LIPIDS AND RELATED PARAMETERS IN SAUDI TYPE II DIABETES MELLITUS PATIENTS

Mohsen A.F. El-Hazmi, PhD, FRCPath; A.R. Al-Swailem, MD;
A.S. Warsy, PhD; A.A. Al-Meshari, MD; R. Sulaimani, MD;
A.M. Al-Swailem, MD; G.M. Magbool, MD

Background: Non-insulin dependent diabetes mellitus (type II DM) is frequently associated with abnormal levels of lipids, particularly in patients with poor diabetic control. This study was designed to investigate the influence of type II DM on levels of plasma lipids and other related parameters in Saudi patients. Saudi Arabia has a high prevalence of diabetes mellitus in the adult population. Since the Saudi population presents a unique group with different dietary habits, lifestyle and genetic make-up, we investigated the lipids, lipoprotein and apolipoprotein pattern in Saudi type II DM patients.

Materials and Methods: This study was conducted on 2835 diabetic patients (1361 males, 1474 females) and 200 age-matched healthy adults from the same areas with no history of diabetes mellitus. Data collected included height, weight, body mass index (BMI), blood pressure and other relevant parameters. Lipids, lipoproteins and apolipoproteins were estimated, and correlation studies were carried out between these parameters. Lipids, lipoproteins and apolipoproteins were also correlated with the fasting blood glucose.

Results: Our results showed significant elevation in cholesterol and triglyceride, apo A and apo B levels in the diabetic males and females compared to the controls. Approximately 37% of the total DM patients fell in the borderline risk group, while 28.4% fell in the high-risk group for development of cardiovascular disease. Lipoproteins did not differ significantly. Cholesterol, triglyceride, VLDL, LDL and Hb A1c correlated positively with glucose (P<0.05), while triglyceride, VLDL, HDL, LDL, apo A and apo B showed significant correlation with cholesterol, where all parameters increased with cholesterol except HDL, which decreased as cholesterol increased.

Conclusion: The findings point toward high prevalence of dyslipidemia in type II DM Saudi patients.
Ann Saudi Med 1999;19(4):304-307.

Key Words: Diabetes mellitus, type II DM, lipids, cholesterol, triglycerides, lipoproteins.

During the last two to three decades, considerable interest has been directed towards the investigation of plasma lipids and related compounds in healthy and diseased individuals, due to the close association between abnormal lipid levels and the development of coronary heart disease (CHD), one of the major killer diseases of modern times.[1-5] The frequency of abnormality of lipids, lipoproteins and apolipoproteins varies in different populations.[6] The lipid levels are affected by age, sex, lifestyle, dietary habits, physical activities, obesity, hypertension, smoking, contraceptive use, and certain genetic predisposing factors.[7-11] In addition, diabetes mellitus is regarded as a major independent factor responsible for hyperlipidemias and CHD development, either by the exacerbation of the conventional atherogenic risk factors or by the production of its own risk factors.[12-13] Furthermore, diabetic patients from different populations seem to differ in their predisposition to development of lipid abnormalities.[1]

This study was conducted on Saudi diabetic patients in an attempt to: 1) determine the levels of plasma lipids, lipoproteins and apolipoproteins in Saudi diabetics; 2) determine the prevalence of lipid abnormalities; 3) correlate the lipid levels with the lipoproteins and apolipoproteins; and 4) correlate the fasting blood glucose level with the lipids, lipoproteins and apolipoproteins.

Patients and Methods

The study was conducted on a group of 2835 patients suffering from non-insulin-dependent diabetes mellitus, of whom 1361 (48%) were males and 1474 (52%) were females. The patients were diagnosed during a national screening program conducted over a period of four years (1992-1996), during which the Saudi population in the different areas of the country were screened through a "Household Screening Program," statistically designed to provide an accurate estimate of the prevalence of diabetes mellitus in different

From the College of Medicine (Drs. El-Hazmi, Al-Meshari and Sulaimani), King Saud University, the Ministry of Health (Drs. Al-Swailem, Al-Swailem and Magbool), and from the College of Science (Dr. Warsy), King Saud University, Riyadh, Saudi Arabia.

