

## PATTERN OF DYSLIPIDEMIA IN TYPE 2 DIABETIC PATIENTS IN THE STATE OF PENANG, MALAYSIA

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### ABSTRACT

A cross-sectional study was conducted at Endocrine Clinic of Penang General Hospital in Penang Island, Malaysia. The aim of the study is to describe the pattern of dyslipidaemia in patients with type 2 diabetes mellitus (DM) and to estimate the correlation of lipid profile with demographics, anthropometric and other clinical characteristics.

Two hundred and forty six type 2 diabetic patients who diagnosed with dyslipidaemia aged  $\geq 40$  years old. The patients who attend the endocrine clinic between 1<sup>st</sup> of January and 31<sup>st</sup> of December 2008 were included in the study. Demographic and laboratory values were obtained from patients' medical records. Low-density lipoprotein cholesterol (LDL-C) was the most common pattern of dyslipidaemia, followed by LDL-C with triglycerides (TG). Total cholesterol (TC), LDL-C and TG were positively correlated with glycated haemoglobin (HbA1c). LDL-C and TC were positively correlated with systolic and diastolic blood pressure. Furthermore, TG was positively correlated with the body mass index (BMI) and waist circumference. LDL-C, TC and TG had a positive relationship with fasting blood glucose (FBG) and HbA1c.

Majority of type 2 diabetic patients in our cohort have inadequate control of plasma lipid. Moreover, poor glycaemic control, over weight and obesity are strongly associated with abnormalities in lipid levels.

**Keywords:** Pattern, Dyslipidaemia, Type 2 diabetes mellitus, Malaysia.

### INTRODUCTION

Diabetes mellitus (DM) is a major cause of various coronary heart diseases (CHD); it is associated with two to four fold excess risk of death from CHD<sup>1-5</sup>. Type 2 DM is a global endemic and increasing rapidly reaching epidemic proportions<sup>6-8</sup>. Usually low High-density lipoprotein-Cholesterol (HDL-C) levels with elevated TG levels are the most predominant pattern of dyslipidaemia in patients with type 2 DM, but these patients have relatively similar levels of LDL-C compared with non-diabetic individuals<sup>9, 10</sup>. Therapeutic management aims to reduce LDL-C and TG and to elevate HDL-C with other modifiable risk factors. This will reduce cardiovascular events and even mortality in patients with type 2 DM<sup>11-13</sup>. Inversely, about 97% of adults with DM have one or more lipid abnormalities<sup>14</sup>. Similarly in Malaysia, high prevalence of dyslipidaemia was shown in type 2 diabetic patients in whom about 97% have at least abnormality in one plasma lipid level<sup>15</sup>.

The prevalence of DM and ischemic heart disease among Malaysian population are rapidly increasing<sup>16-18</sup>. This study was conducted to assess the pattern of dyslipidaemia among type 2 diabetic patients and to examine the demographic, anthropometric and other clinical factors and their correlation with dyslipidaemia in a multi-ethnic population of Penang, Malaysia, in such way may help health care providers to concentrate on the preventive measures that help to reduce the incidence of dyslipidaemia among these patients.

### MATERIALS AND METHODS

#### Study population

The study population comprised of type 2 DM, who diagnosed with dyslipidaemia, aged  $\geq 40$  years old and who attending the endocrine clinic of Penang General Hospital between 1<sup>st</sup>/January and 31<sup>st</sup>/December of 2008. Subjects with at least two laboratory readings for lipid profile, fasting blood glucose and HbA1c with a minimal duration of three months between each reading were included in the study. Pregnant women, patient with cancer, acquired immune deficiency syndrome (AIDS) and Human immunodeficiency virus (HIV) co-infected patients were excluded. The study was approved by National Institutes of Health (NIH) in the Ministry of Health Malaysia.

#### Study design and data collection

This is a cross-sectional study to determine the pattern of dyslipidaemia among type 2 diabetic patients. A convenient sampling method was used in data collection; 246 patients who satisfied the eligibility criteria of the study were reviewed. Demographics, clinical characteristics, treatment options and laboratory data were obtained from patients' medical records. Dyslipidaemia defined as one or more from the following criteria: as diagnosed previously by physician, elevated TC, LDL-C, or TG; a low HDL-C; or a combination of these abnormalities and for patients who reported being prescribed for lipid lowering drugs<sup>19</sup>. Dyslipidaemia divided into two types: isolated dyslipidaemia (one of the lipid fractions is out of the target level) and combination dyslipidaemia (two lipid fractions are out of the target level). Body Mass Index (BMI) which collected or even calculated through the demographic data, were classified to Obese (BMI  $> 27$  kg/m<sup>2</sup>), Overweight (BMI  $\geq 23$  kg/m<sup>2</sup>) and normal weight (BMI  $< 23$  kg/m<sup>2</sup>)<sup>20</sup>. According to the Malaysian clinical practice guideline in Management of type 2 DM and Third Report of the National Cholesterol Education Program (NCEP), optimal lipid levels for LDL-C, TC and TG are ( $\leq 2.6$  mmol/L;  $< 5.2$  mmol/L and  $\leq 1.7$  mmol/L, respectively); while the optimal level for HDL-C is  $> 1.0$  mmol/l for male and  $> 1.3$  mmol/l for female. The optimal target for HbA1c is  $< 6.5$  %<sup>21, 22</sup>.

