

FREQUENCY DISTRIBUTION OF ATHEROGENIC DYSLIPIDEMIA IN SAUDI TYPE 2 DIABETIC PATIENTS

Syed Shahid Habib

Department of Physiology, College of Medicine, King Saud University, King Saud University, Riyadh, Kingdom of Saudi Arabia.

Background: This project was aimed to study the prevalence of desirable and high risk levels of lipid profiles in Saudi type 2 diabetics according to ATP III guidelines. **Methods:** This cross sectional study was conducted at College of Medicine of King Saud University, Riyadh, Saudi Arabia. A total of 507 Saudi type 2 diabetic patients were randomly selected. Selection criteria include Saudi National of any sex aged more than 25 years. No exclusion criteria except those patients who did not complete the investigations needed for this study. Fasting blood samples were analyzed for total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), glucose and glycosylated hemoglobin (HbA1c). We assessed the percentage of patients falling into desirable, borderline and high risk categories according to the criteria laid down by Adult Treatment Panel III of American Medical Association. **Results:** It was found that 56.6, 23.6, 77.1 and 48.9 percent of diabetic subjects had borderline to high risk levels of TC, TG, LDL-C and HDL-C respectively. **Conclusions:** It is concluded that type 2 diabetic patients have a high frequency of atherogenic dyslipidemia especially for TC, LDL-C and HDL-C. It is suggested that along with glycemic control physicians should focus more on lipid profiles also.

Key Words: Type 2 Diabetes Mellitus, Dyslipidemias, Lipoproteins,

INTRODUCTION

The major clinical objective in the management of DM is to control hyperglycaemia and the long term objective is to prevent microvascular and macrovascular complications.¹ Atherogenic dyslipidemia is characterized by 3 lipoprotein abnormalities: elevated very-low-density lipoproteins (VLDL), small dense LDL particles, and low high-density-lipoprotein (HDL) cholesterol. The lipid triad occurs frequently in patients with premature CHD and appears to be an atherogenic lipoprotein phenotype independent of elevated LDL cholesterol (LDL-C).^{2,3} Most patients with atherogenic dyslipidemia are insulin resistant.^{4,5} Atherogenic dyslipidemia in diabetic patients often is called diabetic dyslipidemia. Many patients with atherogenic dyslipidemia also have an elevated serum total apolipoprotein B.⁶ Although there is evidence that each component of the lipid triad low HDL, small LDL, and remnant lipoproteins—is individually atherogenic, yet it is not possible to determine the relative quantitative contribution of each component. For this reason, the lipid triad is viewed as a whole a “risk factor.”

An elevated concentration of serum LDL cholesterol is a major risk factor for CHD.⁷ In fact, some elevation of LDL cholesterol appears to be necessary for the initiation and progression of atherosclerosis. In populations having very low LDL cholesterol levels, clinical CHD is relatively rare, even when other risk factors hypertension, cigarette smoking, and diabetes are common.⁸ In contrast, severe elevations in LDL cholesterol can produce

full-blown atherosclerosis and premature CHD in the complete absence of other risk factors.⁹

Most patients with diabetes do not have marked elevations of LDL cholesterol, but these patients do carry high enough levels to that may lead to atherosclerosis.¹⁰ The Scandinavian Simvastatin Survival Study¹¹ the Cholesterol and Recurrent Events (CARE) trial,¹² and the Long-Term Intervention with Pravastatin in Ischemic Disease (LIPID)¹³ showed a positive role of aggressive LDL-lowering therapy on recurrent CHD events in diabetics.

Syndrome X, the association of raised concentrations of glucose, insulin, and triglyceride, decreased concentrations of high density lipoprotein cholesterol, and increased blood pressure, describes a combination of previously reported risk factors for coronary artery disease.¹⁴ Increased concentrations of low density lipoprotein cholesterol may be more pathogenic in patients with type 2 diabetes mellitus than in non-diabetic patients because of the presence of small dense low density lipoprotein cholesterol particles¹⁵ and oxidation of glycated low density lipoprotein cholesterol.¹⁶

The 1.57 increased risk for an increment of 1 mmol/l in low density lipoprotein cholesterol concentration equates to a 36% risk reduction for a decrement of 1 mmol/l, similar to the 31% risk reduction achieved with a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor in men with hypercholesterolaemia.¹⁷

According to ATP III guidelines Diabetes Mellitus is considered to be a coronary heart disease

(CHD) equivalent. From cardiovascular medicine aspect, it may be appropriate to say that "diabetes is a cardiovascular disease." Diabetics have a very high prevalence of cardiovascular disease morbidity and mortality.⁷

Therefore, we aimed to study the frequency of desirable and high risk levels of lipid profiles in a cohort of Saudi type 2 diabetic patients according to ATP III guidelines.