Address reprint requests and correspondence to Prof. El-Hazmi: Medical Biochemistry Department, College of Medicine & King Khalid University Hospital, P.O. Box 2925, Riyadh 11461, Saudi Arabia.

Accepted for publication 29 March 1999. Received 27 October 1998.

areas of Saudi Arabia. The screening procedure and the results of these investigations have been published elsewhere.[14-20] The patients suffering from diabetes mellitus were diagnosed, based on the criteria published by the World Health Organization,[21-22] as follows: Fasting venous blood glucose ≥6.7 mmol/L (120 mg/dL) and/or two-hour post-glucose load ≥10.0 mmol/L (≥180 mg/dL) were considered diabetic.[21,22] Differential diagnosis between non-insulin-dependent diabetes mellitus (type II DM) and insulin-dependent diabetes mellitus (type I) was based on the age of onset and the mode of treatment. All DM patients with an age of onset <25 years and continuous use of insulin subsequent to diagnosis were classified as type I DM, and were not included in this study. Older patients with an age of onset >25 years and dependence on dietary control or use of hypoglycemics were classified as type II DM and were included in the study. Essential physical data were recorded for each of the patients. Two hundred adult males and females (100 each) from the same population who were identified during the household screening, who were apparently healthy and not suffering from diabetes mellitus as judged from results of blood sugar analysis, were used as controls. They were in the same age range as the diabetics, had no family history of diabetes mellitus, did not smoke and were not obese, as judged by the body mass index (BMI) value.

The fasting blood sample (10 mL) from type II DM patients and controls were collected by venipuncture in heparinized tubes (or calcium oxalate with fluoride), and stored at 4°C for no more than two hours. The plasma was carefully separated from the cells by centrifugation at 1000 rpm for 10 minutes. The levels of lipoproteins were determined following electrophoresis using kits from Helena in fresh plasma samples. The rest of the sample was stored frozen until required for analysis. The blood glucose was estimated in the sample collected in fluoride tube. An autoanalyzer (American Monitor-Parallel^{R}) at the Central Laboratory at King Khalid University Hospital, Riyadh, was used for the estimation of cholesterol (by cholesterol esterase), triglyceride (by lipoprotein lipase), and glucose (by glucose oxidase) levels. The levels of apolipoproteins A and B were determined by Radial Immuno Diffusion (RID), using RID plates from Behring, and Hb A1c was determined (in whole blood), using Quick Column for Hb A1c from Helena.

The results were fed into the mainframe computer at the Computer Center in Riyadh, and using the Statistical Analysis System (SAS), the data analysis were conducted separately for the diabetic males and females and their nondiabetic counterparts (controls). The significance of the difference in the results of any two groups was determined using Student's *t*-test. *P*-value less than 0.05 was considered statistically significant. Regression analysis was carried out and correlation coefficients were determined using the General Linear Model (GLM) Program of SAS. $P<0.05$ indicated a statistically significant correlation.

TABLE 1. *Essential physical data on Saudi diabetic patients and controls (mean±SD).*

	Type II DM		Controls	
	Male	Female	Male	Female
Age (yr)	55.1±16.5	51.6±14.3	54.1±15.9	51.7±14.3
Height (m)	162.1±11.0	153.7±6.9	165.8±8.6	155.1±9.7
Weight (kg)	72.6±13.3	74.3±14.2	69.9±16.1	64.3±15.5
Body mass index (kg/m^2)	27.9±7.4	31.6±6.3	28.9±4.6	31.1±7.7

Results

The essential physical data of the diabetic patients and controls are listed in Table 1. The levels of fasting blood glucose, Hb A1c, plasma lipids, lipoproteins and apolipoproteins in the diabetic patients compared to the controls are presented in Table 2. The levels of the lipids (cholesterol and triglycerides), apo A and B, fasting blood glucose and Hb A1c were significantly higher in the type II DM patients (both males and females), compared to the controls. Among the lipoproteins, chylomicron and very-low-density lipoproteins (VLDL) were higher and high-density lipoproteins (HDL) were lower in the diabetic group, though the difference was not statistically significant ($P>0.05$). Using the cholesterol and triglyceride levels, the diabetic patients and controls were classified as borderline and high-risk for the development of coronary heart disease, according to the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation and treatment of high blood cholesterol in adults[23] (Table 3). Approximately 17.1% of males and 20.1% of females fell in the borderline group ($c^2=6.44$; $P=0.01$), while 11.3% of males and 17.1% of females fell in the high-risk group for developing CHD when cholesterol levels were considered ($c^2=3.7$; $P=0.01$). With triglyceride levels being considered, 12.0% of males and 11.9% of females ($c^2=5.4$; $P=0.02$) were borderline, while 2.4% of male and 1.4% of female diabetics ($P>0.05$) fell in the high-risk group.

