Triglycerides effect on the levels of low density lipoprotein and high density lipoprotein in type 2 diabetic patients.

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ABSTRACT

Background: **Type 2 Diabetes mellitus is a worldwide disease with the recent changes in life styles is associated with increasing complications and hyperlipidemia is hallmark risk factor for most complications.**

Objective: **To evaluate the effect of triglycerides on the levels of other lipid type's mainly low density lipoprotein cholesterol and high density lipoprotein cholesterol in type 2 diabetic patients.**

Patients and method: **From three hundred type 2 diabetic patients who consulted Diabetic and Endocrine Center in Al-Mawani General Hospital complaining from symptoms of diabetes over the period from January 2013 to July 2014, two hundred sixty six patients were eligible for this study. One hundred sixty four (61.7%) patients were males and one hundred two patients (37.3%) were females, their mean age was 50.57±9.28years. All patients were subjected to a thorough history and physical examination including their height, weight and body mass index were calculated, blood pressure was measured and fasting blood sample tested for blood sugar, glycosylated hemoglobin and lipid profile.**

Results: **level of low density lipoprotein lipid was greatly changed by level of triglyceride with mean difference ranges from (-0.05745 to 0.60150*) in patients with normal triglyceride and very high triglyceride with confidence interval (CI/ -0.6517 to 0.5368) in low and (CI/0.00441 to 0.1986) in patients with very high triglyceride. While the mean difference for Non high density lipoprotein ranges from (-0.55268 to -0.53312) and the value of confidence interval was (CI/-01.1761 to 0.0707) and (CI/ -01.15950 to 0.0933) between low and very high triglyceride levels The high density lipoprotein closely related in a parallel direction to level of triglyceride with mean difference ranges from (-0.01095 to -0.01942) with confidence interval (CI/ -0.2150 to 0.1931) and (CI/-0.2245 to 0.1856) between low and very high triglyceride type group.**

Conclusion: **Triglycerides which is frequently elevated in type 2 diabetic patients significantly influence the levels of low density lipoproteins but not high density lipoprotein and was reverse of the first and parallel levels of the second respectively. This lead to underestimation of atherogenic lipid or overestimation of the protective lipid respectively in type 2 diabetic patients.**

Key words: **Type 2 diabetes mellitus, triglycerides, LDL-C, HDL-C.**

تأثير الشحوم على مستويات البروتينات الدهنية منخفضة الكثافة والبروتينات الدهنية عالية الكثافة في مرضى السكري من النوع الثاني

الخلفية: داء السكري النوع الثاني مرض في جميع أنحاء العالم مع التغيرات الأخيرة في أنماط الحياة، المرتبطة بزيادة التعقيدات والدهون عامل خطر والسمة المميزة لمعظم المضاعفات.

الهدف: لتقييم تأثير الشحوم على مستويات أساسا انخفاض كثافة البروتين الدهني نوع الدهن آخر نسبة الكولسترول في الدم والكوليسترول بروتين دهني عالي الكثافة في نوع مرضى السكري ٢.

المرضى والأسلوب: مجموع مائتان وست وستون مريضا الذين يعانون من أعراض السكري من النوع الثاني الذين استشاروا مركز السكري والغدد الصماء في المستشفى الموانئ العام و يشكون من أعراض مرض السكري خلال الفترة من كانون الثاني/يناير ٢٠١٣ إلى ٢٠١٤ تموز/يوليه، كانوا مؤهلين لهذه الدراسة مائة وأربعة وستون من الذكور (٦١.٧%) ، ومائة واثنتان(٣٧.٣ في المائة) من الإناث، معدل أعمارهم يعني ٥٠.٥٧±٩.٢٨. جميع المرضى الذين تعرضوا لتاريخ دقيق وحسبت الفحص البدني بما في ذلك مؤشر كتلة الطول والوزن والجسم وتم قياس ضغط الدم واختبار عينة من الدم أثناء الصيام للسكر في الدم، الغليكوزيلاتي خضاب الدم ومستوى الدهون.

