

The implementation of guidelines in a South African population with type 2 diabetes

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Abstract

Objective: The aim of this study was to identify the treatment gaps that pertain to risk factors in South African patients with type 2 diabetes mellitus, using national treatment guidelines.

Design: Cross-sectional study.

Setting and subjects: The study consisted of 666 patients with type 2 diabetes mellitus, attending a diabetes clinic at the Charlotte Maxeke Johannesburg Academic Hospital.

Outcome measures: Using a public sector database, retrospective data were obtained on the treatment of type 2 diabetes mellitus participants. Patients were randomly selected on the basis of established type 2 diabetes mellitus diagnosis, and if they were receiving oral hypoglycaemic and/or insulin therapy. Age, gender, race, blood pressure, haemoglobin A_{1c} (HbA_{1c}) and fasting lipids were captured and measured. The history of patients' previous coronary artery disease, strokes, nephropathy, neuropathy and retinopathy was recorded.

Results: The mean age of the patients was 63 years [standard deviation (SD) 11.9], 55% of whom were females. The HbA_{1c} was 8.8% (SD 2.5). 26.2% of patients attained HbA_{1c} levels of < 7%. Of the total patients, 45.8% met a < 130/80 mmHg blood pressure target, and 53.8% a low-density lipoprotein (LDL) cholesterol of < 2.5 mmol/l. Only 7.5% obtained the combined target for HbA_{1c}, blood pressure and LDL cholesterol.

Conclusion: Traditionally, type 2 diabetes mellitus treatment has centred on correcting blood glucose levels. Yet, as many as 80% of people with type 2 diabetes mellitus die from some form of cardiovascular disease (CVD). Many trials have demonstrated the benefits of targeting CVD risk factors (HbA_{1c}, blood pressure and lipids) in patients with type 2 diabetes mellitus. Despite the wealth of evidence, our data suggest that significant undertreatment of risk factors in patients with type 2 diabetes mellitus remains.

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Introduction

Diabetes mellitus is a serious, multifaceted condition. The aetiological types of diabetes are type 1, type 2, gestational diabetes and other specific types.¹ Insulin-dependent type 1 diabetes mellitus may present in childhood, and is associated with pancreatic β -cell destruction, but it is outweighed by the more common type 2 diabetes mellitus.² Type 2 diabetes mellitus has emerged as one of the most common chronic conditions throughout the world. The incidence of type 2 diabetes mellitus is approximately 10 times higher than that of type 1 diabetes.³ In 2010, it was estimated that approximately 285-million people globally were diabetic, and that by 2030, an estimated 439-million people will be living with diabetes worldwide.⁴

Treatment in patients with either form of diabetes has centred around the correction of blood glucose levels. Insulin is used to reduce hyperglycaemia in patients with type 1 diabetes, while a more varied and multifaceted armamentarium is available for glycaemic control in those with type 2 diabetes mellitus. Yet, as many as 80% of patients with type 2 diabetes mellitus die from some form of cardiovascular disease (CVD).⁵ This highlights the need for a more intense intervention to reduce cardiovascular risk factors. A number of interventions and other epidemiological surveys have demonstrated that blood pressure targets are far lower in this risk group.⁶ Serum lipid targets are also set at lower levels than those for non-diabetics. As the risk of cardiovascular disease increases by at least three- to

fourfold, this necessitates more intensive therapy for cardiovascular risk factors in this patient population.

The 2009 guidelines issued by the Society for Endocrinology, Metabolism, and Diabetes of South Africa (SEMDSA), and in use at the time of this study, suggested aggressive targeting of haemoglobin A_{1c} (HbA_{1c}), but also of blood pressure and dyslipidaemia.⁷ The question remains: how well are treatment guidelines translated into clinical practice? And how many patients are meeting targets, and if not, how far are they away from doing so?

We wished to document the extent to which patients with type 2 diabetes mellitus were being managed in a South African, public sector setting. The cohort comprised patients who were initially referred from their primary local clinics to a tertiary public sector clinic. This reflects the quality of care that the state can provide, especially to those who cannot afford private health care.

