

Dyslipidemia and Type-2 Diabetics

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Objective: To determine the frequency of type-2 diabetics who have target lipoprotein blood levels and to study these levels in patients with ischemic heart disease and cardiovascular disease risk factors.

Design: Retrospective analytical study of hyperlipidemic type-2 diabetics between January 2000 and January 2001 was undertaken.

Setting: King AbdulAziz University Hospital.

Method: We studied hyperlipidemic type-2 diabetics who were on regular follow up to the medical outpatient clinic of King Abdulaziz University Hospital from January 2000 to January 2001. The mean lipoprotein levels, duration of hyperlipidemia and its treatment, duration of diabetes, its treatment and degree of blood glucose control, presence of hypertension, ischemic heart disease, and smoking.

Results: A total of 202 patients were studied with mean age of 60 years and equal male to female ratio. The mean duration of diabetes was 10 years and it was 7 years for hyperlipidemia. The mean level of LDL was 3.15 mmol/l and it was 1.0 mmol/l and 2.47 mmol/l for LDL and TG respectively. Only 31% of patients had LDL < 2.6 mmol/l, 28% had HDL > 1.1 mmol/l and 37% had TG < 1.7 mmol/l. No significant difference was found in the frequency of target level of LDL in patients with IHD and those without; 26% versus 34% (0.4). Similarly, no difference was found in those with hypertension, obesity, and patients with family history of IHD compared to those without these risk factors; 30%, 26%, 16% versus 34%, 36%, 33% (p 0.2, 0.1, 0.4 respectively). Males were found to have a higher frequency of target LDL level compared to females; 38% versus 25% (p 0.04).

Conclusions: A low frequency of type-2 diabetics has target levels of lipoproteins and this was also evident in diabetics with IHD and CVD risk factors.

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Diabetes mellitus (DM) is one of the most common endocrine disorders. It is closely associated with coronary heart disease (CHD)¹. Diabetes is associated with two to four fold excess risk of CHD². Eighty percent of patients with type 2 diabetes will die of cardiovascular diseases³. The most common pattern of dyslipidemia in diabetics is elevated triglyceride (TG), low high density lipoprotein cholesterol (HDL), and predominance of small dense particle low density lipoprotein (LDL). Baseline data from the UKPD (United Kingdom Prospective Diabetes) Study showed that both low HDL and elevated LDL predicted CHD⁴. According to the American Diabetes Association (ADA) recommendations⁵; treatment goal for lipoprotein therapy in diabetics is as follow: LDL <2.6 mmol/l, HDL>1.1 mmol/l, TG <1.7 mmol/l. The aim of this study is to determine the frequency of type 2 diabetics who have target lipoprotein blood levels and to study these levels in patients with ischemic heart disease and cardiovascular disease risk factors.

METHOD

The study was carried out at King Abdulaziz University Hospital (KAUH), a teaching hospital in the western province of Kingdom of Saudi Arabia. During a one year period – January 2000 through January 2001, type 2 diabetics who were on regular follow up to the medical outpatient clinic were studied. Patients with dyslipidemia (defined as patient is known hyperlipidemic or has LDL >2.6 mmol/l, HDL <1.1 mmol/l, TG >1.7 mmol/l) were included in the study. For those who were recently discovered, they were reassessed after 6 months period. The mean lipoprotein levels of the last two visits were calculated and the duration of hyperlipidemia and type of treatment (diet, statin, fibrates, or combined) were recorded. Data were collected from the duration of DM, type of treatment, degree of blood glucose control (well controlled defined as H1c <7%, fasting <7 mmol/l, post-prandial <9 mmol/l), presence of hypertension (patient is known or having blood pressure >140/90 mmHg), its duration, presence of ischemic heart disease (IHD) (assessed by patients history or changes on electrophysiological studies), smoking (whether active or passive) and mortality.

The frequency of target lipoprotein level were studied as well as its level in patients with (CHD) and (CHD) risk factors. Statistical analysis was performed using the SPSS software. Mean \pm SD was determined for quantitative data, and frequency for categorical variables. Chi-square was used to analyze group difference for categorical variables. For continuous variables t-test were used if comparing two groups. P value <0.05 was considered significant.