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النتائج: مستوى الدهون **LDL–C** قد تغير كثيرا بمستوى الدهون الثلاثية مع نطاقات الموزون من (**–٠.٠٥٧٤٥** إلى **٠.٦٠١٥٠***) في المرضى الذين يعانون من الدهون الثلاثية العادية والدهون الثلاثية عالية جداً مع فاصل الثقة (**CI/–0.6517** إلى **٠.٥٣٦٨**) في منخفض و (**CI/0.00441** إلى **٠.١٩٨٦**) في المرضى الذين يعانون من الدهون الثلاثية مرتفعة جداً. حين الفرق يعني غير **HDL–C** يتراوح من (**–٠.٥٥٢٦٨** إلى**–٠.٥٣٣١٢**)، وكانت قيمة فاصل الثقة (**CI/–01.1761** إلى **٠.٠٧٠٧**) و (**CI/–01.15950** إلى **٠.٠٩٣٣**) بين منخفضة جداً ومستويات الدهون الثلاثية العالية **HDL–C** ارتباطاً وثيقا في اتجاه مواز لمستوى الدهون الثلاثية مع نطاقات الموزون من (**–٠.٠١٠٩٥** إلى**–٠.٠١٩٤٢**) مع فاصل الثقة (**CI/–0.2150** إلى **٠.١٩٣١**) و (**CI/–0.2245** إلى **٠.١٨٥٦**) بين نوع الدهون الثلاثية منخفضة وعالية جداً في المجموعة

الاستنتاج: مستوى الدهون الثلاثية التي كثيرا ما تكون مرتفعة عند مرضى السكري من النوع الثاني إلى حد كبير لها تأثير على مستويات الدهون القليلة الكثافة وعدم وجود تأثير على العالية الكثافة أو الحميدة –فهي معاكسة للأولى وموازية للثانية على التوالي. وهذا يؤدي إلى التقليل من أهمية تأثير تأثرها في القليلة الكثافة أو المبالغة في تقدير الدهن الواقية في مرضى السكري من النوع ٢ على التوالي.

الكلمات المفتاحية: السكري من النوع الثاني، الدهون الثلاثية، الدهون قليلة الكثافة ،الدهون علية الكثافة

INTRODUCTION

Chronic hyperglycemia not only affect carbohydrate metabolism but also implies an effects on various body metabolic processes including lipid and protein metabolism.[1] Hence the chronic effects of diabetes mellitus is associated with various dysfunctions, long term damage and failure of various body organs including heart, renal, nerves, eyes and peripheral vascular system. [2,3] Dyslipidemia in people with type 2 diabetes as one of the well-known metabolic derangements, it involves changes in the levels of high density lipoprotein cholesterol, low density lipoprotein, very low density lipoprotein and triglyceride.[4,5,6] Insulin resistance and deficiency both are the key enzymes and pathways in lipid metabolism.[7] Well known that increased levels of low-density lipoprotein cholesterol (LDL-C) are a widely recognised risk factor for coronary artery disease. Two main patterns for LDL-C subfractions was described.[8,9] In pattern A, there is a preponderance of large floating LDL particles while in pattern B smaller denser LDL particles predominate. Pattern B is usually associated with elevated triglyceride and low HDL-C. Triglyceride concentration seems to be the most important determinant of LDL sub fraction profile. Pattern B is rarely found where serum triglyceride is less than 1 mmol/L but is usual where it exceeds 2 mmol/L. Pattern B is not unusually found in type 2 diabetes and it is a part of the insulin resistance syndrome.[9] Although long-standing association exists between elevated triglyceride levels and cardiovascular disease, [10] its role in diabetes cardiovascular complications is still not completely understood, some researchers kept it as second risk factor after LDL and VLDL as predictor of IHD risk, but its role may attributed to its effect in lowering HDL Level and this may impose a risk for CVS or due to under estimation of LDL and VLDL levels. This underestimations lead to miss managements of already friable patients. [11,12] There is suggestive evidence that increasing level of triglyceride lead disproportionally to decrease in the level of LDL in diabetic patients and if this level are abnormal high lead to miss interpretation of lipid profile.[13] Some researchers look for other way to predict the atherogenic lipids. It has been recently suggested that Non- HDL cholesterol might be a useful marker and better predictor of CVD than LDL cholesterol in diabetic as well as non-diabetic individuals.[14] Non high density lipoprotein cholesterol reflects total cholesterol minus HDL cholesterol and incorporates all cholesterol that is potentially atherogenic. Instead of recommending direct measures of LDL cholesterol, the most effective solution for