#### Statistical analysis

The data collected were analysed using SPSS version 15.0 (SPSS Inc., Chicago, IL) and Microsoft Excel. Descriptive analyses were applied by calculating mean  $\pm$  standard deviation (SD) for continuous variables while percentages and frequency was applied for categorical variables. Independent *t*-test was used for continuous and normally distributed variables; on the other hand Mann-Whitney U test was employed as a substitute. Multilinear regression applied to determine the correlations between lipid fractions and other clinical characteristics. *P* value  $\leq 0.05$  at 95% confidence interval (CI) was considered statistically significant.

### RESULTS

Of 246 (121 males, 125 females) type 2 diabetic patients, 80 (32%) Malay, 95 (39%) Chinese, 67 (27%) Indian and 4 (2%) were foreigners. The mean age for subjects was  $56.7 \pm 8.9$  years as shown in table 1. Majority of patients in our cohort were either

obese (46.7%) or overweight (35.8%); the mean level of BMI was 27.6 kg/m<sup>2</sup>. Unfortunately, the subjects in our cohort had uncontrolled DM with HbA1c above the optimum level (8.4 ± 1.9%).

Mean value of LDL-C was above the optimal level, while TC, HDL-C and TG were within optimal levels. There was no significant difference between males and females in terms of lipid levels except for HDL-C in which females had higher level compared to males ( $P < 0.001$ ) (data is shown in table 2).

The most common pattern of dyslipidaemia in our cohort was the isolated dyslipidaemia in which 37.8% of patients had one of the lipid fractions out of target level. Elevated LDL-C had the highest percentages (46.2%) of isolated dyslipidaemia, followed by lower HDL-C level and elevated TG (35.5% and 18.3%, respectively). 23.2% of subjects had combination dyslipidaemia, which represent the second most common pattern of dyslipidaemia. LDL-C and TG represent the majority of combination dyslipidaemia followed by HDL-C with TG and LDL-C with HDL-C 42.1%, 35.1% and 22.8% respectively (data is shown in table 3). Unfortunately, the majority of subjects in our cohort (70%) had at least one lipid fraction out of target level.

Table 4 demonstrates the correlation of plasma lipid with demographic, anthropometric and other characteristics, including age; sex; race; duration of DM; systolic and diastolic blood pressure. TC positively correlated with type of lipid therapy ( $P = 0.02$ ,  $r =$

0.132), fasting blood glucose ( $P = 0.001$ ,  $r = 0.204$ ), HbA1c ( $P < 0.001$ ,  $r = 0.223$ ), systolic blood pressure ( $P = 0.006$ ,  $r = 0.160$ ) and diastolic blood pressure ( $P = 0.035$ ,  $r = 0.117$ ), but it was negatively correlated with age ( $P = 0.010$ ,  $r = -0.150$ ).

LDL-C significantly correlated with systolic blood pressure, HbA1c, fasting blood glucose and diastolic blood pressure. LDL-C was significantly correlated with age in inverse manner ( $P = 0.010$ ,  $r = -0.149$ ). While it had no significant correlations with waist circumference, body mass index, duration of diabetes, sex, race and type of lipid therapy.

HDL-C negatively correlated with the waist circumference ( $P < 0.001$ ,  $r = -0.214$ ), body mass index ( $P = 0.003$ ,  $r = -0.179$ ) and sex ( $P = 0.005$ ,  $r = -0.163$ ). HDL-C significantly correlated with Chinese ( $P = 0.005$ ,  $r = 0.166$ ) and Indian ( $P = 0.023$ ,  $r = -0.128$ ). LDL-C, HDL-C had no significant correlations with duration of diabetes, type of lipid therapy, Malay ethnicity.

