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Prevalence of Dyslipidaemia in Type 2 Diabetes Mellitus Patients and Its Association to Diabetic Retinopathy in a Malaysian Tertiary Hospital

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ABSTRACT

Background: Diabetic retinopathy (DR) is a microvascular complication of diabetes, which is a cause of visual impairment and blindness. Its development and progression have been linked to dyslipidaemia, although the link remains inconclusive. Aim: This study aimed to determine the prevalence of dyslipidaemia among type 2 diabetic patients with DR in a tertiary setting and to determine the association between dyslipidaemia and DR severity. Materials and methods: This was a cross sectional study using retrospective data of type 2 diabetic patients attending the opthalmology clinic of a tertiary centre from January 2007 to June 2014. Results of their fasting lipid profile and clinical data were retrieved from the hospital information system. Results: A total of 178 patient's data were collected. 120 (n=67.4%) patients had non-proliferative diabetic retinopathy (NDPR) with moderate NPDR being the most prevalent. Dyslipidaemia was noted in 151 (84.8%) of the patients. Patients had a combination of more than one abnormality in the lipid profile with increased LDL-cholesterol being the main abnormality. Dyslipidaemia was however, not significantly associated with DR severity. Conclusion: Dyslipidaemia was highly prevalent in DR patients. The dyslipidaemia was however not associated with severity of DR.

Keywords: Diabetic retinopathy, Dyslipidaemia, Non-proliferative diabetic retinopathy, Proliferative diabetic retinopathy, Type 2 diabetes mellitus

INTRODUCTION

Diabetic retinopathy (DR) is a well-known microvascular complication of diabetes and a cause of visual impairment and blindness worldwide.[1-4] DR can be classified into mild, moderate and severe non-proliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR) and advanced diabetic eye disease (ADED).[5] NDPR is characterised by formation of microaneurysms and retinal vascular permeability and leakage, and PDR is characterised by neovascular proliferation and vitreous haemorrhage.[6]

In Malaysia, the prevalence of DR in various centres has previously been reported as 44.1%,[7] 48.6%[8] and 51.6%[9] whilst the Malaysian 2007 Diabetic Eye Registry reported a DR prevalence of 36.8%.[10] Among well-established risk factors for DR are hyperglycaemia and hypertension.[3] Clinical practice guidelines from several countries recommend that intensive control of high blood glucose and blood pressure not only delay the onset of DR but reduces the rate of its progression.[11,12,13] Dyslipidaemia has been linked to the pathogenesis of DR, but results from past research showed discrepancy on the association of serum lipids with DR severity. Thus, the aim of this study was to determine the association between dyslipidaemia and DR severity in type 2 diabetic patients attending the ophthalmology clinic of a tertiary centre in Malaysia.

MATERIALS AND METHODS

This was a cross sectional study using retrospective data retrieved from the electronic medical records of patients attending the hospital ophthalmology clinic. The sample size was calculated using the prevalence of isolated dyslipidaemia and combined dyslipidaemia, which were reported as 37.8% and 23.2%, respectively in Type 2 DM in Malaysia[14] taking into account 0.05% unresponsive rate. Patients fasting serum lipid (FSL) profile results, demographics (gender, age and race) and DR severity were obtained. Only patients (18 years old and above) with Type 2 DM were included. Patients were classified into mild, moderate and severe NPDR, PDR and Advance Diabetic

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Eye Disease (ADED). Apart from the standard FSL, which include total cholesterol (TC), triglycerides (TG), LDL-C and HDL-C, other calculated lipid parameters were used such as non-HDL-C (obtained by subtracting HDL from TC), LDL-C/HDL-C and TC/HDL-C. Non-HDL provides a single index of all atherogenic, apoprotein B-containing lipoproteins, including LDL, VLDL, IDL, and lipoprotein (a).[15] Non-HDL, LDL-C/HDL-C and TC/HDL-C are found to be more reliable in predicting cardiovascular disease risk than the standard lipid parameters.[15,16] These parameters were included in or study as limited research have looked into them with regards to DR. Chi-square test was used to determine the association between dyslipidaemia and severity of DR; p value of < 0.05 showed statistical significance. This study was approved by the Ethics Committee of the National Medical Research Registry (NMRR-14-452-20733), Ministry of Health, and the Ethics Committee of Universiti Putra Malaysia.

RESULTS

A total of 178 patients' data were obtained. Table 1 shows the demographic characteristics of the patients. There were 94 (52.8%) males and the remaining 84 (47.2%) were females. Age was categorised into more and less than 60 years old, taking 60 as the cut-off age for the definition of elderly in our population. The median age was incidentally 60 years old (IQR=12). Majority were Malays (48.3%), followed by Chinese (30.9%) and Indian (20.8%). Majority (67.4%) had NPDR with moderate NPDR being the most prevalent. There were 151 (84.8%) patients with dyslipidaemia defined as presence of either one or more abnormal results in the lipid profile. The median parameters of the lipid profile are shown in Table 2. Only the median LDL-C and the TC/HDL-C ratio were not within the recommended target values for management of dyslipidaemia. There were no significant differences with regards to age (p=0.396), gender (p=0.466) and race (p=0.44) with dyslipidaemia or age (p=0.947), gender (p=0.06) and race (p=0.165) with DR.

Table 3 shows the association between the parameters of lipid profile and the severity of DR. There were no significant association between dyslipidaemia and severity of DR ($p = 0.184$). However, in all stages of DR, most patients have a combination of more than one abnormality in the parameter of the lipid profile characterised by increased LDL-C, low HDL-C and increased triglycerides (TG).