addressing the misclassification of very low LDL-C levels is to assess Non-HDL-cholesterol levels instead. [15,16] Directly measuring LDL cholesterol would be an extra test on top of a standard lipid panel and cost the health care system more. Also, there are multiple ways of measuring LDL cholesterol directly, and the reliability of measurements from one lab to the next is not known. [17] The proposed aim of this study was to show whether triglyceride levels implies an effect on the other lipids, commonly LDL-C and HDL-C in type 2 diabetic patients.

PATIENTS AND METHODS

This is a prospective descriptive study conducted in Al-Mauwani, General Hospital, Endocrine and Diabetic Center in Basra (Southern Iraq) over the period from January 2013 to July 2014. Two hundred sixty six patients enrolled in this study, after exclusion of patients already being under treatment of hyperlipidemia and those with morbid obesity. Patients were subjected to thorough history and physical examination, their blood pressure measured, weight and height, were measured and body mass index were calculated by the formulae of body weight in kg over the square height in meter. Fasting blood sample sent for blood sugar, HbA1c and lipid profile. Glucometer used for measuring blood sugar, the same recommended tool in the center used for measurement of lipid profile, glycosylated hemoglobin measured for every patients included. NHDL– C, calculated from subtracting HDL – C from total cholesterol. The patients subdivided into four groups according to their triglyceride levels agreeing to the American National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III) guidelines. [18, 19]

Group 1; Patients with normal triglyceride, with levels less than 1.7 mmol/L
Group 2; Patients with border line high triglyceride, with levels 1.7 to 2.29 mmol/L
Group 3; Patients with high triglyceride, with levels from 2.3 to 5.59 mmol/ L
Group 4; Patients with very high triglyceride, with levels more than 5.6 mmol/L

Data were collected and computed on SPSS Version 22, the frequency of variable measured by test of frequency and the mean and standard deviation of fixed variable by relevant test. ANOVA test were used to compare mean of differences among main groups, their confidence intervals, post Hoc tests used to compare between the groups of independents variable, p value of 0.05 was considered significant.

RESULTS

Table 1. General characteristic of the studied groups, matched well among the study groups regarding their age, body mass index, duration of diabetes and their HbA1c, but not in their triglyceride levels.

Group	No. (%)	Age/years	Bmi	Duration/years	Hba1c	Triglyceride levels mmol/l
1	43(16.2)	51.97 ± 9.85	27.57 ± 4.83	7.09 ± 4.74	7.86 ± 1.83	1.34 ± 0.29
2	49(18.4)	50.87 ± 8.25	29.45 ± 5.76	6.89 ± 4.82	8.27 ± 1.75	1.98 ± 0.18
3	126(47.4)	51.15 ± 9.74	27.71 ± 4.34	6.41 ± 5.34	8.42 ± 1.60	3.53 ± 0.83
4	48(18.0)	47.52 ± 8.08	28.03 ± 4.54	6.40 ± 6.34	8.02 ± 1.30	8.23 ± 1.62
Total	266(100.0)	50.57 ± 9.28	28.06 ± 4.76	6.54 ± 5.42	8.08 ± 2.37	3.71 ± 2.50
P. value		0.081	0.149	0.935	0.187	0.000