In this study, TG positively correlated with the waist circumference ( $P = 0.001$ ,  $r = 0.191$ ), body mass index ( $P = 0.011$ ,  $r = 0.146$ ), type of lipid therapy ( $P = 0.018$ ,  $r = 0.135$ ), fasting blood glucose ( $P = 0.002$ ,  $r = 0.185$ ) and HbA1c ( $P < 0.001$ ,  $r = 0.219$ ). TG showed a strong correlation with HbA1c, followed by the waist circumference, fasting blood glucose, body mass index and type of lipid therapy. TG had not significant correlations with age, duration of diabetes, sex, race, systolic blood pressure and diastolic blood pressure.

**Table 1: Basic demographic and anthropometric features of all 246 type 2 diabetic patients**

n = 246	Range	Mean ± SD
Age (years)	(40.0 - 82.0)	56.7 ± 8.9
Waist circumference (cm)	(35.0 - 150.0)	96.4 ± 12.9
Body Mass Index (Kg/m <sup>2</sup> )	(16.1 - 54.9)	27.6 ± 5.4
Duration of diabetes (years)	(0.1 - 37.0)	11.1 ± 7.2
HbA1c (%)	(3.7 - 15.4)	8.4 ± 1.9

**Table 2: Mean lipid levels for overall 246 type 2 diabetic patients**

n = 246	All Mean ± SD	Male Mean ± SD	Female Mean ± SD	P value <sup>a</sup>
Total cholesterol (mmol/L)	4.68 ± 1.1	4.60 ± 1.24	4.74 ± 1.02	0.063
LDL-cholesterol (mmol/L)	2.71 ± 0.9	2.71 ± 1.05	2.70 ± 0.87	0.680
HDL-cholesterol (mmol/L)	1.19 ± 0.3	1.12 ± 0.33	1.24 ± 0.32	<0.001
Triglycerides (mmol/L)	1.70 ± 0.9	1.72 ± 1.03	1.69 ± 0.84	0.917

<sup>a</sup> Mann-Whitney Test

**Table 3: Percentages of pattern of type 2 diabetic patients (n=246) with all within control, one, two and three out of recommended target established by Malaysian guideline <sup>21</sup>**

	Number of patients	Percentage (%)
All within target	73	29.7%
	LDL-cholesterol	43
		33
		46.2%
		35.5%
One out of target 93(37.8%)	HDL-cholesterol	
	Triglycerides	17
	LDL-cholesterol + Triglycerides	24
		18.3%
		42.1%
Two out of target 57(23.2%)	HDL-cholesterol + Triglycerides	20
	LDL-cholesterol + HDL-cholesterol	13
		23
		35.1%
		22.8%
Three out of target		9.3%

Table 4: Lipid levels correlation demographic, anthropometric and other clinical characteristics

Source	Total cholesterol		LDL-cholesterol		HDL-cholesterol		Triglycerides	
	P value	Pearson Correlation	P value	Pearson Correlation	P value	Pearson Correlation	P value	Pearson Correlation
Age (years)	0.010	-0.150	0.010	-0.149	0.468	-0.005	0.110	-0.079
Waist circumference (cm)	0.149	0.067	0.090	0.086	<0.001	-0.214	0.001	0.191
Body Mass Index (kg/m <sup>2</sup> )	0.188	0.057	0.212	0.052	0.003	-0.179	0.011	0.146
Duration of diabetes (years)	0.264	-0.041	0.265	-0.040	0.453	0.008	0.418	0.013
Sex	0.172	-0.061	0.475	0.004	0.005	-0.163	0.423	0.013
Race								
Malay	0.228	0.048	0.179	0.059	0.267	-0.040	0.461	-0.006
Chinese	0.456	0.007	0.225	-0.049	0.005	0.166	0.384	-0.019
Indian	0.192	-0.056	0.499	0.000	0.023	-0.128	0.486	0.002
Others	0.461	-0.006	0.316	-0.031	0.274	-0.039	0.086	0.088
Type of lipid therapy	0.020	0.132	0.169	0.062	0.453	0.019	0.018	0.135
Fasting blood glucose (mmol/L)	0.001	0.204	0.008	0.154	0.387	-0.051	0.002	0.185
HbA1c (%)	<0.001	0.223	0.006	0.159	0.212	-0.075	<0.001	0.219
Systolic blood pressure (mmHg)	0.006	0.160	0.006	0.160	0.123	0.077	0.106	0.080
Diastolic blood pressure (mmHg)	0.035	0.117	0.008	0.154	0.117	-0.007	0.101	0.082

## DISCUSSION

In the present study, we found that the mean levels of TC, LDL-C and HDL-C and TG were (4.68 mmol/L, 2.71 mmol/L, 1.19 mmol/L and 1.70mmol/L), respectively. Compared with other studies in elsewhere in the world, our results regarding lipid levels were consistent with those in Brazil (4.81 mmol/L, 2.78 mmol/L, 1.24 mmol/L and 1.68 mmol/L) for TC, LDL-C, HDL-C and TG<sup>23</sup>. In consistent done in Chile<sup>24</sup>, but our findings lower than those in England and Greece<sup>25, 26</sup> and higher than those in Bangladesh and Vietnam<sup>27, 28</sup>.