Table 1: Demographics and clinical characteristic of study population (N=178)

Chracteristics	n (%)
Gender	
Male	94 (52.8)
Female	84 (47.2)
Age (years)	
< 60	94 (52.8)
≥ 60	84 (47.2)
Ethnicity	
Malay	86 (48.3)
Chinese	55 (30.9)
Indian	37 (20.8)
Dyslipidaemia	
Present	151 (84.8)
Absent	27 (15.2)
Stages of DR	
Mild NPDR	39 (21.9)
Moderate NPDR	50 (28.1)
Severe NPDR	31 (17.4)
PDR	54 (30.3)
ADED	4 (2.3)

Table 2: Lipid profile of study population

Parameter	Median (IQR)	Min-Max	Reference Range
TC (mmol/L)	4.70(1.79)	2.45-10.00	>6.2
TG (mmol/L)	1.56(1.11)	0.48-12.37	>1.7
LDL-C (mmol/L)	2.85(1.5)	0.92-7.22	>2.6
HDL-C (mmol/L)	1.14(0.35)	0.13-2.49	<1.1
Non-HDL-C (mmol/L)	3.62(1.75)	1.33-8.66	≥3.3
LCL-C/HDL-C	2.66(1.75)	0.71-20.69	≥3.0
TC/HDL-C	4.34(2.04)	2.07-34.54	≥4.0

TC: total cholesterol; TG: triglyceride; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol

Table 3: Association between dyslipidaemia with severity of DR

	Mild NPDR n(%)	Moderate NPDR n(%)	Severe NPDR n(%)	PDR n(%)	ADED n(%)	TOTAL N (%)
TC > 6.2mmol/L	3(7.7)	10(20.0)	5(16.0)	15(27.8)	1(25.0)	34(19.1)
TG > 1.7mmol/L	18(46.2)	19(38.0)	18(58.1)	21(38.9)	1(25.0)	77(43.26)
LDL-C > 2.6mmol/L	22(56.4)	28(56.0)	20(64.5)	30(55.6)	3(75.0)	103(57.9)
HDL-C < 1.1mmol/L	13(33.3)	25(50.0)	22(71.0)	22(40.7)	1(25.0)	83(46.6)
Non-HDL-C ≥ 3.35mmol/L	24(61.5)	29(53.0)	25(80.6)	29(53.7)	3(75.0)	110(61.8)
LDL-C/HDL-C ≥ 3.0mmol/L	13(33.3)	18(36.0)	16(51.6)	20(37.0)	2(50.0)	69(38.8)
TC/HDL-C ≥ 4.0mmol/L	18(46.2)	34(68.0)	25(80.6)	31(57.4)	3(75.0)	111(62.3)
Total	39	50	31	54	4	
X^2	1.397	0.021	3.898	0.951	0.700	
p-value			0.184			

DISCUSSION

Majority (84.8%) of the patients had dyslipidaemia, which was expected as the overall prevalence of dyslipidaemias in type 2 DM in Malaysia was reported as 89.1%.[17] The common abnormalities seen were elevated LDL-C, reduced HDL-C and increased TG, consistent with diabetic dyslipidaemia. Majority had a combination of more than one abnormalities in their lipid profile. 67.4% were also diagnosed with NPDR. NPDR will progress to PDR if the risks for its progression are not controlled. Identifying the risk factors for DR, especially modifiable ones, is important for early intervention and thus slowing the progression of DR. We found no significant association between dyslipidaemia and severity of DR which concurred with previous large studies such as Australian Diabetes, Obesity and Lifestyle Study (AusDiab)[18] and Multi-ethnic study of atherosclerosis (MESA)[19] and others.[20, 21] Furthermore, studies indicated that there was no single lipid marker consistently found to be associated with DR.[22] In the Chennai Urban Rural Epidemiology Study (CURES), TC was an independent risk factor for DR,[23] while Sangkora et. al. 2011 found no association with TC but showed that HDL-C level was inversely associated with DR[24] In contrast, the Singapore Malay Eye Study reported that a higher TC was protective against diabetic retinopathy.[2] TG was also shown to be an independent risk factor for DR although it did not correlate with DR severity.[23] Serum lipids were also thought to have

stronger association with clinically significant macular oedema (CSME) rather than DR. Although DR and CSME share similar pathogenesis, it has been suggested that the association of serum lipids with DR differed from CSME due to lack of significant association of serum lipids with DR.[20] In this study, patients with diabetic macular oedema were not included as its association with dyslipidaemia has already been established in previous research.[25,26]
Recently, serum apolipoprotein-A1 (ApoA1) and apolipoprotein B (ApoB) were reported to have better association with DR progression and severity than the traditional lipid markers, suggesting that future research should include these biomarkers.[24,27] ApoA1 was inversely related while ApoB and ApoB/ApoA1 ratio was positively associated with DR severity.[24] This is further supported by clinical evidence that lipid lowering therapies are effective in preventing progression of DR, independent of effects on traditional serum lipid markers.[28] Thus, in future, apolipoprotein might be used as an indicator of DR severity and response to treatment.

Our study had a few limitations. Being a cross-sectional study and using retrospective data of a single centre may not be representative of the whole diabetic population with DR in Malaysia. Other factors which may affect severity of DR such as glycaemic control, duration of diabetes and the use of lipid-lowering medications were not taken into consideration. This was due to lack of recorded clinical data as most of the patients were followed up in various primary care centres for their diabetic management.

CONCLUSION

The prevalence of dyslipidaemia in patients with DR was highly prevalent with most patients having more than one abnormal parameter in the lipid profile. Raised LDL-C was the main abnormality seen. Dyslipidaemia was not associated with the severity of DR in our population of type 2 DM patients.

DECLARATION OF CONFLICT OF INTEREST

We, authors of the article declare that there is no conflict of interest regarding publication of this article.

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