9)	9 (8.0)	27 (23.9)	0 (0.0)
7 to 8%	8 (7.1)	21 (18.6)	4 (3.5)	25 (22.1)
>8%	0 (0.0)	57 (50.4)	0 (0.0)	57 (50.4)
Total	26 (23.0)	87 (77.0)	31(27.4)	82 (72.5)

Table-4, Shows clearly that when BMI was above 30, None of these patients had a goal of LDL below 100 or Non-HDL below 130, while in 42(37.2%) patients had LDL above 100mg/dl and Non-HDL above 130 mg/dl (P-value <0.05). The table also demonstrates that when BMI was below 25, the percentage of LDL

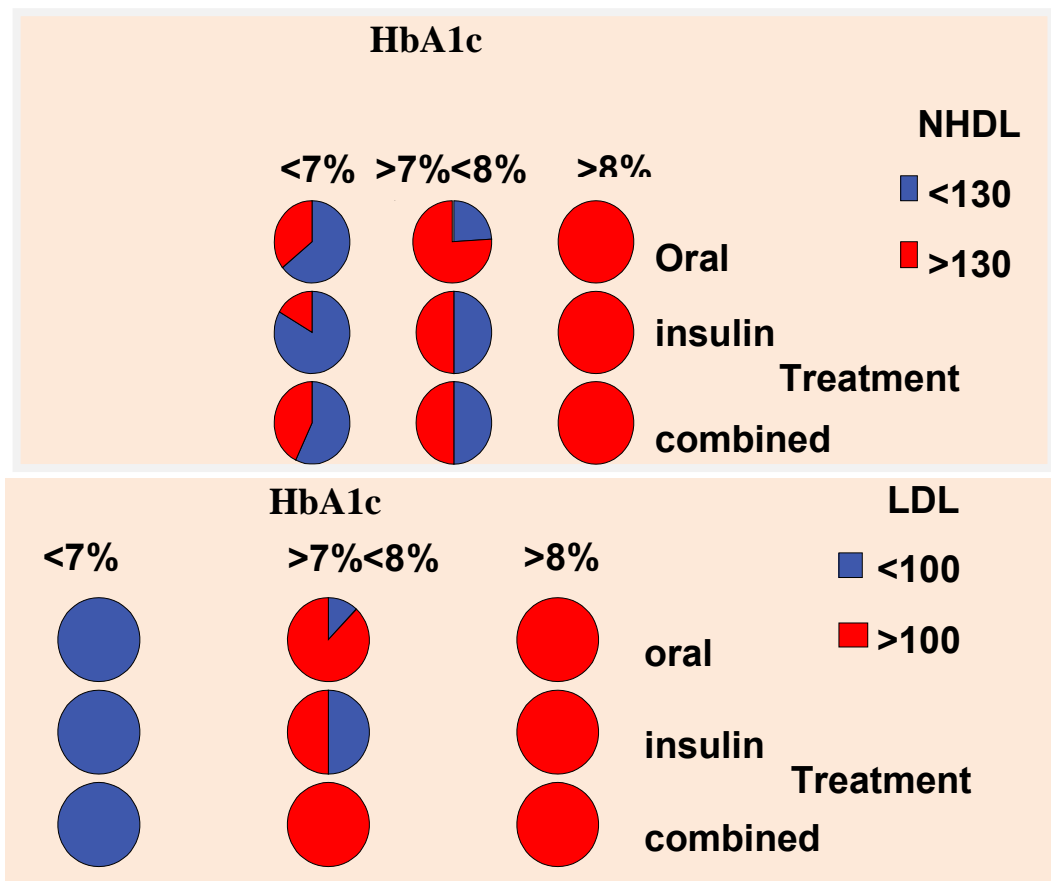
below 100mg/dl and Non-HDL below 130 mg/dl were increasing to 29(25.7%) and 19(16.8%) respectively as compared to lower percentage of LDL above 100mg/dl 0(0%) patients and Non-HDL above 130 mg/dl 10(8.8%) patients.