The mean HbA1c level was 8.4 %, suggesting poor glycaemic control in our diabetic patients, which consistent with earlier reports from Malaysia by Eid et al and Ismail et al. They found that HbA1c level were 8.7% and 8.5% respectively<sup>15, 29</sup>. In United States, Kuwait and Tunisia<sup>30-33</sup>, the authors also found that their diabetic patients had poor glycaemic control.

The most common pattern was an isolated increase in LDL-C; a combination of high LDL-C with high TG was the second most common pattern. In contrast to the results of other studies that done among Jordanian, Kuwaiti and African-American diabetic patients, these studies found a combination of high LDL-C with low HDL-C was the most common pattern; an isolated increase of LDL-C was the second most common pattern<sup>31, 32, 34</sup>. The difference in pattern of dyslipidaemia in our cohort might due to differences in race, diet, and lifestyle, or due to the differences in cut point of clinical target goal compared to those in elsewhere in the world.

Our study demonstrates the correlation of the lipid fractions with different variables. LDL-C was significantly negatively correlated with the age, suggesting that older patients in our sample were more compliant to pharmacologic and/or non-pharmacologic therapy than younger patients. While Eid et al found that LDL-C was not correlated with age<sup>15</sup>.

TC, LDL-C and TG were significantly correlated with FBG, HbA1c in a positive manner. Chan et al and Ladia et al found TC; LDL-C and TG were significantly correlated with HbA1c, which corroborated our findings<sup>35, 36</sup>. Khan H. A. found that TC, LDL-C, HDL-C and TG were significantly correlated with HbA1c<sup>37</sup>. Ko et al found that increasing HbA1c was associated with increasing LDL-C and TC. This significant correlation suggesting that improving glycaemic control can beneficially modify plasma lipid levels<sup>38</sup>. Our findings emphasize the importance of hyperglycaemia as reflected by HbA1c, as a

continuum in the evaluation of cardiovascular risk, which is demonstrated as dyslipidaemia in this study.

It is well known that hypertension and high serum cholesterol are often occur concomitantly<sup>39, 40</sup>. In the present study, TC and LDL-C were positively correlated with systolic blood pressure and diastolic blood pressure. Therefore, elevated blood pressure should be treated in order to control plasma lipid levels which in turn can prevent further cardiovascular complications.

Overweight or obese diabetic patients have a high burden of CHD risk factors including dyslipidaemia (high LDL-C, low HDL-C and high triglycerides)<sup>41, 42</sup>. In this study, we found that LDL-C was positively correlated with the BMI and waist circumference, but these fail to reach statistical significance. HDL-C had a negative linear-relationship with the BMI and waist circumference, while TG had a positive linear-relationship with these variables.

Our results is corresponding to the results of study done in China that showed BMI and waist circumference were significantly negatively correlated with HDL-C and positively with TG while there was no significant correlation in terms of LDL-C and TC<sup>35</sup>.

In United states TC, LDL-C, HDL-C and TG were not significantly correlated with duration of diabetes<sup>43</sup>. Also our result showed that the duration of DM not affecting the level of plasma lipids.

Our findings showed that majority of type 2 diabetic patients with dyslipidaemia have inadequate control of plasma lipid. This fact demonstrates the importance of early interventions for control and treatment of these risk factors for prevention of the cardiovascular complications in these patients. Furthermore, poor glycaemic control in our cohort is strongly associated with abnormalities in lipid levels. These results, along with the high prevalence of overweight and obesity, suggest that diabetic patients should be counselled regarding their diets, physical activity and life habits. These patients also need frequent monitoring to ensure optimal lipid level control.

The conclusion drawn from this study is limited because it was a retrospective data from a routine clinic and not a prospective series. However, the strength of this study lies in the fact that it was the usual clinical setting where most clinicians practice and not in the artificial setting of a clinical trial. Another point; this analysis was based on a clinic population; data from other centres are required to determine whether our findings can be generalized to other diabetes

care settings. Medications that can affect lipid levels (e.g., beta blockers, and diuretics) that patients may have been taking at the time of their visit were not captured in our registry.

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