RESULTS

A total of 202 patients were included in the study. The mean age was 59.9 \pm 12.9 years with equal male to female ratio and mean duration of diabetes 10.3 \pm 7 years. Most of the patients were using oral hypoglycemic agents for blood glucose control followed by insulin and diet; 121/202 (60%), 59/202 (29%), 22/202(11%) respectively. The majority of patients, 190/202 (94%), have poor blood glucose control. The mean duration of hyperlipidemia was 6.6 \pm 1.7 years. Hypertension, obesity and (IHD) were found with

high frequency in the study group (Table 1). A low frequency of diabetics has goal of lipoprotein levels (Table 2). As shown in Table 3; both patients with CHD, CHD risk factors and those without have poor target lipoprotein levels. Males are more likely to have target LDL compared to females. A significant relation was found between poor lipid control and long duration of hyperlipidemia; mean duration of hyperlipidemia in patients with poor control was 6.9 ± 1.8 years versus 5.2 ± 1.4 years in those with good control ($p=0.004$). Patients with poor glycemic control has poor lipid control; 60/190 (32%), patients with poor blood glucose control has goal level of LDL, 70/190 (37%) goal TG, 52/190 (27%) goal HDL versus 130/190 (68%), 120/190(63%) has high LDL,TG, and 138/190(73%) has low HDL levels respectively ($p <0.001, 0.02, 0.001$ respectively) Most of patients, 112/202 (55.4%) , were not taking pharmacological treatment for lipid control while those on statin were 66/202(32.7%), on fibrates 18/202(8.9%) and on combined statin and fibrates 6/202(3%).

Table 1. Some characteristics of the study group

<i>Variable</i>	<i>Total Number=202 N (%)</i>
Ischemic heart disease	81(40)
Hypertension	140(69)
Duration of hypertension in years (mean \pm SD)	8.25 \pm 6.8
Body mass index in Kg/m ² (mean \pm SD)	29.3 \pm 6.3
<30 Kg/m ²	121 (60)
>30 Kg/m ²	81(40)
Smoking	37(18)
Family history of ischemic heart disease	38(19)
Mortality	17(8)

Table 2. Lipoproteins blood levels

<i>Lipoprotein type</i>	<i>Lipoprotein level N(%)</i>
LDL in mmol/l (mean \pm SD)	3.15 \pm 1.9
<2.6 mmol/l	62(3)
2.6 –3.4 mmol/l	60(30)
>3.4 mmol/l	80(39)
HDL in mmol/l (mean \pm SD)	\pm 0.29
>1.1 mmol/l	57(28)
<1.1 mmol/l	145(72)
Triglyceride in mmol/l (mean \pm SD)	2.47 \pm 1.9
<1.7 mmol/l	75(37)
>1.7 mmol/l	127(63)

Table 3. Relation of target lipoprotein level to ischemic heart disease and cardiovascular disease risk factors

<i>Variables</i>	<i>LDL</i> <i>N (%)</i>	<i>P</i>	<i>HDL</i> <i>N (%)</i>	<i>P</i>	<i>TG</i> <i>N (%)</i>	<i>P</i>
IHD (N=81)	23(28)	0.4	16(20)	0.02	27(33)	0.3
No IHD (N=121)	41(34)		41(34)		48(40)	
Hypertension (N=140)	42(30)	0.2	36(26)	0.4	49(34)	0.2
No hypertension (N=62)	21(34)		20(33)		25(42)	
Obese (N=81)	21(26)	0.1	24(30)	0.7	23(28)	0.03
Non-obese (N=121)	43(36)		33(27)		52(43)	
Smokers (N=37)	6(16)	0.02	9(24)	0.5	6(16)	<0.001
Non-smokers (N=165)	58(35)		48(29)		69(42)	
Family history of IHD (N=38)	10(26)	0.4	10(26)	0.7	10(26)	0.1
No family history (N=164)	54(33)		47(29)		65(40)	
Males (N=102)	39(38)	0.04	25(25)	0.2	38(37)	0.9
Females (N=100)	25(25)		32(32)		37(37)	

