Prevalence and pattern of dyslipidaemia in type 2 diabetes mellitus patients at a tertiary care hospital

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**Background:** Diabetes mellitus (DM) is a common secondary cause of dyslipidaemia, particularly if glycaemic control is poor, which in turn is an important risk factor for atherosclerosis and coronary artery disease.

**Objectives:** (1) To study the prevalence and pattern of dyslipidaemia in patients with type 2 DM. (2) To determine the relationship (if any) between HbA1c and the lipid profile in type 2 diabetic patients.

**Methods:** This was a cross-sectional study done in 200 type 2 diabetic patients attending the Diabetic Clinic at the Helen Joseph Hospital. Patients suffering from other known causes of secondary dyslipidaemia were excluded. Each patient’s HbA1c and lipid profile results were recorded from their clinic files. The lipid profile included total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and calculated low-density lipoprotein cholesterol (LDL-C).

**Results:** Of the 200 type 2 DM patients studied, 86 (43%) were male and 114 (57%) female. Despite all patients being treated with lipid-lowering therapy (simvastatin at a mean daily dose of 20 mg), 187 patients (93.5%) did not achieve all their lipid targets. The most prevalent lipid parameter not at target was an LDL-C of ≥ 1.8 mmol/l in nearly 80% of patients. The most common pattern of dyslipidaemia was a combined dyslipidaemia (any two abnormal lipid parameters) affecting a total of 82 out of the 187 patients (43.8%) not reaching recommended targets. No significant relationship was found between HbA1c and any of the lipid parameters.

**Conclusion:** The vast majority of the type 2 diabetic patients studied had dyslipidaemia not meeting recommended targets, despite the use of lipid-lowering therapy in all patients. There is a need for more intensive lipid-lowering therapy, particularly statin therapy in patients with dyslipidaemia. Measures aimed at combating obesity and other lifestyle-related risk factors are also vital and need to be implemented for effectively controlling dyslipidaemia and reducing the burden of CVD.

**Keywords:** combined dyslipidaemia, LDL, lipid targets

**Introduction**

Type 2 diabetes mellitus (DM) is a metabolic disorder, characterised by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both.1

The International Diabetes Federation has estimated that the number of people with diabetes worldwide in 2015 was 415 million and this is projected to reach 642 million by 2040.2 In 2015 diabetes was the leading cause of mortality, whereby 5 million people died from diabetes and diabetes-related complications.3 The long-term macrovascular complications of diabetes contribute to the high morbidity and mortality associated with the disease with as many as 80% dying from some form of cardiovascular disease (CVD).3

Well-known risk factors for CVD include age, gender, hypertension (HT) and DM. Other lifestyle behaviours such as tobacco smoking, excessive alcohol consumption, sedentary lifestyle and poor diet with resultant obesity further contribute to elevating one’s CVD risk.

Diabetic patients often suffer from HT and also have abnormal lipoprotein metabolism.3,4 Dyslipidaemia is one of the major risk factors for CVD in DM. The most common pattern of dyslipidaemia is hypertriglyceridaemia and reduced HDL cholesterol levels and an increased concentration of small dense low-density lipoprotein (LDL) particles. The precise pathogenesis of diabetic dyslipidaemia is not known; however, a large body of evidence suggests that insulin resistance has a central role in the development of this condition. The main cause of the lipid changes associated with DM is attributed to increased free fatty acid flux secondary to insulin resistance.1,4

Bearing this in mind, it should be the clinician’s aim to control hyperglycaemia and HT as well as dyslipidaemia with lifestyle measures and/or medication to try and reduce their CVD risk. As macrovascular disease is the major cause of mortality in diabetic patients, blood pressure and lipid targets are set lower for this high-risk group than in the general population.