Fasting blood glucose was correlated with the levels of plasma lipids, lipoproteins and apolipoproteins. A statistically significant correlation was obtained with cholesterol (r=0.17; $P=0.021$), triglyceride (r=0.356; $P=0.0001$), VLDL (r=0.144; $P=0.001$), LDL (r=0.133; $P=0.001$), and Hb A1c (r=0.133; $P=0.001$), though the correlation coefficient (r) was not very high. With HDL, apo A and apo B, there was no significant correlation ($P>0.05$).

Correlation studies were also carried out between cholesterol and plasma triglycerides, lipoproteins and apolipoproteins. Cholesterol level correlated positively with triglyceride (r=0.452; $P=0.001$), LDL (r=0.216; $P=0.001$), apo A (r=0.192; $P=0.031$) and apo B (r=0.137; $P=0.04$), though the correlation coefficients were not very high. With VLDL (r=0.075; $P=0.025$) and HDL (r=0.209; $P=0.001$), a statistically significant negative correlation was obtained.

Further correlation studies were conducted between plasma

TABLE 2. *Level of plasma lipids, lipoproteins and apolipoproteins in Saudi diabetics (mean±SD).*

Parameters	Type II DM patients		Control group	
	Male	Female	Male	Female
Lipids				
Cholesterol (mmol/L)	5.6±1.4*	5.8±1.4*	4.6±1.7	4.8±1.4
Triglyceride (mmol/L)	2.2±1.6*	2.1±1.3*	1.2±0.8	1.4±0.9
Lipoproteins (%)				
Chylomicron	1.8±1.5	1.79±1.4	1.0±0	1.0±0
VLDL	19.1±11.4	19.6±11.7	10.0±2.5	10.0±2.5
LDL	48.7±9.6	45.96±9.5	47.5±3.7	44.0±2.5
HDL	30.0±0.63	30.0±0.63	32.7±8.3	34.7±8.1
Apolipoproteins				
Apo A (g/L)	2.2±0.5*	2.3±0.6*	1.6±0.2	1.6±0.4
Apo B (g/L)	1.2±0.5*	1.3±0.5*	0.6±0.3	0.65±0.4
FBS (mmol/L)	10.6±4.6*	10.6±4.6*	5.0±1.1	5.2±1.2
Hb Alc (%)	9.7 ±2.5*	9.2±2.4*	7.2±0.9	6.1±0.9

*P<0.05 statistically significant, compared to the control group of the same gender.

TABLE 3. *Frequency of abnormality of plasma lipids in Saudi diabetics.*

	Male (%)		Female (%)	
	Control	DM	Control	DM
Borderline				
Cholesterol 5.18-6.19 mmol/L	7.5	17.1	15.6	20.l
Triglyceride 2.83-5.65 mmol/L	6.5	12.0	6.2	11.9
High risk				
Cholesterol >6.20 mmol/L	6.4	11.3	15.6	17.1
Triglyceride >5.65 mmol/L	0	2.4	0	1.4

Statistical significance of the difference between diabetic patients and control group: borderline: cholesterol χ^2=6.44, P=0.01; triglyceride χ^2=3.7; P=0.01; high risk: cholesterol χ^2=5.4, P=0.02; triglyceride P>0.05.

triglycerides and lipoproteins and apolipoproteins. With VLDL (r=0.140; P=0.0001) and LDL (r = 0.148; P=0.0001), a statistically significant positive correlation was obtained, while with HDL (r=0.335; P=0.0001), a statistically significant negative correlation was obtained.