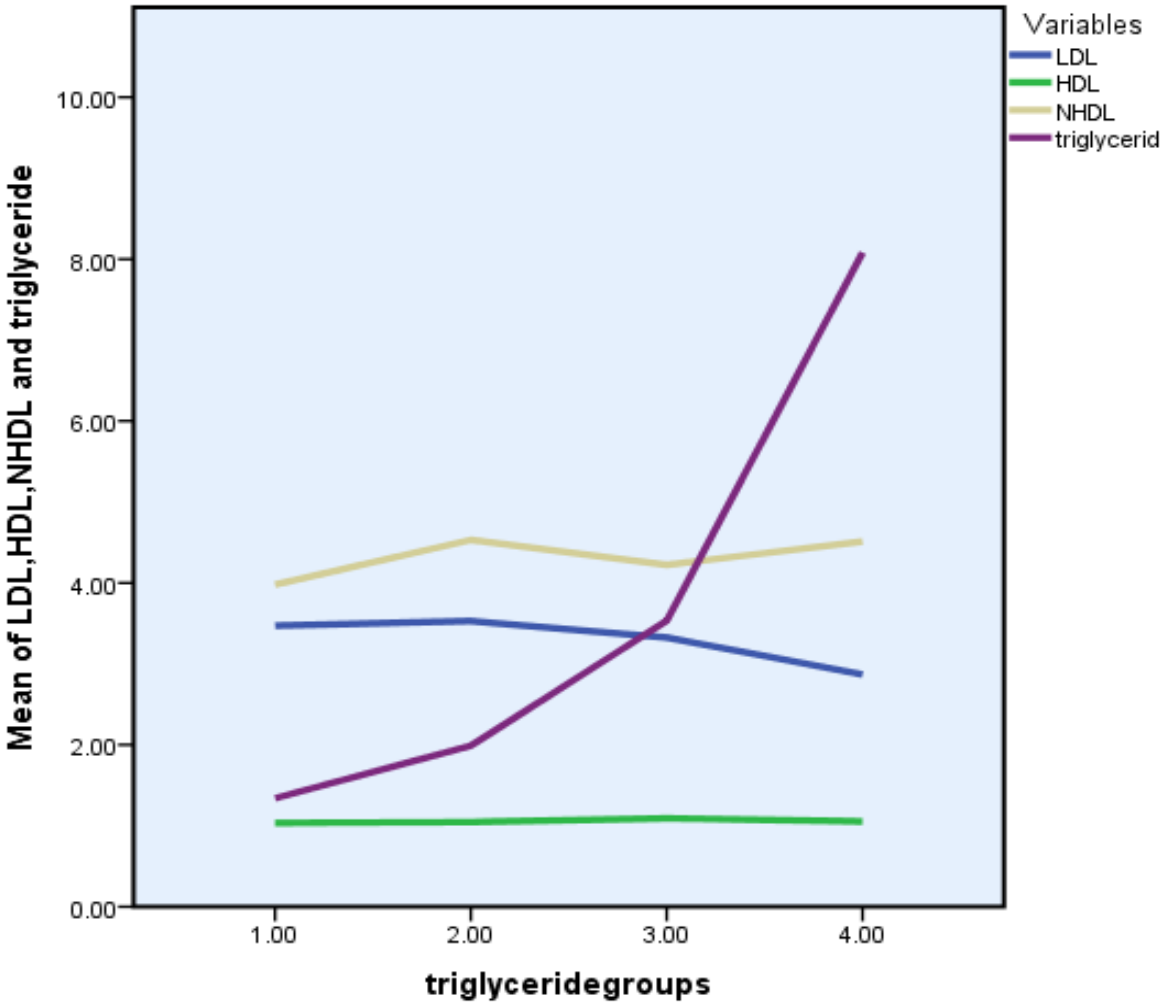
Table 2. One way ANOVA Test to compare between the groups with the triglyceride type according to whether the dependent factor are combined, weighted and un weighted which shows significant results in low density lipoprotein in all measurements type but not for high density lipoprotein and non-high density lipoprotein lipids type.