Apart from the classical risk factors such as dyslipidaemia, elevated HbA1c is regarded as an independent risk factor for CVD in subjects with or without diabetes. The estimated risk of CVD has shown to be increased by 18% for each 1% increase in absolute HbA1c value in the diabetic population.5

In clinical practice, it was previously advocated to use fasting lipid profiles. However, solid evidence is lacking that fasting samples are superior to non-fasting samples when evaluating a patient’s lipid profile for his/her cardiovascular risk assessment. Bearing this in mind other countries have changed their recommendations to using random non-fasting lipid profiles as the standard, i.e. Denmark6 and UK NICE guidelines. This has advantages as it is
more convenient for the patient, which will hopefully ease the patient’s hospital visits and ensure better compliance.6

The aim of statin therapy is to lower LDL-C levels. Statin therapy is used extensively in both primary and secondary prevention of CVD at all levels of healthcare settings.7–11 Several large prospective clinical trials have shown that for every 1 mmol/l reduction in LDL-C levels there is a 23% reduction in CVD risk.12–15 In a further meta-analysis of studies comparing high and low statin doses, more intensive lowering of LDL-C (0.51 mmol/l additional reduction) in the high-dose statin arm was associated with a further 15% reduction in CVD risk.16

In the JUPITER study, a statin cardiovascular outcomes trial that enrolled men and women free of overt CVD over the ages of 50 and 60 years respectively with baseline LDL-C < 3.37 mmol/l and high-sensitivity C-reactive protein of 2 mg/l or greater; who were randomised to rosuvastatin 20 mg/day or placebo statin treatment was associated with a 39% reduction in primary endpoints (myocardial infarction, stroke, admission to hospital for unstable angina, arterial revascularisation or CV death) in patients with at least one risk factor for DM.17,23

The results of these and other studies have given rise to treatment guidelines recommending lower LDL-C target levels.18,19,23 Thus far many studies, local and international, have failed to demonstrate that patients reach these recommended targets.20–22

The aim was to determine the prevalence and pattern of dyslipidaemia in type 2 DM patients and to determine how dyslipidaemia is being managed in patients with type 2 DM in a South African, public sector, tertiary care setting and, second, to determine the relationship (if any) between HbA1C and the lipid parameters.

Materials and methods
Ethics approval was obtained from the Human Research Ethics Committee, University of the Witwatersrand, Johannesburg (protocol number: M120536). This cross-sectional study evaluated 200 type 2 diabetic patients attending the Diabetic Clinic at the Helen Joseph Hospital during July and August 2012. Patients were excluded from the study if they were < 18 years of age, had Type 1 diabetes mellitus, gestational diabetes, steroid-induced diabetes or chronic pancreatitis as a secondary cause of DM. Patients suffering from other causes of secondary dyslipidaemia such as overt hypothyroidism were also excluded.

Using patients’ clinic files, the following clinical data were recorded: gender, age, duration of DM, smoking status, height, weight (BMI), HbA1C, lipid profile, concomitant HT and medication pertaining to the management of their HT, DM and dyslipidaemia. The lipid profile included total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and calculated low-density lipoprotein cholesterol (LDL-C). Lipid profiles were non-fasting, which is in keeping with recent recommendations from the European Society of Cardiology.3

LDL-C is preferred when deciding on whether to treat a patient and for subsequent assessments, as cardiovascular risk reduction is proportional to LDL-C level. However, LDL-C cannot be calculated using the Friedewald equation if the triglyceride level is ≥ 4.5 mmol/l and would need to be measured either directly or by means of ultracentrifugation.

According to the 2012 South African Dyslipidaemia Guidelines,24 target levels in patients with type 2 diabetes are:

- TC < 4.5 mmol/l;
- TG < 1.7 mmol/l;
- HDL-C > 1.0 mmol/l in men and > 1.2 mmol/l in women;
- LDL-C < 1.8 mmol/l.

With the above targets in mind, dyslipidaemia was defined by the presence of one or more abnormal serum lipid concentration outside these recommended target levels.

BMI was defined as the weight in kilograms divided by the height in metres squared expressed as kg/m2. Patients were classified as: underweight (BMI < 20 kg/m2), normal (BMI 20–24.9 kg/m2), overweight (BMI > 25–29.9 kg/m2) or obese (BMI > 30 kg/m2).

The 2012 SEMDSA guidelines25 recommend a target HbA1C of less than 7% for the majority of patients because they prevent or significantly delay complications of DM. Good glycaemic control was defined as an HbA1C level of < 7% and was considered uncontrolled if ≥ 7%. Those subjects with dyslipidaemia were further classified into mixed dyslipidaemia (three abnormal parameters: high TG, low HDL-C as well as raised LDL-C), combined dyslipidaemia (any two abnormal lipid parameters) and isolated (single parameter) dyslipidaemia (high TC, TG, LDL-C or low HDL-C). A comparison was also made of the lipid levels in patients with good control of diabetes (HbA1C <7%) versus those with poorer glycaemic control (HbA1C ≥ 7%). A multiple regression was done in order to determine whether HbA1C correlated with any of the lipid parameters, namely TC, TG, HDL-C and/or LDL-C.