Method

Study design

This was a cross-sectional study designed to evaluate the extent to which the 2009 SEMDSA treatment guidelines were followed in a tertiary-based type 2 diabetic population. The study period coincided with the publication of these guidelines. Therefore, it was appropriate to assess the data against these. This was achieved by comparing blood pressure, serum glucose and lipid levels in treated patients with type 2 diabetes against the national treatment targets.

Setting

The study was conducted at the Charlotte Maxeke Johannesburg Academic Hospital between July 2008 and 2009. This academic tertiary hospital provides healthcare services to patients across Gauteng province. Generally, enrolled patients in this clinic are not covered by the private healthcare industry. In addition, patients in these clinics are only enrolled once their treating physicians at the primary clinics have referred them. Management is carried out at the diabetic clinic and patients attend the clinic for purposes of follow-up and maintenance.

Patients

We extracted data from a sample of 666 patients attending the hospital's diabetic clinic. At the time of the study, the latest diagnosing type 2 diabetes mellitus criteria issued by SEMDSA were applied to the cohort.⁷ Patients were excluded from the study if they were < 18 years of age, had type 1 diabetes, gestational

diabetes, steroid-induced diabetes and chronic pancreatitis which had led to secondary diabetes. As one of the primary measurements was a serum lipid reading, a decision was taken to exclude patients with triglyceride levels > 5.0 mmol/l as this may have been a source of error when calculating low-density lipoprotein (LDL) cholesterol, as measured by the Friedewald formula,⁸ or could have been noncompliance with overnight fasting, leading to anomalous lipid readings, and in particular, falsely low LDL cholesterol readings. The study participants were enrolled in a consecutive sequential manner, based on their assigned computer-generated hospital numbers and the first letter of their surnames.

Using patient records, clinical data were captured into case report forms, including demographics (age, gender and ethnicity), systolic blood pressure (SBP), diastolic blood pressure (DBP), glycated HbA_{1c}, total cholesterol, LDL cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides (TGs), a family history, cardiovascular history and chronic medication. Unfortunately, most patient files had incomplete details of weight, height, diet details and smoking status. These parameters, especially the first two, would have been used to calculate body mass index. Also, patient classification with regard to metabolic syndrome was also omitted from the study owing to absent waist measurements.⁹ Incomplete details of ethnicity in the patient files were denoted as "unknown."

Patients defined as having diabetic nephropathy using laboratory data, i.e. microalbumin to creatinine ratios, serum creatinine concentrations or glomerular filtration rate, often proved inconsistent because many patients did not have the available laboratory reports in their records. It was also found that some patients were concurrently managed at the hospital's renal clinic, separate to the diabetic clinic. For the purposes of this study, patients deemed to have diabetic nephropathy were those with one or more of the following in their records: chronic kidney disease, chronic renal disease, chronic renal failure (CRF), nephropathy and diabetic nephropathy. Only the most recent records and laboratory reports of patients were utilised for the purposes of this study. Data from the CRF were entered into a secure database at the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg. Prior to the study, the University of the Witwatersrand's Human Research Ethics Committee granted ethical approval of the study (ethics protocol number M080409).

Clinical parameters

Where blood samples were required for laboratory tests, registered nurses were in charge of drawing the study patients' blood, using standardised techniques at the diabetes clinic. Patients were informed of the mandatory fasting requirements that pertained to the tests before having their blood drawn for specific tests in prior appointments or visits.

