

Abstract

Introduction

Type 2 diabetes mellitus (T2DM) is common and has devastating outcomes for patients diagnosed with this disease. In Africa, the prevalence of T2DM is reaching epidemic proportions, especially in developing countries like Ghana, Nigeria and South Africa (SA). The financial burden of T2DM is seen in the public and private healthcare sectors in Africa. Major depressive disorder (MDD) frequently co-occurs as a discordant comorbidity with T2DM. MDD is an important component in the holistic management of T2DM care as the outcomes of both conditions are exacerbated by the presence of the other.

T2DM patients are at high risk for cardiovascular (CV) morbidity and mortality. The comorbidity of MDD among these individuals is associated with poor diabetes-related cardiovascular disease (CVD) outcomes such as myocardial infarction, stroke and cardiac failure, because MDD is a highly prevalent risk factor for CVD and T2DM alike. Little is known of the prevalence of MDD as a comorbidity of T2DM in SA or if MDD is a risk factor for the onset of T2DM. It is also unclear whether the treatment of depressive disorders in T2DM would improve glycaemic control. While the association between depression and T2DM in America and Europe is established, understanding the relationship between these two non-communicable diseases (NCDs) is lacking in SA.

The relationship between T2DM and associated co-morbidities, particularly MDD, is poorly acknowledged in chronic disease management practices in SA. The management of co-morbid conditions may influence managed healthcare costs and hospitalisation rates.

Aim and objectives

This thesis investigated the bidirectional relationship between T2DM and comorbid MDD within a South African privately managed healthcare organisation. The objectives of the study were to estimate the comorbidity incidence, resource utilisation (medicine, services and hospital), assess the cost between two T2DM management funding models, the influence of MDD on glycaemia, blood pressure and lipid control (ABC guidelines) and finally identify the depressive symptom and CV risk profiles of patients with T2DM with or without MDD and those with MDD alone.

Method

The thesis comprised four quantitative studies that analysed claims data from a privately funded healthcare insurer and electronic health records (EHR) from 2012 to 2019, and a cross-sectional survey from 2016 to 2019.

The methodology in the first study was a retrospective descriptive analysis of 902 adult patients with T2DM in 2014. Patients were identified with T2DM and their comorbidities and categorised as those with concordant comorbidities (CC), and those with discordant comorbidities (DC). Hospital admissions of patients with T2DM, with MDD (T2DM+MDD) versus those without MDD (T2DM-MDD), were further analysed.

The second study analysed the claims data of patients with T2DM and T2DM+MDD from 2012 to 2016. Annual healthcare costs were assessed between two funding models and categorised as in-hospital and out-of-hospital medicines and out-of-hospital services. Diabetes-related and other medicine-plus-services and hospitalisation costs between T2DM and T2DM+MDD were estimated.

In the third study, the cardiometabolic indices control of 1211 patients with T2DM+MDD, T2DM-MDD and MDD only were measured using their EHR for the year 2019. Claims for lipid-lowering therapy, hypoglycaemic agents, antihypertensives and antidepressant selective-serotonin-reuptake inhibitors (SSRI) were assessed between the study groups. Frequencies of patients achieving target glycated haemoglobin (HbA1c), systolic blood pressure (SBP) and low-density-lipoprotein (LDL-C) were compared between groups. A stepwise multivariate logistic regression analysis was performed to identify predictors of HbA1c and LDL-C control of the study groups.

The fourth study conducted a cross-sectional survey of a random sample of members with T2DM+MDD, T2DM-MDD, MDD only, and a healthy control group between the years 2016 to 2019. The survey comprised a Patient Health Questionnaire-9 (PHQ-9) to assess possible depressive symptoms, and anthropometric measures (body mass index (BMI), family history of diabetes and/or heart disease, and smoking status as CV risk profiles).

Findings

The first study revealed a high incidence of CV concordant comorbidities (hypertension and hyperlipidaemia) in patients with T2DM+MDD, with MDD being the most prevalent discordant comorbidity of T2DM (17%). A higher percentage of patients with T2DM+MDD were admitted to

hospital (42%, $p=0.004$) compared with those with T2DM-MDD (30%). The number of overnight admissions was higher among the T2DM+MDD (76%, $p=0.016$) compared with T2DM-MDD (66%).