A p-value < 0.05 was considered significant. The descriptive analysis of the data was done using statistical software SPSS 19.0™ (IBM Corp, Armonk NY, USA). Graphs and tables were generated using Microsoft Word and Excel (Microsoft Corp, Redmond, USA).

Results
In the sample group of 200 type 2 DM patients, 43% were males and 57% females. The mean age of the sample was 55.89 years (SD ± 12.52). The earliest age of being diagnosed with DM was 18 years and the oldest age 72 years. The mean age of diagnosis was 42.19 years (SD ± 10.74). The demographics of the study cohort are shown in Table 1.

Dyslipidaemia
Despite the use of lipid-lowering therapy (statin therapy) in all of the patients, the prevalence of dyslipidaemia in the cohort was 93.5% (187 out of the 200 patients).

Simvastatin was the only statin therapy used by all patients. The mean dose of simvastatin was 20 mg.

No documentation of any complications from the statin therapy was noted in the files. Compliance was not assessed.

The most prevalent lipid abnormality in our study was LDL-C of ≥ 1.8 mmol/l (81.8%) in nearly 80% of both the male and female patients (Table 2).

The most common pattern of dyslipidaemia was a combined dyslipidaemia (any two abnormal lipid parameters) in a total of 82 of the 187 patients (43.8%) not achieving recommended
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Targets (see Table 3). The most common pattern of combined dyslipidaemia in males was low HDL-C levels (≤ 1 mmol/l) and elevated LDL-C levels (≥ 1.8 mmol/l) (23.25%) and in females was an elevated TG (≥ 1.7 mmol/l) in combination with an elevated LDL-C level (19.29%) (Figures 1 and 2, respectively).

HbA1c
The mean HbA1c in this study was 9.5% (SD 2.4); range 4.5–17.6%). The majority of the patients, 173 out of 200 (86.5%), had poor glycaemic control with an HbA1c of ≥ 7%. Only 28 patients (14.0%) had a target HbA1c of < 7%. The majority of patients (40%) had HbA1c levels > 10%.

Of these 173 patients with an HbA1c of ≥ 7, 49.7%, 43.9%, 46.2% and 76.3% had TC, TG, HDL-C, and LDL-C levels outside the recommended levels respectively. In those with good glycaemic control (HbA1c of < 7) 28%, 32%, 48% and 80% of patients had TC, TG, HDL-C, and LDL-C levels outside the recommended levels respectively.

Table 1: Profile of the patients analysed

| Parameter | Results |
|-----------|---------|
| Total no. of patients | 200 |
| Gender: |
| Males | 86 (43%) |
| Females | 114 (57%) |
| Age (years): |
| Mean ±SD | 55.89 ± 12.52 |
| Median | 58 |
| Range | 30–82 |
| Male, mean ±SD | 53.29 ± 12.73 |
| Female, mean ±SD | 57.85 ± 12.04 |
| Age at diagnosis (years): Results |
| Mean ±SD (years) | 42.19 ± 10.74 |
| Median | 40 |
| Range | 18–72 |
| Male, mean ±SD | 41.34 ± 10.81 |
| Female, mean ±SD | 42.82 ± 10.69 |
| No. of Insulin units used per day |
| Insulin usage | 199 (99.5%) |
| 0.1–40 | 63 (31.7%) |
| 40.1–80 | 89 (44.7%) |
| 80.1–120 | 25 (12.6%) |
| 120.1–160 | 3 (1.5%) |
| 160.1–220 | 4 (2.0%) |
| No insulin use | 1 (0.5%) |
| BMI |
| Underweight (BMI < 20 kg/m 2) | 5 (2.5%) |
| Normal (BMI 20 to 24.9 kg/m 2) | 31 (15.5%) |
| Overweight (BMI > 25 to 29.9 kg/m 2) | 41 (20.5%) |
| Obese (BMI > 30 kg/m 2) | 123 (61.5%) |