As Charlotte Maxeke Johannesburg Academic Hospital is a state hospital, the National Health Laboratory Services (NHLS) was responsible for the study patients' laboratory measurements. Once the results were available, the NHLS issued laboratory results delivered by hospital staff to the diabetes clinic, and filed under respective patient files by clinic administration staff. HbA_{1c} was measured using the Tina-quant Hemoglobin A_{1c} II immunological assay, fasting LDL cholesterol was calculated by means of the Friedewald formula, fasting HDL cholesterol was measured by direct enzymatic methods (third generation), fasting total cholesterol was also calculated by direct enzymatic methods, and TGs were measured by enzymatic colorimetric methods. Measurements were carried out using the Modular Analyser P800 System® (Roche Diagnostics, Mannheim, Germany). Blood pressure readings were measured by registered nurses or treating doctors, using standardised brachial cuff techniques in accordance with the latest (at the time of the study) South African hypertension guidelines and *The seventh report of the Joint National Committee on the prevention, detection, evaluation and treatment of high blood pressure (JNC 7)*.^{10,11} Once data were captured into case reports, the SEMDSA 2009 guidelines for type 2 diabetes mellitus treatment targets were applied to the cohort, namely SBP < 130 mmHg and DBP < 80 mmHg. HbA_{1c} < 7%, total cholesterol < 4.5 mmol/l, LDL cholesterol < 2.5 mmol/l, HDL cholesterol > 1 mmol/l (men), HDL cholesterol > 1.2 mmol/l (women) and TGs < 1.7 mmol/l. The LDL cholesterol target was ≤ 1.8 mmol/l in patients with established vascular disease, such as ischaemic heart disease, cerebrovascular disease or peripheral vascular disease. Hypertension was present if patients were receiving antihypertensive treatment.

Statistical and data analysis

Simple statistics were calculated for age, gender, race, blood pressure, HbA_{1c} and fasting lipids. The percentage of previous coronary artery disease (CAD), strokes, nephropathy, neuropathy and retinopathy

history in patients was reported. Patient usage of chronic medication to treat hyperglycaemia, hypertension and lipids, as well as receiving antiplatelet treatment was analysed. The percentage of patients reaching the SEMDSA treatment goals for various clinical parameters was also calculated. A significance level of 5% was used for the analysis. Where necessary, ratios were compared using the chi-square test. Unpaired Student's t-tests were used to compare mean differences. Microsoft Office® Excel® 2009 was utilised for the study's databases and statistical analysis was carried out using Statistica® version 8.

Results

The cohort consisted of 666 patients, of whom 369 (55%) were women. Ages ranged from 29-94 years. The mean age for men was 62 [standard deviation (SD) 12.0] vs. 63 (SD 11.8) years for the women (p-value 0.56) (Table I). The patient ethnicity of the cohort was 42.8% African, 29.4% Caucasian, 19.5% Asian, 5.9% mixed ancestry and 2.4% unknown (using patient records with incomplete data).

The mean SBP readings for the cohort were 134 mmHg (SD 20.0) and 79 mmHg for DBP (SD 11.7). Of the cohort, 85.4% were hypertensive. More women than men were being treated for hypertension (88.4% vs. 81.9%, p-value < 0.05). Most of the patients were receiving angiotensin-converting enzyme inhibitors (80.0%). Diuretics were prescribed to 69.8%. Approximately 46.6% were taking calcium-channel blockers, and 17.6% β blockers.

DBP targets (< 80 mmHg) were achieved more easily than those for SBP (69.1% vs. 54.6%, p-value < 0.01)