MATERIAL AND METHODS

This cross sectional study was conducted at College of Medicine, King Saud University, Riyadh, Saudi Arabia. A total of 507 Saudi type 2 diabetic patients were randomly studied. Selection criteria included Saudi National of any sex and aged more than 25 years. No exclusion criteria except those patients who did not complete the investigations needed for this study.

Fasting blood samples were analyzed for total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), glucose and glycosylated hemoglobin (HbA1c). We assessed the percentage of patients falling into desirable, borderline and high risk categories according to the criteria laid down by Adult Treatment Panel III of American Medical Association⁷

The data was analyzed by computer software program Statistical Package for Social Sciences (SPSS Version 10). Descriptive

characteristics and lipid profile of the study patients were calculated as Mean ± SD (Standard Deviation) for continuous variables and as percentages for categorical variables.

RESULTS

Descriptive characteristics and lipid profile of diabetic patients including sex, age, BMI, duration of diabetes, SBP, DBP, HbA1c, fasting glucose and lipid profile are summarized in Table 1.

We analyzed the prevalence of dyslipidemias according to ATP III guidelines (Table 2).⁷ The patients were categorized into Optimal, borderline and high risk (Table3). It was found that 56.6, 23.6, 77.1 and 48.9 percent of diabetic subjects had borderline to high risk levels of TC, TG, LDL-C and HDL-C respectively.

Table 1: Clinical characteristics and lipid profile in diabetic population (n=507)

Variable	Values (Mean±SD)
Age (years)	53.12 ±10.29
BMI (kg/m)	30.36 ± 4.46
FBS (mmol/l)	10.3 ± 4.0
2 hour post prandial (mmol/l)	13.85 ± 5.42
HbA1c %	8.9 ± 2.4
Duration (Years)	11.50 ± 7.02
Systolic BP mmHg	138.32 ± 23.41
Diastolic BP mmHg	82.39 ±10.01

Table 2: ATP III Classification of Categories of risk based on lipoprotein levels in adults

Risk Categories	Total Cholesterol		LDL		HDL		Triglyceride	
	Mg/dl	mmol/l	mg/dl	mmol/l	mg/dl	mmol/l	mg/dl	mmol/l
High	= 240	= 6.2	= 130	= 3.4	< 35	< 0.9	= 400	= 4.5
Borderline	200-239	5.2-6.1	100-129	2.6-3.3	35-45	0.9-1.0	200-399	2.3-4.4
Optimal	< 200	< 5.2	< 100	< 2.6	> 45	> 1.0	< 200	< 2.3

For woman values of HDL Cholesterol should be increased by 10 mg/dl

Table 3: Percentage distribution of desirable, moderate risk and high risk levels in DM patients according to criteria by ATP III. (N = 507)

Lipid Types	Desirable	Moderate risk	High risk
Serum total cholesterol	220 (43.4 %)	171 (33.7%)	116 (22.9 %)
Serum triglycerides	387 (76.3 %)	101 (19.9 %)	19 (3.7%)
Serum LDL cholesterol	116 (22.9 %)	149 (29.4%)	242 (47.7 %)
Serum HDL cholesterol	259 (51.1 %)	154 (30.4 %)	94 (18.5 %)

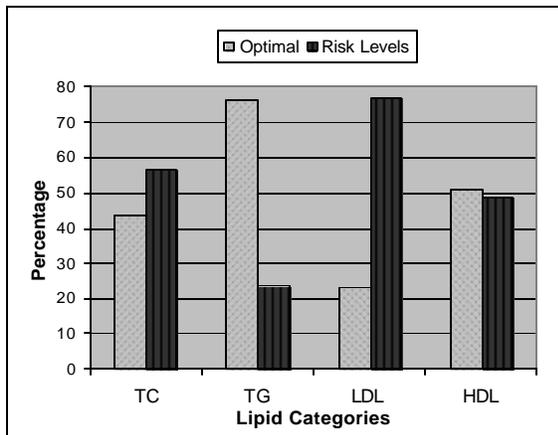


Fig-1: Frequency distribution of Optimal and Risk (Moderate plus High Risk) levels of TC, TG, LDL and HDL in diabetic subjects.