Discussion

This study shows the pattern of lipid abnormalities in the Saudi type II DM patients. The levels of cholesterol and triglycerides were significantly higher in both male and female diabetics compared to their nondiabetic counterparts. When considering values of cholesterol ranging between 5.18-6.19 mmol/L as the borderline risk group and >6.22 mmol/L as the high-risk group for CHD, as considered by the NCEP, our type II DM patients showed that 17.1% of males and 20.1% of females were in the borderline risk group, while 10.3% of males and 7.1% of females fell into the high-risk group. With triglyceride estimation, the borderline (2.83-5.65 mmol/L) and high-risk group (>5.65 mmol/L) for CHD were 11.97% and 2.4%, respectively, in the males, and 11.9% and 1.5%, respectively, in the females. It has been well documented that high levels of cholesterol and LDL play a significant role in the development of arteriosclerosis and hence CHD,[1-3,11-13] and as shown by the results of this study, Saudi type II DM patients with a higher prevalence of lipid abnormalities constitute a moderate- to high-risk group for the development of CHD.

Lipid abnormalities can largely be related to the extent of obesity, dietary habits[9] and genetic makeup[10] of the population, where 57.67% of male diabetics and 69.0% of female diabetic patients were overweight (BMI=25-29.9) or obese, with a body mass index >30.[24]

Obesity is becoming a significant health problem in the Saudis, and in the extensive National Screening Program of the overall Saudi population, we identified 40.3% of males and 45.3% of females to be overweight and obese.[25] Obesity is significantly higher in the diabetic patients compared to the nondiabetics, and this may be one of the factors in type II DM development.[24] As is well documented, higher levels of fat in the cells prevent the action of insulin, and so produce insulin resistance and type II DM development. The high prevalence of obesity in Saudis has largely been attributed to the dietary habits, which include high intake of fatty and sweet foods and dates, lack of physical activity,[25] and genetic factors, since diabetes concentrates in Saudi families.

As blood glucose elevated, a positive correlation was obtained with total cholesterol, triglycerides, LDL and apo B. Due to significant scatter, the correlation coefficient (r) was not high, though the P-value showed significance (<0.05). With HDL and VLDL, a negative correlation was obtained, which was significant only for the latter. This is an important finding and shows that hyperglycemia is closely related to hypercholesterolemia, hypertriglyceridemia and elevation in LDL, which are all documented as risk factors for CHD. Therefore diabetic patients with lack of diabetic control (i.e., high FBS and Hb A1c) have higher lipids, less HDL and are at a higher risk of developing CHD. This also points to the significance of control of blood glucose in diabetic patients.

In addition, correlation studies within the lipid groups also showed interesting results. As cholesterol increased, it was accompanied with increase in triglyceride, LDL and apo A, while HDL decreased significantly (P<0.05). Similar findings were with triglyceride levels, which correlated positively with VLDL and LDL, but negatively with HDL. These results stress the need for control of plasma cholesterol and triglyceride levels in order to have lower LDL levels and elevated HDL levels. These latter two parameters (i.e., low LDL and high HDL) are also protective against CHD. This shows that the various lipids and lipoproteins are closely correlated with each other, and control of one influences the others.

In conclusion, our study has documented several lipid abnormalities in Saudi type II DM patients and has pointed to the significance of diabetic control in control of lipid abnormalities in the diabetic patients. These may involve dietary intervention, increase in physical exercise, control of blood pressure, avoidance of smoking, and control of overweight and obesity. We strongly recommend "lipid and diabetes awareness programs" for the Saudi population in general and diabetic patients, as well as high-risk groups, in particular, in an attempt to improve the overall

health status of the Saudi population, and to encourage the growth of a healthier future generation of young Saudis.