Table I: Patient baseline characteristics of study type 2 diabetics

Characteristics	Total (n = 666)	Men (n = 297)	Women (n = 369)	p-value*
Age (years)	63 ± 11.9	62 ± 12.0	63 ± 11.8	0.56
SBP (mmHg)	134 ± 20.0	132 ± 20.6	136 ± 19.4	< 0.05
DBP (mmHg)	79 ± 11.7	78 ± 13.2	79 ± 10.3	0.58
HbA _{1c} (%)	8.8 ± 2.5	8.5 ± 2.3	8.9 ± 2.6	0.05
Total cholesterol (mmol/l)	4.6 ± 1.2	4.5 ± 1.2	4.8 ± 1.1	< 0.05
Triglycerides (mmol/l)	1.8 ± 1.0	1.8 ± 1.0	1.7 ± 1.0	0.41
HDL cholesterol (mmol/l)	1.2 ± 0.4	1.1 ± 0.4	1.3 ± 0.4	< 0.05
LDL cholesterol (mmol/l)	2.6 ± 0.9	2.5 ± 0.9	2.7 ± 0.9	0.98
Hypertension, n (%)	569 (85.4)	243 (81.8)	326 (88.3)	< 0.05
CAD, n (%)	95 (14.3)	44 (14.8)	51 (13.8)	< 0.05
Stroke, n (%)	20 (3.0)	9 (3.0)	11 (3.0)	0.34
Nephropathy, n (%)	78 (11.7)	41 (13.8)	37 (10.0)	0.54
Neuropathy, n (%)	47 (7.1)	25 (8.4)	22 (6.0)	0.75
Retinopathy, n (%)	42 (6.3)	26 (8.8)	16 (4.3)	0.38

*: p-value for sex differences, significant if p-value < 0.05

CAD: coronary artery disease, DBP: diastolic blood pressure, HbA_{1c}: haemoglobin A_{1c}, HDL: high-density lipoprotein, LDL: low-density lipoprotein, SBP: systolic blood pressure

in patients with no apparent signs of diabetic nephropathy. Only 45.8% reached the goals for both SBP and DBP. In other words, over 54% did not achieve the target.

In this cohort, 11.1% had documented nephropathy. More rigorous blood pressure targets are set by SEMDSA for these patients (SBP \leq 120 mmHg and DBP \leq 70 mmHg). Control rates were poor. 25.5% of these patients achieved the SBP goal, and 32.7% the DBP goal. Only 16.4% met the combined SBP and DBP target.

The mean HbA_{1c} for the cohort was 8.8% (SD 2.5). Patients on insulin monotherapy had the highest HbA_{1c} 9.4% (SD 2.6). HbA_{1c} for patients on insulin and hypoglycaemic combination therapy was 9.1% (SD 2.3). The lowest HbA_{1c} of 6.3% (SD 1.0) was present in patients on diet alone. In the cohort, just over a quarter (26.2%) of patients reached the SEMDSA treatment target of HbA_{1c} < 7%.

The TCs for the population were 4.6 mmol/l (SD 1.2), with a calculated LDL cholesterol of 2.6 mmol/l (SD 0.9). TGs were measured at 1.8 mmol/l (SD 1.0), and HDL at 1.3 mmol/l (SD 0.4) for women and 1.1 mmol/l (SD 0.4) for men. The total cholesterol target of < 4.5 mmol/l was obtained by 53.8% of patients. 60.2% reached the TG target of < 1.7 mmol/l.

Previously established CAD or strokes were present in 103 of the 666 patients. Of these, 81.9% failed to reach LDL cholesterol (\leq 1.8 mmol/l). 53.8% of patients with a lower risk profile (no previous CAD or strokes) reached the SEMDSA LDL cholesterol goal of < 2.5 mmol/l. The majority of statin users (59.1%) were prescribed simvastatin 20 mg.

Of the patients with no history of heart disease, 40.7% received antiplatelet therapy. In the group with a history of CAD only, just over half (56 of the 103 patients) were on antiplatelet therapy.

Discussion

In South Africa, the human immunodeficiency virus/acquired immune deficiency syndrome epidemic has mushroomed over the last two decades and has consumed scarce resources in the public sector.¹² As the South African population becomes urbanised and more affluent, diseases of lifestyle, such as type 2 diabetes mellitus, have proliferated. Mortality rates in South Africa have revealed a 41% increase due to non-communicable diseases, with CVD and type 2 diabetes mellitus growing alarmingly.¹³

This study aimed to investigate the management of a cohort of South African patients with type 2