		Sum of squares	**DF**	**Mean square**	**F**	**SIG.**
LDL	Between Groups	12.786	3	4.262 3	0 .52	0.016
Linear Term	Un weighted	9.481	1	9.481 7	0.83	0.005
	Weighted	8.879	1	8.879 7	0.34	0.007
	Deviation	3.907	2	1.954 1	0.61	0.201
HDL	Between Groups	0.155	3	0.052	0.36	0.780
Linear Term	Un weighted	0.026	1	0.026	0.18	.671
	Weighted	0.044	1	0.044	0.30	.580
	Deviation	0.112	2	0.056	0.39	.677
NHDL	Between Groups	9.945	3	3.315	2.49	061
Linear Term	Un weighted	3.921	1	3.921	2.94	.087
	Weighted	2.769	1	2.769	2.080	.150
	Deviation	7.176 2	3	0.588 2	.69	0.06

Table 3. Multiple Comparisons using Post Hock Test, in the assumed equal variance,Tukey HSD test used to measure mean difference of lipid types and subgroup of triglyceride which demonstrate, that the more levels of triglyceride significantly inversely associated with levels of LDL-C but not with levels of HDL-C or Non-HDL-C.* The mean difference is significant at the 0.05 level.

Dependent variable	Triglyceride group	(J) T. Group	Mean dif (I-J)	Std. Error	Sig.	95% CI	
						Lower	Upper
LDL	**1.00**	2.00	-0.05745	.22984	.995	-.6517	.5368
		3.00	0.14574	.19426	.876	-.3565	.6480
		4.00	0.60150*	.23095	.048	.0044	1.1986
	2.00	1.00	0.05745	.22984	.995	-.5368	.6517
		3.00	0.20319	.18518	.692	-.2756	.6820
		4.00	0.65894*	.22337	.018	.0814	1.2365
	3.00	1.00	-0.14574	.19426	.876	-.6480	.3565
		2.00	-٠.20319	.18518	.692	-.6820	.2756
		4.00	٠.45575	.18656	.072	-.0266	.9381
	4.00	1.00	-٠.60150*	.23095	.048	-1.198	-.0044
		2.00	٠.65894*	.22337	.018	-1.2365	-.0814
		3.00	-٠.45575	.18656	.072	-.9381	.0266
HDL	**1.00**	2.00	-٠.01095	.07892	.999	-.2150	.1931
		3.00	-٠.05754	.06670	.824	-.2300	.1149
		4.00	-٠.01942	.07930	.995	-.2245	.1856
	2.00	1.00	٠.01095	.07892	.999	-.1931	.2150
		3.00	-٠.04659	.06358	.884	-.2110	.1178
		4.00	-٠.00847	.07670	1.000	-.2068	.1898
	3.00	1.00	٠.05754	.06670	.824	-.1149	.2300
		2.00	٠.04659	.06358	.884	-.1178	.2110
		4.00	٠.03812	.06406	.933	-.1275	.2037
	4.00	1.00	٠.01942	.07930	.995	-.1856	.2245
		2.00	٠.00847	.07670	1.000	-.1898	.2068
		3.00	-٠.03812	.06406	.933	-.2037	.1275
NHD	**1.00**	2.00	-٠.55268	.24110	.102	-1.1761	.0707
		3.00	-٠.24445	.20378	.628	-.7713	.2825
		4.00	-٠.53312	.24227	.126	-1.1595	.0933
	2.00	1.00	٠.24110	-.0707	.102	.55268	1.1761
		3.00	٠.30823	.19426	.388	-.1940	.8105
		4.00	٠.01956	.23432	1.000	-.5863	.6254
	3.00	1.00	٠.24445	.20378	.628	-.2825	.7713
		2.00	-٠.30823	.19426	.388	-.8105	.1940
		4.00	-٠.28867	.19571	.454	-.7947	.2173
	4.00	1.00	٠.53312	.24227	.126	-.0933	1.1595
		2.00	-٠.01956	.23432	1.000	-.6254	.5863
		3.00	٠.28867	.19571	.454	-.2173	.7947