**Table 4. Correlation of NHDL and LDL with body mass index.**

BMI	NHDL<130	NHDL>130	LDL<100	LDL>100
<25	20 (17.7%)	9 (8.0%)	29 (25.7%)	0 (.0%)
25 To 30	6 (5.3%)	36 (31.9%)	2 (1.8%)	40 (35.4%)
>30	0 (.0%)	42 (37.2%)	0 (.0%)	42 (37.2%)
Total	26 (23.0%)	87 (77.0%)	31 (27.4%)	82 (72.6%)

**Graph-1**, Shows that none of the treatment type in uncontrolled group (C) had reached a target of non-HDL-C (<130mg/dl), while in fairly controlled group B (7%-8%), both insulin and combined treatment revealed equal result of target non-HDL-C but not for oral anti diabetic

drugs. In control group the best target of N-HDL was with patients using insulin. Regarding LDL, no treatment type in-group C had reached the targets while all-in group A reached the target, but most in group B except in those on insulin had not reached the target.



Graph 1. Non-HDL-C,LDL-C, effects of type of treatment and HbA1c level.

**DISCUSSIONS**

The main purpose of this study is first to know whether the use of non-HDLC as lipid markers in type 2 DM patients than other lipids that need many preparations for assay including the fasting state and the presence of normal triglyceride level to be assessed accurately and to assess whether this lipid type can parallel the degree of control of diabetes mellitus type 2 patients as measured by percentages of glycoselated hemoglobin (HbA1c) as it the only mean to predicts the control state. This study showed that non –HDL-C,which can be easily calculated lipid type is marginally correlated more with the degree of control of glycemia as compaired to LDL-C lipid type. This might be explained by the fact that non-HDL-C containing all lipoproteins i.e. VLD, LDL, IDL and apolipoprotien are considered to be atherogenic as compaired to only lipoprotein present in LDL-C type. In addition to the advantage of its easily calculation, it can be assessed in presence of high triglyceride level

even if higher than 400 mg/dl and in patients investigated in non fasting state.<sup>[7,8]</sup> This property gives a flexibility in lipid monitoring in type 2 diabetic patients specially in obese patients not already assessed in conventional lipids assessments. The majority of studied patients had poorly controlled glycemic state as reflected by high HbA1c,which was statistically significant (P-value <0.05). In addition none of the obese patients had reached the target of atherogenic lipid, while most of patients with normal body mass index had reached. This means that BMI greatly influences both the control of diabetes and atherogenicity of lipids. The managements of dyslipidemia may reduce or delay macro and microvasculare complications, as it has been recently suggested that Non-HDL-C might be a useful marker and better predictors of CVD than LDL in diabetic as well as in non diabetics patients.<sup>[9]</sup> This study had demonstrated no significant effects of gender or duration of disease, but progressively

diminishing control of diabetic state with increasing age of patients. The type of treatments, though not significantly related to degree of control of glycemic state and with lipids (Non-HDL, LDL), none of uncontrolled group (C) had approached the targets regardless treatments used, however patients using insulin had in fairly and well controlled groups (B and A) as compared to those patients using oral anti diabetic drugs. On the other hand the target response of non-HDL-C in controlled group was best seen in patients using insulin while the target of LDL-C in controlled group demonstrated no difference among treatment types. A small sample size of patients using insulin in this study had limited the effect of treatment type on lipid abnormalities and it formed one of draw back on this study. Increasing use of insulin as primary treatment or in secondary failure might improve glycemic control and best target atherogenic lipids, though poor compliance and unfamiliarity in using insulin act as a burden on future management. As far as the incidence of diabetes mellitus grown globally and coronary heart disease accounts for majority of type 2 related morbidity and mortality <sup>[10]</sup> Non-HDL is simple, reliable index of overall for CHD risk that may be equivalent if not superior to total or very low density lipoprotein, that may form a future target in type 2 D.M. Both non-HDL-C and glycosylated hemoglobin are important predictors for coronary artery disease in diabetes mellitus and therapy to lower non-HDL-C and HbA1c are key markers of glycemic control and dyslipidemia.

**In conclusion:** This study had demonstrated the simplicity and effectivity of measurements of non-HDL in type 2 DM to provide an index of atherogenic lipid over other lipid profile and its level below 130 mg/dl was well correlated with glycemic control.

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