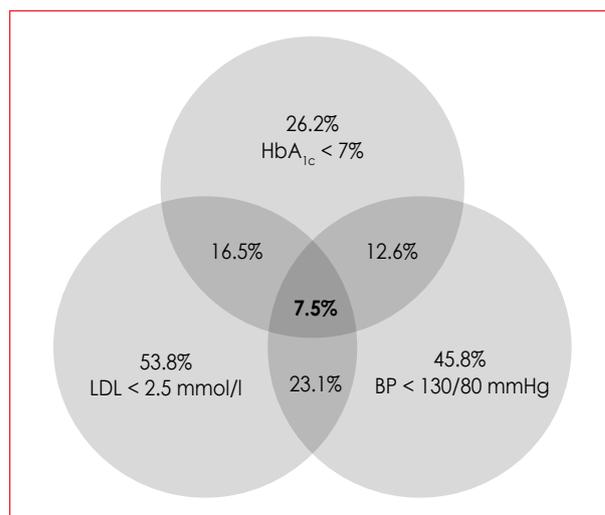


Figure 1: Percentage of study type 2 diabetics at goal using the Society for Endocrinology, Metabolism, and Diabetes of South Africa 2009 targets for glycaemia, blood pressure and lipids
BP: blood pressure, HbA_{1c}: haemoglobin A_{1c}, LDL: low-density lipoprotein

diabetes mellitus based on the SEMDSA 2009 treatment guidelines prevailing at the time of the study. These guidelines advocate strict control of glucose, but also control of blood pressure and lipids. Results from this study indicate that the attainment of treatment goals remains suboptimal. Less than half of the total cohort met their goal pertaining to the blood pressure target, although over 85% were receiving antihypertensive medication. Even more alarmingly, the SEMDSA HbA_{1c} target of < 7% was achieved by just over one quarter of the population, even though almost the entire cohort was receiving glucose-lowering therapy. More patients met the LDL cholesterol, than the blood pressure or glycaemic control for serum lipids, goal (Figure 1). Given that small, dense and atherogenic particles of LDL cholesterol predominate in type 2 diabetes mellitus, these levels may underestimate the actual risk.¹⁴

Overall, less than 10% of the study population achieved the treatment goals for all three risk factors (serum glucose, blood pressure and cholesterol). Comparable findings have been seen in other observational studies. In an Italian study, in which 2 465 patients were recruited, only 5% achieved the recommended goals for LDL cholesterol, blood pressure, glycated HA_{1c} and smoking habits.¹⁵ Similarly, a Czech study concluded that 1% of their patients achieved similar 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.^{16,17} It is clear that the gap between type 2 diabetes mellitus treatment and goals is not necessarily confined to developing countries, but also affects countries with greater available resources.

It is also worthwhile mentioning that this study was set

at a time when the previously issued guidelines were in place. This study may have overestimated the current number of patients who did not achieve the goal as the previously set targets were stricter in comparison to the newer and more individualised targets.¹⁸

In South Africa, resource scarcities in the public sector are a constant reality. Declining numbers of available clinicians lead to shortened consultation times. Patient education may be compromised for patients who do not speak the same first language as their treating practitioners.¹⁹ It is vital for patients with type 2 diabetes mellitus to be fully aware of their risk factors and to know how to manage these effectively.²⁰ Further efforts in resource allocations and practitioner-patient communication are undoubtedly necessary in addressing disease management issues.

In conclusion, the study evaluated adherence to recommended type 2 diabetes mellitus treatment guidelines and actual targets achieved by patients being managed in a resource-limited public sector setting. The results indicate disappointing achievement of national type 2 diabetes mellitus treatment targets. The goal of closing the gap between targets and what is realised remains elusive, given diminishing resources and limited physician-patient interaction.

Most patients with type 2 diabetes mellitus did not meet their targets for blood pressure, lipids and glycaemic control, in spite of receiving the necessary pharmacotherapy. The chasm between the target goals and actually reaching them is massive, and unlikely to narrow. Improvement lies in the form of therapeutic titration adjustment and patient education. Clearly, more aggressive therapeutic efforts, affected earlier, are needed to reduce overall microvascular and macrovascular outcomes.

Conflict of interest

The authors of this article declare that there is no conflict of interest with regard to this work.

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