Target LDL <2.6 mmol/l, target HDL >1.1 mmol/l, target TG <1.7

IHD = ischemic heart disease

DISCUSSION

Diabetes is rapidly becoming a major public health problem worldwide². A study conducted by Mokdad et al⁶ detected 33% increase in the prevalence of diabetes in adults across all age-groups, races, education level, weight level, and level of smoking over 8 year period (1990-1998). Type 2 diabetes is a progressive disease and it is an independent risk factor for CHD. Patients with diabetes and no previous history of IHD have the same risk for cardiac events as patients with previous myocardial infarction¹. It is also associated with a combination of CVD risk factors including; hypertension, high LDL, low HDL, high TG and abdominal obesity, which are primarily attributed to insulin resistance⁷⁻⁹. Patients with type 2 diabetes have an increased prevalence of lipid abnormalities that contribute to high rate of CVD. The Framingham offspring study had shown that there is twice the prevalence of low HDL, high TG, high LDL in diabetics compared to non-diabetics¹⁰. Clinical research has found that these lipid abnormalities to be an independent risk factor for CHD in diabetics^{11,12}. It is clear in our study that minority of diabetics had goal lipoprotein level, where only 31% had goal LDL level. Similar result had been reported by Saaddine et al¹³ and others¹⁴⁻¹⁶. High LDL level was evident in diabetics with CHD risk factors where they are supposed to have better care because of their high risk. Poor lipid control was associated with long duration of hyperlipidemia and poor glucose control. This could be due to the patients being fed up from chronic use of multiple medications. Diabetes itself often require 2 or 3 separate medications each day, without the addition of additional disease treatments It is easy for us as physicians to tell a patient to take 5, 6, or 7 different pills up to 3 three times per day, but for the patient it will be boring. Another reason could be financial, patient can't afford buying multiple medications. An interesting observation is better lipid control in males compared to females, which is also observed in other studies^{13,14}, whether it is related to poor quality of care in diabetic females or other reasons, this needs to be

studied. Studies had also showed a lower risk of death attributed to IHD in diabetic males compared to females¹⁷. Lipid management had been shown to reduce the risk of CHD by 25% to 55% and the risk of death by 43%^{18,19}. Almost half of the patients were not on any pharmacological therapy and statins were the most frequently used medication. In three secondary prevention studies using statins, diabetics achieved significant reduction in coronary events¹⁹⁻²¹. A primary prevention study also using statins showed similar trend of reduced events²². The Helsinki Heart Study, the Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial (VA-HIT) also showed reduction in CHD events using fibrate^{23,24}.

CONCLUSION

It is clear from this study and other studies that lipid control is sub-optimal in diabetics. There is a gap between ADA recommendations and their clinical application. Patients with diabetes often lack sufficient knowledge about their disease and its complications. VHA (Veterans Health Administration) for example recommend reassessing patient's knowledge about diabetes at least three month after educational intervention²⁵. Programs to improve diabetics knowledge about the importance of controlling hyperlipidemia will allow them for better contribution to their care and the benefit of these programs should be reassessed. Also reinforcement and encouragement of physicians for better follow up and more aggressive management of hyperlipidemia is warranted.

REFERENCES

1. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486-97.
2. Malmberg-K, Yusuf-S, Gerstein-H, et al. Impact of Diabetes on Long-Term Prognosis in Patients with Unstable Angina and Non-Q-Wave Myocardial Infarction: Results of the OASIS (Organization to Assess Strategies for Ischemic Syndromes) Registry. *Circulation* 2000;102:1014-19.
3. O'Keefe J, Miles J, Harris W, et al. Improving the adverse cardiovascular prognosis of type 2 diabetes. *Mayo Clin Proc* 1999;74:171-80.
4. Turner RC, Millns H, Neil HA, et al. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus (UKPDS23). *BMJ* 1998;316:823-8.
5. Haffnir MS. Management of dyslipidemia in adults with diabetes. *Diabetes Care* 2002;25(Suppl 1): S74-S77.
6. Mokdad AH, Ford ES, Bowman BA, et al. Diabetes trends in the US:1990-1998. *Diabetes Care* 2000;23:1278-83.
7. American Diabetes Association. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 2001;23:S4-S19.
8. Cavaghan MK, Ehrmann DA, Polonsky KS. Interactions between insulin resistance and insulin secretion in the development of glucose intolerance. *J Clin*