Table 2: Breakdown of dyslipidaemia in males and females

| Factor | Male | Female |
|--------|------|--------|
| Mean levels ± SD | % not at target | Mean levels ± SD | % not at target |
| TC ≥4.5 mmol/l | 5.30 ±0.77 | 37.21% | 5.63 ±0.90 | 54.39% |
| TG ≥1.7 mmol/l | 2.77 ±1.07 | 39.53% | 2.83 ±1.24 | 43.86% |
| HDL ≤1 mmol/l (M) < 1.2 mmol/l (F) | 0.9 ±0.12 | 55.81% | 1.11 ±0.87 | 38.60% |
| LDL ≥1.8 mmol/l | 2.69 ±0.74 | 76.74% | 2.97 ±0.86 | 76.32% |

Note: For TG: Female median 1.5, IQR 1.3; male median 1.5 and IQR 1.1.

Table 3: Breakdown of the pattern of dyslipidaemia in the 187 patients not achieving recommended lipid targets

| Type* | Males (n = 81) | Females (n = 106) | Total (n = 187) |
|-------|----------------|------------------|----------------|
| Isolated | 28 | 47 | 75 (40%) |
| Combined | 39 | 43 | 82 (43.8%) |
| Mixed | 14 | 16 | 30 (16%) |

*Dyslipidaemia was classified into mixed dyslipidaemia (three abnormal parameters: high TG, low HDL-C as well as raised LDL-C), combined dyslipidaemia (any two abnormal parameters) and isolated (single parameter) dyslipidaemia (TC, TG, HDL-C or LDL-C).

Figure 1: shows the percentage breakdown of dyslipidaemia in the male cohort (n = 86), using the 2012 South African Dyslipidaemia Guidelines, target levels.

Figure 2: shows the percentage breakdown of dyslipidaemia in the female cohort (n=114), using the 2012 South African Dyslipidaemia Guidelines, target levels.
A multiple regression was done in order to determine whether HbA1c correlated with any of the lipid parameters, namely TC, TG, HDL-C and/or LDL-C. None of these parameters correlated significantly with HbA1c. F (4,190) = 0.606, p > 0.05, r² = 0.013, and multiple R = 0.112.

**Discussion**

Despite the use of lipid-lowering therapy (statin therapy) in all of the patients, the prevalence of dyslipidaemia in the cohort was very high. This is in accordance with similar studies done in South Africa and Nigeria where the prevalence of dyslipidaemia (at least one abnormal lipid profile) was 90.3% and 90.7% respectively. Comparable findings were observed in international studies. In an Italian study, in which 2,465 patients were recruited, only 5% achieved the recommended goals for LDL-cholesterol, blood pressure, HbA1c, and smoking habits. Similarly, a Czech study concluded that only 1% of their patients achieved their goals, while 6% of the total cohort that consisted of 975 patients in a Norwegian study met the goal for the combined target of glucose, blood pressure and cholesterol control.

This brings to light that controlling diabetes and dyslipidaemia is a global challenge affecting developed and developing countries alike. More resources (monetary, skill, therapeutics) need to be dedicated to trying to achieve better control in our patients.

The reasons for the high prevalence of dyslipidaemia in the cohort could be multifactorial.

It may be partly attributed to the current trend toward urbanisation and adoption of a Western diet and lifestyle, which results in a higher incidence of type 2 DM with its attendant metabolic abnormalities.

The statin used in the study was a less potent statin, simvastatin, at a suboptimal mean dose of only 20 mg daily. This inertia on the part of clinicians to increase the dose of a given medication or move to combination lipid-modifying treatment is not unique to South Africa, as shown in the DYSIS Study.

In the state sector only simvastatin is routinely available for patients with dyslipidaemia. Other more potent statins such as atorvastatin are available on an individual motivational basis for patients with severe primary dyslipidaemia such as familial hypercholesterolaemia or who have established atherosclerotic cardiovascular disease. In addition state pharmacies often have a short supply of stock, leaving patients without any statin therapy. Any possible side effects were not evaluated. Compliance and side effects of statin therapy were also not assessed.

Nonetheless, the results indicate disappointing achievement of targets, particularly lipid targets in state patients with type 2 DM.

The goal of achieving recommended targets remains elusive, given diminishing resources (healthcare workers, pharmacotherapy etc.) and limited physician–patient interaction in the state sector. Improvement can only be achieved by more intensive statin therapy and ongoing patient education.

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