References

1. Pyrorala K, Laakso M, Uusitupa M. Diabetes and atherosclerosis: an epidemiologic view. Diabetes Metab Rev 1987;3:463-524.
2. Grundy SM. Cholesterol and coronary heart disease: a new era. JAMA 1986;256:2849-58.
3. Kannel WB. Lipids, diabetes and coronary heart disease: insights from the Framingham study. Am Heart J 1985;110:1100-7.
4. Anderson KM, Castelli WP, Levy P. Cholesterol and mortality: 30 years of follow-up from the Framingham study. JAMA 1987;257:2176-80.
5. Castelli WP. The triglyceride issue: a view from Framingham. Am Heart J 1986;112:432-7.
6. Labarthe DR, Obvein B, Dunn K. International comparison of plasma cholesterol and lipoproteins. Ann N Y Acad Sci 1992;623:108-19.
7. Webber LS, Hunter SM, Johnson LC, et al. Smoking, alcohol and oral contraceptives. Effect on lipids during adolescence and young adulthood: Bogalusa Heart Study. Ann N Y Acad Sci 1992;623:135-54.
8. Schiekem RM. Effect of exercise on lipids. Ann N Y Acad Sci 1992;623:269-71.
9. Quivers ES, Driscoll DJ, Garvey CD, et al. The effect of diet on serum cholesterol in children. Ann N Y Acad Sci 1992;623:133-4.
10. Tenkate LP, Boman H, Diager SP, Motulsky AC. Familial genetic risk factors. Am J Cardiol 1982;50:945-53.
11. Carlson LA, Bottiger LE. Risk factors for ischaemic heart disease in men and women: results of the 19-year follow-up of the Stockholm prospective study. Acta Med Scand 1985;218:207-11.
12. Reavan GM. Non-insulin dependent diabetes mellitus, abnormal lipoprotein metabolism and atherosclerosis. Metabolism 1987;36(Suppl 1):1-8.
13. Dunn FL. Hyperlipidemia in diabetes mellitus. Diabetes Metab Rev 1990;6: 47-61.
14. El-Hazmi MAF, Warsy AS, Al-Swailem AR, Al-Swailem AM, Sulaimani R, Al-Meshari AA. Diabetes mellitus and impaired glucose tolerance in Saudi Arabia. Ann Saudi Med 1996;16:381-5.
15. El-Hazmi MAF, Warsy AS, Barimah N, Al-Swailem AR, Al-Swailem AM, Sulaimani R, et al. The prevalence of diabetes mellitus and impaired glucose tolerance in the population of Al-Baha. Saudi Med J 1996;17:591-7.
16. El-Hazmi MAF, Al-Khader SM, Warsy AS, Al-Swailem AR, Sulaimani R, Al-Swailem AM, et al. Gender-age-diabetes mellitus relation in Al-Qaseem population. Bahrain Med Bull 1997;19:6-10.
17. El-Hazmi MAF, Warsy AS, Al-Swailem AR, Al-Deeb ABM, Al-Swailem AM, Al-Meshari AA, et al. Diabetes mellitus and IGT in relation to gender and age in Najran, Saudi Arabia. Bahrain Med Bull 1997;19:40-4.
18. El-Hazmi MAF, Al-Swailem AR, Warsy AS, Sulaimani R, Al-Swailem AM. Prevalence of diabetes mellitus in Saudi Arabia. Saudi Med J 1995;16:294-9.
19. El-Hazmi MAF, Al-Swailem AR, Warsy AS, Al-Sudairy F, Sulaimani R, Al-Swailem AM, et al. The prevalence of diabetes mellitus and impaired glucose tolerance in the population of Riyadh. Ann Saudi Med 1995;15:598-602.
20. El-Hazmi MAF, Warsy AS, Al-Swailem AR, Al-Swailem AM, Sulaimani R, Al-Meshari AA. Diabetes mellitus as a health problem in Saudi Arabia and its complications. East Mediterr Health J 1998;4:361-9.
21. World Health Organization Study Group on Diabetes Mellitus. WHO Technical Report Series. WHO, Geneva, No. 727, 1985.
22. World Health Organization. WHO Expert Committee on Diabetes Mellitus Second Report. WHO, Geneva (Tech. Rep. Ser. No. 626), 1980.
23. Summary of the second report of the National Cholesterol Education Programme (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel II). JAMA 1993;269:3015.
24. El-Hazmi MAF, Warsy AS. Obesity, overweight and type II DM in Saudi adult patients. Saudi Med J 1999;20:167-72.
25. El-Hazmi MAF, Warsy AS. Prevalence of obesity in Saudi population. Ann Saudi Med 1997;17:302-6.