DISCUSSION

Patients with Diabetes Mellitus have a high prevalence of coronary artery disease (CAD).¹⁸ The major risk factors in DM are hyperglycemia, dyslipidemias and hypertension. Diabetic dyslipidemia is characterized by elevated levels of very low density lipoproteins cholesterol (VLDL-C), low density lipoprotein cholesterol (LDL-C) and lower levels of high density lipoproteins cholesterol (HDL-C), often referred to as the lipid triad.¹⁹ Lipid abnormalities in diabetic patients are likely to play an important role in the development of atherogenesis and so are called atherogenic dyslipidemia.²⁰ An issue of considerable interest is the relative contribution of each component of atherogenic dyslipidemia to CAD risk. Growing evidence suggests that all the components of lipid triad are independently atherogenic.²¹ The major risk factors in DM are glycaemic status, dyslipidemia and hypertension. The present study was an effort to provide an insight into some of the risk factors in DM. In this study we observed that a high percentage of type 2 diabetic patients have moderate to high risk levels of TC, TG, LDL-C, HDL-C. This percentage is quite higher for TC and LDL-C. According to NCEP guidelines LDL-C is the main target of CVD prevention.

In a study on Indian type 2 diabetic patients, high prevalence of atherogenic dyslipidemias has been reported.²² The prevalence of dyslipidemias is also very high in Kuwait and it is reported that diabetic patients with mixed hyperlipidaemia benefit from tight glycaemic control, appropriate advice on diet and exercise with regular reinforcement by continuing contact with professional dietitians and regular availability of drugs prescribed.²³ It has been

suggested that inspite of ethnic and cultural differences diabetics have significantly higher prevalence of dyslipidemias.²⁴ In terms of benefit for cardiovascular protection, treatment of hyperlipidemia has been reported to be more beneficial than blood pressure or glycaemic control.^{25,26} In a similar study a higher prevalence of undesirable levels of LDL-C has been reported in Pakistani diabetic subjects.²⁷

It is concluded that type 2 diabetic patients have a high frequency of atherogenic dyslipidemia especially for TC and LDL-C. It is suggested that along with glycaemic control physicians should focus more on lipid profiles also.

REFERENCES

1. American Diabetes Association. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Clinical Practice Recommendations. *Diabetes Care* 2000;21(suppl 1):S5–S19.
2. Austin MA, King M-C, Vranizan KM, Krauss RM. Atherogenic lipoprotein phenotype: a proposed genetic marker for coronary heart disease risk. *Circulation*. 1990;82:495–506
3. Grundy SM. Small LDL, atherogenic dyslipidemia, and the metabolic syndrome. *Circulation*. 1997;95:1–4
4. Grundy SM. Hypertriglyceridemia, atherogenic dyslipidemia, and the metabolic syndrome. *Am J Cardiol*. 1998;81:18B–25B.
5. Mostaza JM, Vega GL, Snell P, Grundy SM. Abnormal metabolism of free fatty acids in hypertriglyceridaemic men: apparent insulin resistance of adipose tissue. *J Intern Med*. 1998;243:265–274
6. Lamarche B, Tchernof A, Moorjani S, Cantin B, Dagenais GR, Lupien PJ, Despres JP. Small, dense low-density lipoprotein particles as a predictor of the risk of ischemic heart disease in men: prospective results from the Quebec Cardiovascular Study. *Circulation*. 1997;95:69–75
7. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). 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) final report. *Circulation*. 2002 17;106:3143–421.
8. Grundy SM, Wilhelmsen L, Rose G, Campbell RWF, Assman G. Coronary heart disease in high-risk populations: lessons from Finland. *Eur Heart J*. 1990;11:462–471.
9. Goldstein JL, Hobbs HH, Brown MS. Familial hypercholesterolemia. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. *The Metabolic and Molecular Bases of Inherited Diseases*. New York, NY: McGraw Hill; 1985:1981–2030.
10. National Center for Health Statistics. Plan and operation of the second national health interview survey 1976–1980. In: Vital and Health Statistics. Washington, DC: US Government Printing Office; Ser. 1, No. 15, DHHS Publication 81-1317, 1981.
11. Pyorala K, Pedersen TR, Kjekshus J, Faergeman O, Olsson AG, Thorgeirsson G. Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary heart disease: a subgroup analysis of the