Graph1: The plateau of the HDL, the corresponding of NHDL and the inverse relation of LDL with triglyceride groups which itself shows liner association with mean of triglyceride. Which indicate the mean difference of the tested lipid types.



DISCUSSION

In this study based on measurement of lipids in a known diabetic from both gender and well matched four groups of different triglyceride levels regarding their body mass index, age, duration of their disease after exclusion of morbid obese patients and patients on lipid lowering drugs to get ride its effect on levels of triglyceride. This study demonstrate an inverse correlations between triglyceride levels and LDL-C more significant in in patients with very high triglyceride and less with border line high and plateau with moderate triglyceride. This is similar to other study. The PROVE IT-TIMI 22 trial demonstrate that achieving lower triglyceride levels may be an additional consideration beyond level of LDL-C in reducing events after coronary artery surgery.[20] This in part may reflect the role of triglyceride in prevention of CAD. On other hand in comparison with WOSCOPS group study which demonstrate the effect of triglyceride and other factors including body mass index and alcohol

consumptions on both LDL-C and HDL-C.[21] This study differs in respect to HDL-C that show plateau correlations with triglyceride levels in comparison to levels of LDL-C. The results in this study explain the proposed hypothesis, that triglyceride implies a strong risk factor on the atherogenic lipid type (LDL). Being this study well matched regarding non modifiable risk factors like age, gender, duration and race and also modifiable risk as body mass index, levels of HbA1c,and being the sample of lipid profile measurements tested during fasting state give the study more freedom from limiting factors in addition to the biases of the typical time of triglyceride measurements.[22] Treatment of hypertriglyceridemia in type 2 DM patient when firstly faced and normalized its levels may made a chance of appropriately assess the lipid abnormality and best approach to treatment of other lipid abnormalities especially LDL-C. On the other hand some researchers found that combined hyperlipidemia in a form of raised triglyceride and LDL-C theoretically might raise the possibility of coronary heart disease in diabetic patients and aim to lower both triglyceride and LDL-C may minimize the recurrences of CHD.[19] But the inverse relationship between both lipid types in type 2 DM patients not supports this suggestive theory. Whatever the reactions of lipid type the parallel movement of Non HDL-C & the plateau of HDL-C with triglyceride level might give strong association between them. While the inverse relation between triglyceride and LDL-C that shown in this study may falsely reduce level of LDL-C in diabetic patients and development of CAD. As triglycerides are the common lipids deranged in type 2 diabetic patients, actually we need more study to compare with other studies. Practice direct measurements of LDL-C and its sub fraction to measure pitfall this study. The other results that emerge in this study is the positive movement of both HDL-C with triglyceride level may give falsely high value of HDL-C in diabetic patients that is regarded as protective lipid in prevention of CHD. The well matched study gives another clue to the firmness of the study as the interferences of these factors are excluded. [23,24] Non high density lipoprotein (NHDL) that have been introduced lipid type, easily measured may not affected by levels of triglyceride, may form one of the recent changes in the treatments of lipid derangements.

In conclusion, Focusing on triglyceride levels in type 2 diabetic patients should be considered seriously as part of routine investigations. Initiate treatments for triglyceride may falsely normalized LDL-C and increase HDL-C to use the last both as predictor of atherogenicity become less likely applicable. Increase the use of simple, easily measured Non HDL-C instead of LDL-C may form the future target for diabetic dyslipidemia.

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