The second study focused on health care costs and the funding models associated with managed care. The direct medical costs of patients with T2DM and T2DM+MDD registered with a medical scheme over a 5-year period between two funding models were estimated and compared: a capitation risk-sharing model (CM) versus a traditional fee-for-service (FFS) model. Of the identified T2DM patients, 64% were enrolled in CM in 2012 and this rose to 81% by 2016. The implementation of CM resulted in a significantly higher cost to the scheme (\$1,095) compared to FFS (\$296) in 2016 ($p<0.0001$). Forty-six T2DM patients in this study incurred hospitalisation costs of \geq \$24,243 for T2DM-related or other hospital admissions (non T2DM-related). The healthcare expenditure consumed by patients with T2DM and T2DM+MDD on a capitation model of care for diabetes was high compared to patients on FFS. While the diabetes-related treatment and management were similar between patients with T2DM+MDD and T2DM-MDD, other medicine and services, expenditure was significantly higher in the T2DM+MDD group, for example T2DM+MDD patients had a median expenditure of \$1,414 in 2016 compared to a median of \$614 in T2DM-MDD patients ($p<0.0001$).

The third study assessed the HbA1c, SBP and LDL-C control target attainment (as per South African ABC guidelines) in patients with T2DM+MDD and T2DM-MDD and those with MDD alone. Only 13% of the patients in T2DM+MDD group and 7.1% in the T2DM-MDD group achieved ABC (HbA1c $<$ 7%, LDL-C $<$ 1.8mmol/l and SBP $<$ 140/90 mmHg) targets, despite hypoglycaemic, lipid-lowering therapy and antihypertensive claims, indicating a possible risk for CVD in T2DM+MDD and T2DM-MDD patients. A higher proportion of patients with T2DM+MDD (56%) achieved an HbA1c target of $<$ 7% compared to the T2DM-MDD group (45%, $p<0.05$). Multiple regression analysis showed that HbA1c control was independently associated ($p<0.001$) with older age, claims for statins and having a history of MDD, after adjusting for claims for antihypertensive therapy, metformin, newer hypoglycaemic agents, sex, and interaction factor of newer hypoglycaemic agents and metformin. Only 24% of patients in both the T2DM+MDD and T2DM-MDD groups reached the LDL-C target $<$ 1.8mmol/l. The predictors of LDL-C control between the T2DM+MDD and T2DM-MDD groups were older age ($p<0.0001$) and claiming statin therapy ($p=0.001$), after adjusting for antihypertensive therapy and metformin claims and sex.

The fourth study identified the depressive symptoms and CV risk factors (such as obesity, smoker status and family history of diabetes and heart disease) in individuals with T2DM+MDD, T2DM-MDD or MDD alone compared to a healthy control. The PHQ-9 scores revealed that patients in all four groups were within a range of mild to moderate-severe depressive symptoms. The T2DM+MDD group had moderate-severe (PHQ-9 \geq 10) depressive symptoms (58.8%) similar to the MDD group (54.2%, $p=1.0$) suggesting a poor response to antidepressants. Patients with T2DM-MDD had underlying unrecognized depressive symptoms: 20.5% had moderate-severe (PHQ-9 \geq 10) depressive symptoms and 23.1% had mild (PHQ-9=5-9) depressive symptoms. Of concern was that 25% of the control (healthy) group recorded having moderate-severe (PHQ-9 \geq 10) depressive symptoms and 21.4% of having mild depressive (PHQ-9=5-9) symptoms. The majority of the T2DM+MDD group obese (76.5%) whereas 46.2% of the T2DM-MDD group were overweight. However, the control group, with no stated disease, were overweight (37.5%) or obese (30.4%). This study highlights the undetected MDD and high CV risk prevalent in this setting.

Conclusion

Within this South African private managed healthcare setting, comorbidities associated in patients with T2DM, i.e. MDD and CVD, are managed discretely. High-risk individuals with T2DM increase costs and resource utilisation within the private managed healthcare setting. In summary, the relevance of the research was to increase awareness of the consequences of comorbidity of T2DM and MDD and encourage routine screening for depression in T2DM patients, and glycaemic screening among patients with MDD. Managed care programmes should consider a patient-centric approach to assist patients in engaging with their T2DM and comorbidities more effectively by listening to their difficulties in terms of medication compliance, offering regular glycaemic and lipid blood tests and encouraging healthier diet through visits to dieticians or nurse educators.

Targeting primary healthcare as an intervention has the potential to reduce the hospitalisation burden by initially stabilizing patients with T2DM+MDD, providing cost-effective and appropriate medicine management (i.e. statins), improving attainment of ABC control targets and early screening for depression and non-invasive CV risk factors. Resource allocation for a coordinated care team that includes health professionals such as dieticians, endocrinologists, drug review utilisation (DUR) pharmacists, psychologists and nurse educators to treat patients with T2DM+MDD is indicated.