- Scandinavian Simvastatin Survival Study (4S). *Diabetes Care*. 1997;20:614–620.
12. Goldberg RB, Mellies MJ, Sacks FM, Moya LA, Howard BV, Howard WJ, Davis BR, Cole TG, Pfeffer MA, Braunwald E, for the CARE investigators. 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. *Circulation*. 1998;98:2513–2519.
 13. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. *N Engl J Med*. 1998;339:1349–1357.
 14. Reaven, GM. Role of insulin resistance in human disease. *Diabetes* 1988; 37: 1595–1607 .
 15. Austin, MA., Breslow, JL., Hennekens, CH., Buring, JE., Willett, WC., & Krauss, PM. Low-density lipoprotein subclass patterns and risk of myocardial infarction. *JAMA* 1988; 260: 1917–1921
 16. Kawamura, M., Heinecke, JW., & Chait, A. Pathophysiological concentrations of glucose promote oxidative modification of low density lipoprotein by a superoxide-dependent pathway. *J Clin Invest* 1994; 94: 771–778
 17. Shepherd, J., Cobbe, SM., Ford, I., Isles, CG., Lorimer, AR., MacFarlane, PW., et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. West of Scotland Coronary Prevention Study Group. *N Engl J Med* 1995; 333: 1301–1307 .
 18. Diabetes Drafting Group: Prevalence of small vessel and large vessel disease in diabetic patients from 14 centres: the World Health Organization Study of Vascular Disease in Diabetics. *Diabetologia* 1985; 28:615-640.
 19. King H, Balkau B, Zimmet P, Taylor R, Raper LR, Borger J, Heriot W. Diabetic retinopathy in Nauruans. *Am J Epidemiol* 1983 Jun;117(6):659-67
 20. Pettitt DJ, Knowler WC, Lisse JR, Bennett PH. Development of retinopathy and proteinuria in relation to plasma-glucose concentrations in Pima Indians. *Lancet* 1980 Nov 15;2(8203):1050-2
 21. Haffner SM, Fong D, Stern MP, Pugh JA, Hazuda HP, Patterson JK, van Heuven WA, Klein R. Diabetic retinopathy in Mexican Americans and non-Hispanic whites. *Diabetes* 1988 Jul;37(7):878-84
 22. Udawat H, Goyal RK, Maheshwari S. Coronary risk and dyslipidemia in type 2 diabetic patients. *J Assoc Physicians India* 2001 Oct;49:970-3
 23. Akanji AO. Diabetic dyslipidaemia in Kuwait. *Med Princ Pract* 2002;11 Suppl 2:47-55
 24. Bermudez OI, Velez-Carrasco W, Schaefer EJ, Tucker KL. Dietary and plasma lipid, lipoprotein, and apolipoprotein profiles among elderly Hispanics and non-Hispanics and their association with diabetes. *Am J Clin Nutr* 2002 Dec;76(6):1214-21
 25. Hyman DJ, Pavlik VN. *N Engl J Med*. Characteristics of Patients with Uncontrolled Hypertension in the United States. 2001;345:479-485
 26. UKPDS. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet*. 1998 12;352(9131):837-53.
 27. Habib SS, Aslam M. Risk factors, knowledge and health status in diabetic patients Saudi Med J 2003; Vol. 24 (8):447-52

Address for correspondence

Dr Syed Shahid Habib, Department of Physiology (29), College of Medicine, PO Box 2925, King Saud University, Riyadh 11461, Kingdom of Saudi Arabia. Tel: 01-4671604, Fax: 01-4672567

Email: shahidhabib44@hotmail.com