- Invest 2000;106:329-33.
9. Polonsky KS, Sturis J, Bell GI. Seminars in Medicine of the Beth Israel Hospital, Boston. Non-insulin-dependent diabetes mellitus - a genetically programmed failure of the beta cell to compensate for insulin resistance. *N Engl J Med*. 1996;334:777-83.
 10. Siegel RD, Cupples A, Schaefer EJ, et al. Lipoproteins, apolipoproteins, and low-density lipoprotein size among diabetics in the Framingham offspring study. *Metabolism* 1996;45:1267-72.
 11. Miller M. Is hypertriglyceridemia an independent risk factor for coronary heart disease? The epidemiological evidence. *Eur Heart J* 1998;19:H18-22.
 12. Miller M. The epidemiology of triglyceride as a coronary artery disease risk factor. *Clin Cardiol* 1999;22:3-6.
 13. Saaddine JB, Engelgau MM, Beckles GL, et al. A Diabetes Report Card for the United States: Quality of Care in the 1990s. *Annals of Intern Med* 2002;136:565-574
 14. George PB, Kenneth J, Tobin DO, et al. Treatment of cardiovascular risk factors in diabetic patients: How well do we follow the guidelines. *Am Heart J* 2001; 142:857-63.
 15. Beckles GL, Engelgau MM, Narayan KM, et al. Population-based assessment of the level of care among adults with diabetes in the US. *Diabetes Care* 1998;21:1432-8.
 16. Cowie CC, Harris MI. Ambulatory medical care for non-Hispanic whites, African-American and Mexican-American with NIDDM in the US. *Diabetes Care* 1997;20:142-7.
 17. Barrett-Connor E, Wingard DL. Sex differential in ischemic heart disease mortality in diabetics: a prospective population-based study. *Am J Epidemiol* 1983;118:489-96.
 18. Goldberg RB, Mellies MJ, Sacks FM, et al. Cardiovascular events and their reduction with pravastatin in diabetic and glucose-intolerant myocardial infarction survivors with average cholesterol levels: subgroup analyses in the cholesterol and recurrent events (CARE) trial. The Care Investigators. *Circulation* 1998;98:2513-9.
 19. Pyorala K, Pedersen TR, Kjekshus J, et al. Cholesterol lowering with simvastatin improve prognosis of diabetic patients with coronary heard disease. A subgroup analyses of the Scandinavian Simvastatin Survival Study (4S). *Diabetes Care* 1997;20:614-20.
 20. The Long Intervention with pravastatin in ischemic heart disease (LIPID) study group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of intitial cholesterol levels. *N Eng J Med* 1998;339:1349-57.
 21. Sacks FM, Pfeffer MA, Loyer LA, et al. The cholesterol and recurrent events trial investigators: the effect of prevestatin on coronary events after myocardial infarction I patients with average cholesterol levels: cholesterol and recurrent events trila investigators. *N Eng J Med* 1996;335:1001-9.
 22. Downs JR, Cleafield PA, Langendorfer A, et al. Primary prevention of acute coronary events with lovastatin in men and women with average age cholesterol levels: results of AFCAPS/TexCAPS. *Air Force/Texas Coronary Atherosclerosis*

- prevention Study. JAMA 1998;279:1615-22.
23. Frick MH, Elo O, Haapa K, et al. Helsinki Heart Study: Primary prevention trial with gemfibrozil in middle-aged men with dyslipidemia. Safety of treatment, changes in risk factors and incidence of coronary hear disease. N Eng J Med 1987;317:1237-45.
 24. Rubins HB, Robins SJ, Collins D, et al. The secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotei Cholesterol Intervention Trial Study Group. N Eng J Med 1999;341:410-18.
 25. Diabetes Mellitus Working Group. Veterans Health Administration clinical guidelines for management of diabetes mellitus. Version 4.0. Washington, DC: Veterans Health Administration,1997.